Heterogeneous Treatment Effect in Time-to-Event Outcomes: Harnessing Censored Data with Recursively Imputed Trees

Tomer Meir[1], Uri Shalit[2], and Malka Gorfine[2]

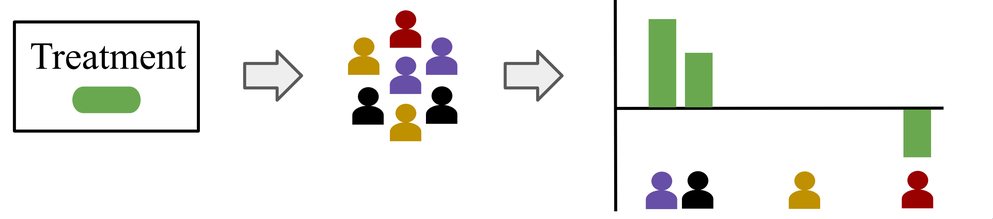
[1] Faculty of Data and Decisions Sciences, Technion - Israel Institute of Technology

[2] Department of Statistics and Operations Research, Tel Aviv University

Goal

Our goal is to estimate heterogeneous treatment effects (HTE) - the way treatments impact different subgroups - in time-to-event data.

Existing methods, such as causal survival forests (CSF) with inverse probability weighting and a doubly robust estimator [1], struggle under heavy censoring and cannot handle instrumental variables (IV).



Methods

Estimand

$$\tau(x) = E\left\{g(\widetilde{T}_i^0) - g(\widetilde{T}_i^1) | X_i = x\right\}$$

for a known function $g(\cdot)$.

For example, with $g(\widetilde{T}_i) = \min(\widetilde{T}_i, h)$, $\tau(\cdot)$ represents the difference in restricted mean survival time (RMST).

Notation

N iid observations

$X_i \in \mathbb{R}^p$ - vector of p covariates of observation i

$\widetilde{T}_i \in \mathbb{R}_+$ - event time

$C_i \in \mathbb{R}_+$ - censoring time

$T_i = \min(\widetilde{T}_i, C_i)$ - observed time

$\delta_i = I(\widetilde{T}_i \leq C_i)$ - event indicator

$W_i \in \{0, 1\}$ - treatment assignment

$\{\widetilde{T}_i^0, \widetilde{T}_i^1\}$ - potential outcomes under $W_i = 0$ and $W_i = 1$

Recursively Imputed Survival Trees

Q-RIST [2] is a forest of M extremely randomized survival trees, trained over Q recursive steps to **estimate the conditional survival function while extracting more information from censored data**.

Each censored observation is imputed M times using the RIST from the previous step.

Generalized Random Forest (GRF)

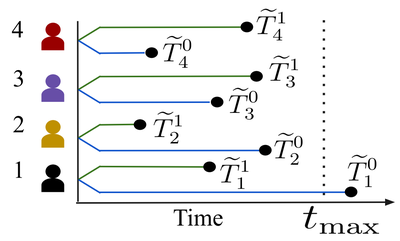
GRF [3] can be used for **estimating HTE** in non-censored data.

Heterogeneity is captured through similarity weights, defined as the fraction of trees in which a given training and test sample share the same leaf.

From Challenges to Solutions: The Proposed Method

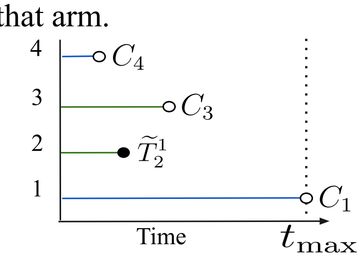
Ideal Data

Each sample would include both potential outcomes - under treatment and under no treatment.



