

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)?
  - 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? Without this information, depending upon the combination, a situation could result in which symptoms decreased, but mortality increased, but the composite masks this untoward outcome.
  - All-cause mortality is an important outcome as it is likely to be "unbiased." If randomization is successful and the study is otherwise valid, any non-treatment related deaths should be likely to be balanced between the groups or be the result of chance. Disease-specific mortality provides additional information about death from specific causes, but disease-specific outcomes may be biased, if groups are not balanced at outset or blinding is not successful. Biases could result from group imbalance or bias or errors in assigning cause of death. Mortality outcomes are prone to power problems.