Delfini Pearls
Basics of Evaluating Evidence in Superiority Trials for Therapies

Healthcare Information & Decision Equation: Information → Decision → Action → Outcome
Is it true → Is it useful → Is it usable?

Quick Assessment
If the results are reliable, are they useful and usable? Would they change your practice? Do they apply to your situation considering your patients and circumstances of care? Consider effects on your patients including benefits, harms, risks, costs, uncertainties, alternatives, applicability, satisfaction, abuse and dependency issues. Consider conflicts of interest.

- Are the results in clinically significant areas (morbidity, mortality, symptom relief, mental/emotional/physical functioning and health-related quality of life)? If not, is there a reliable causal chain of evidence to support use of an intermediate marker?
- Were research questions, outcomes and populations for analyses determined in advance?
- Are definitions of outcomes such as success/failure, improvement/no improvement, etc. reasonable?
- Are the confidence intervals wholly inclusive of clinical benefit? If non-significant, are the confidence intervals wholly exclusive of clinical benefit? Are results likely to be due to chance?
- Is this a new intervention? If yes, safety is likely to be unknown.

Study Design Considerations for Usability
1. Randomized controlled trials (RCTs) for efficacy and safety (tip: choice of intervention was not made by patient or patient’s physician or by other means that would render study observational)
2. Possibly observation studies with all-or-none results (very rare)
3. Observational studies for safety if lacking quality information from RCTs

Validity Considerations to Assess Potential Distortion of Results Due to Bias, Confounding or Chance
Assess methodologic details and outcomes in the 4 Phases of a Study

I. Selection of Subjects
   1. Random allocation of study subjects to their groups (minimization may be acceptable)
   2. Adequate methods for blinding the allocation of subjects to their groups (aka “concealment of allocation”)
   3. Balanced distribution of prognostic variables as assessed through review of baseline characteristics

II. Performance
   1. Comparisons are reasonable
   2. Execution is successful, adherence was achieved, duration of treatment is reasonable
   3. Everything is the same between the groups except for the subject of interest* (e.g., groups are concurrent and balanced, use of co-interventions is the same, same care experiences, adherence is balanced, protocol deviations are balanced, etc.) and no bias is present affecting the groups as a whole (e.g., measurement problems, changes due to time, etc.) *attrition is, at times, an exception
   4. Blinding of subjects and all working with subjects and their data was performed and success was likely

III. Data
   1. Are measurement methods valid and the same between groups? “Validated” may not really be valid. Consider duration of treatment and follow-up.
   2. Could high discontinuation rates distort the outcomes resulting in under reporting of safety problems or otherwise create a distortion due to such issues as subjects using other interventions?
   3. Are missing data likely to distort results?

IV. Assessment of Outcomes
   1. Was assessment blind?
   2. Were analysis methods appropriate including predefined groups for analysis?
   3. If composite outcomes were utilized, were they reasonable?
   4. If appropriate, was analysis done by Intention-to-Treat (all patients evaluated in assigned groups) with missing variables assigned by reasonable methods which will not favor the intervention?
   5. If time-to-event analysis used, were methods appropriate including unbiased censoring rules?
   6. Were assumptions used for modeling reasonable?
   7. Was reporting likely to have been selective?
   8. Was safety assessed and reported?
   9. Have results been confirmed in other valid studies?