Causal parameter estimation with right-censored data using the state learner

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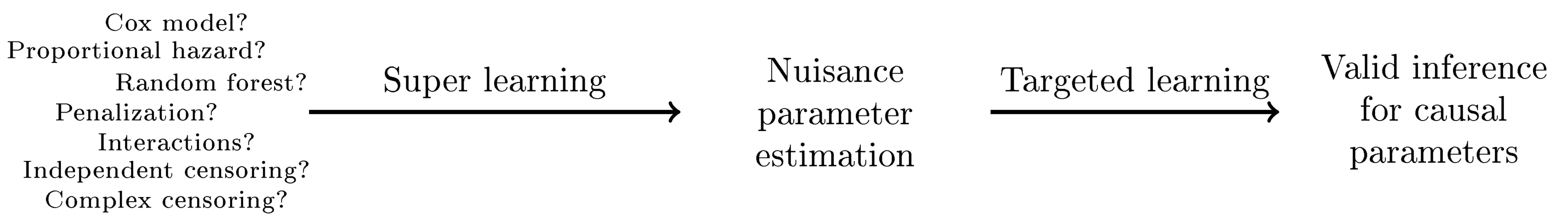
Abstract

The super learner is a machine learning algorithm which combines a library of prediction models into a meta learner based on cross-validated loss. We introduce the state learner, a new super learner for survival analysis, which evaluates the loss based on the observed data simultaneously using libraries of predictions models for the events of interest and the censoring distribution. We establish an oracle inequality for the state learner and investigate its performance through numerical experiments. We illustrate how the state learner allows us to estimate causal effects in a competing risks setting without having to prespecify models for neither the cause-specific hazard functions nor the censoring distribution.

Motivation

Super learning uses cross-validation to decides which estimators best fit the data. In survival analysis the result of super learning can be a risk prediction model. Targeted learning can integrate super learning of nuisance parameters and provide valid post-selection inference for causal parameters.



Problem statement

Ideal data: $(W, T^0, D^0, T^1, D^1) \sim Q$

$W \in \mathcal{W} \subset \mathbb{R}^d$ is a vector of covariates, $T^a \in [0,\tau]$ is a counterfactual time to event variable under treatment a, and $D^a \times \{1,2\}$ denotes the cause of the event. The maximal length of followup is $\tau < \infty$.

Observed data: $O = (W, A, \tilde{T}, \tilde{D}) \sim P$

$A \in \{0,1\}$ is a binary treatment administered in observed data. The pair $(\tilde{T}, \tilde{D})$ is the censored outcome variable, defined as $\tilde{T} = T^a \wedge C^a$ and $\tilde{D}^a = \mathbb{1}\{T^a \le C^a\} D^a$, when $A = a$, for some censoring time C^a.

Targeted estimation of causal effects, such as the average treatment effect

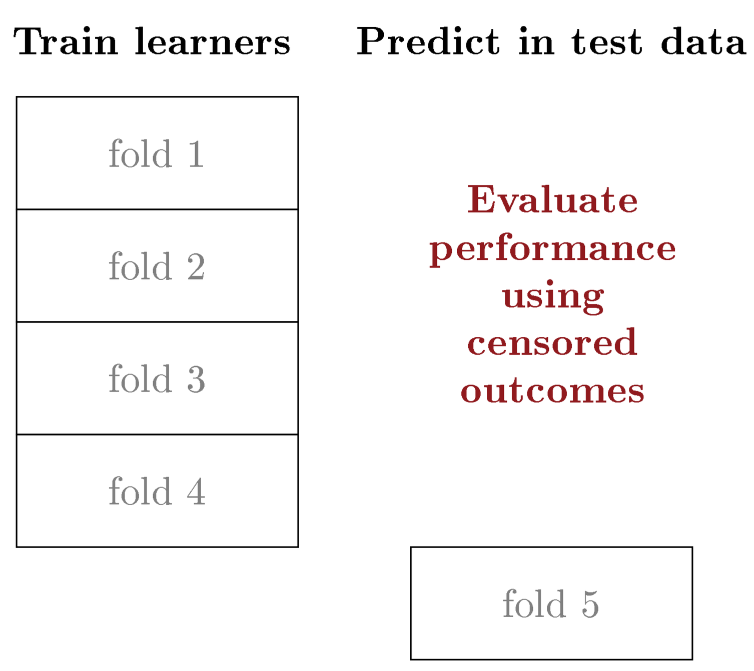
$$\Psi(Q) = Q\big(T^1 \le \tau, D^1 = 1\big) - Q\big(T^0 \le \tau, D^0 = 1\big),$$

rely on estimators of the cause-specific cumulative hazard functions,

$$\Lambda_j(t \mid w, a) = \int_0^t \frac{Q(T^a \in \mathrm{d}s, D^a = j \mid W = w)}{Q(T^a \ge s \mid W = w)}, \quad j \in \{1,2\},$$

