Nonparametric Estimation of Subgroup Mediation Effects with Semi-Competing Risks Data

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Abstract

A treatment may have an effect on a non-terminal event (e.g., disease progression), which in turn may influence a terminal event (e.g., death), or the treatment may affect the terminal event directly. We are interested in evaluating the mediational effect of the treatment through the non-terminal event and the direct treatment effect on the terminal event. However, the conventional definition of natural direct effect and indirect effect is not appropriate here because of the semi-competing risks data structure, where time to a non-terminal event may be censored by a terminal event, but not vice versa. A principal stratification approach is adopted to define the natural direct and indirect effects on one stratum and the total effect on all strata. We propose nonparametric estimators of the direct and indirect effects under suitable assumptions. The theoretical properties of the proposed estimators are established, and their good finite sample performance is illustrated through numerical studies.