Efficient estimation of modified treatment policy effects based on the generalized propensity score

Nima Hejazi

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Department of Biostatistics,
T.H. Chan School of Public Health,
Harvard University

nshejazi
nhejazi
nimahejazi.org

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General setup

The *observed data* unit is $O := (L, A, Y) \sim P_0 \in \mathcal{M}$:

- $L \in \mathbb{R}^d$ is a vector of baseline covariates;
- $A \in \mathbb{R}$ is a continuous or ordinal exposure; and
- $Y \in \mathbb{R}$ is an outcome of interest.

Let $\mathcal{M}$ be a *nonparametric* or infinite-dimensional model. For any $P \in \mathcal{M}$, define the *population intervention effect* (PIE) as

$$\Psi_\delta(P) := \mathbb{E}_P\{Y^{A_\delta} - Y\} \ ,$$

where A_δ is achieved via a modified treatment policy (MTP).

NPSEM-IE with static interventions

- Use a nonparametric structural equation model (NPSEM) to describe the generating process of O (Pearl 2009), that is,

$$L = f_L(U_L); A = f_A(L, U_A); Y = f_Y(A, L, U_Y)$$

- Implies a model for the distribution of counterfactual random variables generated by interventions on this process.
- Applying a *static intervention* would replace f_A with a specific value a in its conditional support $A \mid L$.
- But this requires specifying a particular value of the exposure under which to evaluate the counterfactual outcome *a priori*.

Intervening on continuous-valued exposures

- A *stochastic intervention* would alter the value A takes by drawing randomly from a *modified* exposure distribution.
- Consider the post-intervention value $A_\delta \sim G_\delta(\cdot \mid L)$, which generates the counterfactual RV as $Y^{A_\delta} \leftarrow f_Y(A_\delta, L, U_Y)$.
  - Counterfactual RV Y^{A_δ} has distribution P_0^δ implied by G_δ.
  - Static interventions are only a special case of this, in which G_δ is a degenerate distribution that places all mass on $a \in \mathcal{A}$.
- The goal here is to estimate the counterfactual mean under the modified exposure distribution G_δ — $\psi_{0,\delta} := \mathbb{E}_{P_0^\delta}\{Y^{A_\delta}\}$.

The causal effects of modified treatment policies

- To define $\psi_{0,\delta}$, Díaz and van der Laan (2012) leveraged a *modified intervention distribution* of the following form, $G_\delta := P^\delta(g_{0,A})(A = a \mid L) \equiv g_{0,A}(d^{-1}(A, L; \delta) \mid L)$.
- Haneuse and Rotnitzky (2013) introduced *modified treatment policies* (MTPs), which admit a more tractable expression:

$$d(a, l; \delta) = \begin{cases} a + \delta, & a + \delta < u(l) \quad \text{(if plausible)} \\ a, & a + \delta \geq u(l) \quad \text{(otherwise)} \end{cases},$$

  and were later adopted by Díaz and van der Laan (2018).
- $\psi_{0,\delta}$ is identified by a functional of the distribution of O:

$$\psi_{0,\delta} = \int_{\mathcal{L}} \int_{\mathcal{A}} \mathbb{E}_{P_0}\{Y \mid A = d(a, l; \delta), L = l\} \\ g_{0,A}(a \mid L = l) q_{0,L}(l) d\mu(a) d\nu(l) \ .$$

Towards a causal interpretation of the PIE $\psi_{0,\delta}$

Assumption 1: *Stable Unit Treatment Value (SUTVA)*

- $Y_i^{d(a_i,l_i;\delta)}$ *does not depend on* $d(a_j, l_j; \delta)$ *for* $i = 1, \ldots, n$ *and* $j \neq i$, *or lack of interference (Cox 1958)*
- $Y_i^{d(a_i,l_i;\delta)} = Y_i$ *in the event* $A_i = d(a_i, l_i; \delta)$, $i = 1, \ldots, n$

Assumption 2: *No unmeasured confounding*

$Y_i^{d(a_i,l_i;\delta)} \perp\!\!\!\perp A_i \mid L_i$, *for* $i = 1, \ldots, n$

Assumption 3: *Structural positivity*

$a_i \in \mathcal{A} \implies d(a_i, l_i; \delta) \in \mathcal{A}$ *for all* $l \in \mathcal{L}$, *where* $\mathcal{A}$ *denotes the support of* A *conditional on* $L = l_i$ *for all* $i = 1, \ldots n$

Estimation of the PIE $\psi_{0,\delta}$

A RAL *estimator* $\psi_{n,\delta}$ of $\psi_{0,\delta} := \Psi_\delta(P_0)$ is *efficient* if and only if

$$\psi_{n,\delta} - \psi_{0,\delta} = \frac{1}{n} \sum_{i=1}^{n} D^\star(P_0)(O_i) + o_P(n^{-1/2}) \ ,$$

where $D^\star(P)$ is the *efficient influence function* (EIF) of $\Psi_\delta(\cdot)$ with respect to the nonparametric model $\mathcal{M}$ at P.

