Identifying Direct Causal Effects Under Unmeasured Confounding

Philippe Boileau*[1], Nima S. Hejazi*[2], Ivana Malenica*[1], Sandrine Dudoit[1], Mark J. van der Laan[1]

[1]University of California, Berkeley; [2]Weill Cornell Medicine

Introduction & Motivations

- Developing *mechanistic* understandings of causal effects is a ubiquitous goal across scientific disciplines.
- The natural direct and indirect effects are common target causal parameters since they are nonparametrically identified.
- Identification assumes absence of unmeasured confounders of exposure–mediator, mediator–outcome, and exposure–outcome pathways — but this is *not* completely necessary.
- The natural direct and indirect effects arise from a decomposition of the average treatment effect (ATE), and the
  - natural indirect effect (NIE) captures the portion of the ATE passing through the mediators (Z), while the
  - natural direct effect (NDE) captures the remainder of the ATE, through all paths excluding Z.

The Statistical Problem

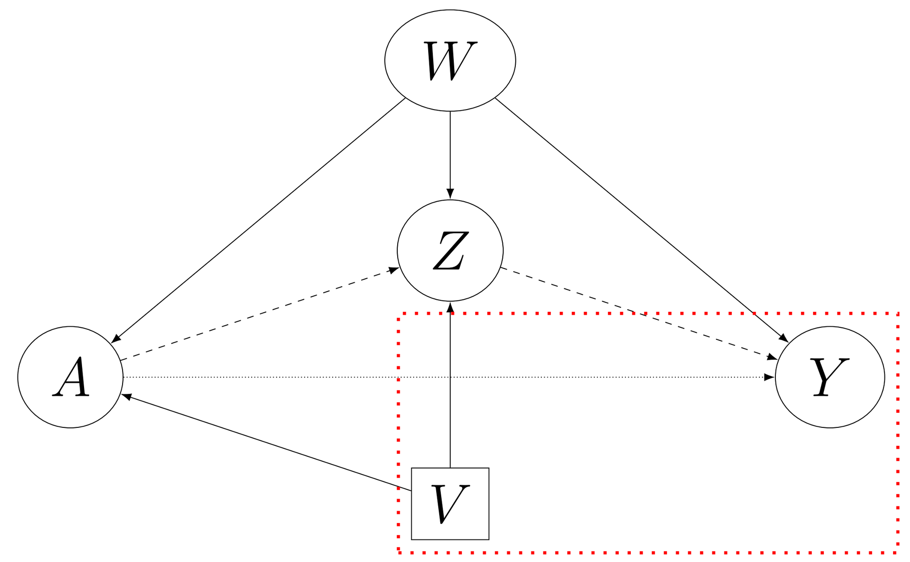
The average treatment effect may be decomposed as

$$\begin{aligned}\Psi^F_{\text{ATE}}(P_{U,X,0}) =& \mathbb{E}_{U,X,0}[Y(1) - Y(0)] \\ =& \underbrace{\mathbb{E}_{U,X,0}[Y(1, Z(1)) - Y(1, Z(0))]}_{\text{NIE}} \\ & + \underbrace{\mathbb{E}_{U,X,0}[Y(1, Z(0)) - Y(0, Z(0))]}_{\text{NDE}},\end{aligned}$$

where $Y(1, Z(0))$ arises from a *joint* intervention on treatment and mediators (Z), setting them to incompatible values. The NDE is

$$\Psi^F_{\text{NDE}}(P_{U,X,0}) = \int_{\mathcal{W},\mathcal{Z}} \mathbb{E}[Y(1,z) - Y(0,z) \mid W = w] \\ p_Z(z \mid A = 0, w) p_W(w) \, d\mu(z) \, d\nu(w) \; .$$

Causal Identification



(A1) No unmeasured endogenous pathways:
$f_Y(Z, A, W, V, U_Y) \equiv f_Y(Z, A, W, U_Y)$.

(A2) Conditional expectation equivalence:
$\mathbb{E}(Y \mid Z, A = 1, W, V) \equiv \mathbb{E}(Y \mid Z, A = 1, W)$

Theorem

Under assumptions A1 and A2, $\Psi^F_{\text{NDE}}(P_{U,X,0})$ is identified by

$$\begin{aligned}\Psi(P_0) = \mathbb{E}_{P_0}\mathbb{E}_{P_0}\{&\mathbb{E}_{P_0}(Y \mid W, A = 1, Z) \\ &- \mathbb{E}_{P_0}(Y \mid W, A = 0, Z) \mid A = 0, W\} \; .\end{aligned}$$

Estimation & Inference

Existing estimation and testing approaches are compatible with with this relaxed identification strategy. Examples include the

- targeted maximum likelihood estimator of Zheng and van der Laan [2012], and the
- one-step bias-corrected estimator based on the efficient influence function [Tchetgen Tchetgen and Shpitser, 2011].

