A unified approach for the statistical analysis of post-randomisation variables in clinical trials

MRC-NIHR Trials Methodology Research Partnership PhD project

Project Description

Background

In randomized trials the primary analysis is based on an intention-to-treat approach which answers the question "What is the effect of offering treatment?". There are many other questions that investigators could pose such as "Does this treatment work if it is received?", "What factors make the treatment work better?" and "How does the treatment work?". Understanding how and why an intervention works can deliver improved understanding of interventions and how these should be implemented in routine care. It can also help to explain why a trial might have produced a null treatment effect.

The statistical methods required to answer these questions can be complicated in real life applications, due to several factors that occur after the patient is randomised and are collectively referred to as post-randomisation variables. Often these factors are outside the control of the investigators, including missing outcome data and non-compliance with random allocation. Sometimes they are built into the design of the trial, such as measuring mediators to assess how treatments work and using surrogate outcomes. In skills-based interventions, it has been increasingly acknowledged that clustering effects are a concern, particularly if the clustering is only present in one arm of the trial.

We will review the analysis approaches for post-randomisation variables, including non-compliance, mediation analysis, surrogate outcomes, missing data and clustering effects. Currently all these issues are considered separately. This project seeks to unify the theory and analysis to provide a comprehensive approach for the statistical analysis of post-randomisation variables in clinical trials.

Aims

The PhD student will undertake a methodological literature review and obtain the practical skills in the statistical methods described in the background; conduct an investigation of real clinical trial data to produce a working model for mediation and sensitivity analyses to check the robustness of the model(s) to assumptions; extensions to repeated measures of intermediate variables; incorporation of time-varying therapist effects into the models; and a systematic series of Monte Carlo simulations to optimise strategies for these analyses.

Supervisors:

- Professor Richard Emsley, Professor of Medical Statistics and Trials Methodology, Department of Biostatistics and Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London
- Professor Sabine Landau, Professor of Biostatistics, Department of Biostatistics and Health Informatics, Institute of Psychiatry, Psychology and Neuroscience, King's College London

Training opportunities:

The student will have the opportunity to gain training through courses on the [PGCert in Applied Statistical Modelling and Health Informatics](#) at the Institute of Psychiatry, Psychology and Neuroscience, and courses at other institutions in the MRC-NIHR Trials Methodology Research Partnership (TMRP). The student will be part of the wider cohort of TMRP PhD students and to attend meetings organized for cohort.

Requirements

A strong academic track record with a 2:1 or higher in a relevant undergraduate degree with substantial statistical content, or its equivalent if outside the UK. It is also desirable to have a strong performance in a relevant postgraduate degree (e.g. medical statistics, clinical trials, epidemiology).

The successful candidate will work in a highly interdisciplinary environment and should be able to work independently and in collaboration with members of the MRC-NIHR Trials Methodology Research Partnership.

Application procedure

The closing date for applications is **31st August 2019**.

Interviews will be held in **mid-September** (exact date TBC).

The start date for the project is **1st February 2020**, and is offered full time for 3 years.

This studentship is offered as one of a set in the Department of Biostatistics and Health Informatics. Full details of how to apply are here: https://www.kcl.ac.uk/ioppn/study/prospective-students/programmes-of-study/pgr/fundedresearchopportunities/01-bio-2020

For further information, please contact Professor Richard Emsley: richard.emsley@kcl.ac.uk

Funding provided

- Stipend at UKRI rate (£15,009 p.a. in 19/20) for 3 years
- Tuition Fees at UK/EU rates (£5,700 p.a. in 19/20) for 3 years
- Conference travel of up to £500p.a. for 3 years
- Note that this studentship covers UK/EU tuition fees only