Causal Inference with Observational Survival Data

Bo Lu

Abstract:
Investigating the causal relationship between exposure and time-to-event outcome is an important topic in biomedical research. Previous literature has discussed the potential issues of using hazard ratio (HR) as the marginal causal effect measure due to noncollapsibility. In this article, we advocate using restricted mean survival time (RMST) difference as a marginal causal effect measure, which is collapsible and has a simple interpretation as the difference of area under survival curves over a certain time horizon. To address both measured and unmeasured confounding, a matched design with sensitivity analysis is proposed. Matching is used to pair similar treated and untreated subjects together, which is generally more robust than outcome modeling due to potential misspecifications. Our propensity score matched RMST difference estimator is shown to be asymptotically unbiased, and the corresponding variance estimator is calculated by accounting for the correlation due to matching. Simulation studies also demonstrate that our method has adequate empirical performance and outperforms several competing methods used in practice. To assess the impact of unmeasured confounding, we develop a sensitivity analysis strategy by adapting the E-value approach to matched data. We apply the proposed method to the Atherosclerosis Risk in Communities Study (ARIC) to examine the causal effect of smoking on stroke-free survival.