EVIDENCE-BASED MEDICINE (EBM) Overview: Notes on Validity, Precision & Contextualization of Results[1,2,3,4,5]

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Critical Appraisal of Drug Studies [6,7]

A) Is the study valid?

1. Were patients **randomized** to treatment (tx) groups & was allocation **concealed** (AC)? {Without concealment, 37% bias in favor of tx. Sealed, opaque envelopes or central registry used to attain AC[8,9]}
2. Was everyone (patients, physicians, investigators, assessors) **blinded** to tx? {Especially important for assessors of subjective outcomes e.g. pain.}
3. Was the study **controlled**? (e.g. RCT: inclusion of **placebo or active** control group/arm; in an "N of 1" trial, patient is their own control.)
4. Were treatment & control **groups similar at baseline** for prognostic factors related to outcome of interest? If not, were adjustments made?
5. Were **all patients accounted for** at end? {Missing patients addressed?}
6. Was data analyzed based on groups patients were initially randomized to? {Intention to treat or **ITT**; protects integrity of prognostic randomization; per protocol (**PP**) analysis also of interest for harms, non-inferiority RCTs.
7. Were **groups treated similarly** apart from the intervention studied?
8. How was the study **funded** (**role** of funder)? Was study stopped early?
9. Was study type, design & comparator drug & dose a good choice?

B) What are the study results?

1. What was the primary (1°) endpoint? What were the secondary (2°) endpoints? Were endpoints & subgroups pre-specified?[10] Avoid data mining!
2. What was the difference in outcomes? (Both benefits & harms.)
3. Were the differences statistically significant? …clinically significant? {What were the 95% confidence intervals (**CIs**) or p values? Does the CI $_{95}$ cross line of no effect?}
4. What are the absolute and relative risk reductions, or increases?
5. What is the number needed to treat (**NNT**) &/or harm (**NNH**)?

C) How does this study matter to my patients?

1. How **clinically relevant/important** are the outcomes?
2. Were the patients similar to those in my practice? (Generalizability) {Consider **inclusion & exclusion criteria**; very sick, old, young, drug interactions & complicated/co-morbid patients often excluded.}
3. Do treatment **benefits outweigh the harms, costs & impact on life**?

Study Types for Tx (from low to **high level** of evidence) [11]

- **Case-control study**: a retrospective observational study which selects patients a) with the outcome of interest (cases) & b) without that outcome (controls); attempts to find exposures linked to the outcome.
- **Cohort study**: an observational study in which 2 groups (cohorts) are observed over time for an outcome. One cohort has exposure to a condition/treatment that the other does not. {**Observational studies**: association does not prove causation! Allow for, or assess for, confounding!} Strength of association: RR: 1.01-1.5 *weak*; 1.51-3 *moderate*; >3 *strong*.[12]}
- **Randomized controlled trial** (**RCT**): a prospective study in which patients are randomized to treatment or control groups (equal/random chance at being assigned to any group). Groups are followed for the outcome of interest. (Good for efficacy; often limited for in safety outcomes.)
- **Crossover RCT**: a design in which each patient receives both treatments in two phases separated by a washout period. Each patient serves as own control, thus less variability in outcomes, & smaller sample size OK; period effects may limit findings
- **Systematic Review (SR)**: a systematic collection, review & presentation of available evidence addressing a clinical question using specific criteria & methods; may, or may not, include meta-analysis. e.g. *Cochrane*[13]*/Campbell*[14]*/CADTH Reviews*[36]

{**Meta-analysis (MA)**: the combining of studies meeting prespecified criteria, addressing a clinical question. Results are calculated from each study's data, then pooled. ↑ sample size & statistical power useful if single trial or subgroup analysis underpowered,. **Assess appropriateness** of a) variables & outcomes; b) studies included; c) if study quality & heterogeneity accounted for.}

Evidence Pyramid: SR {MA >RCT >observational study >expert opinion}.[15]
Observational studies useful to assess safety, generalization-different populations & insights into real world effect, especially when specific RCT not practical.[38]