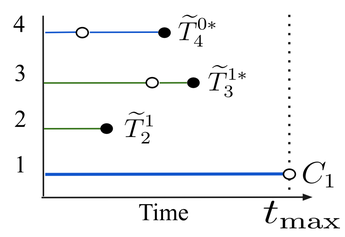
Observed Data

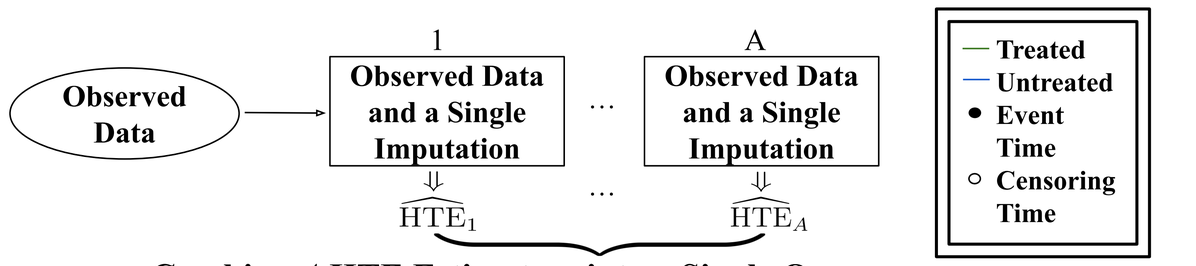
Each sample receives a single treatment, with right-censored observations providing only a lower bound on survival under that arm.



Observed Data and a Single Imputation

Censored data are efficiently imputed by Q-RIST.



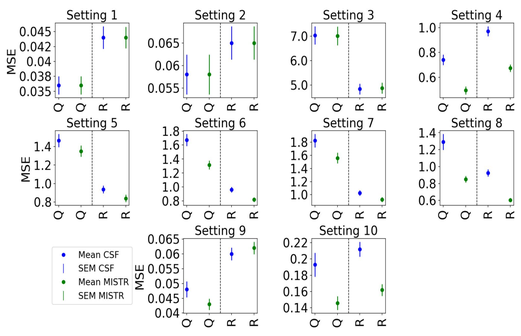


Combine A HTE Estimators into a Single One

Simulations

Performance

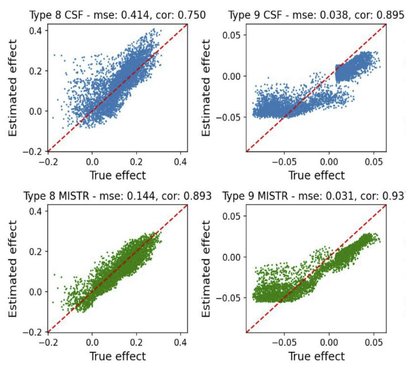
Mean squared error on randomly sampled test set (R) and on covariates quantiles test set (Q).



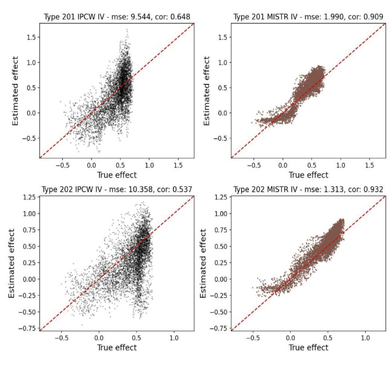
True vs Estimated Effect

Calculated over one random test sample of 5000 observations.

Without confounding



With confounding



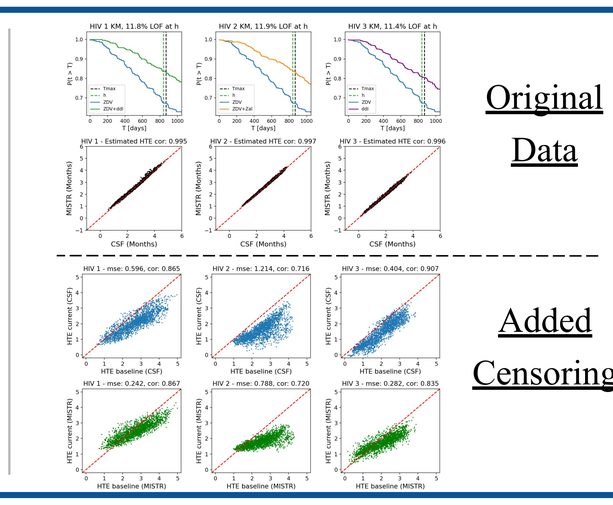
HIV Clinical Trial

Goal: HTE estimation - **which treatment results in longer survival with no AIDS progression?**

