Subgroup identification for treatment response using observational cohort data in the presence of complex confounding

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Detailed description: Clinical and biological evidence suggests that subgroups may exist within the population of patients with systemic lupus erythematosus (SLE), offering the possibility of a more targeted use of existing and novel therapeutic agents to improve remission/low disease activity (LDA) rates. In the recent MASTERPLANS (Maximizing SLE Therapeutic Potential by application of Novel and Systematic approaches) consortium, the key objective is to use clinical, genetic and other predictors to identify subgroups of SLE patients who had better responses to mycophenolate mofetil (MMF) and a B-cell targeted therapy (rituximab).

Many statistical methods have recently been developed for identifying subgroups of patients who may benefit from different available treatments (Lipkovich et al. 2017). These methods are diverse and include both parametric regression with regularization and non-parametric approaches from the machine learning literature. In particular, they were developed mainly for clinical trial settings with random treatment assignment, where confounding is not an issue.

Observational cohort studies with longitudinal data over long study periods provide valuable information about chronic diseases such as SLE, but time-varying confounding is a severe problem for treatment effect estimation because patients could switch between treatments as disease progresses. This creates a significant challenge for subgroup identification using such observational cohort data.

The aim of this PhD project is to develop methods for subgroup identification using longitudinal observational data with complex confounding. This will involve: (1) exploring and adapting G-methods for estimating causal effects from longitudinal data with time-dependent confounding (Daniel et al. 2013); (2) exploring and adapting statistical and machine learning approaches for heterogeneous treatment effect identification and estimation; and (3) dealing with high-dimensional covariate/confounder data which can be partially missing.

This research is mainly motivated by the stratified medicine initiative for improving patients benefit. However, it can also help to select promising subgroups with enhanced efficacy or desirable safety profiles to inform the recruitment and design of future clinical trials using existing observational data sources.

References:


Start date: Michaelmas Term 2018

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

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Deadline for applications: 4th January 2018