The EIF of $\Psi_\delta(\cdot)$ is indexed by two common nuisance parameters

$$\overline{Q}_{P,Y}(A, L) := \mathbb{E}_P(Y \mid A, L) \qquad \textit{outcome mechanism}$$

$$g_{P,A}(A, L) := f(A \mid L) \qquad \textit{generalized propensity score}$$

IPW Estimation of the PIE $\psi_{0,\delta}$

We can estimate the *counterfactual mean* $\psi_{0,\delta}$, using the inverse probability weighted (IPW) estimator,

$$\psi_{n,\delta} = \frac{1}{n} \sum_{i=1}^{n} \frac{g_{n,A}(d^{-1}(A_i, L_i; \delta) \mid L_i)}{g_{n,A}(A_i \mid L_i)} Y_i \ .$$

But why? Isn't simplicity dead?

- IPW estimators are the oldest class of causal effect estimators.
- IPW estimators are still very commonly used in practice today.
- Easy to implement and appropriate in many settings, but...
  1. requires a correctly specified estimate of the propensity score;
  2. can be inefficient, never attaining the efficiency bound; and
  3. suffers from an (asymptotic) curse of dimensionality.

IPW estimators

The IPW estimator $\psi_{n,\delta} \equiv \Psi_\delta(P_n, g_{n,A})$ is a Z-estimator based on solving the score equation $P_n D_{\text{IPW}}(\cdot) \approx 0$, where D_{IPW} is defined,

$$D_{\text{IPW}}(O; \Psi_\delta) := \left[\frac{g_{n,A}(d^{-1}(A_i, L_i; \delta) \mid L_i)}{g_{n,A}(A_i \mid L_i)}\right] Y - \Psi(P) \ .$$

A few properties of and problems with the IPW estimator:

- Consistency and convergence rate of IPW relies on those same properties of the generalized propensity score estimator $g_{n,A}$.
- Generally, finite-dimensional (i.e., parametric) models are not flexible enough to consistently estimate $g_{0,A}$.

Conditional density estimation via classification

- Our IPW estimator requires the generalized propensity score (GPS), so we need to estimate a conditional density.
- There is a rich literature on density estimation. We follow an approach first explored by Díaz and van der Laan (2011).
- To build a conditional density estimator, consider that

$$g_{n,A,\alpha}(A \mid L) = \frac{\mathbb{P}(A \in [\alpha_{t-1}, \alpha_t) \mid L)}{|\alpha_t - \alpha_{t-1}|} \ .$$

  - This is a classification problem, where the probability of A falling in a given bin $[\alpha_{t-1}, \alpha_t)$ is estimated, then re-scaled.
  - The choice of the tuning parameter t corresponds vaguely to the choice of bandwidth in classical kernel density estimation.

Conditional density estimation via pooled hazard regression

- Díaz and van der Laan (2011) propose a reformulation of this classification approach as a series of hazard regressions:

$$
\begin{aligned}
\mathbb{P}(A \in & [\alpha_{t-1}, \alpha_t) \mid L) = \\
& \mathbb{P}(A \in [\alpha_{t-1}, \alpha_t) \mid A \geq \alpha_{t-1}, L) \times \\
& \prod_{j=1}^{t-1} \{1 - \mathbb{P}(A \in [\alpha_{j-1}, \alpha_j) \mid A \geq \alpha_{j-1}, L)\}
\end{aligned}
$$

- Likelihood may be re-expressed as the likelihood of a binary variable in an artificial repeated measures data structure.
- Specifically, the observation of O_i is repeated as many times as intervals $[\alpha_{t-1}, \alpha_t)$ are prior to the interval to which A_i falls, and the indicator variables $A_i \in [\alpha_{t-1}, \alpha_t)$ are recorded.

