

A Liberating Framework from Truncation and Censoring, with Application to Learning Treatment Effects

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Left truncation – selection due to delayed entry

- Example: aging studies.
 - ▶ Age is the time scale of interest.
 - ▶ Subjects enrolled at various ages instead of at the time origin (time at birth).

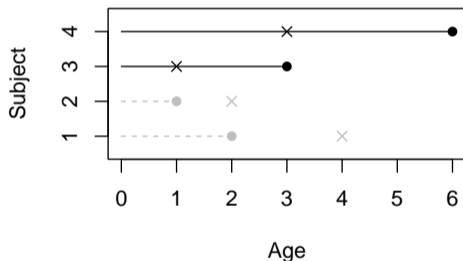
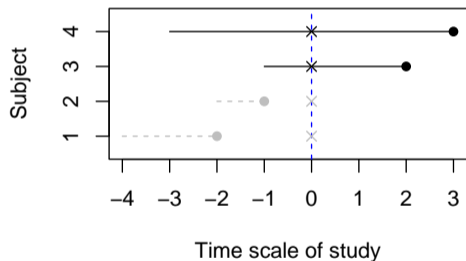


Figure: A toy example for aging study; 'x' - enrollment times; dots - times to events.

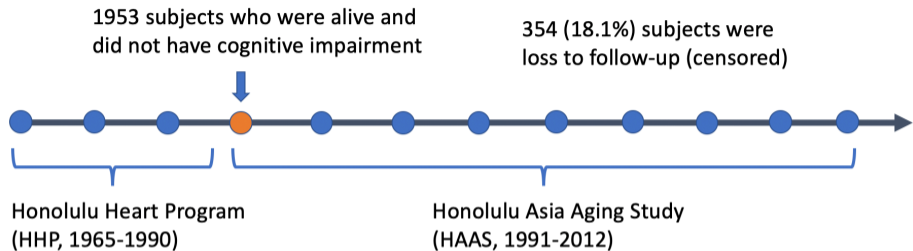
Left truncation – mathematical formulation

- Time-to-event: T^*
- Left truncation time: Q^* – usually the study enrollment time
- T^* is **left truncated** by Q^* if only subjects with $T^* > Q^*$ are included in the data.
- Subjects with early event times tend not to be captured → **selection bias**

Examples:

- Aging studies – age is the time scale of interest
- Pregnancy studies
- Some cancer survivorship studies, e.g., SJLIFE.

HAAS data



- T^* : age to moderate cognitive impairment or death; Q^* : age at entry of HAAS.
- Causal questions:
e.g., the effect of midlife alcohol exposure on late-life cognitive impairment.
- **Triple biases:**
 - **Selection bias from left truncation** – early event times are underrepresented.
 - Confounding in observational data.
 - Informative right censoring.

Literature on left truncation

Conventional methods on left truncation

- Under random left truncation/quasi-independence assumption
- Extended to conditional (quasi-)independence assumption under regression settings
 - ▶ when the dependence-inducing covariates are included as regressors

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For marginal estimands under covariate dependent left truncation

- Inverse probability of truncation weighting (Vakulenko-Lagun et al., 2022)
- Efficient influence function (EIF)-based doubly robust (DR) approaches (Wang et al., 2024)
 - ▶ Constructed model DR and rate DR estimators in the presence of left truncation
 - selection bias that does NOT fall under the established framework of coarsened data

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Complexities of right censoring in the presence of left truncation

- Informative right censoring for estimating a marginal parameter
- Truncation-induced dependence between the right censoring time and the event time

Our contributions

- Introduce a liberating framework for handling covariate dependent **L**eft **T**runcation and **R**ight **C**ensoring (LTRC).
 - ▶ Allows existing estimating functions and loss functions from LTRC-free settings to be easily applied to the observed LTRC data
 - ▶ Maintain their desirable properties in LTRC-free data, e.g., orthogonality, double robustness (DR).
- As an illustration:
 - ▶ Average treatment effect (ATE): model DR and rate DR estimators.
 - ▶ Conditional Average Treatment Effect (CATE): orthogonal and doubly robust learners.
- The framework can also be applied to other problems with LTRC data.

Notation

- Q : left truncation time; T : event time;
- C : censoring time; $D = C - Q$: residual censoring time;
- A : binary treatment assignment; Z : covariates.

