Doubly robust estimation of treatment effects under covariate dependent left truncation and right censoring

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Introduction

- Outcome of interest: time to event (T^*)
- T^* is **left truncated** by the enrollment time (Q^*) if only subjects with $T^* > Q^*$ are included in the data. $\Rightarrow$ **Selection bias**.
  - Usually present in studies with *delayed entry.*
  - E.g., prevelant cohort studes with follow-up, aging studies, pregnancy studies.
- A toy example of aging study:

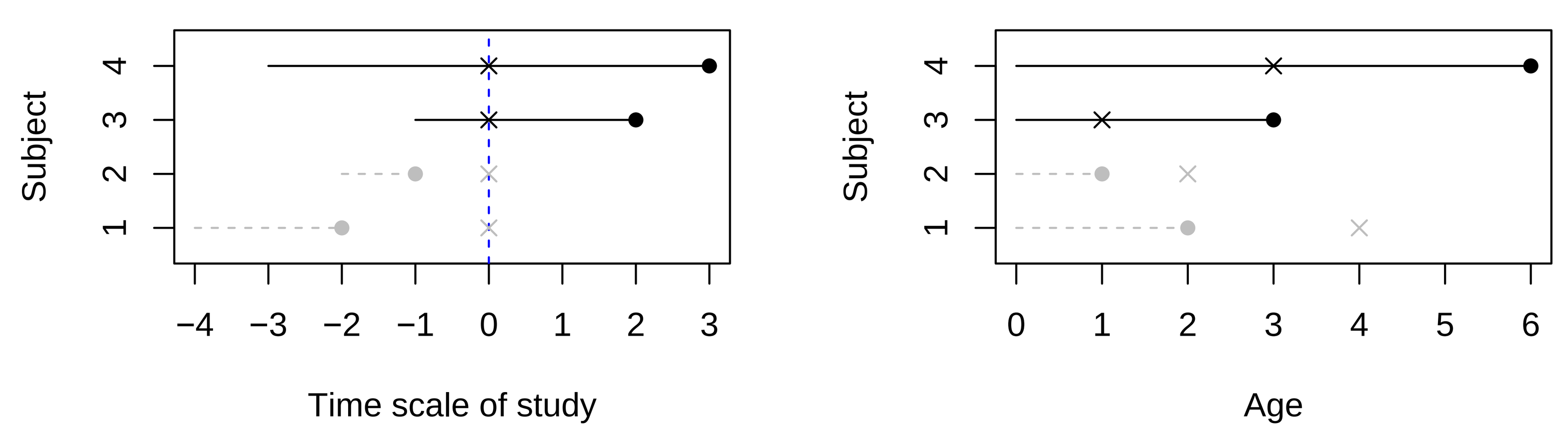
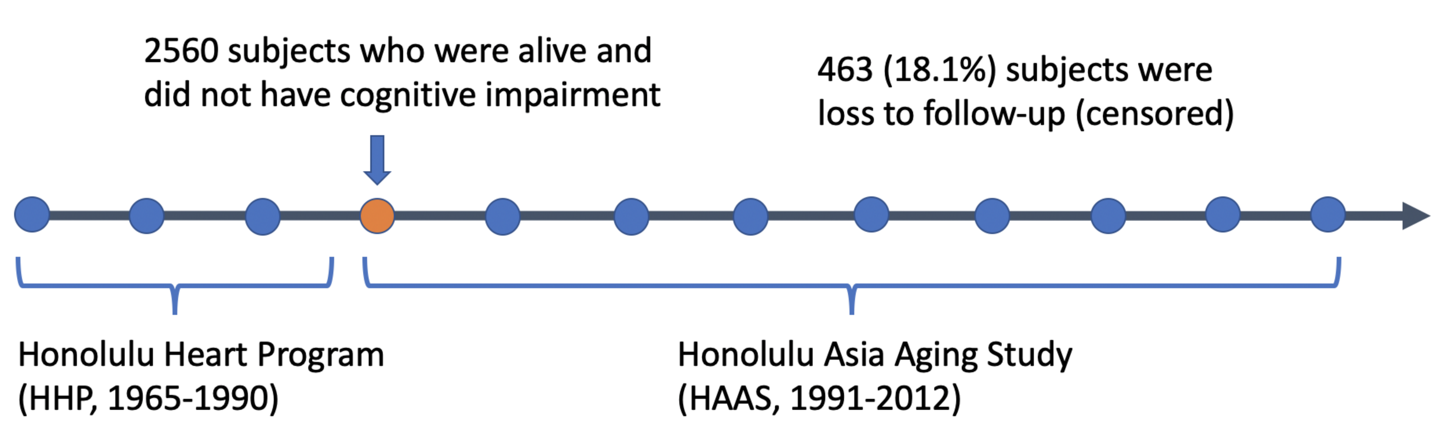


