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

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General setup

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

- $L \in \mathbb{R}^d$ is a vector of possible confounders;
- $A \in \mathbb{R}$ 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):

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

where A_δ is set by a *modified treatment policy* (MTP).

NPSEM-IE with static interventions

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

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

  where $U_L \perp\!\!\!\perp U_A \perp\!\!\!\perp U_A$, i.e., "independent errors" (IE).

- Counterfactual RVs arise from interventions on NPSEM.
- A *static* intervention replaces f_A with an a in support $\mathcal{A}$.
  - What specific value $a \in \mathcal{A}$ is of interest *a priori*?
  - Consider all $a \in \mathcal{A}$ for the causal dose-response curve, but challenging to identify, estimate (e.g., Kennedy et al. 2017).

Causal effects of stochastic interventions

- A *stochastic* intervention alters A to A_δ by drawing randomly from a *modified* exposure distribution $G_\delta(\cdot \mid L)$.
  - Leads to counterfactual RV as $Y^{A_\delta} \leftarrow f_Y(A_\delta, L, U_Y)$, with $Y^{A_\delta} \sim P_{0,\delta}$.
  - Static interventions are only a special case of this, in which G_δ is a degenerate distribution that places all mass on $a \in \mathcal{A}$.
- Goal: Estimate counterfactual mean under the modified exposure distribution G_δ, that is, $\psi_{0,\delta} := \mathbb{E}_{P_{0,\delta}}\{Y^{A_\delta}\}$.
- Díaz and van der Laan (2012)'s *intervention distribution*: $G_\delta := P_\delta(g_{0,A})(A = a \mid L) \equiv g_{0,A}(d^{-1}(A, L; \delta) \mid L)$.

Causal effects of modified treatment policies

- Haneuse and Rotnitzky (2013) introduced *modified treatment policies* (MTPs), which adopt the intervention scheme:

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

  and were also studied and extended by Young et al. (2014), Díaz and van der Laan (2018), and Díaz et al. (2021).

- $\psi_{0,\delta}$ is identified by a functional of the distribution of O as

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

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

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

$g_{P,A}(A, L) := f_P(A \mid L)$ *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,

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

or could use stabilized IPW instead...

Why bother? Isn't simplicity dead? (Ahem, double robustness...)

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

IPW estimators

The IPW estimator $\psi_{n,\delta} \equiv \Psi_\delta(P, g_{n,A})$ is a Z-estimator solving the score equation $\mathbb{E}_P D_{\text{IPW}}(\cdot) = 0$, where D_{IPW} is defined as

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

Hiccups along the way:

- 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 $g_{0,A}$.
- Our IPW estimator requires the generalized propensity score (GPS), so we need to estimate a conditional density.

The GPS and conditional density estimation

- There is a rich literature on density estimation. We follow an approach outlined by Díaz and van der Laan (2011).
- To build a conditional density estimator, note that

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

  for $[\alpha_{t-1}, \alpha_t)$, $t = 0, \ldots, k$ a discrete partitioning of $\mathcal{A}$.

  - Classification problem: probability of A falling in a given bin $[\alpha_{t-1}, \alpha_t)$ is estimated, then re-scaled.
  - Classification approach as a series of hazard regressions:

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

  - Other: Poisson intensity (Rytgaard et al. 2022), Cox PH.

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*.
    - Rates tied to specific learning algorithms and function classes (e.g., functions being Hölder-smooth, s-sparse, etc.).
    - Hirano et al. (2003) took a series regression approach but required 7-times differentiability of $g_{0,A}(A \mid L)$ wrt d.
2. Cross-validation with machine learning or ensemble machine learning (e.g., van der Laan et al. (2007)'s *Super Learner*), but no *general* guarantee of $n^{-1/4}$ *convergence rates*.

A 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:

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

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

Variation norm

We can represent the function θ as

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

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

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

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

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

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

If the nuisance functional $g_{0,A}$ is cadlag with a finite sectional variation norm, logit g can be expressed (van der Laan 2015):

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

where ϕ_s are indicator basis functions.

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

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

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., incorrect tradeoff optimizing $g_{n,A,\lambda}$ instead of $\psi_{n,\delta}$.

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

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

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

[1] Used for nonparametric IPW (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.

