

**Critical Appraisal of Drug Studies<sup>6,7</sup>**

**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)<sup>8,9</sup>
2. Was everyone (patients, physicians, investigators, assessors) **blinded** to tx? (Especially important for assessors of subjective outcomes eg. 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 patient **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<sup>o</sup>) endpoint? What were the secondary (2<sup>o</sup>) endpoints? Were endpoints & subgroups pre-specified?<sup>10</sup> Avoid data mining!
2. What was the difference between treatments? (Benefits & Harms)
3. Were the differences **statistically significant**? ... **clinically significant**? (What were the 95% confidence intervals (CIs) or p values? Does the CI 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)<sup>11</sup>**

- **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*.<sup>12</sup>}
- **Crossover study**: 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.
- **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.
- **Systematic Review (SR)**: a systematic collection, review & presentation of available studies addressing a clinical question using specific criteria & methods; may include meta-analysis. e.g. *Cochrane*<sup>13</sup>/*Campbell*<sup>14</sup> *Reviews*

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

[**Level of evidence for Tx**: SR>RCT>observational study>expert opinion.<sup>15</sup> Observational studies useful for safety, generalization to different populations, & insights into real world effects, especially when specific RCT not practical.]

**Caution**: Lots of low quality RCTs may not be better than 1 good quality RCT!  
A low quality SR, or a SR of low quality trials does not constitute high-level evidence.]

**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<sup>16,17,18,19</sup>**

- **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](http://www.cebm.net): tool for converting OR to NNT<sup>20</sup>)
- **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<sup>21</sup>**

- **Confidence Interval (CI)**: a 95% CI provides the range of values we are 95% certain that overlaps 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 eg. *trends* -provide clues for future research & uncertainties.}
- **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.<sup>22</sup> {**Q statistic**: measure of within-study variance; **I<sup>2</sup>**: ratio of variability among studies to total variation.}

**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 <sup>45</sup>	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
↓ pain by ≥50% with TCAs (e.g. amitriptyline 100mg/day) vs placebo in neuropathic pain (short-term trials)	4

**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.

**Do the study results matter to me & my patients?**

- **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.<sup>23,24</sup>}
- **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.<sup>25</sup>)
- **Surrogate endpoints**: an endpoint meant to reflect / be correlated with another endpoint (eg. 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.<sup>26</sup> {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? Has drug been studied in enough patients to detect serious rare adverse events? What duration of intervention is studied & what are the potential benefits & harms over a longer term of exposure? Does real-world experience appear to be consistent with clinical trial data? Cost? How benefits & harms are described e.g. RR vs NNT will also affect decisions.<sup>27</sup>
- **What patient specific and 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 2<sup>nd</sup> 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 NNTs & NNHs.** {e.g. *Vioxx* monograph 2004<sup>46</sup>PS: 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 complications reductions 0.59% vs 1.37% (ARR=0.78; NNT=129); whereas thrombotic risk was worse (NNH=83).} {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 are often given per year. {e.g. UKPDS-33: aggressive glucose control benefit on microvascular endpoints given per 10 years; risks of hypoglycemia were given per year.<sup>28</sup>}
- **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.<sup>29</sup>}

## Other Online EBM Resources/Links:



EBM Portal Links (SK): [http://web.mac.com/malees/Primary\\_Care\\_Portal/EBM.html](http://web.mac.com/malees/Primary_Care_Portal/EBM.html); Evidence Updates service: <http://plus.mcmaster.ca/EvidenceUpdates/Default.aspx>

General: U of T: <http://www.cebm.utoronto.ca/>; Oxford: <http://www.cebm.net/?o=1011>; McMasters: How to teach evidence based clinical practice – Links: <http://hsl.mcmaster.ca/ebcp/>. Dynamed: [www.ebscohost.com/dynamed/](http://www.ebscohost.com/dynamed/)  
User's Guide: UoFA, Centre for Health Evidence: <http://www.cche.net/usersguides/main.asp>; UBC: <http://www.ti.ubc.ca/>; Grey Literature Searching: <http://www.cadth.ca/index.php/en/cadth/products/grey-matters>  
SchHARR Intro to Evidence Based Practice (Sheffield, UK) <http://www.shef.ac.uk/scharr/ir/netting/>; BMJ – Clinical Evidence Links: [http://clinicalevidence.bmj.com/ceweb/resources/useful\\_links.jsp](http://clinicalevidence.bmj.com/ceweb/resources/useful_links.jsp); NNTs <http://www.thennt.com/>  
Clinical significance CALCULATORS: UBC: <http://sph.ubc.ca/sites/healthcare/files/calc/clinisig.html>; Wisconsin: <http://intsmain.is.mcw.edu/clinical/bayes.html>. Essential Evidence Plus: <http://www.essentialevidenceplus.com/>  
Dalhousie Katie Clinical Significance Calculator: <http://ktcalc.cme.dal.ca/site/login.php> Z-score: <http://www.socscistatistics.com/pvalues/normaldistribution.aspx> Teaching EBM Videos: McMaster Guyatt: [http://ebm.mcmaster.ca/materials\\_videos.htm](http://ebm.mcmaster.ca/materials_videos.htm)

## RxFiles – Select Trial Summaries (more available online at [www.RxFiles.ca](http://www.RxFiles.ca))

**Anemia:** Trials Summary: <http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Anemia-Key-Trials.pdf>  
**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 P, 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>

## Online Extras

### Guidelines, Evidence and Patients

- Guidelines provide guidance based on evidence, clinical experience and someone's values and preferences.
  - Considerations: Evidence
    - How current? Has level/strength of evidence (evidence quality) been assessed for recommendations? (e.g. May have more confidence if high quality, multiple, trials.)
    - What outcomes are evaluated? Are they patient orientated or surrogate?
    - 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 (<https://www.cmaj.ca/content/193/2/E49>)
    - Are conflicts of interest disclosed
    - Conflicts may be financial or non-financial
    - Methods should be transparent and rigorous to inform objectively on best available evidence
  - Values
    - In what way are values and preferences included?
    - Who's values: 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?
- 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 reason for your decision.

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

## RxFiles: Evidence Based Medicine (EBM) Overview - References

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- Jadad A, Enkin M. Randomized Controlled Trials: Questions, Answers and Musings 2<sup>nd</sup> edition. Blackwell Publishing 2007; BMJ Books
- Edited by: Geyman J, Deyo R, Ramsey S. Evidence-Based Clinical Practice: Concepts and Approaches. Butterworth Heinemann 2000.
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- 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 0.60 [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.)
- Fletcher J. Subgroup analyses: how to avoid being misled. BMJ. 2007 Jul 14;335(7610):96-7.
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- Olecko WA. Essential Epidemiology Principles and Applications. Long Grove IL: Waveland Press Inc, 2002. (page 108)
- <http://www.cochrane.org/>; <http://www.cfp.ca/cgi/content/full/55/11/1155?etoc>
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