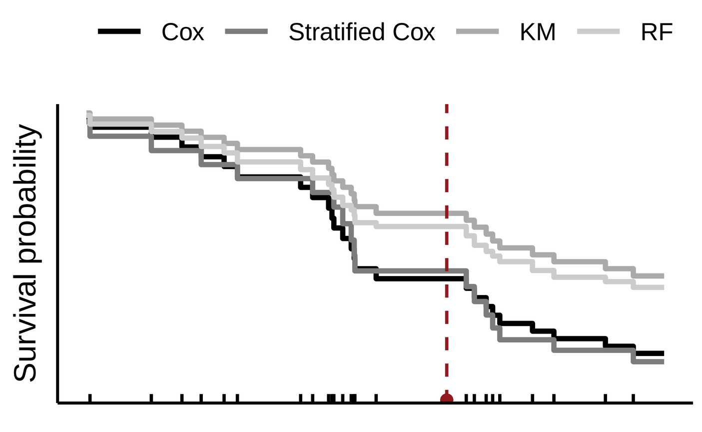
and the censoring probability. Assuming coarsening at random [2, 9], the cause-specific hazard functions and the censoring probability can be estimated based on samples from P. Many existing methods are available for this task, including the Nelson-Aalen estimator, Cox models, random survival forests, Poisson regression, and neural networks.

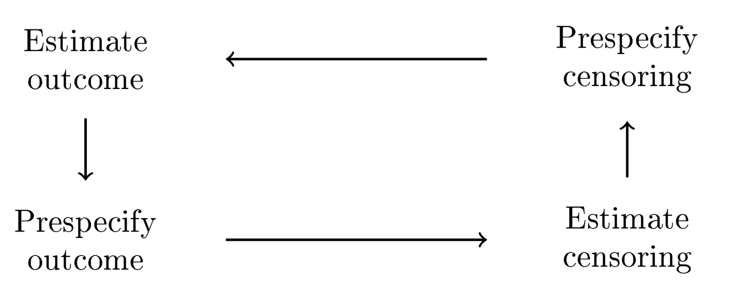
A super learner can be used to data-adaptively select an estimator (called a learner) from a library of candidates. Super learning uses cross-validation to estimate and evaluate the performance of each learner in the library using a given loss function. Our focus in this work is on how a super learner can assess performance in a right-censored validation set without prespecification of an estimator of the censoring probability.



Existing methods

A commonly used loss function in survival analysis is the negative partial log-likelihood loss. This loss is not perfectly suited for super learning because many common survival estimators have infinite loss in a hold out sample. This is illustrated in the figure below to the left. Alternative methods such as inverse probability of censoring weighting [4, 3], pseudo-observations [1, 7], and censoring unbiased transformations [8] rely on a prespecified estimator of the censoring probability. This can lead to a circular reasoning as illustrated in the figure below to the right. A recent proposal is to iteratively estimate the survival and the censoring probabilities [10]. However, no general theoretical guarantees seem to exist for this procedure, and it has not yet been extended to the situation with competing risks.