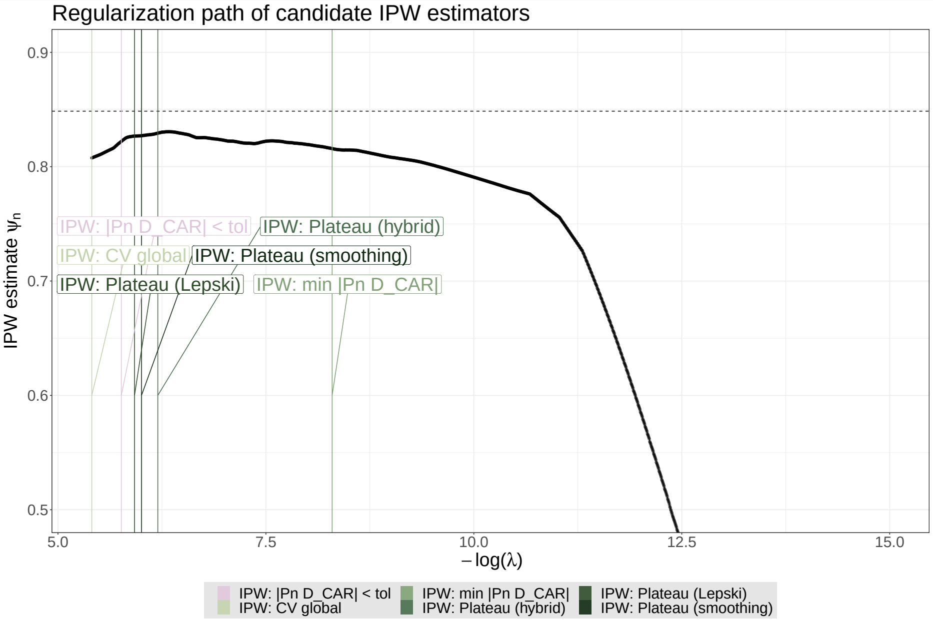
$$|\psi_{n,\delta,\lambda_{j+1}} - \psi_{n,\delta,\lambda_j}| \leq \frac{Z_{(1-\alpha/2)}}{\log n} |\sigma_{n,\lambda_{j+1}} - \sigma_{n,\lambda_j}| \quad \text{for } j = \{1, \ldots, K-1\}$$

   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 estimator's 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:

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

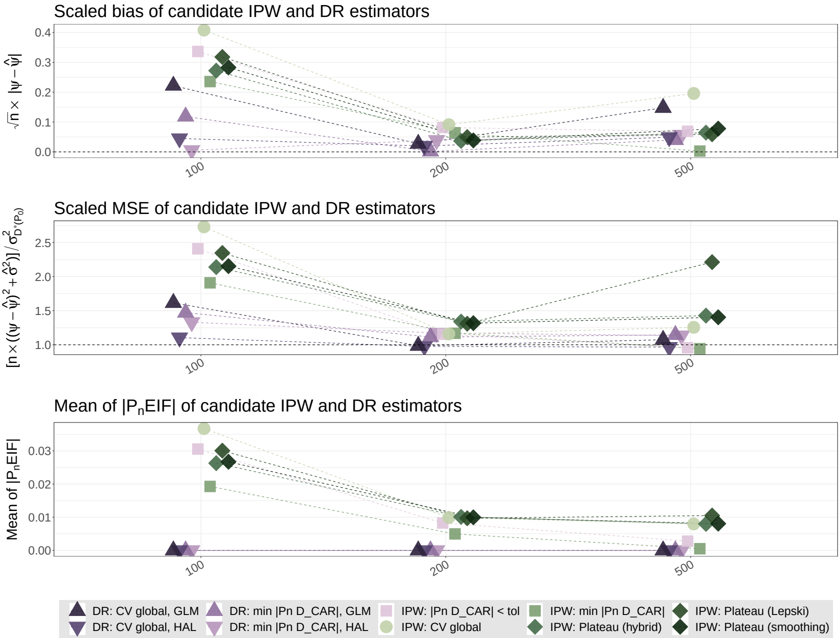
- A TML estimator updates initial estimates of $\overline{Q}_{n,Y}$ by tilting:

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

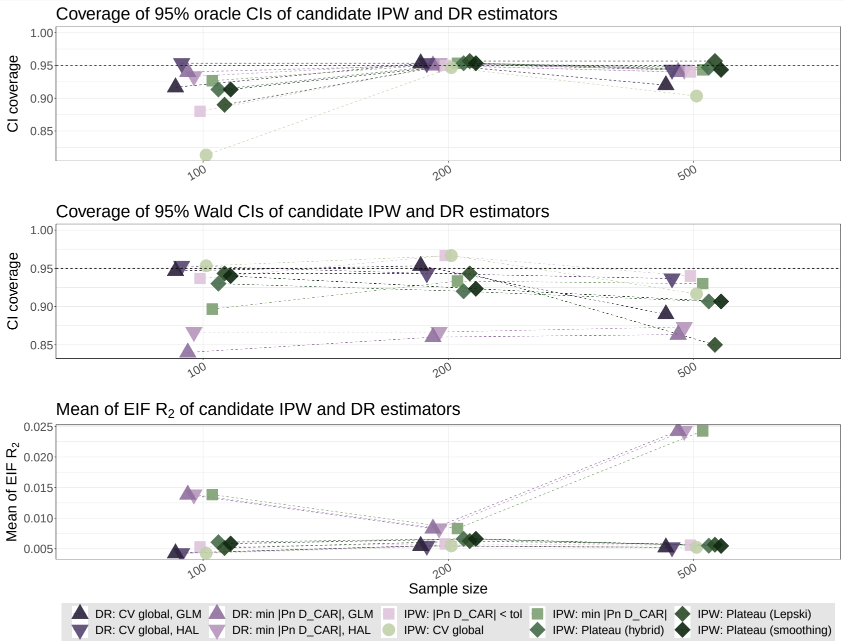
  where $\overline{Q}^{\star}_{n,Y}$ is arrived at by updating its initial counterpart:
  $\text{logit}(\overline{Q}^{\star}_{n,Y}(A_i, L_i)) = \text{logit}(\overline{Q}_{n,Y}(A_i, L_i)) + \epsilon\frac{g_{n,A}(d^{-1}(A_i, L_i; \delta)|L_i)}{g_{n,A}(A_i|L_i)}$.

- 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



Augmenting TMLE via undersmoothing

- Consider again the TML estimator (with a twist):

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

  but adjust the update of $\overline{Q}_{n,Y}^{\star}$ to now involve $g_{n,A,\lambda}$, that is, $\text{logit}(\overline{Q}_{n,Y}^{\star,\lambda}(A_i, L_i)) = \text{logit}(\overline{Q}_{n,Y}(A_i, L_i)) + \epsilon \frac{g_{n,A,\lambda}(d^{-1}(A_i, L_i; \delta) \mid L_i)}{g_{n,A,\lambda}(A_i \mid L_i)}$.
- Update to $\overline{Q}_{n,Y}^{\star,\lambda}$ involves ϵ_n and selection of λ_n via selectors.
- What might be gained from this augmentation?
  - If $\overline{Q}_{n,Y}$ consistent, asymptotic efficiency by bias correction.
  - If $\overline{Q}_{n,Y}$ and $g_{n,A}$ both consistent, then influences higher-order behavior (e.g., second-order bias).

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.

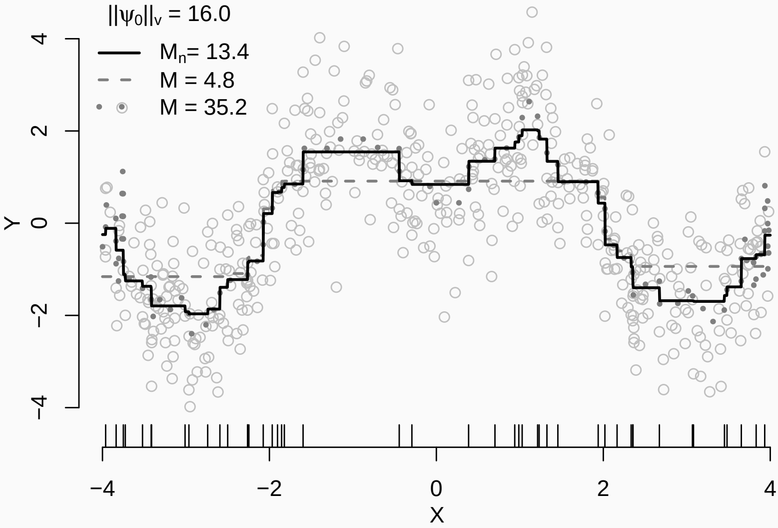
Literature: Díaz and van der Laan (2018)

- 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 2024), 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.

