Clinical Reading Questions #9

HST 190: Introduction to Biostatistics

These discussion questions are based on Weir, Dufault, and Phillips (2024).

1. What were the major goals of the study? What is the ICH E9(R1) addendum and what are its major implications for the design and analysis of clinical trials?
2. What is an estimand and what are the five attributes of an estimand defined within the ICH E9(R1) addendum?
3. The authors take great care to distinguish between an *estimand* and an *estimation method*. What is the difference between these two concepts?
4. The authors re-analyze data from the REMoxTB Phase III placebo-controlled RCT. What was the study population for the REMoxTB clinical trial and what was the primary endpoint?
5. What was the primary objective of REMoxTB and was it attained in the primary analysis reported for that clinical trial? What was the primary unfavorable outcome definition used by the authors in their re-analysis of REMoxTB?
6. In the authors' re-analysis of the individual patient data (IPD) from the REMoxTB trial, what was the sample size, how many patients experienced the endpoint of interest, and what were the most commonly occurring intercurrent events (ICEs)?
7. After using the ICH E9(R1) estimands framework to guide their re-analysis of REMoxTB, what conclusions do the authors reach about non-inferiority of the two investigational regimens versus the standard of care? Do these differ from the conclusions reached in the primary analysis of the REMoxTB trial?
8. What are the primary contributions of the manuscript to the development and analysis of clinical trials (both in TB and more generally)?

References

Weir, Isabelle R, Suzanne M Dufault, and Patrick P J Phillips. 2024. "Estimands for Clinical Endpoints in Tuberculosis Treatment Randomized Controlled Trials: A Retrospective Application in a Completed Trial." *Trials* 25 (1). https://doi.org/10.1186/s13063-024-07999-w.