Inverse Probability Weighting-based Mediation Analysis for Microbiome Data

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Abstract

Mediation analysis is an important tool to study casual associations in biomedical and other scientific areas and has recently gained attention in microbiome studies. With a microbiome study of acute myeloid leukemia (AML) patients, we investigate whether the effect of induction chemotherapy intensity levels on the infection status is mediated by the microbial taxa abundance. The unique characteristics of the microbial mediators—high-dimensionality, zero-inflation, and dependence—call for new methodological developments in mediation analysis. The presence of an exposure-induced mediator-outcome confounder, antibiotics usage, further requires a delicate treatment in the analysis. To address these unique challenges brought by our motivating microbiome study, we propose a novel nonparametric identification formula for the interventional indirect effect (IIE), a measure recently developed for studying mediation effects. We develop the corresponding estimation algorithm and test the presence of mediation effects via constructing the nonparametric bias-corrected and accelerated bootstrap confidence intervals. Simulation studies show that the proposed method has good finite-sample performance in terms of the IIE estimation, and type-I error rate and power of the corresponding test. In the AML microbiome study, our findings suggest that the effect of induction chemotherapy intensity levels on infection is mainly mediated by patients' gut microbiome.