Curse of dimensionality

Construct nuisance parameter *estimators* that are *consistent* and *suitably* ($n^{-1/4}$) *rate-convergent* without *superfluous* assumptions.

Challenging for moderately large d — *curse of dimensionality*.

For example, consider *kernel regression* with bandwidth h and kernels orthogonal to polynomials in L of degree k.

- Assume k-times *differentiability* of parameter. (psst, but is it?)
- Optimal bandwidth $O(n^{-1/(2k+d)})$
- Optimal convergence rate $O(n^{-k/(2k+d)})$

Curse of dimensionality

Broadly, *two approaches* for handling the *curse of dimensionality*.

1. Enlist *smoothness or sparsity assumptions* on the nuisance parameter space (i.e., for the GPS $g_{0,A}(A \mid L)$ in our case).
   - No *general* guarantee of achieving *consistency*.
   - An early example: Hirano et al. (2003) take a series regression approach, which requires k-times differentiability of $g_{0,A}(A \mid L)$.
2. Cross-validation with machine learning or ensemble machine learning (e.g., van der Laan et al. (2007)'s *Super Learner*).
   - No *general* guarantee of $n^{-1/4}$ *convergence rates*.
   - Necessary rates can be proven for specific machine learning algorithms within certain function classes.

But we intended for IPW estimation to simplify our lives...

A useful class of functions

Consider space of *cadlag* functions with *finite variation norm*.

Def. cadlag = *left-hand continuous* with *right-hand limits*

Variation norm Let $\theta_s(u) = \theta(u_s, 0_{s^c})$ be the *section* of θ that sets the coordinates in *s equal to zero*.

The *variation norm* of θ can be written:

$$|\theta|_v = \sum_{s \subset \{1,\ldots,d\}} \int |\ d\theta_s(u_s)\ |,$$

where $x_s = (x(j) : j \in s)$ and the sum is over all subsets.

Variation norm

We can represent the function θ as

$$\theta(x) \quad = \quad \theta(0) + \sum_{s \subset \{1,\ldots,d\}} \int \mathbb{I}(x_s \geq u_s) d\theta_s(u_s),$$

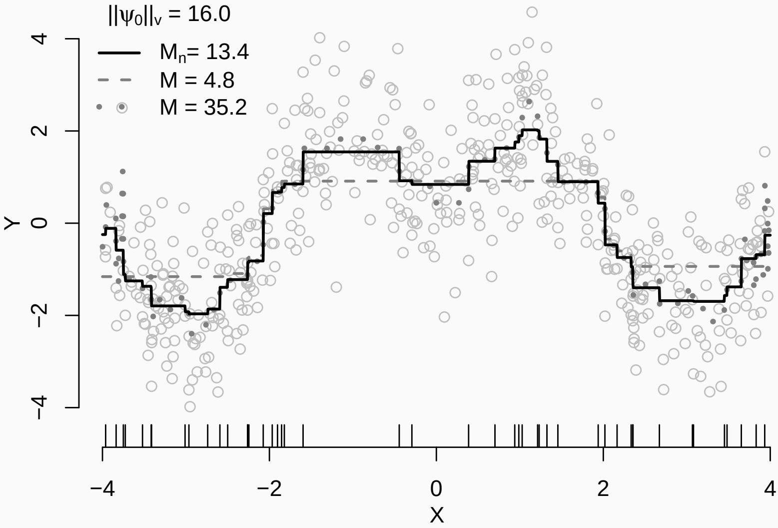
For discrete measures $d\theta_s$ with *support points* $\{u_{s,j} : j\}$ we get a *linear combination* of indicator *basis functions*:

$$\theta(x) = \theta(0) + \sum_{s \subset \{1,\ldots,d\}} \sum_j \beta_{s,j} \theta_{u_{s,j}}(x),$$

where $\beta_{s,j} = d\theta_s(u_{s,j})$, $\theta_{u_{s,j}}(x) = \mathbb{I}(x_s \geq u_{s,j})$, and

$$|\theta|_v = \theta(0) + \sum_{s \subset \{1,\ldots,d\}} \sum_j |\beta_{s,j}|.$$

Highly Adaptive Lasso (HAL) illustration



HAL estimator of GPS $g_{0,A}$

If the nuisance functional $g_{0,A}$ is cadlag with a finite sectional variation norm, $\operatorname{logit} g$ can be expressed (Gill et al. 1995):

$$\operatorname{logit} g_{\beta} = \beta_0 + \sum_{s \subset \{1,\ldots,d\}} \sum_{i=1}^{n} \beta_{s,i} \phi_{s,i},$$

where ϕ_s are indicator basis functions.

