

Generalized interventional approach for causal mediation analysis with causally ordered multiple mediators

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Abstract: Causal mediation analysis has demonstrated the advantage of mechanism investigation. In conditions with causally ordered mediators, path-specific effects (PSEs) are introduced for specifying the effect subject to a certain combination of mediators. However, most PSEs are unidentifiable. To address this, an alternative approach termed interventional analogue of PSE (iPSE), is widely applied to effect decomposition. Previous studies that have considered multiple mediators have mainly focused on two-mediator cases due to the complexity of the mediation formula. This study proposes a generalized interventional approach for the settings, with the arbitrary number of ordered multiple mediators to study the causal parameter identification as well as statistical estimation. It provides a general definition of iPSEs with a recursive formula, assumptions for nonparametric identification, a regression-based method, and a g-computation algorithm to estimate all iPSEs. We demonstrate that each iPSE reduces to the result of linear structural equation modeling subject to linear or log-linear models. This approach is applied to a Taiwanese cohort study for exploring the mechanism by which hepatitis C virus infection affects mortality through hepatitis B virus infection, liver function, and hepatocellular carcinoma. Software based on a g-computation algorithm allows users to easily apply this method for data analysis subject to various model choices according to the substantive knowledge for each variable. All methods and software proposed in this study contribute to comprehensively decompose a causal effect confirmed by data science and help disentangling causal mechanisms when the natural pathways are complicated.