

BIostatistics 740 (BIOS7400)
Clinical Trials

Lecture 17

Data Analysis III
**(Handling of Various Issues, Reporting,
Interpreting)**

Primary, Secondary, and Tertiary Data Analysis

- *Primary Analysis*: to answer the *primary* question by analyzing the *primary* outcome measure
 - Possible to specify > 1 *primary* outcome in the design of a clinical trial, but the use of *multiple primary* outcomes often *inflates* sample size to achieve the necessary statistical power
 - A “*composite*” primary outcome can be created by combining a # of *individual* (i.e., “*component*”) primary outcomes, e.g., APTC events (i.e., non-fatal myocardial infarction, and non-fatal stroke, and CV death) in the 1-Year Post-treatment Follow-up of the APPROVe trial, but there are also limitation of using such an outcome
 - *Usually reported* in the “*main paper*” (or “*primary outcome paper*”)
- *Secondary (or Tertiary) Analysis*: to answer the *secondary* (or *tertiary*) questions by analyzing the *secondary* (or *tertiary*) outcome measures
 - Trials are powered to answer the *primary* question, and *secondary* (or *tertiary*) questions may be posed, but clinical trials are *not statistically powered* to address these
 - *Secondary* (or *tertiary*) outcome results must be viewed and interpreted *with caution*
 - Results are often summarized in the “*main paper*”, but details of these outcomes are *usually reported* in subsequent publications (i.e., “*secondary* (or *tertiary*) outcome paper”)

Counting Rules for Events

- *Early Events* [i.e., those that are observed in *immediate* (i.e., a *very short* timeframe) *post-randomization* follow-up period]:
 - *Not counting such events* should be applied *rarely and cautiously*, e.g., a *negative* impact of the experimental treatment could have a *more immediate* effect that could be missed *as easily* or *as quickly*
 - If *such events* were *decided not to be counted*, data must be presented in *both* ways, i.e., *with* and *without excluding such events*
- *Events* when study participants have *been lost to follow-up* or have *reached some level of nonadherence*
 - It is *not clear* what *length of time* is *appropriate* for *not counting such events*
 - If a study participant develops an *event* within a *certain time period* after *going off the study intervention*, bias could be introduced if that *event* is *not counted* by applying an *arbitrarily-defined threshold* because the *study intervention itself* could contribute to the *event* due to *AEs* [e.g., in the APPROVe trial, the decision *not counting events* (i.e., *CV events*) *after 14 days* and *not to follow up* study participants *after this 14-day time period* led to controversy. In fact, results and interpretation were *different* when *1-year post-treatment follow-up* was *obtained* from a majority (84%) of the study participants]