Highly Adaptive Lasso (HAL) illustration



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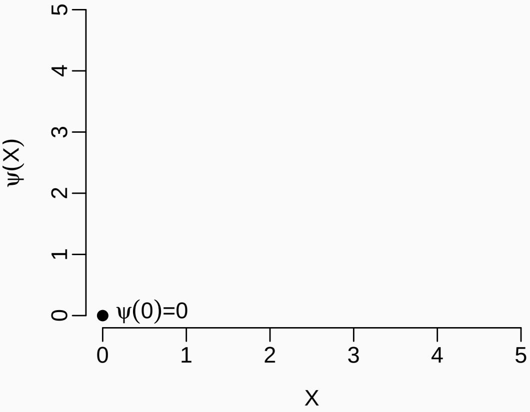

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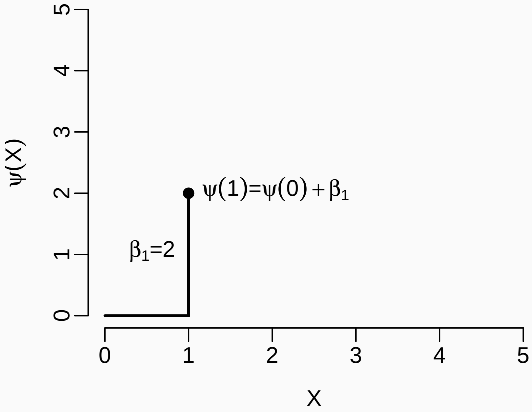

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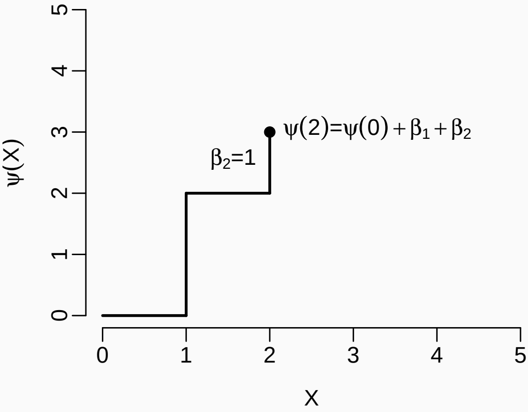

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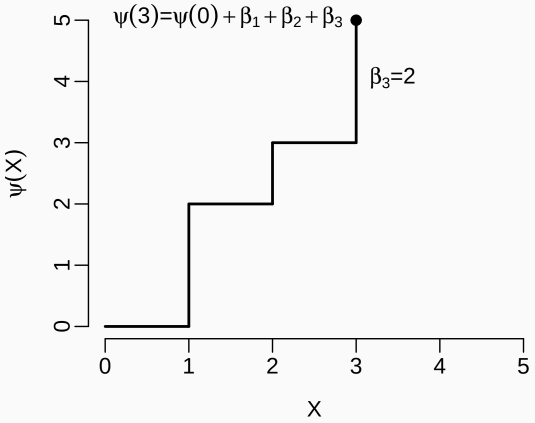

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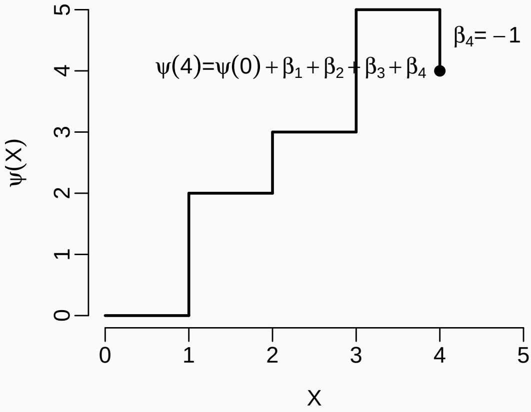

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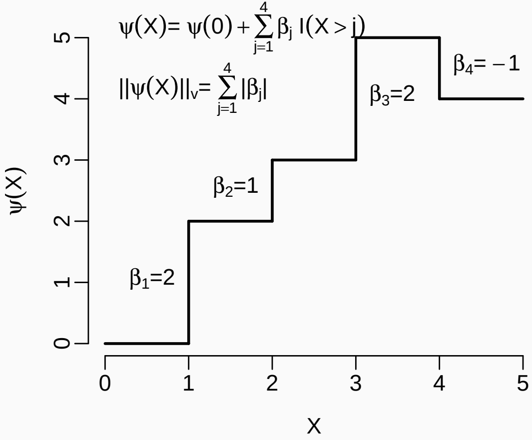

Convergence rate of HAL

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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