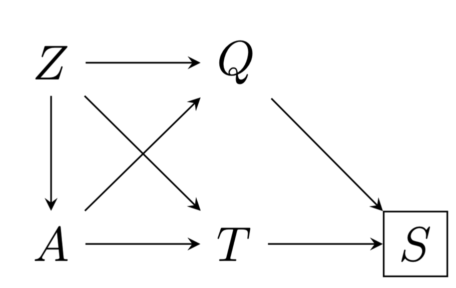
Figure: People's lifespans on the time scale of study (left) and on the age scale (right). Solid dots: event times; '×': enrollment times.

- HAAS data:



Outcome of interest: Cognitive impairment-free survival on the age scale.
T^* - age to moderate cognitive impairment or death.
Q^* - age at entry of HAAS.

- **Triple biases**:
  - Confounding in observational data.
  - **Selection bias from left truncation**
    - Early event times are underrepresented.
  - Informative right censoring.



EIC for $\mathbb{E}\{\nu(T^*)\}$ under left truncation

- The efficient influence curve (EIC) for $\theta = \mathbb{E}\{\nu(T^*)\}$: $\beta \cdot U(\theta; F, G)$,

$$U(\theta; F, G) = \frac{\nu(T) - \theta}{G(T|A, Z)} - \int_0^\infty m_\nu(v, A, Z; \theta, F) \cdot \frac{F(v|A, Z)}{1 - F(v|A, Z)} \cdot \frac{d\bar{M}_Q(v; G)}{G(v|A, Z)},$$

where $\beta = \mathbb{P}(Q^* < T^*)$, $G(t|a, z) = \mathbb{P}(Q^* \le t|A^* = a, Z^* = z)$, $F(t|a, z) = \mathbb{P}(T^* \le t|A^* = a, Z^* = z)$, and $m_\nu(v, a, z; \theta, F) = \mathbb{E}\{\nu(T^*) - \theta \mid T^* < v, A^* = a, Z^* = z\}$.
- **Double robustness**: $\mathbb{E}\{U(\theta_0; F, G)\} = 0$ if either $F = F_0$ or $G = G_0$, where F_0, G_0 denote the truth.
- Constructed *model doubly robust* estimators under asymptotic linearity and *rate doubly robust* estimators under cross-fitting.
- Provided technical conditions for the asymptotic properties that appear to not have been carefully examined in the literature for time-to-event data.
- Represents the **first attempt** to construct doubly robust estimators in the presence of left truncation (selection bias)
  $\rightarrow$ Does *NOT* fall under the established framework of coarsened data where doubly robust approaches are developed.

AIPTW and AIPCW operators

For any $\zeta_1(T^*(a), A^*, Z^*)$ and any $\zeta_2(Q, T, A, Z)$,

$$\mathcal{V}_a(\zeta_1; \pi, \mu_a) = \frac{(A^*)^a(1 - A^*)^{1-a}}{\pi(Z^*)^a\{1 - \pi(Z^*)\}^{1-a}}\zeta_1(T^*, A^*, Z^*) + \frac{(-1)^a\{A^* - \pi(Z^*)\}}{\tilde{\pi}(a, Z^*)}\mathbb{E}\{\zeta_1(T^*, A^*, Z^*)|A^* = a, Z^*\}$$

$$\mathcal{V}_C(\zeta_2; F, S_D)(Q, X, \Delta, A, Z) = \frac{\Delta\, \zeta(Q, X, A, Z)}{S_D(X - Q|Q, A, Z)} + \int_0^\infty \mathbb{E}\{\zeta_@(Q, T, A, Z)|T - Q \ge u, Q, A, Z\}\frac{dM_D(u; S_D)}{S_D(u|Q, A, Z)}.$$

truncAIPW operator

- For any function $\zeta(T^*, Z^*; \theta)$ of the truncation free data, consider the following truncation AIPW operator:

$$\mathcal{V}_Q(\zeta; F, G)(Q, T, A, Z) = \frac{\zeta(T, A, Z; \theta)}{G(T|A, Z)} - \int_0^\infty m_\zeta(v, A, Z; \theta, F) \cdot \frac{F(v|A, Z)}{1 - F(v|A, Z)} \cdot \frac{d\bar{M}_Q(v; G)}{G(v|A, Z)},$$

