Statistical Performance Guarantee for Subgroup Identification with Generic Machine Learning

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January 19, 2023

Winter Workshop on Causal Inference and Its Applications
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Motivation

- Rise of causal machine learning (causal ML)
  1. heterogeneous treatment effects
  2. individualized treatment rules

- Experimental evaluation of causal ML
  1. causal ML algorithms may not work well in practice
  2. need for assumption-lean evaluation with uncertainty quantification

- Today, I will show how to experimentally evaluate:
  1. heterogeneous treatment effects discovered by causal ML
  2. subgroup of exceptional responders identified by causal ML

Setup

- Notation: n experimental units
  1. $T_i \in \{0, 1\}$: binary treatment
  2. X_i: pre-treatment covariates
  3. $Y_i(t)$ where $t \in \{0, 1\}$: potential outcomes
  4. $Y_i = Y_i(T_i)$: observed outcome

- Assumptions:
  1. no interference between units: $Y_i(T_1 = t_1, \ldots, T_n = t_n) = Y_i(T_i = t_i)$
  2. randomization of treatment assignment: $\{Y_i(1), Y_i(0)\} \perp\!\!\!\perp T_i$
  3. random sampling of units: $\{Y_i(1), Y_i(0)\} \overset{\text{i.i.d.}}{\sim} \mathcal{P}$

Evaluation of Heterogeneous Treatment Effects

- How can we make statistical inference for heterogeneous treatment effects discovered by a generic ML algorithm?
- Conditional Average Treatment Effect (CATE):

$$\tau(x) \ = \ \mathbb{E}(Y_i(1) - Y_i(0) \mid X_i = x)$$

- CATE estimation based on ML algorithm

$$s : \mathcal{X} \longrightarrow \mathcal{S} \subset \mathbb{R}$$

- Sorted Group Average Treatment Effect (GATES; Chernozhukov et al.)

$$\tau_k \ = \ \mathbb{E}(Y_i(1) - Y_i(0) \mid c_{k-1} \leq s(X_i) < c_k)$$

  for $k = 1, 2, \ldots, K$ where c_k is a quantile cutoff ($c_0 = -\infty$, $c_K = \infty$)
- Could also use the baseline risk $\mathbb{E}(Y_i(0) \mid X_i = x)$ or some other score

GATES Estimation

- A natural GATES estimator:

$$\hat{\tau}_k \;=\; \frac{K}{n_1}\sum_{i=1}^{n} Y_i T_i \hat{f}_k(X_i) - \frac{K}{n_0}\sum_{i=1}^{n} Y_i(1-T_i)\hat{f}_k(X_i),$$

where $\hat{f}_k(\mathrm{X}_i) \;=\; 1\{s(X_i) \geq \hat{c}_k\} - 1\{s(X_i) \geq \hat{c}_{k-1}\}$ is the group indicator

- Bias is small: finite-sample bound is derived
- Variance:

$$\mathbb{V}(\hat{\tau}_k) \;=\; K^2\left(\frac{\mathbb{V}(\hat{f}_k(X_i)Y_i(1))}{n_1} + \frac{\mathbb{V}(\hat{f}_k(X_i)Y_i(0))}{n_0}\right) \underbrace{-\frac{K-1}{n-1}\mathbb{E}[Y_i(1)-Y_i(0) \mid \hat{f}_k(X_i)=1]^2}_{\text{negative because } \mathrm{Corr}(\hat{f}_k(X_i),\hat{f}_k(X_j))<0}$$

GATES Inference

- Two regularity conditions:
  1. continuity of $\mathbb{E}[Y_i(1) - Y_i(0) \mid s(X_i)]$ at thresholds and bounded variation elsewhere
  2. moment conditions
- Rewrite the GATES estimator as an induced order statistic

$$\hat{\tau}_k = \frac{1}{n} \sum_{i=1}^{n} 1\left\{ \frac{(k-1)n}{K} < i \leq \frac{kn}{K} \right\} \underbrace{K Y_{[i,n]} \left(\frac{T_{[i,n]}}{n_1/n} - \frac{1 - T_{[i,n]}}{n_0/n} \right)}_{:= U_{[i,n]}}$$

where $(Y_{[i,n]}, T_{[i,n]}, X_{[i,n]})$ is ordered s.t. $s(X_{[1,n]}) \leq \cdots \leq s(X_{[n,n]})$

