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

Anders Munch & **Thomas Gerds**

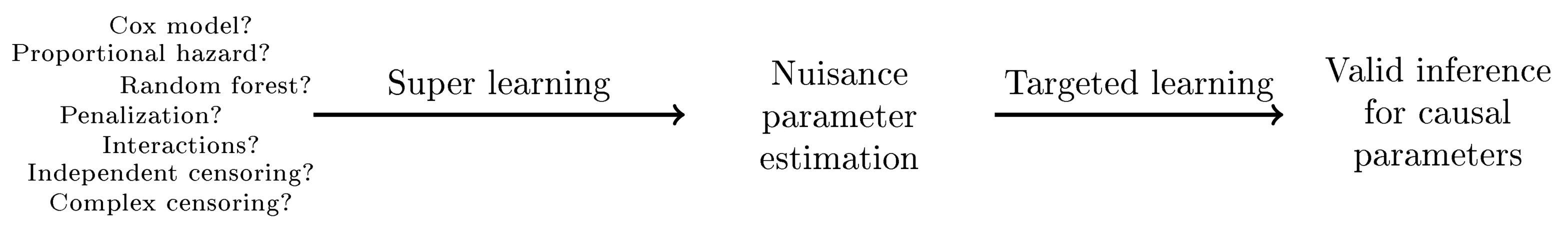
Section of Biostatistics, University of Copenhagen

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. Unfortunately, when data are right-censored the commonly used partial likelihood loss is not suited for super learning, and inverse probability of censoring weighted loss functions require a prespecified estimator of the censoring distribution. To relax this, 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 event(s) 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

Prespecification of estimators for survival and censoring probabilities can be difficult with observational data. Super learning uses the data to decides which estimators best fit the data. Targeted learning can correct the bias stemming from this data-adaptive model selection step, providing valid post-selection inference for causal parameters.



Problem statement

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

$W \in \mathcal{W} \subset \mathbb{R}^d$ 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 $\tilde{D}^a = \mathbb{1}\{T^a \leq C^a\} D^a$, when $A = a$, for some censoring time C^a.

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

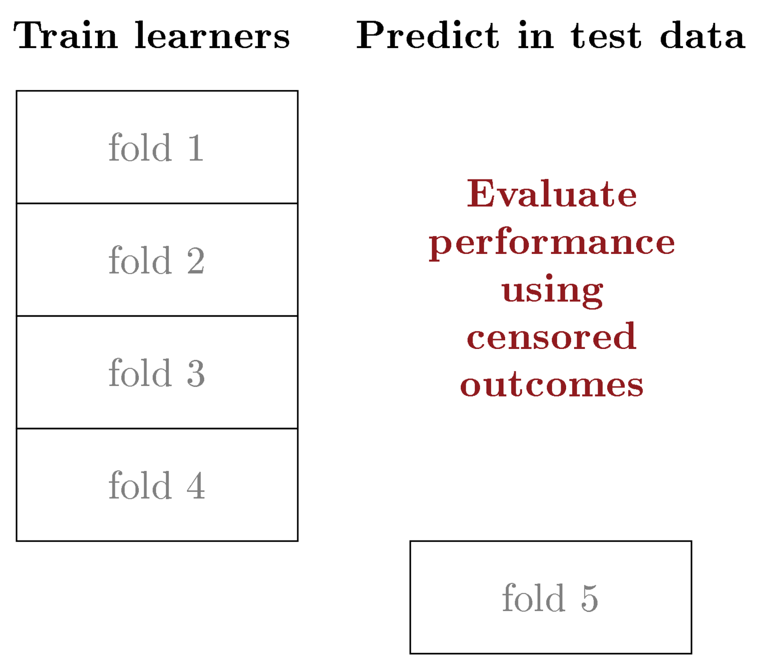
$$\Psi(Q) = Q\big(T^1 \leq \tau, D^1 = 1\big) - Q\big(T^0 \leq \tau, D^0 = 1\big),$$

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

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

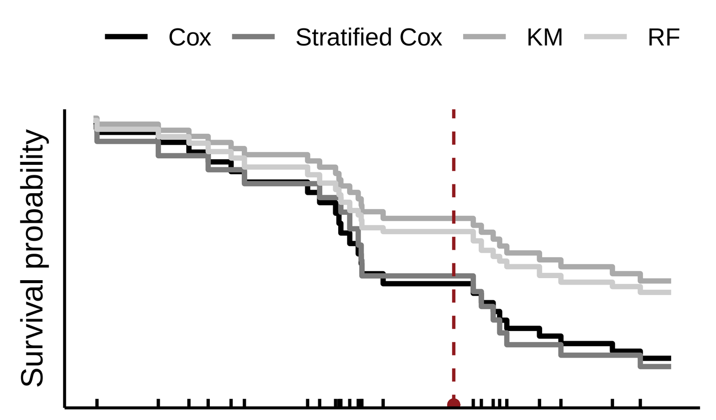
and the censoring probability. Assuming coarsening at random [2, 9], the cause-specific hazard functions and the censoring probability can be estimated based on samples from P. Many existing methods are available for this task, including the Nelson-Aalen estimator, Cox models, random survival forests,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

