Project title: Developing Bayesian non-myopic response-adaptive randomisation for the case of delayed endpoint observation

Supervisor(s): Sofía Villar and David Robertson

Abstract:

Before a novel treatment is made available to the wider public, clinical trials are undertaken to provide unbiased and reliable information that the treatment is safe and efficacious. The standard approach for such confirmatory clinical trials is to compare only two treatment options and requires a large number of patients to be recruited in a trial. This approach does not fit well with the development of treatment for many conditions, in which there is a large number of potential treatments to explore and relatively very few patients affected by the disease that could be enrolled in a trial. This is the case for drug development for rare types of cancer.

A promising alternative to the standard approach within the above described context is the use of response-adaptive randomization (i.e. changing the allocation probabilities as outcome data is collected to favour promising treatments). Promising treatments can be quickly identified, allocating more patients to them while doing so, by designing a trial that incorporates a response-adaptive randomization patient allocation rule. The type of response-adaptive randomization rules that exhibit the best performance in terms of patient benefit are the so called non-myopic rules which unfortunately suffer from a binding computational burden. Developing computational feasible and practical methods to apply these ideas into trial design as a way for improving the success rate of Phase III clinical trials are therefore of great current interest. At the Biostatistics Unit we have made a start with this by developing a non-myopic group response-adaptive randomisation method called the ‘forward looking Gittins index’ rule (1,2) for the case of dichotomous endpoints. This PhD project will look at extending existing non-myopic response-adaptive randomisation methodology to cover the case of delayed outcomes. This is particularly relevant for trials in which the endpoint is survival. The project will investigate novel optimal adaptive designs that can use both observed response and partial information (derived from the delayed response). Therefore, these methods will be closer to the real world situations being handled by trials in which the endpoint is not necessarily best modelled as binary and immediately observable. The PhD will cover some of the following areas:

• To model the patient allocation problem with delayed patients responses as an optimal sequential decision making problem in the stochastic dynamic programming framework.
• To design index policies and compare them to existing approaches in terms of statistical and optimality performance
• To develop and study efficient algorithms for optimal solutions, create a software package and collaborate with statisticians and clinicians to apply the designed solutions in real clinical trials

The student also will have the opportunity to collaborate with researchers from Lancaster University that are experts in stochastic dynamic programming approaches and in adaptive designs.

References:

Start Date: Easter Term 2020 (UK applicants only) or Michaelmas Term 2020 (all applicants)

All application queries regarding eligibility should be directed to phdstudy@mrc-bsu.cam.ac.uk

How to Apply: Applications should be made on-line via www.graduate.study.cam.ac.uk/applicant-portal selecting course details MDBI22 PhD in Biostatistics

Deadline for applications: 7th January 2020