The loss-based HAL estimator β_n may then be defined as

$$\beta_{n,\lambda} = \underset{\beta: |\beta_0| + \sum_{s \subset \{1,\ldots,d\}} \sum_{i=1}^{n} |\beta_{s,i}| < \lambda}{\arg\min} P_n \mathcal{L}(\operatorname{logit} g_{\beta}),$$

where $\mathcal{L}(\cdot)$ is an appropriately selected loss function.

Denote by $g_{n,\lambda} \equiv g_{\beta_{n,\lambda}}$ the HAL estimator of the GPS $g_{0,A}$.

Targeted selection of λ_n for IPW estimation

1. CV: select λ_n as cross-validated empirical risk minimizer of negative log-density loss (Dudoit and van der Laan 2005):

$$\mathcal{L}(\cdot) = -\log(g_{n,A,\lambda}(A \mid L)).$$

   n.b., "targeted" but incorrect tradeoff ($g_{n,A,\lambda}$ instead of $\psi_{n,\delta}$).

2. EIF[1]: select λ_n to minimize mean of EIF estimating equation:

$$\lambda_n = \arg\min_{\lambda} |P_n D_{\text{CAR}}(g_{n,A,\lambda}, \overline{Q}_{n,Y})|,$$

   where $\overline{Q}_{n,Y}$ is an estimate of $\overline{Q}_{0,Y}$ and $D^\star = D_{\text{IPW}} - D_{\text{CAR}}$ by the AIPW representation (Robins and Rotnitzky 1992; 1995).

[1] Used for efficient IPW estimation (when $A \in \{0, 1\}$) by Ertefaie et al. (2022).

Agnostic selection of λ_n for IPW estimation

What if we dispensed with criteria based on the EIF altogether?

1. Plateau-based[2]: Choose λ_n as the first in $\lambda_1, \ldots, \lambda_K$ s.t.

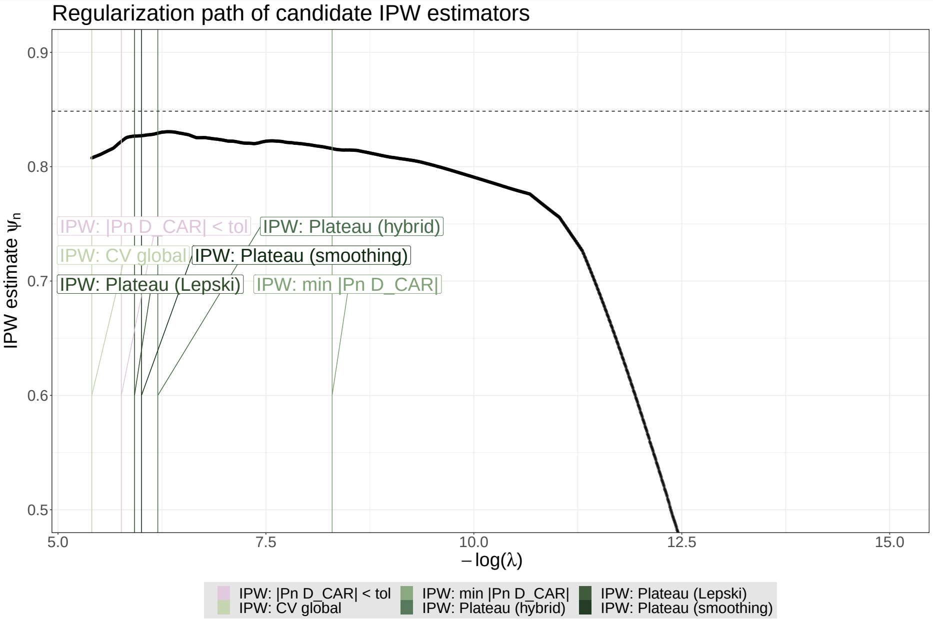
$$|\psi_{n,\delta,\lambda_{j+1}} - \psi_{n,\delta,\lambda_j}| \leq \frac{Z_{(1-\alpha/2)}}{\log n} |\sigma_{n,\lambda_{j+1}} - \sigma_{n,\lambda_j}| \quad \text{for } j = \{1, \ldots, K-1\}$$

   where σ_{n,λ_j} is a standard error estimate for $\psi_{n,\delta,\lambda_j}$ at λ_j.