- $U_{[i,n]} - \mathbb{E}[U_{[i,n]} \mid s(X_{[i,n]})]$ is independent of one another given all X
- Asymptotic distribution:

$$\frac{\hat{\tau}_k - \tau_k}{\sqrt{\mathbb{V}(\hat{\tau}_k)}} \xrightarrow{d} N(0, 1)$$

Estimation and Evaluation Using the Same Data

- Cross-fitting:
  1. randomly split the data into L folds: $\mathcal{Z}_1, \ldots, \mathcal{Z}_L$
  2. estimate the CATE using $L-1$ folds: $\hat{f}_{-\ell}$
  3. estimate GATES with the hold-out set: $\hat{\tau}_k^{(\ell)}(\hat{f}_{-\ell})$
  4. repeat the process for each ℓ and average

$$\hat{\tau}_k(S) \;=\; \frac{1}{L}\sum_{\ell=1}^{L}\hat{\tau}_k^{(\ell)}(\hat{f}_{-\ell})$$

  where $S : \mathscr{Z} \longrightarrow \mathcal{S}$ is a generic but stable ML algorithm with $\mathcal{Z}_{\text{train}} \in \mathscr{Z}$ and $\hat{s}_{\mathcal{Z}_{\textbf{train}}} = S(\mathcal{Z}_{\text{train}}) \in \mathcal{F}$

- Estimand: average performance of S

$$\tau_k(S) = \mathbb{E}_{\mathcal{Z}_{\text{train}}}[\mathbb{E}\{Y_i(1) - Y_i(0) \mid c_{k-1}(\hat{f}_{\mathcal{Z}_{\text{train}}}) \leq \hat{f}_{\mathcal{Z}_{\text{train}}}(\mathrm{X}_i) < c_k(\hat{s}_{\mathcal{Z}_{\text{train}}})\}]$$

- Inference without resampling (see Imai and Li. 2023. *JASA*)

Simulation Study

- A highly nonlinear specification from the 2016 ACIC competition
  - 58 covariates (3 categorical, 5 binary, 27 counts, 13 continuous)
  - sample size: $n = 4802$
  - use empirical distribution of X_i as true distribution

- Machine learning algorithms
  - Causal forest and Lasso
  - $L = 5$ and also use 5-fold cross validation for tuning

Evaluation Bias and Coverage under Cross-fitting

	$n = 100$			$n = 500$			$n = 2500$		
	bias	s.d.	coverage	bias	s.d.	coverage	bias	s.d.	coverage
Causal Forest									
$\hat{\tau}_1$	−0.05	2.97	94.0%	−0.01	1.57	95.6%	−0.01	0.59	97.7%
$\hat{\tau}_2$	−0.06	2.58	95.9	−0.04	1.08	98.2	0.01	0.54	98.6
$\hat{\tau}_3$	−0.01	2.56	96.7	−0.05	1.06	97.7	0.02	0.47	98.1
$\hat{\tau}_4$	−0.12	2.87	97.4	0.05	1.15	97.9	−0.01	0.51	98.6
$\hat{\tau}_5$	0.14	3.45	94.1	0.00	1.62	96.0	−0.01	0.62	98.3
LASSO									
$\hat{\tau}_1$	−0.13	3.20	97.6%	−0.03	1.49	96.0%	−0.00	0.67	96.0%
$\hat{\tau}_2$	0.04	2.28	97.5	−0.07	1.03	97.9	−0.02	0.59	98.9
$\hat{\tau}_3$	−0.13	2.35	96.6	−0.02	1.00	97.9	0.04	0.49	97.5
$\hat{\tau}_4$	−0.00	2.54	96.8	0.04	1.17	96.8	0.03	0.64	97.2
$\hat{\tau}_5$	0.11	3.62	96.2	0.05	1.81	95.0	0.02	0.70	95.3