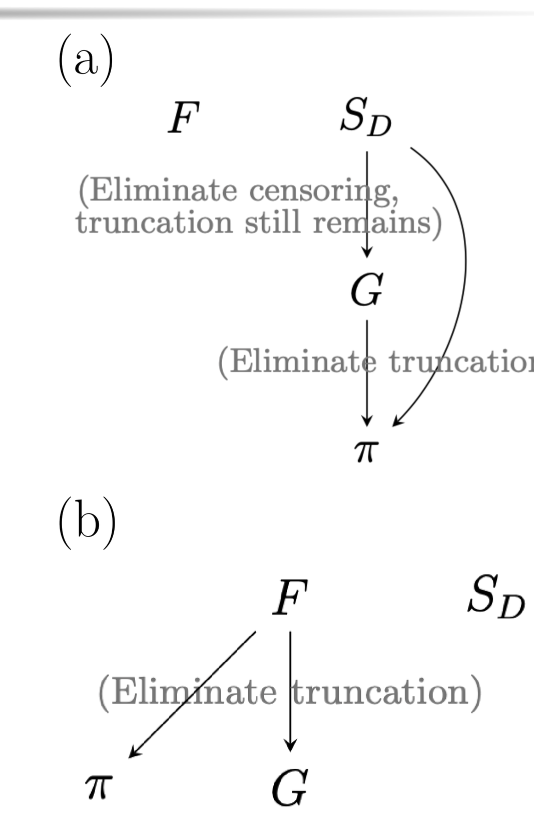
where $m_\zeta(v, a, z) = \mathbb{E}\{\zeta(T^*, Z^*; \theta) \mid T^* < v, A^* = a, Z^* = z\}$.
- **Double robustness**: if either $F = F_0$ or $G = G_0$, then

$$\mathbb{E}\{\mathcal{V}_Q(\zeta; F, G)(Q, T, A, Z)\} = \beta^{-1} \cdot \mathbb{E}\{\zeta(T^*, A^*, Z^*; \theta)\},$$

where $\beta = \mathbb{P}(Q^* < T^*)$.

Framework for handling triple biases

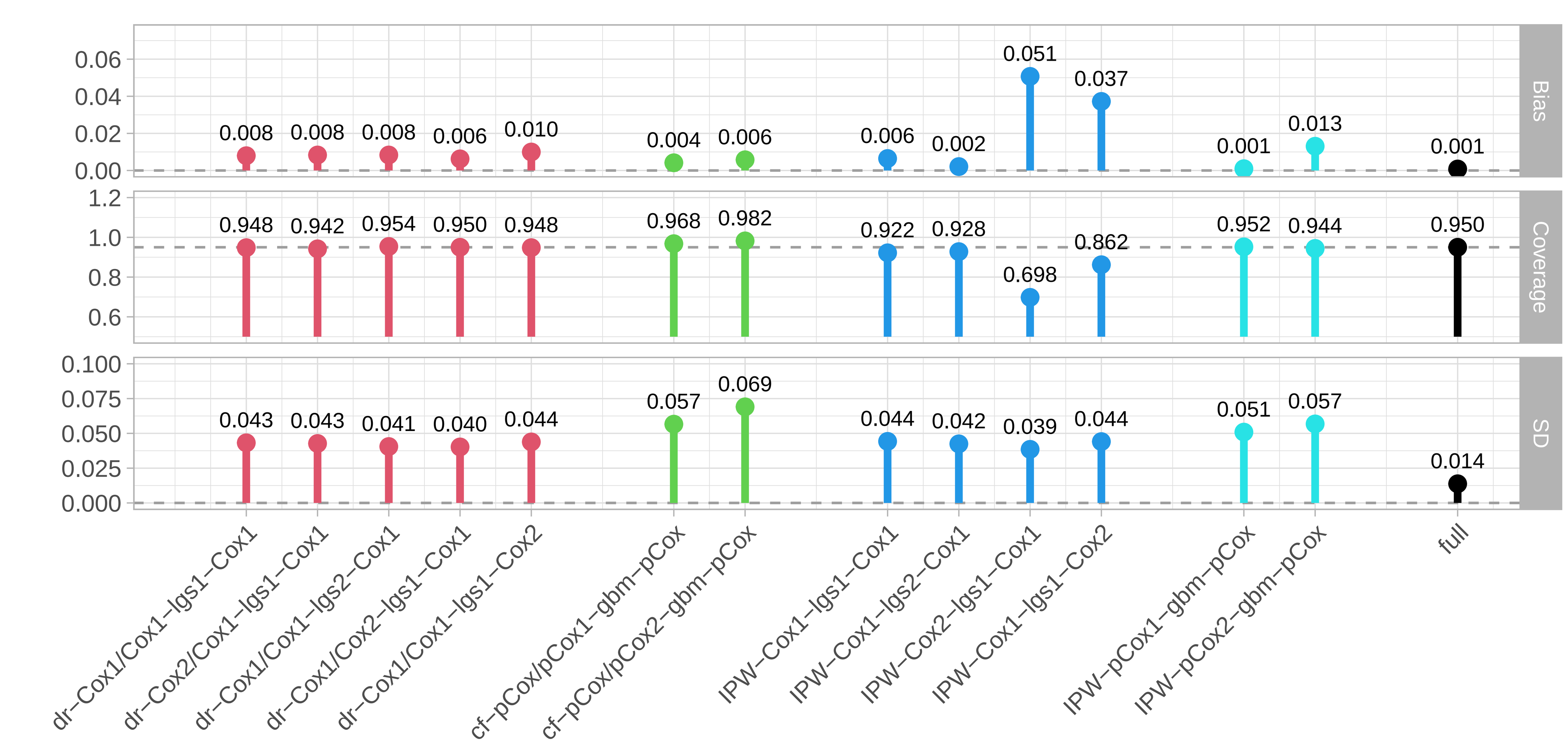
- Estimand θ – defined by the distribution of $(T^*(1), T^*(0), Z^*)$; e,g, ATE: $\mathbb{E}[\nu\{T^*(1)\} - \nu\{T^*(0)\}]$.
- $A \in \{1, 0\}$ – treatment. $T^* = A^*T^*(1) + (1 - A^*)T^*(0)$.
- D – residual censoring. $X = \min(T, Q + D)$, $\Delta = I(T < Q + D)$.



