Estimands and analyses of longitudinal continuous outcomes in clinical trials

For more than a decade, a mixed model for repeated measures (MMRM) approach has been the de facto standard for the primary analysis of clinical trials with longitudinal outcomes. The conventional MMRM model provides valid inference under a basic missing-at-random assumption. However, it is increasingly appreciated that more complex analysis methods may be required to fully align the analysis strategy with the targeted estimand and flexible missing data assumptions.

Course outline

This short course provides a thorough introduction to estimands and estimation strategies for clinical trials with longitudinal continuous outcomes. A particular focus will be on estimation methods based on multiple imputation of missing data and their implementation in the R package rbmi.

Specifically, the course will cover the following topics:

- Introduction to continuous longitudinal estimands, missing data assumptions (basic and extended MAR, reference-based missingness), and traditional analysis approaches.
- Estimators based on multiple imputation and their implementation in statistical software.
- Case study: Estimands and estimators in early Parkinson's disease.

After the course, attendees will understand the strengths and limitations of conventional MMRM analyses in view of the estimands framework. They will be familiar with alternative analysis methods based on multiple imputation which are of increasing importance for primary and sensitivity analyses. Finally, they will understand how such analyses can be implemented with statistical software.

Target audience

Statisticians from the pharmaceutical industry and academic clinical research units.
No prior knowledge except for basic familiarity with the statistical software R and the estimands framework as described in the "ICH E9(R1) addendum on estimands and sensitivity analyses in clinical trials" is required.

Instructors:

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