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Title: Addressing immortal-time bias in emulated trials from cancer registry data

Abstract:
Real world evidence from observational studies is becoming increasingly important to influence health care policies. However, unlike randomised trials, observational studies are prone to bias, such as confounding or immortal-time bias. A general framework to emulate randomised trial from observational data has been proposed by Miguel Hernan to estimate causal effects while addressing these two issues.
In this talk, we will illustrate how this framework can be used for the estimation of the causal effect of early surgery (within 6 months following diagnosis) on 1-year survival among older lung cancer patients. Immortal-time bias is accounted for using a cloning and censoring procedure. At baseline, two exact copies of every patient's record are created. One copy is allocated to each treatment arm of the emulated trial. Then, one of these copies is censored when the treatment actually received by the patient is no longer compatible with the definition of one of the two arms (for instance, if a patient had surgery at 3 months, the copy allocated to the "no surgery" arm will be censored at 3 months). This artificial censoring is then accounted for in the analysis using inverse-probability-of-censoring weighting. We will compare this approach to more standard models that account for immortal-time bias: a Cox regression model with a time-updated treatment variable and the delayed entry method. In particular, we will show that the emulated trial approach focuses on an estimand more likely to be relevant for real-life evaluations of treatments and interventions.
However, a complexity of the approach is the estimation of the censoring weights. We will present different methods to estimate these weights, among which generalized additive models and random forests, and we will show how the performance of these weights to balance groups over time can be easily assessed using graphs.
The aim of this presentation is therefore to provide some practical recommendations for the implementation of trial emulation in the presence of confounding and immortal-time bias.