Covariate Dependence and Effect Modification by Covariates: Extending the Regression-Based Causal Mediation Analysis

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Background

- The closed-form mediation mediation analysis approach by Valeri & VanderWeele (VV2013) estimates the natural direct effect (NDE) and natural indirect effect (NIE), conditional on covariates.
- VV 2013 includes a treatment-mediator interaction term in outcome model.
- However, in some cases, there is effect modification by covariates.

Objectives

- **Extend the model** by VV2013, including additional interaction terms.
- Demonstrate **effect measure modification (EMM) by covariates** by a simulation study.
- Investigate the impact of **model misspecification** on NDE and NIE estimates where a product term is omitted.

Methods

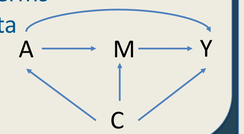
- Treatment A; Mediator M; Outcome Y; Covariates C.
- Extended mediator model:

$g_{a,c}[E(M|A, C)] = \beta_0 + \beta_1 a + \beta_2 c + \mathbf{\beta_3 ac}$

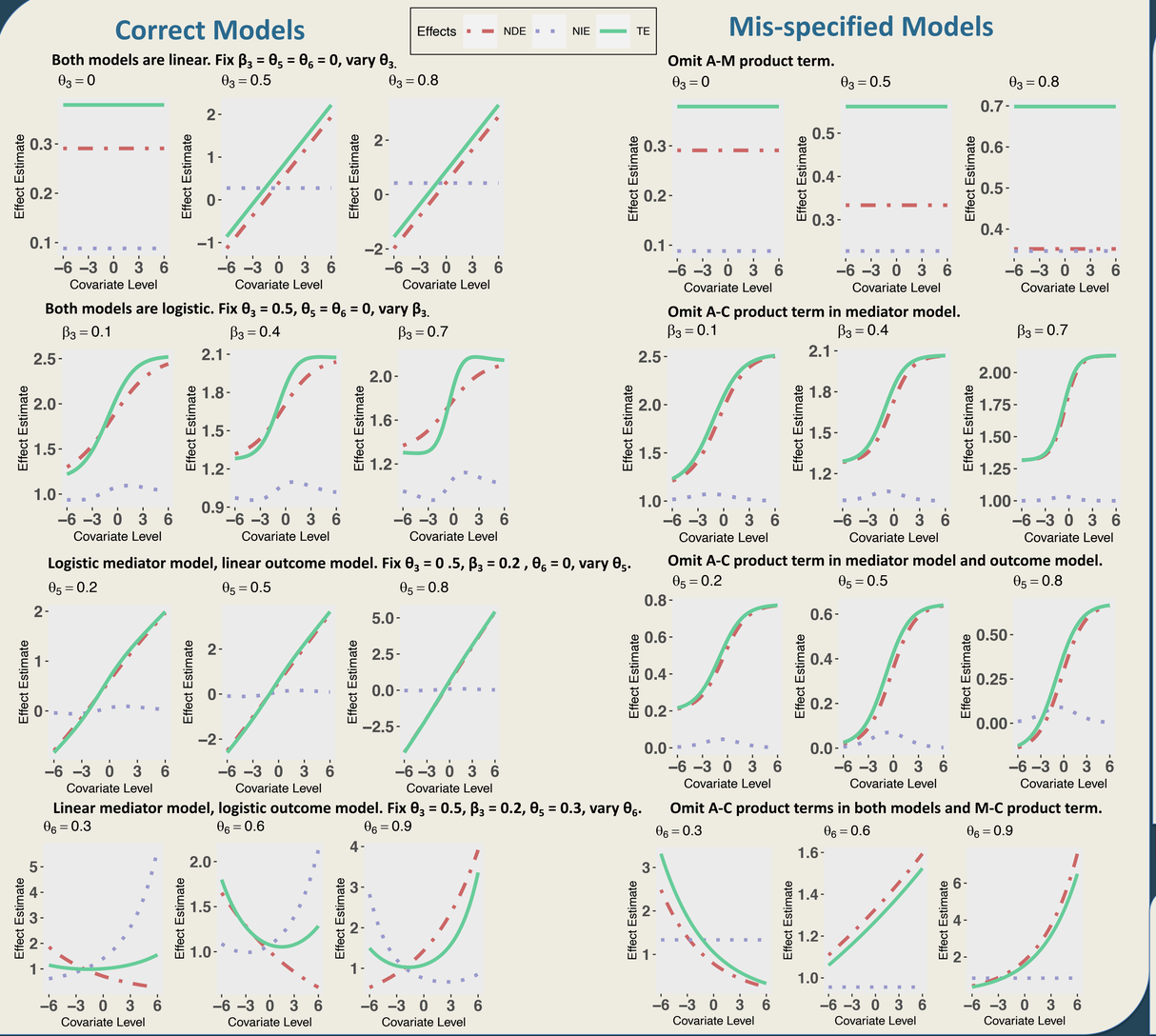
- Extended outcome model:

$g_{a,m,c}[E(Y|A, M, C)] = \theta_0 + \theta_1 a + \theta_2 m + \theta_3 am + \theta_4 c + \mathbf{\theta_5 ac + \theta_6 mc}$

- $\beta_3 ac$, $\theta_5 ac$, $\theta_6 mc$: newly added terms
- We use the same simulated data for both correct and mis-specified models.



Simulation Results



Conclusions

- Covariate levels affect the **direction** and **magnitude** of natural effects (NDE and NIE).
- Whether and how natural effects depend on covariate dependence is affected by the **magnitude of A-M interaction, EMM by C, and link functions.**
- The omission of product terms where they should be present **oversimplifies the relationship** between covariates and natural effects, and **biases the effect estimates.**

References

Valeri L & VanderWeele TJ. (2013). Mediation analysis allowing for exposure-mediator interactions and causal interpretation: theoretical assumptions and implementation with SAS and SPSS macros. *Psychological Methods*, *18*(2), 137.