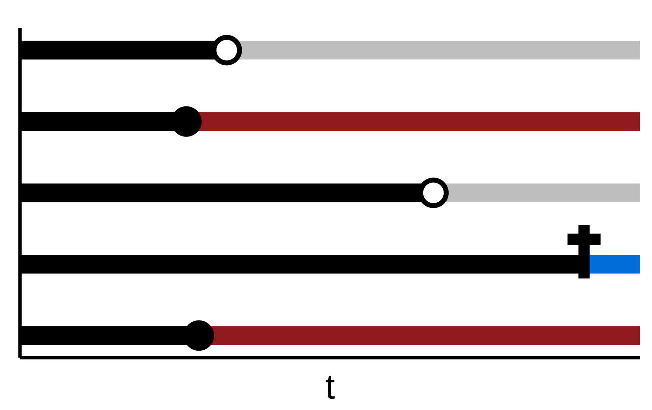


The state learner

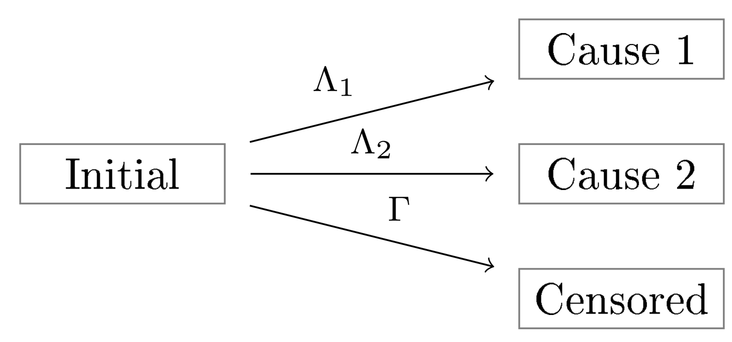
The state learner is a new super learner for survival analysis with competing risks. The input to the state learner are libraries of learners for all transitions of the multi-state model where censoring is considered a state. The observed data can be regarded as realizations of the process $\eta(t) \in \{-1, 0, 1, 2\}$ defined by

$$\eta(t) = \mathbb{1}\{\tilde{T} \le t, \tilde{D} = 1\} + 2\,\mathbb{1}\{\tilde{T} \le t, \tilde{D} = 2\} - \mathbb{1}\{\tilde{T} \le t, \tilde{D} = 0\}, \quad \text{for} \quad t \in [0,\tau].$$

The process η



The states of the observed system



The state learner is a super learner for the conditional state-occupation probability function,

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

Performance of a learner for F is cross-validated in the observed data using the integrated Brier score:

$$\bar{B}_\tau(F, O) = \int_0^\tau B_t(F, O)\,\mathrm{d}t, \quad \text{where} \quad B_t(F, O) = \sum_{j=-1}^{2} \Big(F(t, j, W, A) - \mathbb{1}\{\eta(t) = j\}\Big)^2.$$

Building a library for state learning

Learners of F are obtained using libraries of learners of the cause-specific cumulative hazard functions Λ_1 and Λ_2, and a library for learning the cumulative hazard of censoring, denoted by Γ:

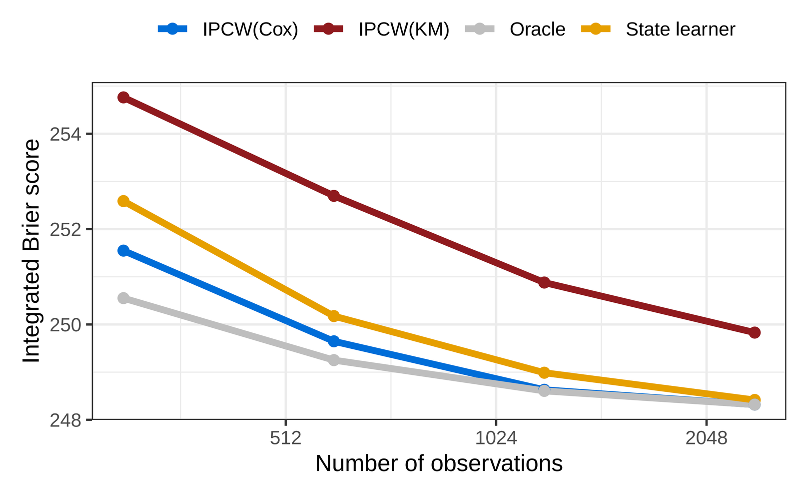
$$F(t, 0, w, a) = P\big(\tilde{T} > t \mid W = w, A = a\big) = \prod_0^t \left(1 - [\Lambda_1 + \Lambda_2 + \Gamma](\mathrm{d}s \mid w, a)\right),$$

$$F(t, j, w, a) = P\big(\tilde{T} \le t, \Delta = j \mid W = w, A = a\big) = \int_0^t F(t-, 0, w, a)\Lambda_j(\mathrm{d}s \mid w, a), \quad j \in \{1,2\},$$

