

### I. Should I bother with this article? Do not automatically trust authors or sources. Details must be evaluated.

If the Results are Reliable, Are They Usable? ↓	Pertinent Study Issues For Determining Reliability & Usability ↓
<ol style="list-style-type: none"> <li>1. Will I change my practice? Will my patients benefit?</li> <li>2. Meaningful benefit = size of benefit + areas of clinical significance to patients (morbidity, mortality, symptom relief, physical and emotional functioning and health-related quality of life)</li> <li>3. Applicability to my patient (see inclusions, exclusions and baseline characteristics)</li> <li>4. Look at the boundaries of the confidence intervals (CIs) of valid studies to compare to your requirements for meeting clinical significance. See * below. Then →</li> </ol>	<ol style="list-style-type: none"> <li>5. Was choice involved in determining who got the therapy? If yes, this is an observational study, and there is a high risk of misleading results, with rare exception (e.g., all-or-none results).</li> <li>6. Is the comparison fair?</li> <li>7. Question, endpoints and analysis groups should be determined in advance, otherwise there is a high risk of chance results.</li> <li>8. Do you agree with how they defined outcomes such as success/failure, improvement/no improvement, etc.?</li> <li>9. If this study is for a new agent, safety may be unknown.</li> </ol>

### II. How do I know the results are likely to be true?

10. What could possibly explain the results other than the intervention? Could **bias**, **confounding** or **chance** explain or affect the outcomes? Or can I rule them out and comfortably presume results are true (**cause and effect**)?
11. The burden of proof is on the intervention: Could anything advantage the intervention?
12. Review the 4 phases of a study for bias: **selection** phase + **performance** phase + **follow-up** phase + **assessment** phase. Always use a critical appraisal checklist. See the **Delfini Study & Usability Tool** (short checklist) for validity considerations.

- Bias tends to favor the intervention. Biases in areas such as randomization, concealment of allocation to study groups, blinding or using models can inflate benefits by up to a relative 50 percent.
- Are there **any differences** between groups except for what is being studied? If yes, this is an automatic bias.
- Look for other biases. For example, frequently information on co-interventions or adherence will be lacking. This could result in misleading results due to confounding. Were methods used to measure the outcomes appropriate, etc.?
- How much **data** are **missing**? (e.g., discontinuations, etc.)? Even non-differential loss can mean differences in prognostic variables. Primary analysis should be Intention-to-Treat (ITT), with people being analyzed in their assigned groups plus using reasonable choices to “make up” entries for missing data. Most analyses involve modeling and modeling requires unverifiable assumptions.

### III. For valid studies, how do I know the results are likely to be useful?

13. \*For valid studies, consider what *you judge* to be a reasonable range for **clinical significance**. For **statistically significant findings**, is the confidence interval wholly within *your* bounds for clinical significance? For **non-significant findings**, is the confidence interval wholly beneath your limit for clinical significance? A yes to these two questions means likely conclusive findings for valid studies. No, means findings are inconclusive.
14. **Non-significant findings** may mean there truly is no difference or they didn't have enough people to show a difference.
15. Equivalence does not mean two drugs are actually equivalent. There are special issues for evaluating “equivalence” and “non-inferiority” available from Delfini.

**IV. Suggestions for quality information sources are available from Delfini.** Most all sources vary in quality and should be critically appraised. Delfini has tools available for appraising primary and secondary sources for interventions.

### Best Experiments for Interventions: Prevention & Therapies ^

- a. Questions in advance (a priori) and questions that matter to patients (clinical significance)
- b. Right people, enough people and low number of missing data points (possible to solve via analysis)
- c. Comparison group (concurrent controls) and good comparator (eg, placebo)
- d. Randomization to assign study groups
- e. Blinding successful (assignment to groups, all people, intervention, all working with data)
- f. Reasonable design, execution, measurement and analysis methods (including composite endpoints)
- g. Sameness except for intervention
- h. No bias or confounding
- i. Tests for probability of coincidental findings (chance)
- j. Results large enough to be useful or, if no difference between groups, assurance results are conclusive (review confidence intervals)
- k. Safety considered

^ Special issues: cross-over design, screening, diagnostic testing, equivalence and non-inferiority trials