- Reduction in standard errors compared with fixed S of the same evaluation size (see the paper) is more than 50% in some cases

Empirical Application

- National Supported Work Demonstration Program (LaLonde 1986)
- Temporary employment program to help disadvantaged workers by giving them a guaranteed job for 9 to 18 months

- Data
  - sample size: $n_1 = 297$ and $n_0 = 425$
  - outcome: annualized earnings in 1978 (36 months after the program)
  - 7 pre-treatment covariates: demographics and prior earnings

- Setup
  - ML algorithms: BART, Causal Forest, and LASSO
  - Sample-splitting: 2/3 of the data as training data
  - Cross-fitting: 3 folds

GATES Estimates (in 1,000 US Dollars)

	$\hat{\tau}_1$	$\hat{\tau}_2$	$\hat{\tau}_3$	$\hat{\tau}_4$	$\hat{\tau}_5$
Sample-splitting					
BART	2.90	-0.73	-0.02	3.25	2.57
	$[-2.25, 8.06]$	$[-5.05, 3.58]$	$[-3.47, 3.43]$	$[-1.53, 8.03]$	$[-3.82, 8.97]$
Causal Forest	3.40	0.13	-0.85	-1.91	7.21
	$[-1.29, 3.40]$	$[-5.37, 5.63]$	$[-5.22, 3.52]$	$[-5.16, 1.34]$	$[1.22, 13.19]$
LASSO	1.86	2.62	-2.07	1.39	4.17
	$[-3.59, 7.30]$	$[-1.69, 6.93]$	$[-5.39, 1.26]$	$[-2.95, 5.73]$	$[-2.30, 10.65]$
Cross-fitting					
BART	0.40	-0.15	-0.40	2.52	2.19
	$[-3.79, 4.59]$	$[-2.54, 2.23]$	$[-3.37, 2.56]$	$[-0.99, 6.03]$	$[-0.73, 5.11]$
Causal Forest	-3.72	1.05	5.32	-2.64	4.55
	$[-6.52, -0.93]$	$[-2.28, 4.37]$	$[2.63, 8.01]$	$[-5.07, -0.22]$	$[1.14, 7.96]$
LASSO	0.65	0.45	-2.88	1.32	5.02
	$[-3.65, 4.94]$	$[-3.28, 4.18]$	$[-5.38, -0.38]$	$[-1.83, 4.48]$	$[-0.14, 10.18]$

Data-driven Subgroup Identification

- In GATES estimation, the percentile cutoff p is given
- How do you choose p based on the data?
  1. those who benefit from treatment the most (exceptional responders)
  2. those who are harmed by treatment

- Challenges:
  1. sample size may not be large
  2. ML estimates of CATE may be biased and noisy
  3. proportion of exceptional responders may be small
- Can we provide a *statistical* guarantee?

Problem of the Standard Approach

- The problem is trivial if we had an infinite amount of data

$$p^* = \operatorname*{argmax}_{p \in [0,1]} \Psi(p) \quad \text{where } \Psi(p) \; = \; \mathbb{E}[\underbrace{Y_i(1) - Y_i(0)}_{:=\psi_i} \mid F(s(X_i)) \geq p],$$

- Standard method suffers from multiple testing problem:

$$\hat{p}_n \; = \; \operatorname*{argmax}_{p \in [0,1]} \widehat{\Psi}_n(p) \quad \text{where } \widehat{\Psi}_n(p) \; = \; \frac{1}{np} \sum_{i=1}^{\lfloor np \rfloor} \hat{\psi}_{[n,i]}$$

where $s(X_{[n,1]}) \geq \cdots \geq s(X_{[n,n]})$ and

$$\hat{\psi}_{[n,i]} = \frac{T_{[n,i]} Y_{[n,i]}}{n_1/n} - \frac{(1 - T_{[n,i]}) Y_{[n,i]}}{n_0/n}$$

