ConCR-TMLE R Paper

David Chen, Thomas Gerds, Helene Rytgaard

Abstract

An abstract of less than 150 words.

1 Introduction

Introductory section which may include references in parentheses (**?**), or cite a reference such as **?** in the text.

2 Data Structure

Consider a survival analysis on an interval $[0, t_{max}]$ with competing risks. Let T_j^a denote counterfactual time-to-event variables for event j and intervention a, for competing events $j \in \mathcal{J} = \{1, 2, \ldots, J\}$ and an intervention $a \in \mathcal{A}$. Our counterfactual data structure can then be denoted by

$$(T_j^a, \mathbf{X} \, : \, a \in \mathcal{A}, \, j \in \mathcal{J})$$

where $\mathbf{X} \in \mathbb{R}^d$ is a d-dimensional vector of baseline covariates. For a single time-point binary intervention, as in many randomized control trials, $\mathcal{A} = \{0, 1\}$ and the corresponding counterfactual data is

$$(T_j^1, \, T_j^0, \, \mathbf{X} \, : \, j \in \mathcal{J})$$

> ## sample data.table for counterfactual data

Let O denote the corresponding coarsened observed data where $O \sim P_0$. The observed data would include the time-to-censoring C, and observed intervention A. The time to first event (censoring or otherwise) we denote as $\widetilde{T} = \min(C, \, T_j \, : \, j \in \mathcal{J})$ with $\Delta = (\operatorname*{argmin}_j T_j) \times \mathbf{1}(\min_j T_j \leq C)$ marking which outcome is observed ($\Delta = 0$ being that censoring occurred). The observable right-censored survival data with competing events can then be represented as

$$O = (\widetilde{T}, \, \Delta, \, A, \, \mathbf{X})$$

> ## sample data.table of the observed data correlating to
>   the above counterfactual data example

This observed data also allows the "long-format" formulation, where with single time-point intervention variable A and baseline covariate vector $\mathbf{X}$,

$$O = (N_j(t),\ N_c(t),\ A,\ \mathbf{X}\ :\ j \in \mathcal{J}, t \le \widetilde{T})$$

Here $N_j(t) = \mathbf{1}(\widetilde{T} \le t, \Delta = j)$ and $N_c(t) = \mathbf{1}(\widetilde{T} \le t, \Delta = 0)$ denote counting processes for event j and censoring respectively.

Under coarsening at random (CAR), the observed data likelihood can be factorized as

$$p(O) = p(\mathbf{X})\,\pi(A \mid \mathbf{X})\,\lambda_c(\widetilde{T} \mid A,\ \mathbf{X})^{\mathbf{1}(\Delta=0)} S_c(\widetilde{T}\text{-} \mid A,\ \mathbf{X}) \prod_{j=1}^{J} S(\widetilde{T}\text{-} \mid A,\ \mathbf{X})\lambda_j(\widetilde{T} \mid A,\ \mathbf{X})^{\mathbf{1}(\Delta=j)}$$

where $\lambda_c(t \mid A,\ \mathbf{X})$ is the hazard of the censoring process and $\lambda_j(t \mid A,\ \mathbf{X})$ is the hazard of the jth event process. Additionally

$$S_c(t \mid a,\ \mathbf{x}) = \exp\left(-\int_0^t \lambda_c(s \mid a,\ \mathbf{x})\,ds\right)$$

while in a pure competing risks setting

$$S(t \mid a,\ \mathbf{x}) = \exp\left(-\int_0^t \sum_{j=1}^{J} \lambda_j(s \mid a,\ \mathbf{x})\,ds\right)$$

and

$$F_j(t \mid a,\ \mathbf{x}) = \int_0^t S(s\text{-} \mid a,\ \mathbf{x})\lambda_j(s \mid a,\ \mathbf{x})\,ds$$

$$= \int_0^t \exp\left(-\int_0^s \sum_{j=1}^{J} \lambda_j(u \mid a,\ \mathbf{x})\,du\right)\lambda_j(s \mid a,\ \mathbf{x})\,ds$$

