Separable effects under semicompeting risks

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Abstract

The separable effect has recently been proposed to study causal effects under the setting of competing risks. In this work, we extend the separable effect approach to semicompeting risks involving a primary and intermediate outcome. We decompose the exposure into two disjoint components: the first component affects the primary outcome directly, i.e., direct effect and the other affects the primary outcome only through the intermediate outcome, i.e., indirect effect. Under such an effect separation, the identification formula of counterfactual risk that we derive for semicompeting risks is a function of cause-specific hazards and transition hazards of multistate models and can be reduced to the formula for competing risks as a special case. We propose nonparametric and semiparametric methods to estimate the causal effects and study their asymptotic properties. The model-free nonparametric method is robust but less efficient for confounder adjustment; the model-based semiparametric method flexibly accommodates confounders by treating them as covariates. We conduct comprehensive simulations to study the performance of the proposed methods. Finally, we apply the proposed methods to characterize the effect of hepatitis C infection on the incidence of liver cancer through liver cirrhosis.

Keywords: Causal inference; Separable effects; Mediation model; Multistate model, Semicompeting risks.