Caution: Lots of low-quality RCTs not better than 1 good quality RCT! A low-quality SR, or a SR of low-quality trials, does not high-level evidence make. SR = a lens for understanding.[41]

GRADE: a systematic approach for making clinical practice recommendations in EBM - Link

Terms: Related To Validity

- **Risk of Bias**: design flaws leading to over/underestimation of tx effect e.g. recall bias, selection bias, publication bias; confounding factors esp observational studies {*Risk of Bias* should be distinguished from a) *Reporting*, & b) *Quality* ssessment.[45]}
- **Blinding**: if investigators, patient etc. are unaware of who receives tx vs control, they are less likely to inappropriately report better results with tx.

{ **CONSORT Statement**: a checklist of standards for standardized reporting of RCTs intended to reduce bias, Update 2022; & 2022 Checklist }

Study Results: Size Of The Treatment Effect [16,17,18,19]

- **Event rate** (**ER**): the number of people experiencing the event as a proportion of total number of people in the population or group
  -Experimental ER (**EER**): {# events in experimental group / total in exp. group}
  -Control group ER (**CER**): {# events in control group / total in control group}
- **Relative risk** (**RR**) or **risk ratio**: {EER/CER}
- **Relative risk reduction** (**RRR**): the RR subtracted from 1 {RRR=1–RR} [Whereas ARR varies with type of population treated, RRR is often more constant.]
- **Absolute risk reduction** (**ARR**): the arithmetic difference between the 2 event rates {CER–EER} [If ↑ risk: **ARI**= absolute risk increase]
- **Number needed to treat** (**NNT**): the number of people who would have to be treated with the studied intervention for the studied time period to see 1 extra benefit compared to the control. {**NNT**=100/ARR%}
- **Number needed to harm** (**NNH**): number of people who would have to be treated with the studied intervention for the studied time period for 1 extra person to experience an adverse outcome (ie an AE. {**NNH**=100/ARI%}
- **Odds ratio** (**OR**): = experimental event odds / control event odds; especially used in case-control studies where baseline risk is not known; also used in meta-analysis. When events are rare, the OR is similar to the RR; however, OR rate exaggerated relative to RR when events more common. {Link www.cebm.net: tool for converting OR to NNT[20]}
- **Point estimate**: the trial result used as best estimate of the true effect
- **Hazard ratio** (**HR**): like RR but more accurate; accounts for the time each participant was in the study before having *a 1st event* or withdrawing.

Study Results: Precision of Treatment Effect [21]

- **Confidence Interval** (**CI**): a 95% CI provides the range of values we are 95% certain overlap the true value. CI's indicate the precision of the estimate; where CI's are wide, they indicate less precise estimates of effect (an estimate of the worst & best case scenario of the outcome; related to p-value) {For ratios, a CI that includes "1" means possibility of no difference. For ARR, ARI, NNT, NNH, a CI that includes "zero" means possibility of no difference between tx. Non-significant results, *trends,* may provide clues re uncertainties & future research.}
- **Type 1 (or α) error**: *the false positive*; to find a difference when there is none. **p-value**: reflects type 1 error. A p <0.05 suggests a <1 in 20 probability that any difference is due to chance (statistically significant by convention). The smaller the **p-value**, the less likely that the result is due to chance.
- **Type 2 (or β) error**: *the false negative*; to conclude there is no difference when there really is a difference (e.g. if not enough patients enrolled)
- **Heterogeneity**: when studies within a meta-analysis have more variation than expected; may indicate its inappropriate to combine studies.[22] {***Q statistic***: measure of within-study variance; I^2: ratio of variability among studies to total variation.}

How do the results matter to me, my patients & society?

