Targeted learning with right-censored data using the state learner

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Targeted or debiased machine learning

Low-dimensional target parameter

$$\Psi\colon \mathcal{P} \to \mathbb{R}, \quad \text{such that} \quad \Psi(P) = \tilde{\Psi}(\nu_1(P), \dots, \nu_B(P)),$$

for high-dimensional nuisance parameters $\nu_1, \dots, \nu_B$.

(Picture from PhD with multi-state model)

Examples of estimands

Available data $O = (X, \tilde{T}, \tilde{D}) \sim P \in \mathcal{P}$, where

$$\begin{aligned} X &= W \in \mathbb{R}^d \text{ or } X = (W, A) \in \mathbb{R}^d \times \{0, 1\}, \\ \tilde{T} &= T \wedge C \\ \tilde{D} &= \mathbb{1}\{T \leq C\}D, \quad D = 1 \text{ or } D \in \{1, 2\}. \end{aligned}$$

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$$Q(T > t) \overset{(!)}{=} \mathbb{E}_P[e^{-\Lambda_P(t|X)}], \quad (T, X) \sim Q,$$

where

$$\Lambda_P(\mathrm{d}t \mid x) = P(\tilde{T} \in \mathrm{d}t, \tilde{D} = 1 \mid \tilde{T} \geq t, X = x).$$

For (!) to hold we need $C \perp\!\!\!\perp T \mid X$.

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Use $\{(T^a, D^a) : a \in \{0,1\}\} \sim Q$, to denote potential outcomes.

$$Q(T^a \leq t, D^a = 1) \overset{(!)}{=} \mathbb{E}_P\left[\int_0^t e^{-[\Lambda_{1,P}+\Lambda_{2,P}](u|a,W)} \Lambda_{1,P}(\mathrm{d}u \mid a, W)\right],$$

$$\Lambda_{d,P}(\mathrm{d}t \mid a, w) = P(\tilde{T} \in \mathrm{d}t, \tilde{D} = d \mid \tilde{T} \geq t, A = a, W = w).$$

For (!) to hold we need both $C \perp\!\!\!\perp T \mid X$ and causal assumptions.

Targeted learning with super learning

$$\Psi(P) = \mathbb{E}_P\left[\int_0^t e^{-[\Lambda_{1,P}+\Lambda_{2,P}](u|a,W)}\Lambda_{1,P}(\mathrm{d}u \mid a, W)\right]$$

can be written as

$$\Psi(P) = \tilde{\Psi}(\Lambda_{1,P}, \Lambda_{2,P}, P_W).$$

$$\tilde{\Psi}(\hat{\Lambda}_{1,n}, \hat{\Lambda}_{2,n}, \mathbb{P}_n) \quad + \quad \begin{matrix}\text{Targeting/debiasing step} \\ \text{using } \hat{\Gamma}_n \text{ and } \hat{\pi}_n\end{matrix} \quad \longrightarrow \quad \hat{\Psi}_n^*$$

Asymptotic valid inference and $O_P(n^{-1/2})$ convergence for $\hat{\Psi}_n^*$ if

$$\|\hat{\nu}_n - \nu\|_{P,2} = o_P(n^{-1/4}), \quad \text{for all } \hat{\nu}_n \in \{\hat{\Lambda}_{1,n}, \hat{\Lambda}_{2,n}, \hat{\Gamma}_n, \hat{\pi}_n\}.$$

To achieve this we can use a super learner to data-adaptively select an estimator from a library of candidates.

Super learning*

$$\mathcal{D}_n \quad = \quad \boxed{O_1 \,|\, O_2 \,|\, \quad \cdots \qquad \cdots \qquad \cdots}$$

$$\begin{aligned}
\text{Learner} \quad & \mathcal{D}_n \longmapsto a(\mathcal{D}_n) = \hat{\nu}_n \\
\text{Library} \quad & \mathcal{A} = \{a_1, a_2, \dots, a_M\} \\
\text{Loss function} \quad & \mathcal{V} \times \mathcal{O} \ni (\nu, O) \longmapsto L(\nu, O) \in \mathbb{R}
\end{aligned}$$

$$\text{Discrete SL} = \hat{a}_n = \underset{a \in \mathcal{A}}{\operatorname{argmin}} \frac{1}{K} \sum_{k=1}^{K} \frac{1}{|\mathcal{D}_n^k|} \sum_{O_i \in \mathcal{D}_n^k} L\big(a(\mathcal{D}_n^{-k}), O_i\big),$$

*Stone [1974], Geisser [1975], Wolpert [1992], Breiman [1996], van der Laan et al. [2007]

Super learning*

$\mathcal{D}_n^{-1} =$ | $\cdots$ | $\cdots$ |

$\mathcal{D}_n^{1} =$ | O_1 | O_2 | $\cdots$ |

$$
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Super learning*

$\mathcal{D}_n^{-2} = \boxed{O_1 \,|\, O_2 \,|\, \quad \cdots \quad} \qquad \qquad \boxed{\quad \cdots \quad}$

