An Unsupervised Adaptive Approach for Causal Inference in Competing Risks Data Using Separable Effects

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Abstract

This study investigates causal effects when the primary time-to-event outcome is unobserved due to truncation caused by competing risks, wherein a competing event precludes its observation. Employing the separable effects framework, we disentangle the direct effect of exposure on the primary outcome from the indirect effect mediated through the competing event. Our goal is to develop a robust, unsupervised method that accommodates such data structures while retaining flexibility and estimation efficiency, thereby addressing biases due to dependent censoring. We propose a method based on the generalized transformation model, which adapts to a wide range of data distributions without requiring excessive parameterization. This unsupervised approach incorporates confounders as covariates for proper adjustment and is computationally efficient, making it suitable for moderate sample sizes. We theoretically establish that the proposed estimator is asymptotically consistent and weakly converges to a Gaussian process, thereby ensuring valid statistical inference. Simulation studies demonstrate that the proposed method outperforms existing nonparametric approaches by mitigating model misspecification, even when the true model lies outside the transformation class. Moreover, it efficiently adjusts for confounding without incurring heavy computational costs. Finally, we apply the method to assess the causal effect of hepatitis B virus (HBV) infection on the incidence of liver cancer as the first primary cancer, accounting for competing risks using data from the REVEAL study. The results suggest that HBV infection directly increases the incidence of liver cancer.

Keywords: Causal inference, Separable effect, Competing risks