- **Clinical significance vs statistical significance**: some studies may detect extremely small statistically significant differences between groups; however magnitude of effect may be too small (e.g.high **NNT #**) to change practice. Evaluate both 1) the endpoint, & 2) the **NNT** or **NNH**. {e.g. small cognitive score improvement not noticeable to patient.[23,24]}
- **Composite endpoints**: combining endpoints can increase a study's power allowing for smaller or shorter trials. Outcomes should have **similar value**. Examination of individual outcomes can be important in interpretation as one endpoint may be the primary *driver*. {e.g. In **DREAM**, outcome of "diabetes diagnosis the driver **or** death" =example of unequal endpoints.[25]}
- **Surrogate endpoints**: an endpoint meant to reflect / be correlated with another endpoint (e.g. BP/LDL/A1c for CV events; CD4 cell count for HIV mortality). Clinical outcomes are more important since surrogate endpoints **assume** correlation with an outcome which may,or may not always be true.[26] {eg. lower A1c target ≤6% **ACCORD**: but ↑ death; doxazosin ↓ BP **ALLHAT** but ↑ HF/stroke; & clofibrate **WHO-CLOF** ↓ LDL but ↑ death.}
- **Other considerations**: What uncertainties remain, & how should they be weighed (e.g. legitimate vs illegitimate uncertainty[39])? Has the drug been studied well enough to detect rare serious adverse events (SAE)? What duration is studied & what are the potential benefits/harms over a longer term of exposure? Is real-world experience consistent with clinical trial data? Any insights for interpretation from subgroup analysis (see ICEMAN tool[40])? What are the cost considerations? Any evidence of data-dredging?[42] How benefits & harms are described e.g. RR vs **NNT** will also affect decisions.[27]
- **What *patient specific* &/or *societal* values need to be considered?**

Heads Up! Know what the numbers are telling you.

⇨ *You "double" your chance of winning a lottery if you buy a 2nd ticket; however your chance of winning is impacted more by whether 2 tickets or 2 million tickets are sold!*

- ***Beware of the Relatives***
  - Benefits are often given as **relative** numbers, whereas harms are often given as **absolute** numbers. This tends to exaggerate benefits & minimize the harms. ⇨Look for **NNT**s & **NNH**s.
    {e.g. **VIOXX** monograph 2004[CPS]: reported ~50% ↓ in GI complications with Vioxx 50mg/day vs naproxen 500mg BID & a thrombotic event rate of 1.8% (Vioxx) vs 0.6% (naproxen). Actual GI complication reductions 0.59% vs 1.37% (ARR=0.78; **NNT=129**); whereas thrombotic risk worse (**NNH=83**). **VIGOR**}
    {e.g. Oral contraceptives: risk of DVT in a younger, non-smoking ♀ may be ↑300% but absolute risk is <1.5/10,000 /yr, & lower than risk in pregnancy}
- ***Non-Equivalent Durations & Risk/Benefit Perception***
  - Benefits are often given for total duration of trial which may be several years, whereas harms may be reported as per year.
    {e.g. **UKPDS-33**: benefits listed over **10 yrs**; risk of hypoglycemia **per yr**.[28]}
- ***Analysis: Pooling Together or Dividing Out***
  - Discussing the multiple benefits of a composite endpoint while only sorting out individual harms may minimize risk perception.
    {e.g. **In WHI**, risk of just breast ca with HRT was **8/10,000 pt-years**; yet risk of any harm (DVT, CHD, stroke, PE & breast cancer) was **1/66 over 5.2yrs**.[29] }

Calculations Example: 1 yr trial	**RRR**		**ARR**	**NNT**	**NNH**: if 60% of patients in tx group experienced *headaches* compared with 27% in control group (ARI=33%)
◆200 patients in Control group ◆200 patients in Treatment (tx) group	= (0.20 - 0.15)/0.20 X 100 = 25% {risk of event is reduced by 25%}		20% - 15% = 5% {absolute risk of event is reduced by 5%}	= 100/5% = **20**	**NNH** = 100/33% **= 3**