- Variables with '*' – truncation-free data; without '*' – truncated data.
- $T^*(a)$ – potential event time under treatment a .

- Observe $O = (Q, X, \Delta, A, Z)$ only if $Q^* < T^*$.
- $X = \min(T, C)$, $\Delta = I(T < C)$.

- Estimand:
 - ▶ ν : a given transformation; V^* a subset of covariates,
 - ▶ **CATE**: $\tau(\nu) = \mathbb{E}[\nu\{T^*(1)\} - \nu\{T^*(0)\} \mid V^* = \nu]$.
 - ▶ **ATE**: a special case with $V^* = \emptyset$, $\theta = \tau(\emptyset)$.

Assumptions

- 1 SUTVA, no unmeasured confounding, consistency.
- 2 Conditional independent truncation: $Q^*(a) \perp\!\!\!\perp T^*(a) \mid Z^*$.
- 3 Conditional noninformative residual censoring: $D^*(a) \perp\!\!\!\perp (T^*(a), Q^*(a)) \mid Z^*$.
- 4 Strict positivity.

$\pi(z) = \mathbb{P}(A^* = 1 \mid Z^* = z)$;

F, G : conditional CDF of $T^* \mid A^*, Z^*$, and $Q^* \mid A^*, Z^*$, respectively;

S_D : the conditional survival function of $D \mid Q, A, Z$.

(i) There exist $\delta_1 > 0$ such that $\delta_1 \leq \pi(Z^*) \leq 1 - \delta_1$ a.s.;

(ii) There exist $0 < \tau_1 < \tau_2 < \infty$ and $\delta_2 > 0$ such that $T^* \geq \tau_1$ a.s. and $Q^* < \tau_2$ a.s., $1 - F(\tau_2 \mid A^*, Z^*) \geq \delta_2$ a.s. and $G(\tau_1 \mid A^*, Z^*) \geq \delta_2$ a.s.;

(iii) There exists $\delta_3 > 0$ such that $1 - F(t_{\max} \mid A, Z) \geq \delta_3$ a.s. and $S_D(t_{\max} - Q \mid Q, A, Z) \geq \delta_3$ a.s..

Doubly robust operator for left truncation

- Motivated by the EIF derived in Wang et al. (2024).
- For any function in the LTRC-free data $\zeta(T^*, A^*, Z^*)$,
- $\mathcal{V}_Q(\zeta; F, G) =$

$$\underbrace{\frac{\zeta(T, A, Z)}{G(T|A, Z)}}_{\text{IPW}} - \underbrace{\int_0^\infty m_\zeta(v, A, Z; F) \cdot \frac{F(v|A, Z)}{1 - F(v|A, Z)} \cdot \frac{d\bar{M}_Q(v, G)}{G(v|A, Z)}}_{\text{Augmentation}}$$

- F : the conditional CDF of $T^* | A^*, Z^*$.
- G : the conditional CDF of $Q^* | A^*, Z^*$.
- $m_\zeta(v, a, z; \theta, F) = \mathbb{E}\{\zeta(T^*, A^*, Z^*; \theta) | T^* \leq v, A^* = a, Z^* = z\}$.

Doubly robust operator for censoring

- Adapt the **AIPCW** (Rotnitzky and Robins, 2005) to the **residual time scale**.
- Recall $D = C - Q$: the residual censoring time.
- For any function $\xi(Q, T, A, Z)$ in the truncated but censoring-free data,
- $\mathcal{V}_C(\xi; F, S_D) =$

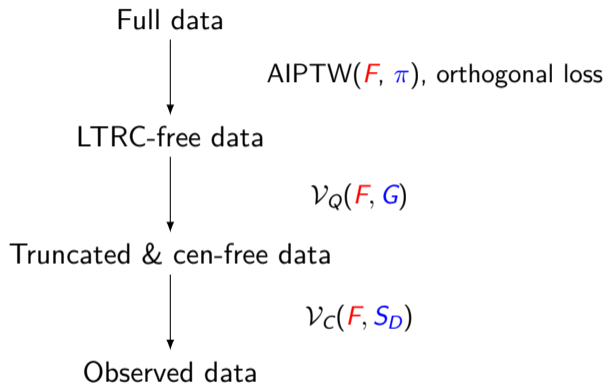
$$\underbrace{\frac{\Delta \xi(Q, X, A, Z)}{S_D(X - Q | Q, A, Z)}}_{\text{IPCW}} + \underbrace{\int_0^\infty \bar{m}_\xi(u, Q, A, Z; F) \cdot \frac{dM_D(u; S_D)}{S_D(u | Q, A, Z)}}_{\text{Augmentation}}$$