$\mathcal{D}_n^{2} = \qquad \qquad \boxed{\quad \cdots \quad}$

$$
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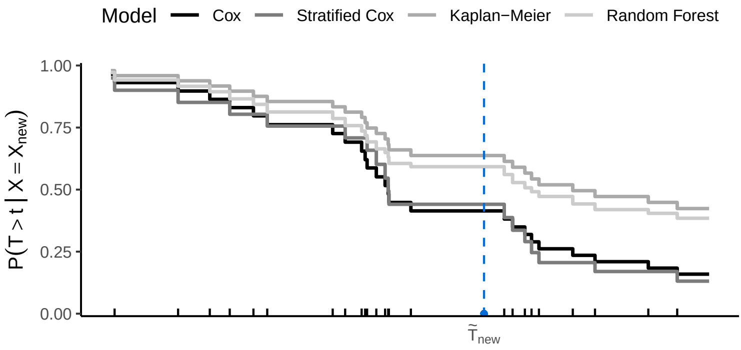
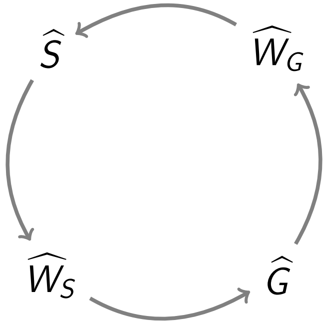
Evaluating performance in hold-out folds is a challenge with right-censored data

The negative log-likelihood is unsuited for super learning

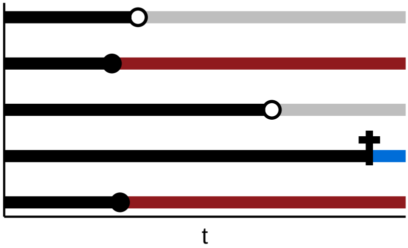


IPCW and pseudo-outcome require pre-specified censoring estimator



The state learner: Model all 'states' of the *observed* data

$$N(t) = \mathbb{1}\{\tilde{T} \leq t, \tilde{D} = 1\} + 2\,\mathbb{1}\{\tilde{T} \leq t, \tilde{D} = 2\} - \mathbb{1}\{\tilde{T} \leq t, \tilde{D} = 0\}$$



Build a super learner for the function

$$F(t, k, w, a) = P(N(t) = k \mid W = w, A = a).$$

Back and forth calculations

Use

$$F(t,0,w,a) = \prod_{0}^{t} \left(1 - [\Lambda_1 + \Lambda_2 + \Gamma]\,(\mathrm{d}s \mid w,a)\right),$$

$$F(t,j,w,a) = \int_0^t F(t-,0,w,a)\Lambda_j(\mathrm{d}s \mid w,a), \quad j \in \{1,2\},$$

$$F(t,-1,w,a) = \int_0^t F(t-,0,w,a)\Gamma(\mathrm{d}s \mid w,a),$$

to build a library for F from libraries for Λ_1, Λ_2, Γ,

$$\mathcal{F}(\mathcal{A},\mathcal{B},\mathcal{C}) = \{F_{a,b,c} : a \in \mathcal{A}, b \in \mathcal{B}, c \in \mathcal{C}\}.$$

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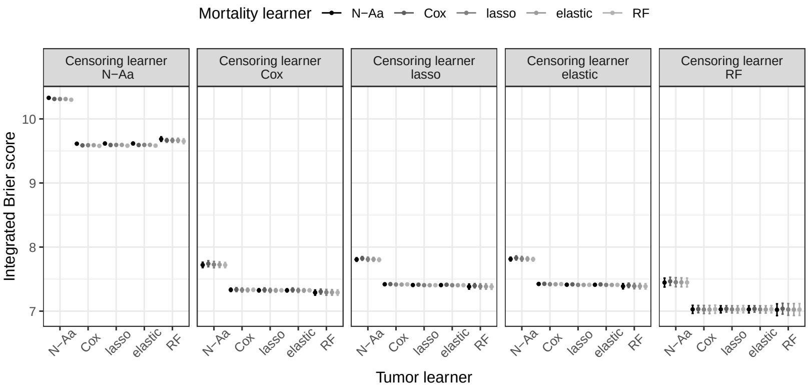
$$

$$
L(F,O) = \int_0^\tau \sum_{j=-1}^{2} \Big(F(t,j,W,A) - \mathbb{1}\{N(t)=j\}\Big)^2 \,\mathrm{d}t.
$$

Illustration with data from a prostate cancer study[†]



[†]Kattan et al. [2000].

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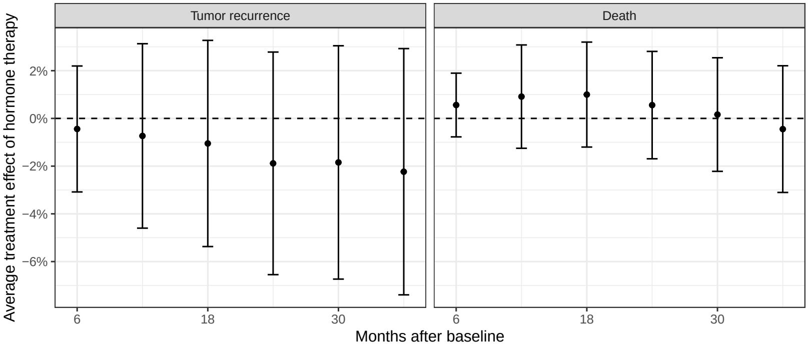

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Theoretical results etc – reference to paper Github

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