A few NNTs / NNHs of interest (NOTE that duration matters for NNT interpretation)	**NNT**
↓ mortality with simvastatin 20-40mg/day over 5.4yrs vs placebo in patients with CHD [4S; see link to statin trials cht]	30 / 5.4yrs
↓ mortality with metformin 2550mg/day over 10.7 years vs non-intensive tx in obese T2DM patients [UKPDS-34; see link]	14 / 10 yrs
↓ CV death/MI/stroke; clopidogrel 75mg/day + ASA vs ASA alone in ACS pts (↑ bleeding: **NNH=99**) [CURE]	48 / 9mo
↓ neuropathic pain by ≥50% vs placebo: TCAs ~75mg/day, gabapentinoids, SNRIs duloxetine 60mg/day; (short-term) [37]	4, 7, 8

What makes for a good NNT? *It all depends!!!* NNTs will vary greatly with variations in baseline population risk, duration of tx, & type & number of endpoints included in composite. Values & preferences also impact interpretation.

Evidence-Based Medicine

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💻 EBM Online Extras

Table 1. Assessing Guidelines.

Guidelines provide guidance based on evidence, clinical experience and someone's values and preferences. When evaluating guidelines, you may ask:

Evidence	• How current is the evidence? Has level/strength of evidence (evidence quality) been assessed for recommendations? (Readers may have more confidence if multiple high quality trials.) • What outcomes are evaluated? Are they patient-orientated or surrogate outcomes? • Has evidence been allowed to inform pre-existing assumptions, biases, and beliefs? • Is the evidence applicable to your patient(s)?
Clinical Experience / Consensus	• Is expert opinion, and extent of agreement acknowledged?
Conflicts of Interest	• Are conflicts of interest disclosed? Conflicts may be financial or non-financial. • Was the guideline methodology transparent and rigorous to inform objectively on best available evidence?
Values	• In what way are values and preferences included? • Whose values are included: patient? Society? Payer? Professional?
Overall Assessment	• Look for transparency, evidence ratings, peer review, conflicts of interest. • Do the guidelines allow for, and enable, shared decision making with patients?

see analysis at www.cmaj.ca/content/193/2/E49

If the guidelines don't apply, don't apply them! Almost all guidelines contain a chapter/disclaimer noting that any recommendations must be assessed and individualized for the patient in front of you. Recommendations are often intended to apply to a majority of patients, but may not be suitable for the patient in front of you. If so, document the reason for your decision. See also *The Value, Role & Limitation of Clinical Practice Guidelines*, published online at RxFiles, June 2015.

Table 2. Useful EBM Resources.

- Evidence Alerts (McMaster): www.evidencealerts.com
- EBM Focus (DynaMed): www.ebsco.com/clinical-decisions/dynamed-solutions/about/ebm-focus
- Centre for Evidence-Based Medicine (CEBM-Oxford): www.cebm.ox.ac.uk
  Critical Appraisal Tools (CEBM): https://www.cebm.ox.ac.uk/resources/ebm-tools/critical-appraisal-tools
  - Critical appraisal worksheets to help appraise the reliability, importance and applicability of clinical evidence
  - Covers: systematic reviews, diagnostics, prognosis, randomized controlled trials, qualitative studies
  - Includes "**PICO**" critical appraisal worksheet
    - **P**atients
    - **I**ntervention
    - **C**omparator
    - **O**utcomes
- RxFiles Critical Appraisal – RCT – Alternate Worksheet Tool (Links to a) pdf version; b) word version
- PEER Evidence (Alberta College of Family Physicians): https://peerevidence.ca; U of A, EBM Workshops
- Therapeutics Initiative (University of British Columbia): www.ti.ubc.ca. Wisconsin Appraisal mcw EBM
- CADTH Guide to Searching the Grey Literature: www.cadth.ca/grey-matters-practical-tool-searching-health-related-grey-literature
- Knowledge Translation Clinical Significance Calculator (Dalhousie): contact to see if available
- Z Score Calculator for Statistical Significance www.socscistatistics.com/tests/ztest/default2.aspx
- Instrument for assessing the Credibility of Effect Modification Analyses (ICEMAN):[40] www.iceman.help/overview
- BMJ Talk Evidence Podcast: www.bmj.com/podcasts/talkevidence
- The NNT: www.thennt.com
- Essential Evidence Plus (Wiley); including InfoPOEMS: www.essentialevidenceplus.com
- Users' Guide to the Medical Literature – Text – 3rd Ed. http://thepafp.org/website/wp-content/uploads/2017/05/Users-Guides-to-the-Medical-Literature-3rd-ed-2016.pdf
- Top POEMs (Patient-Oriented Evidence that Matters) – annually from American Family Physician
- Therapeutics Education Collaboration: Medication Mythbusters – Best Science (BS) Medicine Podcast
- Duke University – Evidence Based Practice: Home – PICO, Study Design, Search, Appraise, Calculate Results, Teach

