Abstract Title Page

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Title: Identifying the Average Causal Mediation Effects with Multiple Mediators in the Presence of Treatment Non-compliance

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Abstract Body

Background / Context:
Identifying the causal mechanisms is becoming more essential in social and medical sciences. In the presence of treatment non-compliance, the Intent-To-Treated effect (hereafter, ITT effect) is identified as long as the treatment is randomized (Angrist et al., 1996). However, the mediated portion of effect is not identified without additional unverifiable assumptions (Yamamoto, 2013; Robins, 2003). The inability to identify the mediated portion of ITT effect presents a serious problem in conducting causal mediation analysis in the presence of treatment non-compliance, and a researcher often uses the naïve approach for estimating the mediated ITT effect where 1) the treatment assigned is used as if it was the treatment received and 2) a standard causal mediation analysis is conducted. Yamamoto (2013) proposed an alternative approach to identifying the mediated portion of the ITT effect using the instrumental variable approach, and compares his proposed approach to the naïve approach when a single mediator exists.

Purpose / Objective / Research Question / Focus of Study:
Considering the complexity of the causal mechanisms in reality, it may be natural to assume multiple variables that mediate through the causal path. Thus, this paper extends Yamamoto (2013)'s approach to the multiple-mediators case where mediators do not or do influence one another. Due to page limitation, this article only presents the case where mediators influence one another.

Significance / Novelty of study:
The proposed approach to multiple mediators can solve the identification problem that occurs in the presence of treatment non-compliance with multiple mediators. In addition, less stringent assumptions are needed to identify the natural direct and indirect effects when mediators influence one another.

Statistical, Measurement, or Econometric Model:
In this section, I introduce causal mediation analysis with multiple mediators in the presence of treatment non-compliance.

Notation and Assumptions
Let *Z* and *T* represent treatment assigned and received, respectively; let *W* and *M be* two mediators, respectively, and let *Y* be the outcome. In the data generating model that was used in this article, the dependent-mediators case indicates that mediator *M* is causally dependent to mediator *W*.

In the case of dependent mediators, $W(t)$, $M(t,w)$, and $Y(t,w,m)$ represent the potential mediator *W* under *t*, *M* under *t* and *w* and the potential outcome *Y* under *t*, *w* and *m*. The Local Average Causal Mediation Effect (hereafter LACME) under *t* is defined as $E[Y_i\ (t, M_i\ (1, W_i\ (1)), W_i\ (t)) - Y_i\ \ (t, M_i\ (0, W_i\ (0)), W_i\ (t)) | P_i = C]$, and the Local Average Natural Direct Effect (hereafter LANDE) under *t* is defined as $E[Y_i\ (1, M_i\ (t, W_i\ (t)), W_i\ (1)) - Y_i\ \ (0, M_i\ (t, W_i\ (t)), W_i\ (0)) | P_i = C]$ where $t \in \{0,1\}$, and *P* indicates compliance types where $P \in \{C, A, N, D\}$. C, A, N, and D represents compliers, always takers, never takers and defiers, respectively.

The assumptions that are needed to identify the LACME as well as the mediated ITT effects with causally dependent mediators are given as,

1) The exclusion restriction: the assigned treatment has its effect on W, M and Y only through the treatment received.
2) No defiers: Defiers are those who received the opposite treatment status to whatever they have assigned.
3) The local sequential ignorability assumption

$$\{Y_i(t,m,w), M_i(t,w), W_i(t)\} \perp T_i = t, X_i = x, P_i = C$$
$$\{Y_i(t,m,w), M_i(t,w)\} \perp W_i \mid T_i = t, X_i = x, P_i = C$$
$$\{Y_i(t,m,w)\} \perp M_i \mid W_i(t) = w, T_i = t, X_i = x, P_i = C$$

The first part of the local sequential ignorability assumption implies that there is no confounding between Z and potential outcomes of Y, M, W, and T among compliers. The assumption can be satisfied by the treatment randomization. The second part of the local sequential ignorability assumption implies that 1) there is no confounding between mediator W and outcome Y given X and treatment status among compliers, and 2) there is no confounding between mediator W and another mediator M given X and treatment status among compliers. The third part of the local sequential ignorability assumption implies that there is no confounding between mediator M and outcome Y given X and treatment status among compliers.