2. Smoothing-based: Choose λ_n by trimming $\lambda_1, \ldots, \lambda_K$ to run from λ_{CV} to a multiple $C\lambda_{\text{CV}}$, and then finding an inflection point in the IPW estimator trajectory $\{\psi_{n,\lambda_{\text{CV}}}, \ldots, \psi_{n,C\lambda_{\text{CV}}}\}$.

[2] Inspired by ideas proposed by Lepskii (1993), Lepskii and Spokoiny (1997).

Proof by picture: Smoothing-based selection



Some other efficient estimators

- The one-step bias-corrected estimator:

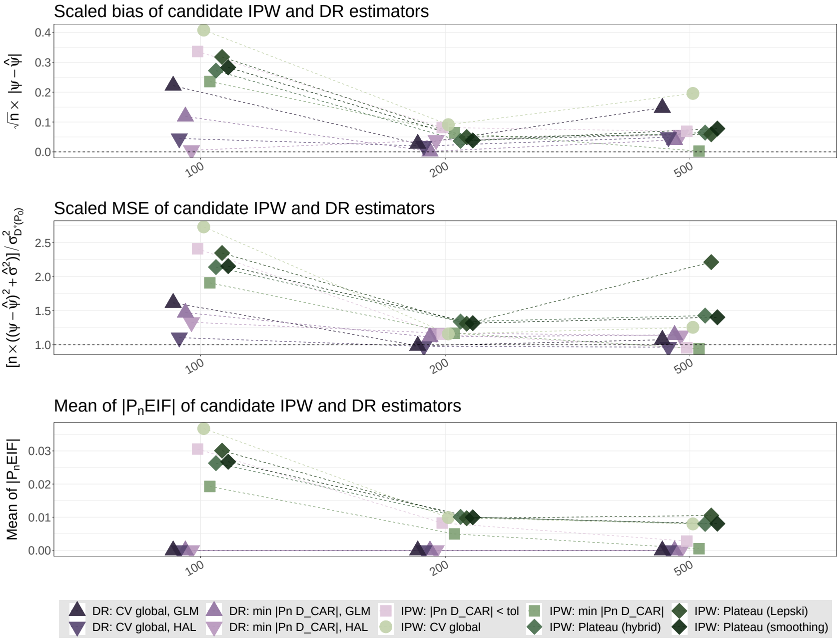
$$\psi_n^+ = \frac{1}{n}\sum_{i=1}^{n} \overline{Q}_{n,Y}(d(A_i, L_i), L_i) + D_n^\star(O_i).$$

- A TML estimator updates initial estimates of $\overline{Q}_{n,Y}$ by tilting:

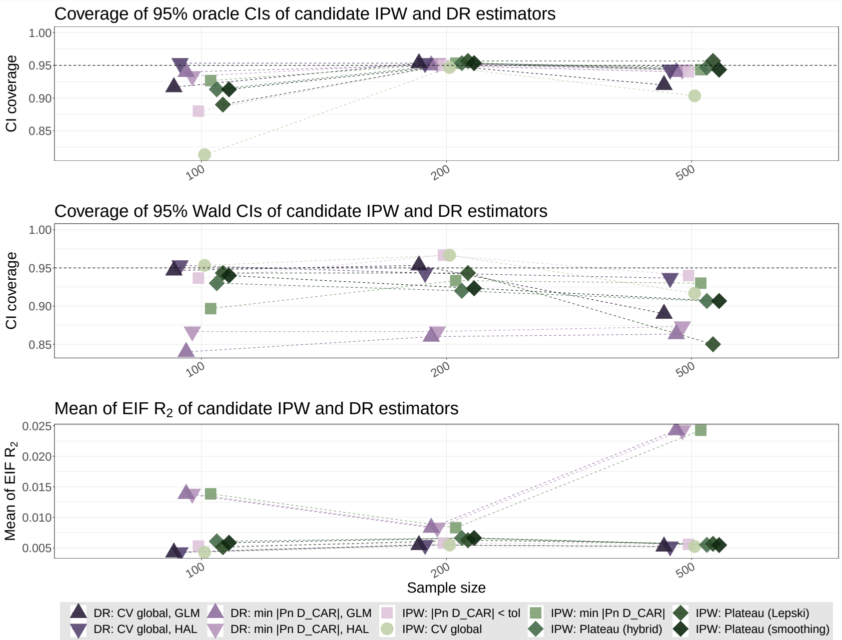
$$\psi_n^\star = \frac{1}{n}\sum_{i=1}^{n} \overline{Q}_{n,Y}^\star(d(A_i, L_i), L_i).$$

- Both are doubly robust (DR), allowing flexible methods to estimate the nuisance parameters $g_{n,A}$ and $\overline{Q}_{n,Y}$.

