

**Harvard Medical School Department of
Continuing Education and the Cardiovascular
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Cardiology Rounds
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**Statistical Methods in Clinical Trials:
Using your Allocated Statistical Firepower**

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Objectives: As physicians practicing evidence-based medicine, we have to be able to understand new developments and, when appropriate, utilize or abandon certain therapeutic approaches for the care of our patients. Even if we are comfortable with statistics, most of us are not fully trained in the nuances of statistics. As such, we rely on experts to assure us that the conclusions reached from clinical trials are valid and appropriate. We are aware that group differences from randomized trials may or may not apply to our individual patients. In this issue of *Cardiology Rounds*, Dr. Moyé, a physician-statistician with extensive experience in conducting and interpreting clinical trials, helps us improve our understanding of the statistical interpretation of clinical trials.

The objective of this issue is to understand some of the pitfalls of data analysis. Dr. Moyé sympathizes with the need for clinicians and investigators to glean as much from the data set as possible. However, he clearly spells out the difference between primary analyses, as intended, secondary analyses, and the much more common exploratory analyses. It is important for the physician to better understand this distinction when viewing clinical trial data. The same P value that is usually associated with a highly significant difference in one set of assumptions, should not be interpreted in the same manner in another set. Specifically, Dr. Moyé uses case histories from major trials to distinguish between a prespecified primary endpoint and what should be considered as more exploratory analyses. The reader will also understand the limitations of subgroup analyses. The overall objective of these rounds is to make our physician readers more knowledgeable of statistical limitations "beyond P values," enabling them to be more educated consumers of clinical trials.

TEST:

1. Selecting a random sample from the overall target population always assures that all of the responses observed will accurately reflect the true response from the overall population.
True___ False___
2. Use of statistics acknowledges potential sampling errors and provides guidance for the interpretation of data. This guidance requires that critical assumptions regarding the conduct of the trial and data analysis are satisfied.
True___ False___

3. In the original ELITE study, the finding of fewer deaths in the losartan group 17/352 (0.048%) versus the captopril group 32/370 (0.086%), a risk reduction of 46%, and a 95% confidence interval, 5% - 69%, $P=0.035$, provides a vivid example of potential pitfalls where the non-primary data analysis may no longer be a reliable indicator of the true effect in the population.
True___ False___
4. Once the primary analyses are conducted, the investigators should stop all further analyses.
True___ False___
5. Hypothesis generating analyses are an important means to learn more from valuable data sets, however, the conclusions from these analyses, even though using same formal test statistics, must be viewed outside of the boundaries of the original statistical assumptions and are therefore exploratory in nature.
True___ False___
6. It is now possible to design a trial that simultaneously tests more than one primary hypothesis. The prespecified design for more than one analysis would require a so-called splitting of the type I error level. In effect, one declares how much of the probability the type I error we are assigning to each of the questions prior to the conduct of the trial.
True___ False___
7. Although subgroup analyses can yield important information, a straight P value comparison within a subgroup is often outside of the statistical bounds of the study and for the most part should be considered exploratory.
True___ False___

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