- S_D : the conditional survival function of $D | Q, A, Z$.
- Recall F : the conditional CDF of $T^* | A^*, Z^*$.

$$\begin{aligned} \bar{m}_\xi(u, q, a, z; F) &= \mathbb{E}\{\xi(Q, T, A, Z) | T - Q \geq u, Q = q, A = a, Z = z\} \\ &= \frac{\int_{q+u}^\infty \xi(q, t, a, z) dF(t | a, z)}{1 - F(q + u | a, z)}. \end{aligned}$$

General framework and double robustness

- **General framework:**



- **Double robustness:** The expectation is maintained (up to a constant factor) by $\mathcal{V}_C \circ \mathcal{V}_Q$ if either F or (G, S_D) is the truth.

ATE estimation

- Estimand: $\theta = \mathbb{E}[\nu\{T^*(1)\} - \nu\{T^*(0)\}]$. Propensity score: $\pi(z) = \mathbb{P}(A^* = 1|Z^* = z)$.
- AIPTW estimating function $U_0(\theta; F, \pi) \xrightarrow{\nu_C \circ \nu_Q} U(\theta; F, \pi, G, S_D)$
- **Double robustness:** $\mathbb{E}\{U(\theta; F, \pi, G, S_D)\} = 0$ if either F or (π, G, S_D) is the truth.
- Estimation:

$$\sum_{i=1}^n U_i(\theta; \hat{F}, \hat{\pi}, \hat{G}, \hat{S}_D) = 0 \quad \Rightarrow \quad \text{closed-form solution } \hat{\theta}$$

Theorem 1 (Model double robustness)

Assume that $\hat{\pi}, \hat{F}, \hat{G}, \hat{S}_D$ converge uniformly to π^*, F^*, G^*, S_D^* , respectively, and that π^*, F^*, G^*, S_D^* also satisfy the strict positivity assumption. Then

(i) $\hat{\theta} \xrightarrow{P} \theta_0$ if either $F^* = F_0$ or $(\pi^*, G^*, S_D^*) = (\pi_0, G_0, S_{D0})$.

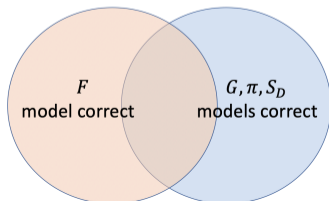
(ii) In addition, if $\hat{\pi}, \hat{F}, \hat{G}, \hat{S}_D$ are asymptotically linear, then

$$\sqrt{n}(\hat{\theta} - \theta_0) \xrightarrow{d} N(0, \sigma^2).$$

Furthermore, when both $F^* = F_0$ and $(\pi^*, G^*, S_D^*) = (\pi_0, G_0, S_{D0})$, we have

$\sigma^2 = \beta^2 \mathbb{E}\{U(\theta_0; \pi_0, F_0, G_0, S_{D0})^2\}$, which can be consistently estimated by

$$\hat{\sigma}^2 = n \sum_{i=1}^n U_i^2(\hat{\theta}; \hat{\pi}, \hat{F}, \hat{G}, \hat{S}_D) / \{\sum_{i=1}^n \mathcal{V}_i(1; \hat{F}, \hat{G}, \hat{S}_D)\}^2.$$



Rate double robustness

Cross-fitted estimator:

$$\sum_{k=1}^K \sum_{i \in \mathcal{I}_k} U_i \left(\theta; \hat{\pi}^{(-k)}, \hat{F}^{(-k)}, \hat{G}^{(-k)}, \hat{S}_D^{(-k)} \right) = 0 \Rightarrow \hat{\theta}_{cf}$$

Assumptions:

