A Simple Nonparametric Least-Squares-Based Causal Inference for Heterogeneous Treatment Effects

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ABSTRACT

Estimating treatment effects is a common practice in making causal inferences. However, it is a challenging task for observational studies because the underlying models for outcome and treatment assignment are unknown. The concept of potential outcomes has been widely adopted in the literature on causal inference. Building on potential outcomes, we propose a simple nonparametric least-squares spline-based causal inference method to estimate heterogeneous treatment effects in this manuscript. We use empirical process theory to study its asymptotic properties and conduct simulation studies to evaluate its operational characteristics. Based on the estimated heterogeneous treatment effects, we further estimate the average treatment effect and show the asymptotic normality of the estimator. Finally, we apply the proposed method to assess the biological anti-rheumatic treatment effect on children with newly onset juvenile idiopathic arthritis disease using electronic health records from a longitudinal study at Cincinnati Children's Hospital Medical Center.

Keywords: Causal inferences; Empirical process theory; Heterogeneous treatment effects; Potential outcome; Regression splines

Using Negative Controls to Adjust for Unmeasured Confounding in Continuous Exposure Settings

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ABSTRACT

This talk introduces approaches for using negative controls to adjust for unmeasured confounding in observational dose–response studies where both exposure and outcome are continuous. I will present several machine learning techniques and a Bayesian nonparametric method we developed to estimate the causal exposure–response function (CERF) using negative control information. Our Bayesian nonparametric method models the CERF as a mixture of linear models, enabling flexibility to capture nonlinear patterns while preserving computational efficiency and benefiting from closed-form results under linear assumptions. I will share simulation studies evaluating these methods' performance. As an illustration, I will show how to select negative controls and use our open-source tools to assess the relationship between long-term ambient $PM_{2.5}$ exposure and cardiovascular hospitalization rates among older adults in the continental United States, accounting for potential unmeasured confounders. Finally, I will discuss ongoing methodological improvements and alternative estimands to consider for causal inference with continuous exposures.

Keywords: bias; confounding; negative controls; Bayesian analysis

Causal Mediation Analysis for Survival Outcome and Recurrent Event Mediators with Time-Varying Confounding

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ABSTRACT

Recurrent events and repeated measures are commonly encountered in clinical longitudinal studies, often holding strong associations with patient outcomes. Although joint models for repeated measure, recurrent events, and a terminal event have been developed to account for their correlation, limited methodologies exist to rigorously examine causal mediation mechanisms involving multiple types of intermediate time-varying variables, especially when these variables are causally related. This study addresses this gap by proposing a novel causal mediation analysis framework to quantify natural direct and indirect effects when the recurrent events and survival outcome are confounded by longitudinal measured time-varying variable. We extend joint modeling approaches by incorporating shared random effects (frailties) structures, relaxing the commonly used "sequential ignorability" assumption, and accounting for unmeasured time-independent confounders through shared random effects. Simulation studies demonstrate the robustness and finite sample performance of our estimators for natural direct and indirect effects. We apply our method to the Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA) study and demonstrate that recurrent opportunistic infections (OIs) mediate the effects of prior AIDS-defining conditions on survival outcomes after taking into account the potential confounding effect of time-varying CD4 count measurements.

Keywords: Causal mediation analysis; Joint modeling; Recurrent event; Repeated measurement