

# Nonparametric-efficient Causal Mediation Analysis for Stochastic Interventions Nima Hejazi, Mark van der Laan, and Iván Díaz

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## OVERVIEW & MOTIVATIONS

- Using stochastic interventions, we present a decomposition of the *population intervention effect* into <u>direct</u> and <u>indirect</u> effects.
  - Define causal contrasts of effects of continuous and categorical exposures
  - **–** ...
- We propose estimators of these direct and indirect effects:
  - Classical parametric: substitution and re-weighted (IPW) estimators
  - Nonparamtric-efficient: one-step and TML estimators with machine learning
- Our efficient estimators are asymptotically linear under a condition requiring  $n^{1/4}$ -consistency of nuisance regression functions

### SOFTWARE IMPLEMENTATION

- The medshift R package [3] implements these estimators and leverages state-of-theart machine learning in the procedure.
  - Construction of all estimators via the eponymous medshift () function.
  - Uses the s13 R package to provide machine learning facilities.
- Construction of TML estimators using tools from the tlverse software ecosystem.
- ...

#### CONSTRUCTION OF NONPARAMETRIC-EFFICIENT ESTIMATORS

- To avoid entropy conditions on initial estimators, we rely on cross-fitting [6, 1], letting  $\hat{\eta}_j$  be the estimator of  $\eta = (g, e, m, \phi)$  and j(i) the index of the validation set containing observation i.
- A one-step estimator [4] may be constructed by augmenting the substitution estimator with the auxiliary scores ( $D^A$  and  $D^Y$ ) in the efficient influence function:

$$\hat{\theta}_{OS}(\delta) = \frac{1}{n} \sum_{i=1}^{n} D_{\hat{\eta}_{j(i)}, \delta}(O_i) = \frac{1}{n} \sum_{i=1}^{n} \left\{ D_{\hat{\eta}_{j(i)}, \delta}^{Y}(O_i) + D_{\hat{\eta}_{j(i)}, \delta}^{A}(O_i) + D_{\hat{\eta}_{j(i)}, \delta}^{Z,W}(O_i) \right\}.$$

- **-** ...
- **–** ...
- A targeted minimum loss-based estimator may be constructed by using the efficient influence function as an estimating equation, updating estimates of nuisance components:

$$\hat{\theta}_{\text{TMLE}}(\delta) = \dots,$$

where

- Unlike the one-step estimator, the TMLE is a substitution estimator.
- Use unversal least favorable submodels for one-step estimation [5].

### STOCHASTIC POPULATION INTERVENTION (IN) DIRECT EFFECTS

- Consider  $O = (W, A, Z, Y) \sim P_0 \in \mathcal{M}$ , for W a set of baseline covariates, A an intervention, Y the outcome, and Z a mediator between A and Y, with no assumptions on nonparametric model  $\mathcal{M}$ .
- We decompose the total population intervention effect (PIE) in terms of a population intervention direct effect (PIDE) and a population intervention indirect effect (PIIE):

$$\psi(\delta) = \underbrace{\mathbb{E}\{Y(g,q) - Y(g_{\delta},q)\}}_{\text{PIDE}} + \underbrace{\mathbb{E}\{Y(g_{\delta},q) - Y(g_{\delta},q_{\delta})\}}_{\text{PIDE}}.$$

• We show the causal parameter  $\mathbb{E}\{Y(g_{\delta},q)\}$  is identified by the observed data parameter [2]:

$$\theta(\delta) = \int m(a, z, w) g_{\delta}(a \mid w) p(z, w) d\nu(a, z, w),$$

which corresponds to implementing a stochastic intervention (indexed by  $\delta$ ) on A while drawing Z as though A were generated by its natural (observed) distribution.

• Letting  $\eta = (g, e, m, \phi)$ , the efficient influence function for  $\theta(\delta)$  in the nonparametric model M is  $D_{\eta,\delta}^Y(o) + D_{\eta,\delta}^A(o) + D_{\eta,\delta}^{Z,W}(o) - \theta(\delta)$  for

$$D_{\eta,\delta}^{Z,W}(o) = \int m(z,a,w)g_{\delta}(a \mid w)d\kappa(a), \quad D_{\eta,\delta}^{Y}(o) = \frac{g_{\delta}(a \mid w)}{e(a \mid z,w)} \{y - m(z,a,w)\},$$

$$D_{\eta,\delta}^{A}(o) = \frac{\delta\phi(w)\{a - g(1 \mid w)\}}{\{\delta g(1 \mid w) + 1 - g(1 \mid w)\}^{2}}, \quad \phi(w) = \mathbb{E}\{m(1,Z,W) - m(0,Z,W) \mid W = w\},$$

where, for simplicity, we present the case  $A \in \{0, 1\}$ . For an unabridged treatment, see [2].

#### RESULTS & DISCUSSION

- All estimators approx. unbiased in large samples; however, inefficient TMLE with HAL has bias not converging at  $n^{-\frac{1}{2}}$ .
- Fitting II with HAL or GLM, efficient TMLE has lower variance than the inefficient.

#### REFERENCES

- [1] V. Chernozhukov, D. Chetverikov, M. Demirer, E. Duflo, C. Hansen *et al.*, "Double machine learning for treatment and causal parameters," *arXiv preprint arXiv:1608.00060*, 2016.
- [2] I. Díaz and N. S. Hejazi, "Causal mediation analysis for stochastic interventions," in revision 2019. [Online]. Available: https://arxiv.org/abs/1901.02776
- [3] N. S. Hejazi and I. Díaz, medshift: Causal mediation analysis for stochastic interventions in R, 2019, R package version 0.0.8. [Online]. Available: https://github.com/nhejazi/medshift
- [4] J. Pfanzagl and W. Wefelmeyer, "Contributions to a general asymptotic statistical theory," *Statistics & Risk Modeling*, vol. 3, no. 3-4, pp. 379–388, 1985.
- [5] M. van der Laan and S. Gruber, "One-step targeted minimum loss-based estimation based on universal least favorable one-dimensional submodels," *The international journal of biostatistics*, vol. 12, no. 1, pp. 351–378, 2016.
- [6] W. Zheng and M. J. van der Laan, "Cross-validated targeted minimum-loss-based estimation," in *Targeted Learning*. Springer, 2011, pp. 459–474.

#### BUT WAIT, THERE'S MORE!

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- https://arxiv.org/abs/1901.02776
- Check out Iván's talk tomorrow morning!