

Randomized Controlled Trials(RCT) are the golden standard for evaluating the causal effect. Although treatment effects will be accurately measured, causal mechanisms often remain unmeasured. Causal mediation analysis divides treatment effect (TE) into two effects, one representing the effect pathing through a specific mediator, the other represents an unknown mechanism or direct effect without mediators. The two effects are called natural indirect effect (NIE) and natural direct effect (NDE).

In a typical RCT framework, baseline characters are measured upon trial enrollment and some select criteria may apply, and then drugs are being assigned randomly. Follow-up measures are often made to verify the treatment effect. This framework creates a very clean data generating process for apply causal mediation analysis since causal mediation analysis requires more strict assumptions than causal inference. In detail, randomized treatment will neutralize treatment-mediator and treatment-outcome confounding; baseline covariates will also provide confidence of mediator-outcome confounding; follow-up measures will help to identify other potential pathways.

However, causal mediation analysis with biomolecular measurements as a mediator often facing measurements varies over time. This is commonly referred to as measurement error in epidemiology, which would create bias in causal mediation analysis. Also the selection of measurements in addition to measurement error will create additional bias for mediation analysis.

Confirm additional bias exists in causal mediation analysis when baseline selection is performed on variables with measurement error. And more extreme selection will further bias the results, where the original adjustment method wouldn't obtain unbiased results.

Proposed a solution, a modification based on an existing adjustment formula, which will correct bias when the variation of the measurement can be estimated from data or using metadata from elsewhere.

Another novelty coming from this research is the consideration of exposure- mediator interaction existed while adjusting for measurement error in mediators that previous research has no mention. Although the proposed solution didn't address this problem fully from a theoretical perspective, only solved the cases when exposures are categorical, from an applicational viewpoint, most of the exposures in epidemiological and clinical studies are categorical. Furthermore, some estimates are difficult to acquire from real-world data due to the strong assumptions required for measurement error and adjustment and causal media- tion analysis. The proposed solution can handle exposure-mediator interaction without demanding additional assumptions.

