PhD Project 2, 2023: Developing models of causal effects of therapies in multiple sclerosis

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Project background: Multiple sclerosis (MS) is the second most common cause of disability in young adults. The focus of multiple sclerosis management lies in preventing episodic inflammation and relapse-related disability accrual.
Methods of causal inference, such as marginal structural models (MSM), enable clinical researchers to estimate causation between treatments and observed outcomes in cohort and registry data. Because of their limitations, MSM have so far been restricted to emulation of clinical trials. There is an unmet need to broaden the scope of research using causal inference beyond emulation of trials in clinical cohorts and registries. The unmet needs include studies of cohorts with variable time of patient entry, long- term effects of interventions, delayed effects of interventions and comparing multiple interventions.

Aim: This project will expand the capabilities of MSM for study of MS therapy by addressing the following aims:
- To develop a method enabling analysis of left-censored longitudinal cohorts with variable time of patient entry
- To enable evaluation of long-term treatment effects in counterfactual framework
- To develop a method that will allow evaluation of delayed treatment effects
- To generalise MSM to enable comparison of multiple MS therapies and pairwise comparison of MS therapies.

This project uses innovative contemporary statistical methods and simulation methods for longitudinal observational data with complex confounding.

Impact: This PhD project will transform the analysis of longitudinal observational MS datasets (registry and cohort data) by greatly expanding the utility of MSM. It will allow clinical researchers and epidemiologists to answer questions about causal effects of therapies that cannot be addressed in standard randomised clinical trials. The results will be presented in scientific journals and at national and international conferences.

Availability: This PhD project is suitable for students with interest in statistics and research of treatment effectiveness. During the project, you will improve your statistical skills, learning techniques of causal inference and simulation of longitudinal data. Knowledge of elementary statistics is a requisite. The offer of the project is conditional on a successful application for a University of Melbourne scholarship.