- Uniform consistency:

$$\|\hat{\pi} - \pi_0\|_2 = o_p(1), \|\hat{F} - F_0\|_{\text{sup},2} = o_p(1), \|\hat{G} - G_0\|_{\text{sup},2} = o_p(1), \|\hat{S}_D - S_{D0}\|_{\text{sup},2} = o_p(1).$$

- Product rate condition:

$$\begin{aligned} & \|\hat{F} - F_0\|_{\text{sup},2} \cdot \left\{ \|\hat{\pi} - \pi_0\|_2 + \|\hat{G} - G_0\|_{\text{sup},2} + \|\hat{S}_D - S_{D0}\|_{\text{sup},2} \right\} \\ & + \|K_1(\hat{g}, g_0)\|_1 + \|K_2(\hat{g}, g_0)\|_1 + \|K_3(\hat{g}, g_0)\|_1 = o_p(n^{-1/2}). \end{aligned}$$

$$g = (F, G, S_D), \hat{g} = (\hat{F}, \hat{G}, \hat{S}_D).$$

$K_1(g, g_0)$, $K_2(g, g_0)$, and $K_3(g, g_0)$ are integral products between the estimation errors of F and (G, S_D) , containing terms such as

$$\int_Q^X \left\{ \frac{\int_0^v \nu(t) dF(t|A, Z)}{1 - F(v|A, Z)} - \frac{\int_0^v \nu(t) dF_0(t|A, Z)}{1 - F_0(v|A, Z)} \right\} \cdot d \left\{ \frac{1}{G(v|A, Z)} - \frac{1}{G_0(v|A, Z)} \right\}.$$

Rate double robustness

Theorem 2 (Rate double robustness)

- (i) Under uniform consistency of the nuisance estimators, $\hat{\theta}_{cf} \xrightarrow{P} \theta_0$.
(ii) In addition, if the product rate condition holds,

$$n^{1/2}(\hat{\theta}_{cf} - \theta_0) \xrightarrow{d} N(0, \sigma^2),$$

where $\sigma^2 = \beta^2 \mathbb{E}\{U(\theta_0; \pi_0, F_0, G_0, S_{D0})^2\}$, which can be consistently estimated by

$$\hat{\sigma}_{cf}^2 = n \sum_{i,k} U_i^2 \left(\hat{\theta}_{cf,i}, \hat{\pi}^{(-k)}, \hat{F}^{(-k)}, \hat{G}^{(-k)}, \hat{S}_D^{(-k)} \right) / \left\{ \sum_{i,k} \mathcal{V}_i(1; \hat{F}^{(-k)}, \hat{G}^{(-k)}, \hat{S}_D^{(-k)}) / n \right\}^2.$$

CATE estimation

- Estimand: $\tau(v) = \mathbb{E}[\nu\{T^*(1)\} - \nu\{T^*(0)\} \mid V^* = v]$, where $V^* \subseteq Z^*$
- Loss function $\ell(T^*, A^*, Z^*; \tau, F, \pi) \xrightarrow{\nu_C \circ \nu_Q} \tilde{\ell}(O; \tau, F, \pi, G, S_D)$
 - ▶ R-loss \rightarrow ltrcR-loss, for the special case with $V^* = Z^*$.
 - ▶ DR-loss \rightarrow ltrcDR-loss
- **Neyman orthogonality** and **double robustness** are maintained.

CATE estimation

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 - ▶ R-loss \rightarrow ltrcR-loss, for the special case with $V^* = Z^*$.
 - ▶ DR-loss \rightarrow ltrcDR-loss
- **Neyman orthogonality** and **double robustness** are maintained.
- Empirical risk minimization with sample splitting:

$$\hat{\tau} = \arg \min_{\tau \in \mathcal{T}} \left[\frac{1}{m} \sum_{i=1}^m \tilde{\ell}\{O_i; \tau, \hat{F}, \hat{\pi}, \hat{G}, \hat{S}_D\} \right],$$

where $\hat{\pi}$, \hat{F} , \hat{G} and \hat{S}_D are estimated from data $\{O_i : i = m + 1, \dots, n\}$, and m is roughly $n/2$.

Oracle rate results

Assume the nuisance estimators are consistent.