Simulation evidence: A first look



Simulation evidence: A bit deeper



The big picture

1. Unlike classical IPW estimators, ours avoid the asymptotic curse of dimensionality and are asymptotically efficient;
2. Our approach leverages flexible conditional density estimation for initial generalized propensity score estimates; and
3. In contrast with popular DR estimators, these IPW estimators can be formulated without the form of the EIF.
4. Analogous ideas (as for IPW) can improve DR estimators too.
5. Check out the `R` packages that make this possible
   - `hal9001`: `https://github.com/tlverse/hal9001`
   - `haldensify`: `https://github.com/nhejazi/haldensify`

Thank you!

https://nimahejazi.org

https://twitter.com/nshejazi

https://github.com/nhejazi

https://arxiv.org/abs/2205.05777

Appendix

Literature: Haneuse and Rotnitzky (2013)

- *Proposal:* Re-characterization of stochastic interventions as *modified treatment policies* (MTPs).
- Assumption of *piecewise smooth invertibility* allows for the intervention distribution of any MTP to be recovered:

$$g_{0,\delta}(a \mid l) = \sum_{j=1}^{J(s)} S_{\delta,j}\{h_j(a,l), s\} g_0\{h_j(a,l) \mid s\} h_j^{'}(a,l)$$

- Such intervention policies account for the natural value of the intervention A directly yet are interpretable as the imposition of an altered intervention mechanism.
- Only requires that the MTP $d(A, L; \delta)$ have an "amenable" form, by way of a j-sectional inverse $h_j(a,l)$ existing.

Literature: Young et al. (2014)

- Establishes equivalence between G-formula when proposed intervention depends on natural value of A vs. when not.
- This equivalence leads to a sufficient positivity condition for estimating the counterfactual mean under MTPs via the same statistical functional studied in Díaz and van der Laan (2012).
- Extends earlier identification results, providing a way to use the same statistical functional to assess $\mathbb{E}Y^{d(A,L;\delta)}$ or $\mathbb{E}Y^{d(L;\delta)}$.
- The authors also consider some limits on implementing MTPs $d(A, L; \delta)$, and address working in a longitudinal setting.

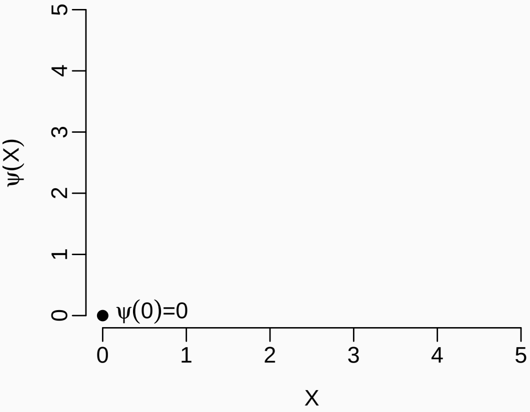
Literature: Díaz and van der Laan (2018)

- Builds on the proposal of Haneuse and Rotnitzky (2013) to accommodate MTPs $d(A, L; \delta)$, proposed after Díaz and van der Laan (2012)'s work with interventional distributions.
- To protect against *structural* positivity violations (Hernán and Robins 2023), considers an MTP mechanism that can avoid these via the guardrail encoded in $u(l)$:

$$d(a, l; \delta) = \begin{cases} a + \delta, & a + \delta < u(l) \\ a, & \text{otherwise} \end{cases}$$

- Proposes an improved TMLE algorithm, with a single auxiliary covariate for constructing the TML estimator.