Identification

Under the assumptions shown above and the SUTVA, the LACME is identified as

$$\delta_i(t) = \iiint \frac{S_{mwttx} H_{m|wttx} G_{w|ttx} Q_{t|tx} - S_{mwtt'x} H_{m|wtt'x} G_{w|tt'x} Q_{t|t'x}}{H_{m|wttx} G_{w|ttx} Q_{t|tx} - H_{m|wtt'x} G_{w|tt'x} Q_{t|t'x}} \cdot \frac{G_{w|ttx} Q_{t|tx} - G_{w|tt'x} Q_{t|t'x}}{Q_{t|tx} - Q_{t|t'x}}$$
$$\cdot \left\{ \int \frac{H_{m|w11x} G_{w|11x} Q_{1|1x} - H_{m|w10x} G_{w|10x} Q_{1|0x}}{G_{w|11x} Q_{1|1x} - G_{w|10x} Q_{1|0x}} \cdot \frac{G_{m|w11x} Q_{1|1x} - G_{m|w10x} Q_{1|0x}}{Q_{1|1x} - Q_{1|0x}} \right.$$
$$\left. - \frac{H_{m|w00x} G_{w|00x} Q_{0|0x} - H_{m|w01x} G_{w|01x} Q_{0|1x}}{G_{w|00x} Q_{0|0x} - G_{w|01x} Q_{0|1x}} \cdot \frac{G_{w|00x} Q_{0|0x} - G_{w|01x} Q_{0|1x}}{Q_{1|1x} - Q_{1|0x}} \, dw \right\} dw\,dm\,dF(x),$$

and the LANDE is identified as

$$\zeta_i(t) = \iiint \left[\left\{ \frac{S_{mw11x} H_{m|w11x} G_{w|11x} Q_{1|1x} - S_{mw10x} H_{m|w10x} G_{w|10x} Q_{1|0x}}{H_{m|w11x} G_{w|11x} Q_{1|1x} - H_{m|w10x} G_{w|10x} Q_{1|0x}} \right. \right.$$
$$\left. - \frac{S_{mw00x} H_{m|w00x} G_{w|00x} Q_{0|0x} - S_{mw01x} H_{m|w01x} G_{w|01x} Q_{0|1x}}{H_{m|w00x} G_{w|00x} Q_{0|0x} - H_{m|w01x} G_{w|01x} Q_{0|1x}} \right\} \cdot \frac{G_{m|wttx} Q_{t|tx} - G_{m|wtt'x} Q_{t|t'x}}{Q_{t|tx} - Q_{t|t'x}}$$
$$+ \frac{S_{mwt't'x} H_{m|wt't'x} G_{w|t't'x} Q_{t'|t'x} - S_{mwt'tx} H_{m|wt'tx} G_{w|tt'x} Q_{t'|tx}}{H_{m|wt't'x} G_{w|t't'x} Q_{t'|t'x} - H_{m|wt'tx} G_{w|tt'x} Q_{t'|tx}}$$
$$\left. \cdot \left\{ \frac{G_{m|w11x} Q_{1|1x} - G_{m|w10x} Q_{1|0x} - G_{m|w00x} Q_{0|0x} + G_{m|w01x} Q_{0|1x}}{Q_{1|1x} - Q_{1|0x}} \right\} \right]$$
$$\cdot \left\{ \int \frac{H_{m|w11x} G_{w|11x} Q_{1|1x} - H_{m|w10x} G_{w|10x} Q_{1|0x}}{G_{w|11x} Q_{1|1x} - G_{w|10x} Q_{1|0x}} \cdot \frac{G_{w|ttx} Q_{t|tx} - G_{w|tt'x} Q_{t|t'x}}{Q_{t|tx} - Q_{t|t'x}} \, dw \cdot \right\} dw\,dm\,dF(x)$$

