Matching approaches for efficient and robust causal inferences in Mendelian randomization

Supervisors: Sofia Villar and Adrian Mander

Location: MRC Biostatistics Unit, University of Cambridge

Detailed description: In dose finding studies the aim is to find the maximum tolerated dose of an agent or to find a dose which is closest to a target dose. In dose-ranging studies different doses of an agent are tested against each other to establish which dose works best and/or is least harmful by estimating a response-dose relationship. However, achieving either of these goals with a high precision can imply exposing a large number of patients to highly toxic doses, imposing a learning-earning trade-off. Despite extensive recent work has been done in using decision theory for addressing such a trade-off in the context of designing clinical trials [1], little work has been done to extend such a framework for dose-finding/dose-ranging studies. Using a decision-theoretic approach allows to take into account the interests of the patients both within and outside the trial to derive a patient allocation rule which can acknowledge the existing conflict between the interests of each individual patient and the following patients. This idea was proposed earlier in the literature (e.g. a framework for dose-finding trials using the theory of bandit problems was proposed by Leung and Wang [2]) yet because finding the optimal strategy for this type of bandits with dependent arms is in most relevant cases not computationally feasible the approach has not been further developed.

This PhD project will look at developing decision-theoretic non-myopic response-adaptive dose-ranging methodology for dose-ranging and dose-finding studies. The project will make use of recent advances in bandit theory to try and reduce the computational complexity of finding the optimal (or nearly optimal) solution derived from a set of relevant optimisation problems. The PhD will cover some of the following areas:

- Use and extend existing response-adaptive randomisation rules to be incorporated into the design of dose-escalation studies.
- Investigate novel optimal response-adaptive adaptive designs that can handle multivariate conflictive outcomes (efficacy-toxicity).
- Assess how these methods perform in terms of estimation purposes and patient gain decisions (administering doses nearest to the target toxicity level).
- Use of the dynamic optimisation (bandit) literature to develop suitable and practical non-myopic adaptive randomisation methods specifically designed for dose adaptive trials;
- Produce easy to use software in R and/or Stata to implement methods;
- Compare the resulting decision-based designs to the real trial.

References:


Start date: Michaelmas Term 2018

All application queries regarding eligibility should be directed to phdstudy@mrc-bsu.cam.ac.uk
How to Apply: Applications should be made online via www.graduate.study.cam.ac.uk/applicant-portal selecting course details MDBI22 PhD in Biostatistics

Deadline for applications: 4th January 2018