- Using the ltrcR-loss, $\hat{\tau}_R$ achieves the oracle error rate if

$$\begin{aligned} & \|\hat{\pi} - \pi_0\|_4^2 + \|\hat{F} - F_0\|_{\text{sup},4} \cdot \left\{ \|\hat{\pi} - \pi_0\|_4 + \|\hat{G} - G_0\|_{\text{sup},4} + \|\hat{S}_D - S_{D0}\|_{\text{sup},4} \right\} \\ & + \|K_1(\hat{g}, g_0)\|_2 + \|K_2(\hat{g}, g_0)\|_2 + \|K_3(\hat{g}, g_0)\|_2 = o_p(n^{-1/2}). \end{aligned}$$

- Using the ltrcDR-loss, $\hat{\tau}_{DR}$ achieves the oracle error rate if

$$\begin{aligned} & \|\hat{F} - F_0\|_{\text{sup},4} \cdot \left\{ \|\hat{\pi} - \pi_0\|_4 + \|\hat{G} - G_0\|_{\text{sup},4} + \|\hat{S}_D - S_{D0}\|_{\text{sup},4} \right\} \\ & + \|K_1(\hat{g}, g_0)\|_2 + \|K_2(\hat{g}, g_0)\|_2 + \|K_3(\hat{g}, g_0)\|_2 = o_p(n^{-1/2}). \end{aligned}$$

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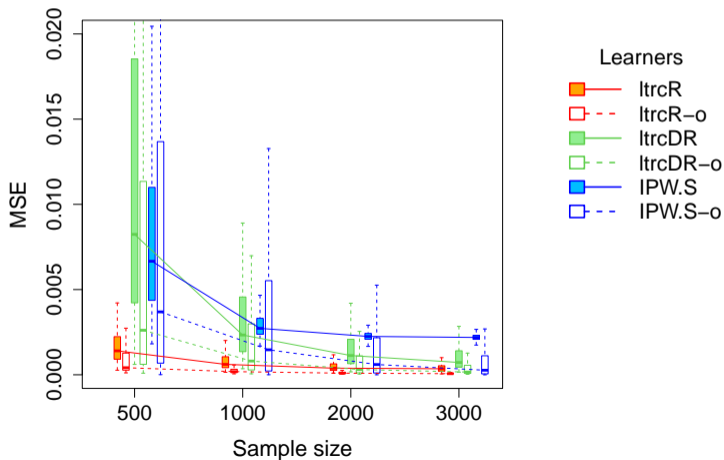
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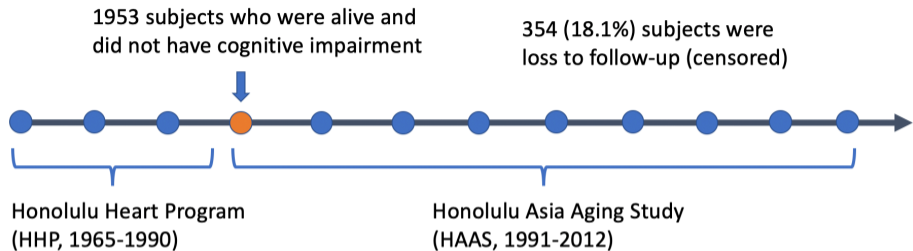
Simulation - CATE

- 500 simulated data sets. Estimand: $\tau(z) = \mathbb{E}\{\log T^*(1) - \log T^*(0) \mid Z^* = z\}$.
- Truncation rate: around 30%; treatment rate: around 50%; censoring rate: around 50%.

$$MSE = \frac{1}{n} \sum_{i=1}^n \{\hat{\tau}(V_i) - \tau_0(V_i)\}^2.$$



HAAS data



- T^* : age to moderate cognitive impairment or death; Q^* : age at entry of HAAS.
- The effect of midlife alcohol exposure (heavy/non-heavy) on late-life cognitive impairment-free survival.
- Covariates:
 - ▶ Education (≤ 12 years or otherwise)
 - ▶ ApoE genotype (positive/negative)
 - ▶ Systolic blood pressure (mmHg)
 - ▶ Heart rate (beats per minute)