Related RxFiles Presentations/Discussions/Seminars, Articles:

- Ways Drug Trials, and Our Own Assumptions, May Fool Us
- Evidence, Opinion & the Art of Using Science for Better Patient Care
- Drug Advertisements - What not to miss, that might be missing!
- RxFiles – Getting Evidence Into Practice with Academic Detailing
- The Value, Role & Limitation of Clinical Practice Guidelines - Link
- Critical Appraisal - Trial Summary Template; …Template Word version

Table 3. RxFiles Selected RCT/Trial Summaries

more available online at RxFiles.ca/Trials

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

Asthma: Asthma Landmark Trials: Treatment of "Mild" or Intermittent Adult & Adolescent Asthma 2021;
Asthma Trials/SR Overview/Summary 2006

Novel-START: https://www.rxfiles.ca/RxFiles/uploads/documents/members/ts-NovelStart.pdf 2021
PRACTICAL: https://www.rxfiles.ca/RxFiles/uploads/documents/members/ts-PRACTICAL.pdf 2021
SYGMA-1: https://www.rxfiles.ca/RxFiles/uploads/documents/members/ts-SYGMA1.pdf 2021
SYGMZ-2: https://www.rxfiles.ca/RxFiles/uploads/documents/members/ts-SYGMA2.pdf 2021

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

Diabetes: Landmark Trials Summary: Glucose
Landmark Trials Summary: NON-Glucose
ACCORD-ADVANCE Comparison: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-A1C-ACCORD-vs-ADVANCE-COMPARISON.pdf
ACCORD-BP & LIPID: http://www.rxfiles.ca/rxfiles/uploads/documents/ACCORD-BP-Lipid-Trial-Overview.pdf
ACCORD: Glucose http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Targets-ACCORD-A1C.pdf
ADVANCE: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-ADVANCE-trial.pdf
AVANDIA & CV risk – Meta-analysis: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Avandia-CV-Meta-Comments.pdf
DREAM: http://www.rxfiles.ca/rxfiles/uploads/documents/Dream-QandA.pdf
ELIXA: Lixisenatide : http://www.rxfiles.ca/rxfiles/uploads/documents/Lixisenatide-ELIXA%20Trial%20Summary.pdf 2016
EMPA-REG: http://www.rxfiles.ca/rxfiles/uploads/documents/EMPA-REG%20Trial%20Summary.pdf 2016
LEADER: Liraglutide: http://www.rxfiles.ca/rxfiles/uploads/documents/Leader-Liraglutide%20VICTOZA%20and%20Cardiovascular%20Outcomes%20in%20Type%202%20Diabetes.pdf 2016
RECORD:http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-RECORD-Trial-Summary.pdf
SAVOR-TIMI 53: http://www.rxfiles.ca/rxfiles/uploads/documents/SAVOR-TIMI-53-Saxagliptin-CV-Outcomes-Trial-Summary.pdf
TECOS: Sitagliptin CV outcomes: http://www.rxfiles.ca/rxfiles/uploads/documents/TECOS-Trial-Summary.pdf 2016