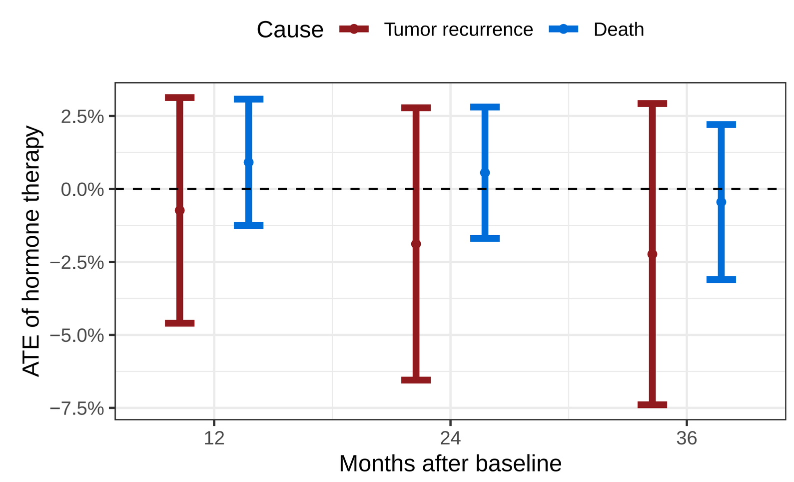
$$F(t, -1, w, a) = P\big(\tilde{T} \le t, \Delta = 0 \mid W = w, A = a\big) = \int_0^t F(t-, 0, w, a)\Gamma(\mathrm{d}s \mid w, a),$$

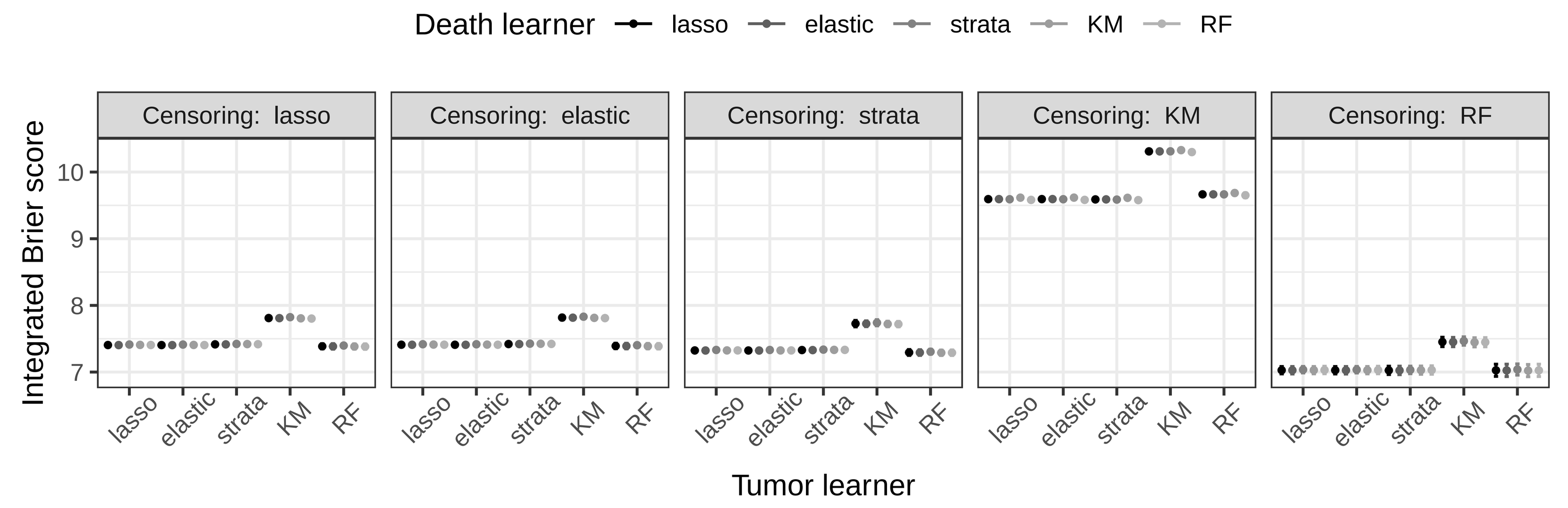
Theoretical and empirical results

In [6] we provide a finite sample oracle inequality for the state learner along with other theoretical results. We confirm these results in a simulation study, where the state learner performs as well as a super learner that uses a correctly specified model to estimate inverse probability of censoring weights. The state learner learns the correct censoring model from the data at the same time as learning the outcome model. This is illustrated in the figure to the right.



We apply the state learner to data from an observational prostate cancer study [5]. The state learner's ranking of all triples of learners from the provided libraries are visualized in the figure below. In [6] we show how estimators of the average treatment effect of hormone therapy on tumor recurrence and death can be obtained from the output of the state learner. The results are shown in the figure to the right.





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