HAAS: ATE

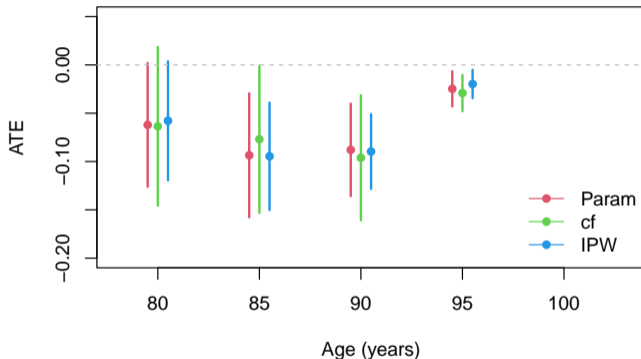


Figure: Estimates of ATE as difference of the potential DFS probabilities at various ages for heavy versus non-heavy drinkers in the HAAS data, with 95% confidence intervals.

HAAS – CATE

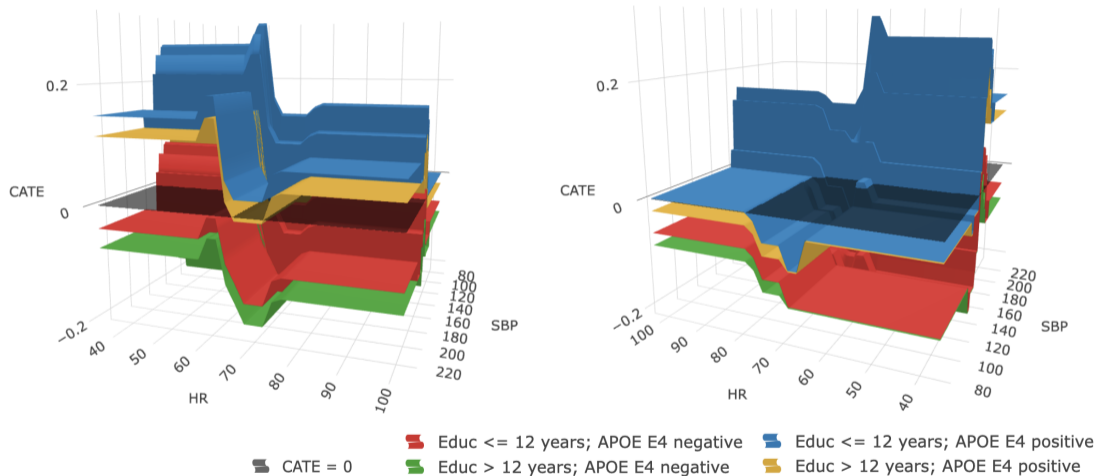


Figure: Estimated CATE surfaces of DFS at age 90 from the ltrcR-learner for different education and ApoE genotype subgroups (views from four different angles).

HAAS – CATE

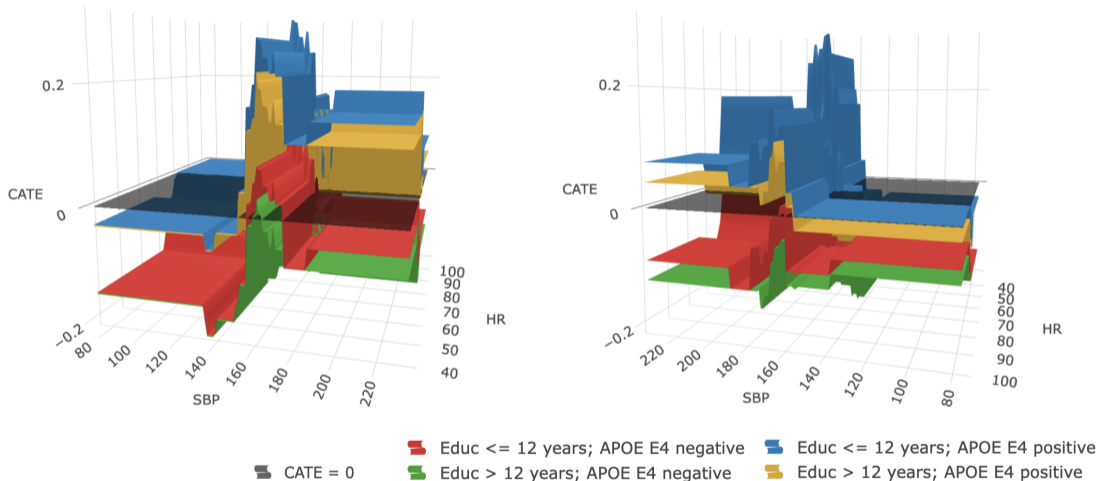


Figure: Estimated CATE surfaces of DFS at age 90 from the ltrcR-learner for different education and ApoE genotype subgroups (views from four different angles).