3 Target Parameter

For a target parameter of the treatment regime a^*, cause $k \in J$ cumulative risk at time τ

$$\Psi_{a^*,k,\tau}(P_0) = \mathbb{E}\left[F_k(\tau \mid A = a^*,\ \mathbf{X})\right]$$

the corresponding efficient influence function $D^*_{a^*,k,\tau}(P)(O)$ is

$$\sum_{j=1}^{J} \int_0^\tau \frac{\mathbf{1}(A = a^*)\,\mathbf{1}(s \le \tau)}{\pi(A \mid \mathbf{X})\,S_c(s\text{-} \mid A,\ \mathbf{X})}\left(\mathbf{1}(\delta = k) - \frac{F_k(\tau \mid A,\ \mathbf{X}) - F_k(s \mid A,\ \mathbf{X})}{S(s \mid A,\ \mathbf{X})}\right)$$

$$\left(N_j(ds) - \mathbf{1}(\widetilde{T} \ge s)\,\lambda_j(s \mid A,\ \mathbf{X})\right)\,ds$$

$$+ F_k(t \mid A = a^*,\ \mathbf{X}) - \Psi_{a^*,k,\tau}(P_0)$$

with a clever covariate $h_{a^*,k,j,\tau,s}$

$$h_{a^*,k,j,\tau,s} = \frac{\mathbf{1}(A = a^*)\,\mathbf{1}(s \le \tau)}{\pi(A \mid \mathbf{X})S_c(s\text{-} \mid A,\ \mathbf{X})}\left(\mathbf{1}(\delta = k) - \frac{F_k(\tau \mid A,\ \mathbf{X}) - F_k(s \mid A,\ \mathbf{X})}{S(s \mid A,\ \mathbf{X})}\right)$$

The components of the data distribution that must be estimated are $g(A \mid \mathbf{X})$ and $S_c(t \mid A,\ \mathbf{X})$, $\lambda_j(t \mid A,\ \mathbf{X})$, $F_j(t \mid A,\ \mathbf{X})$, and $S(t \mid A,\ \mathbf{X})$

2

4 Estimation

4.1 Cross-Validation Specification

Let $D_n = \{O_i\}_{i=1}^n$ be an observed sample of n i.i.d observations of $O \sim P_0$. For V-fold cross validation, let $B_n = \{1, ..., V\}^n$ be a random vector that assigns the n observations into V validation folds. For each v in $\{1, ..., V\}$ we then define the set of training indices $\mathcal{T}_v = \{i : B_n(i) = v\}$ with the corresponding set of validation indices $\mathcal{V}_v = \{i : B_n(i) \neq v\}$.

4.1.1 Stratified Cross-Validation

```
# StrataIDs <- as.numeric(factor(paste0(Data[["Trt"]],
    ":", Data[["Event"]])))
# CVFolds <- origami::make_folds(n = Data, fold_fun =
    origami::folds_vfold, strata_ids = StrataIDs)
```

4.2 Propensity Score

For $\pi : D_n \rightarrow$ Let L_π be a loss function such that the risk $\mathbb{E}_0\left[L_\pi(\hat{\pi}, O)\right]$ is minimized when $\hat{\pi} = \pi_0$. For instance, with a binary A, we may specify the negative log loss $L_\pi(\hat{\pi}, O) = \text{-}\log\left(\hat{\pi}(1 \mid \mathbf{X})^A \, \hat{\pi}(0 \mid \mathbf{X}))^{1-A}\right)$. Let $\mathcal{M}_\pi$ be the set of candidate propensity score models. The discrete superlearner selector chooses the candidate propensity score model with the minimal cross validated risk

$$\hat{\pi}^{SL} = \underset{\mathcal{M}_\pi}{\operatorname{argmin}} \sum_{v=1}^{V}$$