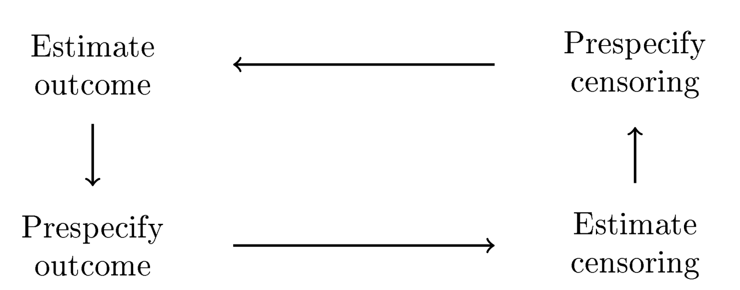
A super learner can be used to data-adaptively select an estimator (called a learner) from a library of candidates. Super learning uses cross-validation to estimate and evaluate the performance of each learner in the library using a given loss function. Our focus in this work is on how a super learner 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 unsuited for super learner because many common survival estimators will have infinite loss in any hold out sample as 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 in a context without competing events is based on iterative estimation of the survival and the censoring probabilities in the hope that this is not a vicious circle [10].

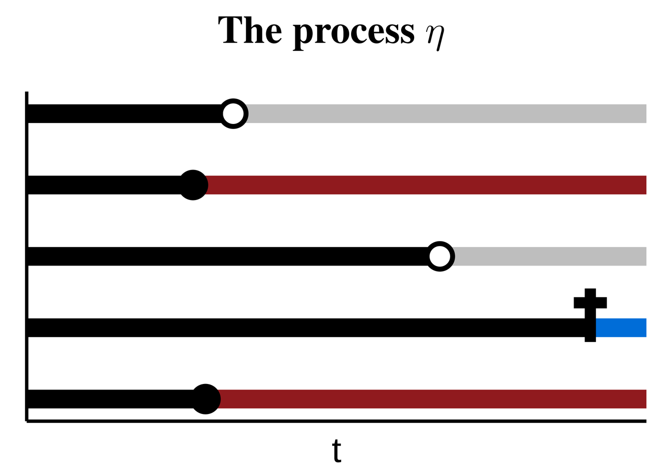


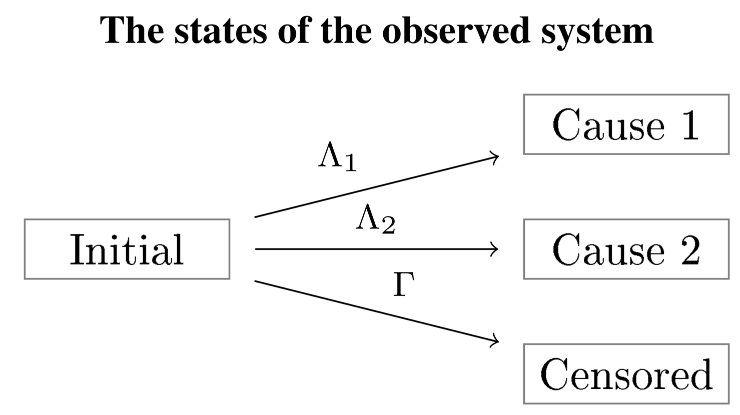


The state learner

The state learner models the observed system as an *artificial* multi-state system where censoring is considered a state. After baseline the observed data can be encoded by the process $\eta(t) \in \{-1, 0, 1, 2\}$ defined as

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





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 model for F can be estimated directly in the observed data, e.g., 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 not directly available. However, given libraries of learners of cause-specific cumulative hazard functions Λ_1 and Λ_2, and a library for learning the cumulative hazard of censoring, denoted by Γ, we can obtain a library of learners for F using the relations below. Most existing survival estimators provide estimates of cumulative hazard functions, so these learner are easily available.

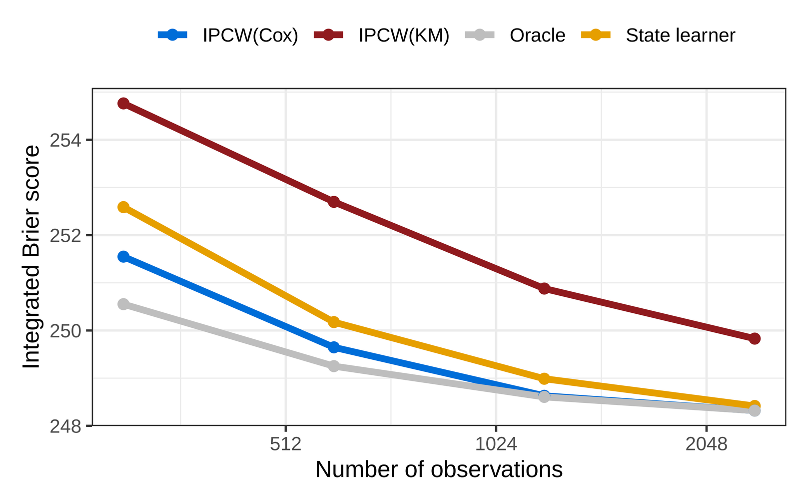
$$F(t, 0, w, a) = P\big(\tilde{T} > t \mid W = w, A = a\big) = \prod_0^t \left(1 - [\Lambda_1 + \Lambda_2 + \Gamma](\mathrm{d}s \mid w, a)\right),$$