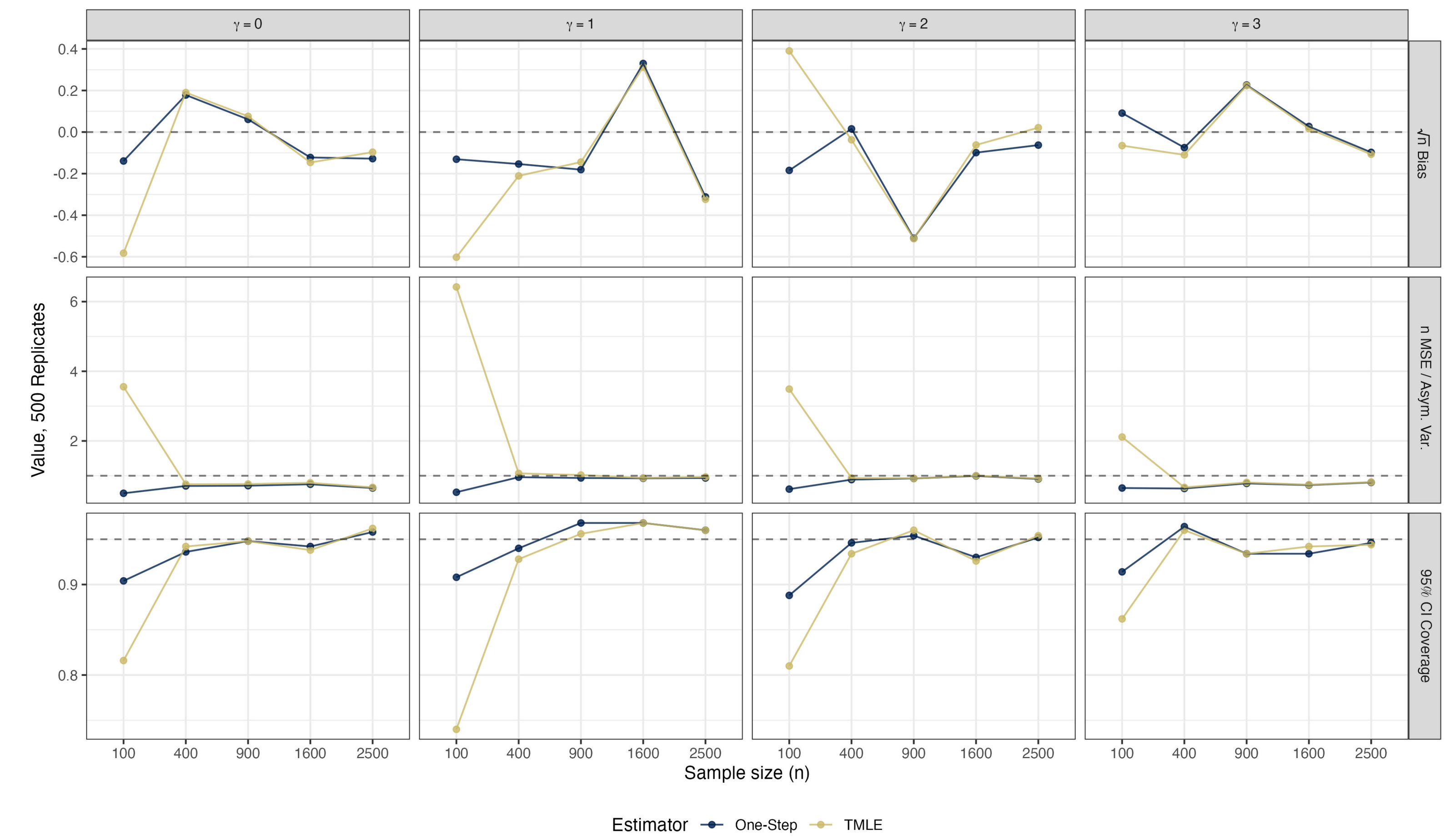
Both estimators are multiple-robust, asymptotically linear under fairly non-restrictive assumptions, and compatible with cross-fitting. Both estimators are implemented in the `medoutcon` R package.

Funding

Numerical Experiments

We consider the following data-generating process:

$$\begin{aligned} W_1 &\sim \text{Unif}(-1, 1), \; W_2, V \sim \text{Norm}(0, 1) \\ A|W, V &\sim \text{Bern}\left((1 + \exp\{-W_1 - W_2 - V\})^{-1}\right) \\ Z|A, W, V &\sim \text{Bern}\left((1 + \exp\{-W_1 - W_2 - \gamma V - 3A\})^{-1}\right) \\ Y|Z, A, W, V &\sim \text{Norm}(3A + W_1 + W_2 + Z, 1) \; .\end{aligned}$$



Conclusions

- Here are the important takeaways.
- There are many important takeaways.
- Didn't this change your life?

References

Wenjing Zheng and Mark J. van der Laan. Targeted maximum likelihood estimation of natural direct effects. *The International Journal of Biostatistics*, 8 (1):1–40, 2012. doi: doi:10.2202/1557-4679.1361. URL `https://doi.org/10.2202/1557-4679.1361`.

Eric J Tchetgen Tchetgen and Ilya Shpitser. Semiparametric estimation of models for natural direct and indirect effects. Working Paper 129, Harvard University, 2011. URL `https://biostats.bepress.com/harvardbiostat/paper129/`.

* *indicates shared first-authorship*