Delfini Pearls
Analyzing Results: Composite Endpoints

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

Composite endpoint refers to individual endpoints grouped together for results reporting to serve as a single outcome measure

- Examples—
  - Major cardiovascular events = consisting of several individual outcome measures = cardiovascular death, nonfatal myocardial infarction, stroke
  - Diabetic nephropathy = decreased renal-function, end-stage renal disease, death
  - In oncology, disease-free survival = No tumor recurrence, alive at time of measurement

Synonyms for Endpoint: Measure or measurement; outcome measure or outcome (eg, cardiovascular mortality, number of pain-free days)

Reasons for composite endpoints—

- Greater frequency for otherwise infrequent events
- Allows for smaller sample size
- May form a more robust picture when dealing with a variety of hoped for outcomes (eg, reduction in mortality from MI + prevention of MI)
- There is also a potential for misleading readings—
  - Point being that you have to **watch out** because an investigator can set up the composite endpoint (intentionally or not) to have a high likelihood of showing a desirable outcome. ↓

Cautions

Watch out for what component of the endpoint is driving the results and determine how clinically significant and valid it is—

- "It will either rain or be dark tomorrow."

Considerations & Critical Appraisal Issues

- Is the combination valid, reasonable, fair and clinically useful? Is there any way that its construction is likely to favor the intervention? Watch out for –
  - Subjective outcomes especially if no blinding
  - Combinations including severe outcomes with mild ones, process measures, intermediate markers without a direct chain of causality to a clinical outcome, items under control or influence of a participant in the research
  - Did the researchers avoid double-counting (eg, if someone dies of stroke, did they get counted in both stroke and death)?
  - If applicable, are all relevant events included (eg, not only fewer symptoms resulted, but mortality was not increased)
  - How meaningfully-related is the combination?
  - Are there other ways the combination could be misleading?
  - Disease-free survival when a treatment reduces risk of tumor recurrence but increases risk of death
  - Did they report results on the individual components?