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

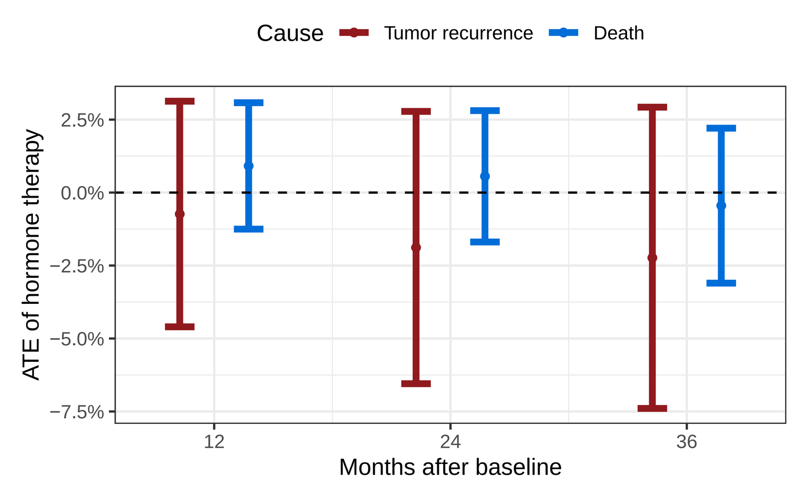
$$F(t, -1, w, a) = P\big(\tilde{T} \leq t, \Delta = 0 \mid W = w, A = a\big) = \int_0^t F(t-, 0, w, a)\Gamma(\mathrm{d}s \mid w, a),$$

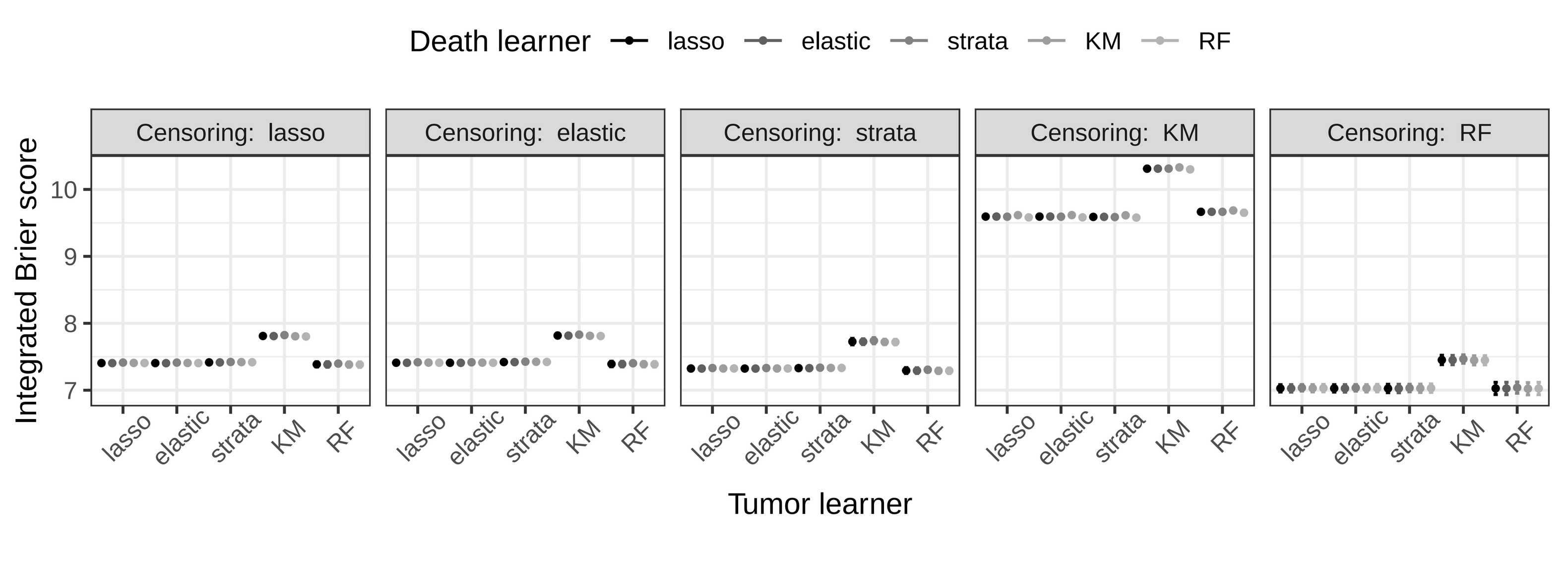
Theoretical and empirical results

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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