Hypertension: Summary Table: http://www.rxfiles.ca/rxfiles/uploads/documents/HTNLandmarkHypertensionTrials.pdf
ACCOMPLISH: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-Accomplish.pdf
ALLHAT: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-Update-2003-Final.pdf
ANBP2: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-ANBP2.pdf
ASCOT-BPLA: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-ASCOT.pdf
SPRINT: http://www.rxfiles.ca/rxfiles/uploads/documents/SPRINT-BP-Trial-Overview.pdf 2015
Trial Summary table - abridged: http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-HTN-trial-summary.pdf

HF: CHARM: http://www.rxfiles.ca/rxfiles/uploads/documents/CHARM-Comments.pdf
DAPA-HF: Dapagliflozin versus Placebo in Patients with Heart Failure & Reduced EF
DELIVER: Dapagliflozin 10mg versus Placebo in Patients with Heart Failure With Mildly Reduced or Preserved Ejection Fraction
EMPEROR: -Preserved 2021 ; -Reduced 2020
FINEARTS-HF: Finerenone versus Placebo in Patients with Mildly Reduced or Preserved Ejection Fraction 2024
PARADIGM-HF: http://www.rxfiles.ca/rxfiles/uploads/documents/PARADIGM-HF-Trial-Sacubitril.pdf 2015
VICTORIA: Vericiguat versus Placebo in Patients with Heart Failure & Reduced EF 2020

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

Infectious Disease
Hoberman et al – 5 day vs 10 day Antimicrobial Treatment for Acute Otitis Media (AOM) in Young Children. 2024
Papi et al – RSV Prefusion F Protein (RSVPreF3; AREXVY) Vaccine in Older Adults 2024

HRT/MHT: WHI: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT Post-WHI-2002-Header.pdf
WHI & Age: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT-Age-and-the-WHI.pdf ;
WHI & Extras/Perspectives on NNTs, NNHs: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT-WHI-Extras-Perspectives.pdf
Efficacy and Safety of Menopause Hormone Therapy (MHT): Trial Evidence Summary 2023

Lipid: Summary Table: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-lipid agents-major trials.pdf
& Q&A 2004: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-Update-Oct04.pdf
AIM-HIGH: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-AIM-HIGH-nicotinic-acid-Niaspan-trial.pdf
ASCOT-LLA: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-ASCOT.pdf
CARDS: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-CARDS.pdf
ENHANCE: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-ENHANCE trial overview.pdf
FOURIER: https://www.rxfiles.ca/RxFiles/uploads/documents/members/ts-FOURIER.pdf
FIELD Substudy: http://www.rxfiles.ca/rxfiles/uploads/documents/FIELD-Sub-Analysis-Women-Trial-Summary.pdf 2015
IDEAL: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-IDEAL.pdf
IMPROVE-IT: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-IMPROVE-IT-Trial-Summary-QandA.pdf 2014
JUPITER: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Jupiter-trial-overview.pdf
LODESTAR: LODESTAR Trial Summary - treat to target vs fire and forget | www.RxFiles.ca 2024
PROVE-IT: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-Prove-It.pdf
REDUCE-IT: https://www.rxfiles.ca/RxFiles/uploads/documents/members/ts-REDUCE-IT.pdf 2023
REPRIEVE: Pitavastatin LIVALO to prevent CV disease in HIV 2024
SHARP: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Sharp-CKD-trial.pdf
SPARCL: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-SPARCL.pdf