Summary:

- We developed a general orthogonal and doubly robust framework for handling covariate dependent LTRC, and applied it to estimate ATE and CATE.
- The framework can be applied to a broad range of estimation problems with LTRC data.
 - ▶ e.g., survival integral considered in Morenz et al. (2024),
 - ▶ e.g., weighted orthogonal learners developed in Morzywolek et al. (2023).

Acknowledgment:

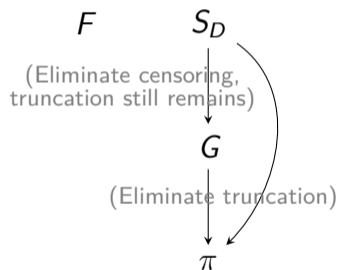
- We thank Drs. Steve Edland, Jue (Marquis) Hou and Kendrick Li for helpful discussions.

References and contact info:

- **Wang, Y.**, Ying, A. and Xu, R. (2024). Doubly robust estimation under covariate-induced dependent left truncation. *Biometrika* 111: 789–808.
- **Wang, Y.**, Ying, A. and Xu, R. (2024). A liberating framework from truncation and censoring, with application to learning treatment effects. *arXiv:2411.18879*.
- Github: <https://github.com/wangyuyao98/truncAC> R-package: `truncAIPW`
- Email: yuya.wang@northeastern.edu

Appendix

Nuisance parameter estimation



- F : use existing software for LTRC data.
- S_D : use existing software for right censored data.
- G : use IPCW weights $\Delta / \hat{S}_D(X - Q | Q, A, Z)$
+ use existing software for left truncated data on the reversed time scale.
- π : use weights $\Delta / \{\hat{G}(X | A, Z) \hat{S}_D(X - Q | Q, A, Z)\}$
+ existing software for regressing A on Z .

Nuisance parameter estimation

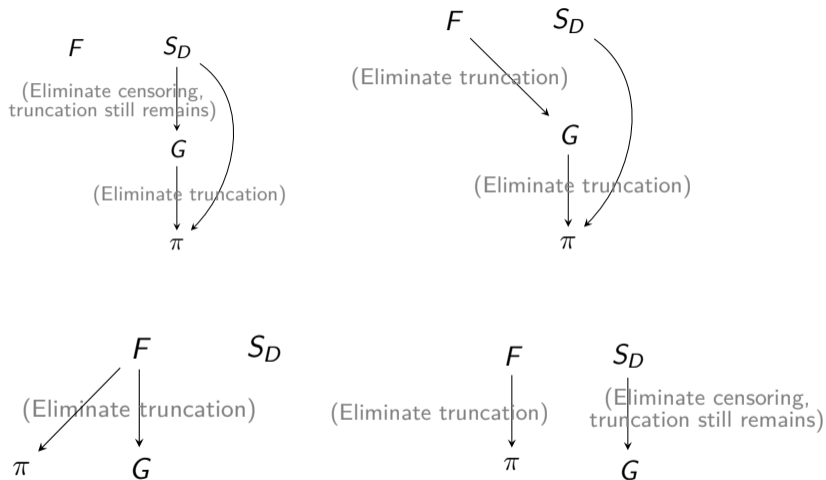


Figure: Different schemes for nuisance parameter estimation.

Instantiation for the ItrcR- and ItrcDR-learners

- ItrcR-learner:

$$\begin{aligned} & \|\hat{\pi} - \pi_0\|_4^2 + \|\hat{F} - F_0\|_{\text{sup},4} \cdot \|\hat{\pi} - \pi_0\|_4 \\ & + \|\hat{F} - F_0\|_{\text{sup},4} \cdot \left\{ \|\hat{G} - G_0\|_{\text{sup},4} + \|\hat{S}_D - S_{D0}\|_{\text{sup},4} \right\} \\ & + \|K_1(\hat{g}, g_0)\|_2 + \|K_2(\hat{g}, g_0)\|_2 + \|K_3(\hat{g}, g_0)\|_2 \end{aligned}$$

- $\hat{g} = (\hat{F}, \hat{G}, \hat{S}_D)$; $g_0 = (F_0, G_0, S_{D0})$.
- $K_1(\hat{g}, g_0)$: integral product between $\hat{F} - F_0$ and $\hat{G} - G_0$;
- $K_2(\hat{g}, g_0)$: integral product between $\hat{F} - F_0$ and $\hat{S}_D - S_{D0}$;
- $K_3(\hat{g}, g_0)$: higher order integral products.