Full data	$\zeta\{T^*(1), T^*(0), Z^*; \theta\}$
	↓ AIPTW
Trunc-free & cen-free data	$\mathcal{V}_A(\zeta; \mu, \pi)(T^*, A^*, Z^*; \theta)$
	↓ truncAIPW
Truncated & cen-free data	$\mathcal{V}_Q \circ \mathcal{V}_A(\zeta; F, \pi, G)(Q, T, A, Z; \theta)$
	↓ AIPCW
Observed data	$\mathcal{V}_C \circ \mathcal{V}_Q \circ \mathcal{V}_A(\zeta; F, \pi, G, S_D)(Q, X, \Delta, A, Z; \theta)$

Simulation results

- 500 simulated data sets each with sample size 1000; estimand: $\theta = \mathbb{P}^*\{T^*(1) > 3\} = 0.5529$.
- Truncation rate: 22.8%; treatment rate: 50%; censoring rate 47.6%.



Orthogonal learning for HTE

- Conditional average treatment effect (CATE): $\tau_0(z) = \mathbb{E}[\nu\{T^*(1)\} - \nu\{T^*(0)\}|Z^* = z]$
- Loss function for truncation-free and censoring-free data: $\ell(T^*, A^*, Z^*; \tau, m, \pi)$; e.g., R-loss (Nie and Wager 2021), DR-loss (Kennedy 2023), etc.
- Apply $\mathcal{V}_C \circ \mathcal{V}_Q$ to ℓ:

$$L(\tau; m, \pi, F, G, S_D) = \mathcal{V}_C \circ \mathcal{V}_Q(\ell; F, \pi, G, S_D)(Q, X, \Delta, A, Z).$$

We have

$$\tau_0 = \arg\min_\tau \mathbb{E}\{L(\tau; F, \pi, G, S_D)\}.$$

- L is a Neyman orthogonal loss
  $\Rightarrow$ Achieve oracle rate if the nuisance parameters are estimated at faster than $n^{-1/4}$ rate.

Additional Information

- Wang, Y., Ying, A., & Xu, R. (2024). Doubly robust estimation under covariate-induced dependent left truncation. *Accepted in Biometrika.* arXiv:2208.06836.
- Code: https://github.com/wangyuyao98/left_trunc_DR.
- Email: yuw079@ucsd.edu (Yuyao Wang).