where $S_{mwtzx} = E[Y_i|M_i = m, W_i = w, Z_i = z, X_i = x]$, $H_{m|wtzx} = p[M_{i=m}|W_i = w, Z_i = z, X_i = x]$, $G_{w|tzx} = p[W_i = w|\ Z_i = z, X_i = x]$ and $Q_{t|zx} = p[T_i|Z_i = z, X_i = x]$. Mediated and unmediated ITT effects are identified by multiplying the proportion of compliers $(Q_{t|tx} - Q_{t|t'x})$ to the LACME and LANDE, respectively.

Estimation

A regression-based estimator is used to obtain S_{mwtzx}, $H_{m|wtzx}$, $G_{w|tzx}$ and $Q_{t|zx}$, and standard errors are obtained from the bootstrapping technique. I used 1000 bootstraps.

A small simulation study is conducted comparing the naïve and proposed approach. As shown in Table 1, a bias in the proposed $\delta^M(1)$ becomes smaller with larger sample size and higher compliance rate while a bias in the naive $\delta^M(1)$ does not show any pattern. 95% Confidence Intervals of proposed $\delta^M(1)$ cover the true value more than 95 times out of 100 iterations in all conditions.

Case study

I applied the proposed approach of estimating the LACME and LANDE for multiple mediators in the case of treatment non-compliance using Families And Schools Together (FAST) data. The case study shows that the estimated LACME and LANDE by proposed and naive approaches present a different picture, and demonstrates that a researcher who uses a naive approach may derive a wrong conclusion. On the other hand, the case study also reveals the limitation of the proposed approach. Although the local sequential ignorability assumption is weaker than the global sequential ignorability assumption where the sequential ignoriability asumption is required for all population, it is still very strong and empirically untestable even after adjusting covariates. In practice, thorough investigation on selecting covariates is required and, if possible, sensitivity analysis may be desirable.

Conclusions:

The paper outlines a framework for causal mediation analysis with multiple mediators in a setting where a treatment is randomized and there is imperfect compliance. The paper contributes to the literature by identifying the LACME and LANDE as well as the mediated and unmediated ITT effects in the presence of treatment non-compliance with multiple mediators. In addition, less stringent assumptions are needed to identify the mediated and unmediated portion of causal effects when mediators influence one another. An important area of the future study would be developing a sensitivity analysis for the sequential ignorability assumption for compliers.

Appendix A. References

Angrist, J. D., Imbens, G. W., & Rubin, D. B. (1996). Identification of causal effects using instrumental variables. Journal of the American statistical Association, 91(434), 444-455.

Robins, J. M. (2003). Semantics of causal DAG models and the identification of direct and indirect effects. Highly structured stochastic systems, 70-81.

Yamamoto, T. (2013). Identification and estimation of causal mediation effects with treatment noncompliance. Unpublished manuscript.

Appendix B. Tables and Figures

		80% compliance			40% compliance			20% compliance		
	Sample size	Bias	RMSE	95% CI coverage	Bias	RMSE	95% CI coverage	Bias	RMSE	95% CI coverage
Proposed $\delta^M(1)$	200	-0.07	1.24	100.0	0.62	2.66	100.0	-4.03	117.05	100.0
	1000	-0.06	0.31	99.3	0.13	3.31	98.4	0.31	3.65	99.6
	2000	-0.03	0.19	95.9	-0.12	2.92	97.4	0.25	3.15	99.2
Naïve $\delta^M(1)$	200	-0.48	0.60	39.6	-0.08	0.54	73.2	-0.67	2.04	58.4
	1000	-0.48	0.50	0.4	-0.09	0.23	59.2	-0.64	0.69	3.8
	2000	-0.48	0.49	0.0	-0.08	0.17	47.0	-0.62	0.65	0.0

Table 1. Comparison between the naïve and proposed approaches for the dependent-mediators case (based on 500 iterations and 1000 bootstraps)