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** in prognostic factors for outcome of interest at beginning of study? 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 may also be of interest (e.g. non-inferiority trials}
7. Were **groups treated similarly** except for study intervention?
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) 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? {Consider **inclusion & exclusion criteria**; very sick, old, young, drug interactions & complicated/co-morbid patients often excluded.}
3. Do treatment **benefits outweigh the risks**, costs & impact on life?

Types of Studies (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! 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 chance at being assigned to any group, like the flip of a coin). Groups are followed for the outcome of interest.
- **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 studies 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 for safety, generalization to different populations, & insights into real world effect, especially when specific RCT not practical.[38]}

Caution: Lots of low-quality RCTs not be 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]

Terms: Related To Validity

- **Bias**: design flaws leading to over/underestimation of treatment effect e.g. recall bias, selection bias, publication bias; confounding factors esp observational studies
- **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. http://www.consort-statement.org/ }

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 of them benefit. {**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 the adverse event. {**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 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 that overlap the true value. CI's indicates the precision of the estimate; where CI's are wide, they indicate less precise estimates of effect (just 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 inappropriate to combine studies.[22] {***Q statistic***: measure of within-study variance; ***I²***: 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 (e.g. **NNT**) may be too small 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 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 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 individually sorting out 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

- 200 patients in Control group
- 200 patients in Treatment (tx) group
- Deaths: Control grp: 40. **CER**=40/200=0.2
  tx grp: 30. **EER**=30/200=0.15

RRR
= (0.20 - 0.15)/0.20 X 100
= 25% {risk of event is reduced by 25%}

ARR
20% - 15% = 5%
{absolute risk of event is reduced by 5%}

NNT
= 100/5%
= **20**

NNH: if 60% of patients in tx group experienced *headaches* compared with 27% in control group (ARI=33%)
NNH = 100/33% **= 3**

For every **20** patients treated for 1yr, there is 1 less *death*; & for every **3** patients treated there will be 1 extra *headache*.

A few NNTs / NNHs of interest	NNT
↓ mortality with simvastatin 20-40mg/day over 5.4yrs vs placebo in patients with CHD [4S]	30 / 5.4yrs
↓ mortality with metformin 2550mg/day over 10 years vs non-intensive tx in obese T2DM patients [UKPDS-34]	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. The value of the endpoint also varies from patient to patient.

Evidence-Based Medicine

Acknowledgements: Written by Loren Regier. Thanks to our reviewers: Alex Crawley, Brent Jensen, G Michael Allen MD, CCFP, Associate Professor, Director of EBM, Dept of Fam Med, U of A. Michael Allen MD, Associate Professor, Director Evidence-based Programs, Dalhousie University CME, Pam Maclean-Veysey, Drug Eval Unit, Halifax. Derek Jorgenson, PharmD, U of S. Darcy Lamb, C of Pharmacy, U of S. David Blackburn, C of Pharmacy, U of S. G. Turcotte MD, FM/EBM teaching, Gatineau, Quebec.
Disclosures: No conflicts of interest are reported by Loren Regier.

💻 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.

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 (Oxford): www.cebm.ox.ac.uk
- BMJ Talk Evidence Podcast: www.bmj.com/podcasts/talkevidence
- The NNT: www.thennt.com
- Essential Evidence Plus (Wiley): www.essentialevidenceplus.com
- PEER Evidence (Alberta College of Family Physicians): https://peerevidence.ca
- Therapeutics Initiative (University of British Columbia): www.ti.ubc.ca
- 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): ktcalc.cme.dal.ca/site/main.php
- 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

Table 3. RxFiles Selected 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: http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Diabetes-Landmark-Trials-Links.pdf

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

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

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

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

HRT: 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

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

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

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

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

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

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

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

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	1
Evidence Based Medicine	1
NNH	1
NNT	1
Precision	1
Validity	1

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

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