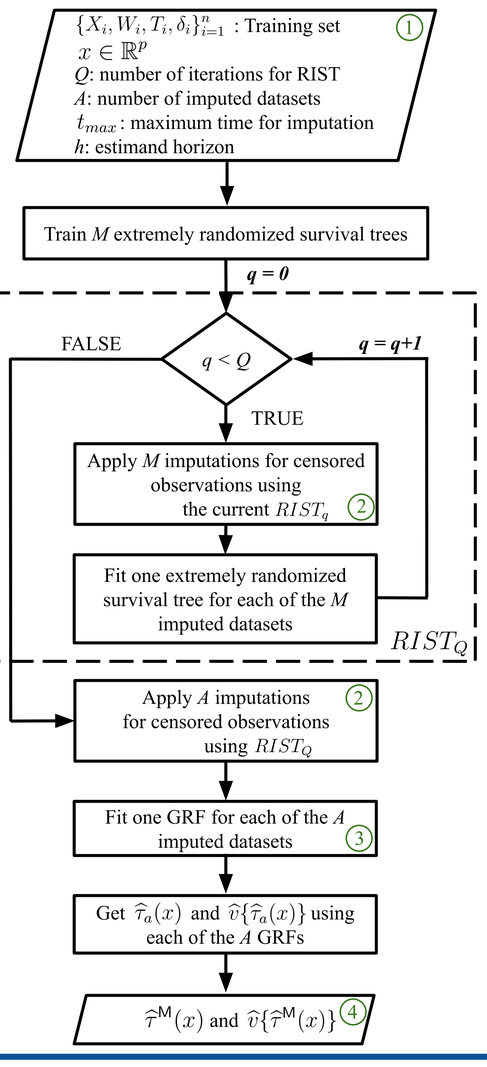
Dataset: N = 2,139 HIV-infected patients with p = 12 covariates, randomized into four treatment groups.

We analyze both the original data and the data with added censoring using MISTR and CSF.

Both methods yield similar results when censoring rate is low; however, MISTR outperforms CSF at high censoring rates.



MISTR Algorithm



Notes

(1) In the IV setting, the training set includes an IV, Z_i, i.e.,

$$\{X_i, W_i, Z_i, T_i, \delta_i\}_{i=1}^n$$

(2) Event times for censored observations are sampled using the estimated conditional survival function:

$$\Pr(\widetilde{T}_i > t \mid X_i, W_i, C_i, \widetilde{T}_i > C_i) = \frac{\Pr(\widetilde{T}_i > t \mid X_i, W_i)}{\Pr(\widetilde{T}_i > C_i \mid X_i, W_i, C_i)}$$

(3) In this step, MISTR employs causal forests [3], while MISTR-IV uses instrumental forests [3].

(4) The final MISTR estimator of the HTE is given by:

$$\widehat{\tau}^{\mathsf{M}}(x) = A^{-1} \sum_{a=1}^{A} \widehat{\tau}_a(x)$$

and the variance of the HTE can be estimated by:

$$\widehat{v}\{\widehat{\tau}^{\mathsf{M}}(x)\} = \overline{v}(x) + \frac{1 + A^{-1}}{A - 1} \sum_{a=1}^{A} \{\widehat{\tau}_a(x) - \widehat{\tau}^{\mathsf{M}}(x)\}^2$$

where

$$\overline{v}(x) = A^{-1} \sum_{a=1}^{A} \widehat{v}\{\widehat{\tau}_a(x)\}$$

is the average of the estimated variances $\widehat{v}\{\widehat{\tau}_a(x)\}$ estimated by each GRF.

Conclusion

This work presents **MISTR - a novel non-parametric approach for estimating HTE and its variance in survival data**:

- **MISTR eliminates the need for estimating the censoring mechanism** and thus expands the range of cases that can be effectively addressed.
- **MISTR outperforms other existing approaches**, especially in heavy censoring rates.
- **MISTR can incorporate an instrumental variable for estimating HTE in presence of unobserved confounding.**

The paper includes additional simulations with realistic covariates, variance sensitivity analysis, weak instrument evaluation, and a real-world use case with unobserved confounding using data from the Illinois Unemployment Insurance Experiment.

References

[1] Cui, Y., Kosorok, M. R., Sverdrup, E., Wager, S., and Zhu, R. ***Estimating heterogeneous treatment effects with right-censored data via causal survival forests***. Journal of the Royal Statistical Society Series B: Statistical Methodology, 85(2):179–211, May 2023.

[2] Zhu, R. and Kosorok, M. R. ***Recursively Imputed Survival Trees***. Journal of the American Statistical Association, 107(497):331–340, March 2012.

[3] Athey, S., Tibshirani, J., and Wager, S. ***Generalized random forests***. The Annals of Statistics, 47(2), April 2019.