Instantiation for the ItrcR- and ItrcDR-learners

- **ItrcR-learner:**

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- **ItrcDR-learner:**

$$\begin{aligned} & \|\hat{F} - F_0\|_{\text{sup},4} \cdot \|\hat{\pi} - \pi_0\|_4 \\ & + \|\hat{F} - F_0\|_{\text{sup},4} \cdot \left\{ \|\hat{G} - G_0\|_{\text{sup},4} + \|\hat{S}_D - S_{D0}\|_{\text{sup},4} \right\} \\ & + \|K_1(\hat{g}, g_0)\|_2 + \|K_2(\hat{g}, g_0)\|_2 + \|K_3(\hat{g}, g_0)\|_2 \end{aligned}$$

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- $K_3(\hat{g}, g_0)$: higher order integral products.

Simulation – ATE

- Estimand: $\theta = \mathbb{P}^*\{T^*(1) > 3\} - \mathbb{P}^*\{T^*(0) > 3\} = -0.1163$.
- 500 simulated data sets each with sample size 1000; 200 bootstrap replications are performed.
- Truncation rate: around 20%; treatment rate: around 50%; censoring rate: around 50%.

Methods	$F/G-\pi-S_D$	bias	SD	SE/bootSE	CP/bootCP
Param	Cox1/Cox1-lgs1-Cox1	0.0014	0.0481	0.0494/0.0519	0.960/0.966
	Cox2/Cox1-lgs1-Cox1	0.0010	0.0477	0.0500/0.0515	0.966/0.960
	Cox1/Cox2-lgs1-Cox1	0.0035	0.0450	0.0451/0.0488	0.950/0.964
	Cox1/Cox1-lgs2-Cox1	0.0010	0.0456	0.0456/0.0487	0.952/0.970
	Cox1/Cox1-lgs1-Cox2	0.0031	0.0496	0.0518/0.0532	0.960/0.964
	Cox2/Cox2-lgs1-Cox1	0.0060	0.0451	0.0475/0.0500	0.964/0.964
	Cox2/Cox1-lgs2-Cox1	0.0195	0.0454	0.0460/0.0479	0.930/0.944
	Cox2/Cox1-lgs1-Cox2	-0.0025	0.0495	0.0524/0.0529	0.968/0.954
cf	pCox/pCox-gbm-pCox	-0.0028	0.0631	0.0635/0.0627	0.960/0.951
IPW	- /Cox1-lgs1-Cox1	-0.0013	0.0528	0.0514/0.0515	0.946/0.942
	- /Cox2-lgs1-Cox1	0.0753	0.0477	0.0494/0.0476	0.662/0.648
	- /Cox1-lgs2-Cox1	0.0067	0.0511	0.0474/0.0496	0.928/0.940
	- /Cox1-lgs1-Cox2	-0.0393	0.0521	0.0517/0.0519	0.872/0.866
	- /pCox-gbm-pCox	0.0430	0.0583	0.0567/0.0516	0.866/0.837
full		-0.0009	0.0185	0.0184/0.0184	0.938/0.944

HAAS – CATE

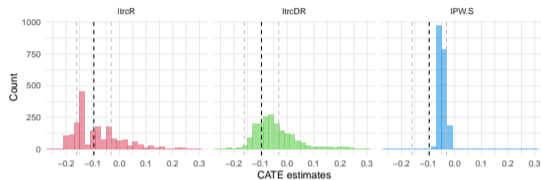


Figure: Histogram of the CATE estimate from different learners; $\nu(t) = I(t > 90)$; the black and grey vertical dashed lines denote the estimate of ATE for the survival probability at 90 years old from the 'cf' estimator and its 95% confidence intervals based on bootstrapped standard errors.