Thrombotic (antithrombotics: ASA, clopidogrel, anticoagulants: warfarin) :
ACTIVE-A & ACTIVE-W trials http://www.rxfiles.ca/rxfiles/uploads/documents/ACTIVE-A-Trial-Summary.pdf
Antithrombotics Summary Chart:: http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-AntiThrombotics.pdf
ARISTOTLE: Apixaban vs warfarin in A Fib: http://www.rxfiles.ca/rxfiles/uploads/documents/ARISTOTLE-AF-Apixaban.pdf
CHARISMA: http://www.rxfiles.ca/rxfiles/uploads/documents/Charisma-QandA.pdf
Clopidogrel-PPI drug interaction: http://www.rxfiles.ca/rxfiles/uploads/documents/Clopidogrel-PPI-interaction-QandA.pdf
DAPT: 12 vs 30months http://www.rxfiles.ca/rxfiles/uploads/documents/DAPT-Trial-12vs30months.pdf
MATCH: Clopidogrel PLAVIX + ASA ASPIRIN vs Clopidogrel PLAVIX in high-risk Patients with recent stroke or recent TIA
PCI-Clarity: http://www.rxfiles.ca/rxfiles/uploads/documents/PCI-CLARITY%20Trial%20Summary.pdf 2016
PCI-CURE: http://www.rxfiles.ca/rxfiles/uploads/documents/PCI-CURE%20Trial%20Summary.pdf 2016
PEGASUS-TIMI 54: Ticagrelor vs PI, prior-MI: http://www.rxfiles.ca/rxfiles/uploads/documents/PEGASUS%20Trial%20Summary.pdf 2016
PIONEER AF-PCI: Rivaroxaban + P2Y12 Inhibitor or Rivaroxaban + DAPT vs. Warfarin + DAPT in Patients with Atrial Fibrillation & PCI
PLATO: Ticagrelor vs clopidogrel ACS: http://www.rxfiles.ca/rxfiles/uploads/documents/PLATO%20Trial%20Summary.pdf 2016
RE-LY: Dabigatran vs warfarin in Atrial Fibrillation http://www.rxfiles.ca/rxfiles/uploads/documents/RE-LY-Trial-Dabigatran.pdf
ROCKET-AF: Rivaroxaban vs warfarin in A Fib: http://www.rxfiles.ca/rxfiles/uploads/documents/ROCKET-AF-Rivaroxaban.pdf
TRITON-TIMI 38: Prasugrel vs clopidogrel, ACS: http://www.rxfiles.ca/rxfiles/uploads/documents/TRITON-TIMI%2038%20Trial%20Summary.pdf 2016

MISC.:
Catie-AD: Atypical Antipsychotics in Patients with Alzheimer's http://www.rxfiles.ca/rxfiles/uploads/documents/Psych-CATIE-AD-trial-summary.pdf
FLAME: *Indacaterol+Glycopyrronium vs Salmeterol+Fluticasone for COPD:http://www.rxfiles.ca/rxfiles/uploads/documents/FLAME-Trial-Summary.pdf* 2016
Meloxicam: SELECT, MELISSA; *celecoxib* CLASS, *rofecoxib* VIGOR,: http://www.rxfiles.ca/rxfiles/uploads/documents/QandA-Meloxicam-2.pdf
OAB: Darifenacin-Oxybutynin Memory Trial : http://www.rxfiles.ca/rxfiles/uploads/documents/UI-Darifenacin-Kay-Trial-QandA.pdf
PALLAS: Dronedarone in High-Risk Permanent Atrial Fibrillation
RACE-II: https://www.rxfiles.ca/RxFiles/uploads/documents/RACE-II-trial.pdf
SELECT: Semaglutide versus Placebo in Patients with Obesity without Diabetes 2024
SENIOR: http://www.rxfiles.ca/rxfiles/uploads/documents/Senior-Trial-Oxybutynin-Solifenacin-Elderly-Cognitive-Impairment.pdf
Vitamin D: Effect of High-Dose Vitamin D on Bone Density and Bone Strength 2020
WARFASA: http://www.rxfiles.ca/rxfiles/uploads/documents/Aspirin-warfarin-trial-summary-WarfASA.pdf

Pandemic: COVID-19
EPIC-HR: Paxlovid in patients unvaccinated high-risk patients with COVID-19
Other COVID-19 RCT Summaries: COMET-ICE (sotrovimab tx) , PROVENT (Evusheld prevention, TACKLE (Evusheld tx), PINETREE (remdesivir tx)

Search Terms

EBM	230
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NNH	230
NNT	230
Precision	230
Validity	230

References for EBM (Evidence Based Medicine):

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