Project Title: Methods for deterministic treatment effect estimates for clinical trials with missing data

Principal Supervisor: Jonathan Bartlett

Secondary Supervisor: James Carpenter (LSHTM) and Marcel Wolbers (Roche)

Department & Institution: Department of Medical Statistics, LSHTM

Collaborative Organisation: Roche

Project description

The statistical analysis of clinical trials is often complicated by missing data. Patients may dropout from clinical trials, which often (although not always) leads to subsequent outcome measurements being missing for such individuals. Intermediate missing values may also occur when a patient misses a scheduled follow-up visit. In the last 20 years methods have been developed for obtaining estimates from trials which accommodate such missingness in a principled way, by making an assumption about how the missing data relate to the observed data. Because such assumptions cannot be verified from the observed data, a range of methods have been developed for assessing the sensitivity of inferences to these untestable assumptions.

Nowadays such analyses are often performed using the method of multiple imputation, where each missing value is replaced multiple times by plausible values based on a statistical model. This leads to multiple completed datasets, each of which is analysed. The estimates from each dataset are then pooled. A drawback of standard multiple imputation methods is that because the imputations are drawn randomly, the treatment effect estimates obtained are (to some extent) random - it will give slightly different answers depending on the computer's random number seed. For the primary analysis of a clinical trial, which decides whether a new medical treatment is licensed by regulatory agencies (such as the MHRA) or not, this is quite undesirable and deterministic methods would be much more preferable.

This PhD project will investigate deterministic single imputation methods for handling missing data in clinical trials, as an alternative to multiple imputation. The project will be in collaboration from statisticians at Roche, one of the world's largest biotech companies. The project will build on previous award winning work (see paper here) between the primary academic supervisor and statisticians at Roche. This work developed an approach for continuous outcome variables, and this PhD project will investigate the extension of this approach to other types of outcome variable (e.g. binary or count data).

Collaboration partner

During the PhD the student will work closely with the collaboration partner Roche. This will involve regularly visiting Roche's site at Welwyn Garden City near London. Dr Marcel Wolbers from Roche in Basel will serve as a secondary supervisor to the student.

Skills development
This project will enable the student to develop skills and experience in a number of areas, including:

- Developing and applying novel statistical methodology for application in clinical trial analyses, using both analytical and simulation based approaches
- Statistical programming using a modern statistical software package (e.g. R)
- Experience of working collaboratively within the environment of an internationally leading biotech company
- Transferrable skills, including research ethics, scientific writing, presentation skills

Environment
The student will join a highly active and collaborative group of researchers in the Medical Statistics Department and Centre for Statistical Methodology at LSHTM, including existing PhD students at different stages and other early career researchers. The student would also have the opportunity to participate in statistical methodology groups, including one focus on missing data. The student will make regular visits to Roche's Welwyn Garden City site, where around 30 statisticians are based, throughout the project.

Candidate Requirements
Ideally, applicants should have an excellent undergraduate degree (first or upper second) in mathematics, statistics or a related field and an MSc in statistics, medical statistics, health data science, or a related field, or equivalents for qualifications gained outside the UK.

UK and international students are eligible to apply. For eligibility criteria for the DTP please see: https://ubeldtp.ac.uk/esrc-studentships/. Further information about the level of funding available for international students is available here: https://www.lshtm.ac.uk/study/fees-funding/funding-scholarships/esrc-2023-24

Key References
Wolbers, M., Noci, A., Delmar, P., Gower-Page, C., Yiu, S. and Bartlett, J.W., 2022. Standard and reference-based conditional mean imputation. Pharmaceutical Statistics, 21:1246-1257. Open access link here.

Further details
If you would like to discuss the project further, please contact Jonathan Bartlett Jonathan.bartlett1@lshtm.ac.uk

Deadlines and how to apply
If you would like to apply, please complete the UBEL DTP co-funded and collaborative student application form in Survey Monkey (link here). This opens on Monday 16th January 2023 and the deadline for applications is 28 February 2023 (23:59 GMT).