HAL illustration



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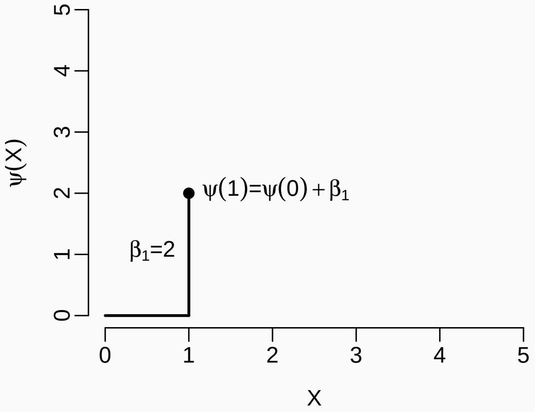

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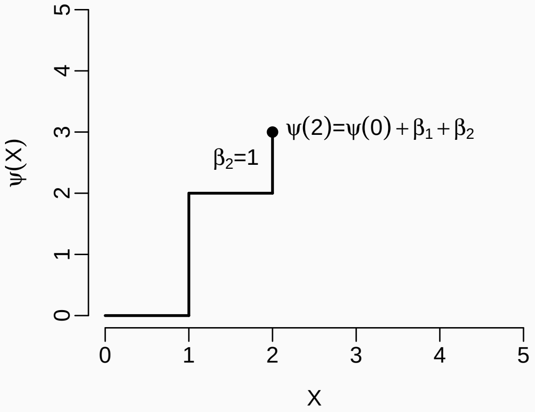

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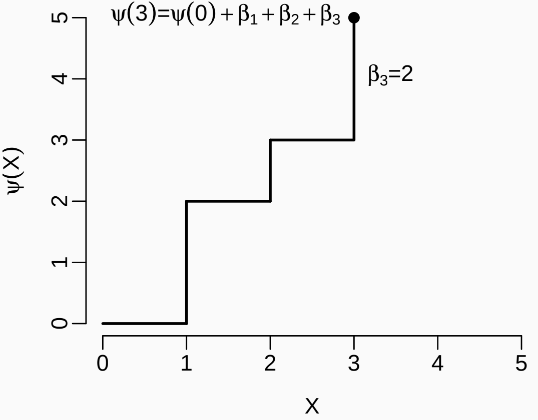

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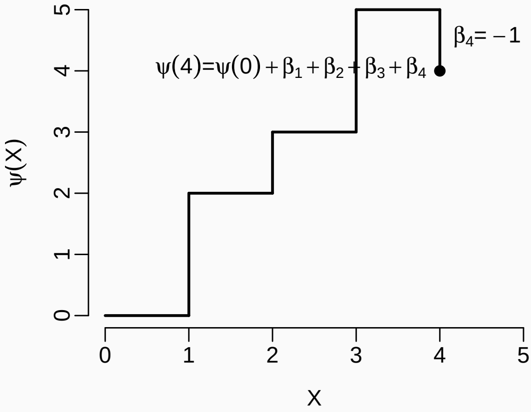

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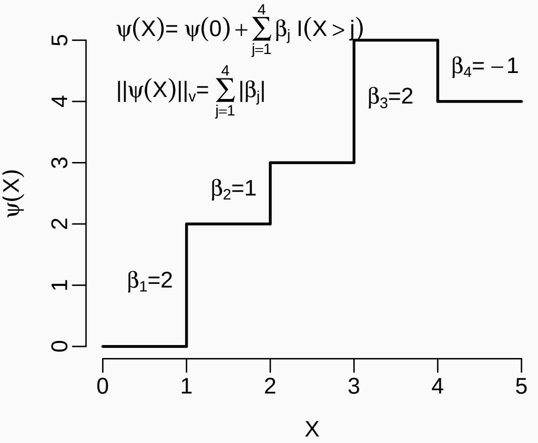

Convergence rate of HAL

We have, for $\alpha(d) = 1/(d+1)$,

$$|\theta_{n,M} - \theta_{0,M}|_{P_0} = o_P(n^{-(1/4+\alpha(d)/8)}).$$

Thus, if we select $M > |\theta_0|_v$, then

$$|\theta_{n,M} - \theta_0|_{P_0} = o_P(n^{-(1/4+\alpha(d)/8)}) \; .$$

Due to oracle inequality for the cross-validation selector M_n,

$$|\theta_{n,M_n} - \theta_0|_{P_0} = o_P(n^{-(1/4+\alpha(d)/8)}) \; .$$

Improved convergence rate (Bibaut and van der Laan 2019):

$$|\theta_{n,M_n} - \theta_0|_{P_0} = o_P(n^{-1/3} \log(n)^{d/2}) \; .$$

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