Providing a Statistical Performance Guarantee

- (one-sided) Uniform confidence band:

$$\mathbb{P}\left(\forall p \in [0,1],\ \Psi(p) \geq \widehat{\Psi}_n(p) - C_n(p,\alpha)\right) \geq 1-\alpha.$$

- Safe identification of exceptional responders:

$$\underline{\hat{p}}_n \;=\; \operatorname*{argmax}_{p\in[0,1]} \widehat{\Psi}_n(p) - C_n(p,\alpha),$$

implying

$$\begin{aligned}\mathbb{P}\left(\Psi(p^*) \geq \widehat{\Psi}_n(\underline{\hat{p}}_n) - C_n(\underline{\hat{p}}_n,\alpha)\right) &\geq\; \mathbb{P}\left(\Psi(\underline{\hat{p}}_n) \geq \widehat{\Psi}_n(\underline{\hat{p}}_n) - C_n(\underline{\hat{p}}_n,\alpha)\right)\\ &\geq\; 1-\alpha.\end{aligned}$$

- Other data-driven selection of p is possible: e.g., for a given c

$$\begin{aligned}\text{estimate}\ \ \underline{\hat{p}}_n(c) &= \sup\{p\in[0,1] : \widehat{\Psi}_n(p) - C_n(p,\alpha) \geq c\},\\ \text{to target}\ \ p^*(c) &= \sup\{p\in[0,1] : \Psi(p) \geq c\}\end{aligned}$$

Constructing Uniform Confidence Band

1. Obtain finite-sample bias bound and variance of $\widehat{\Psi}_n(p)$ as before
2. Use a generalized version of Donsker's invariance principle to show:

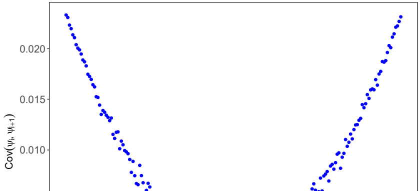
$$\left(\frac{\mathbb{V}(\frac{i}{n}\widehat{\Psi}_n(\frac{i}{n}))}{\mathbb{V}(\widehat{\Psi}_n(1))}, \frac{\frac{i}{n}\Psi(\frac{i}{n}) - \frac{i}{n}\widehat{\Psi}_n(\frac{i}{n})}{\sqrt{\mathbb{V}(\widehat{\Psi}_n(1))}} \right) \xrightarrow{d} (p, G(p)) \quad \text{for } i = 1, \ldots, n.$$

Recall

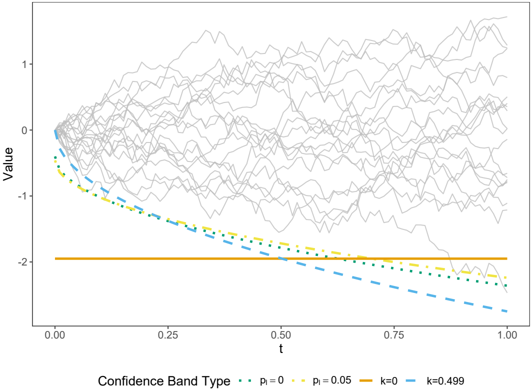
$$\widehat{\Psi}_n(p) \;=\; \frac{1}{np} \sum_{i=1}^{\lfloor np \rfloor} \hat{\psi}_{[n,i]}$$

3. Sorted individual treatment effects are always non-negatively correlated

$$\text{Corr}(\hat{\psi}_{[n,i]}, \hat{\psi}_{[n,j]}) \geq 0 \quad \text{for any } 1 \leq i < j \leq n$$



Minimum-Area Confidence Band



$$\lim_{n\to\infty} \mathbb{P}\left(\forall p \in [0,1], \Psi(p) \geq \widehat{\Psi}_n(p) - \underbrace{\frac{\beta_0^*(\alpha)}{p}\sqrt{\mathbb{V}(\widehat{\Psi}_n(1))}}_{\text{extra CI}} - \underbrace{\beta_1^*(\alpha)\sqrt{\mathbb{V}(\widehat{\Psi}_n(p))}}_{\text{standard CI}} \right) \geq 1-\alpha$$

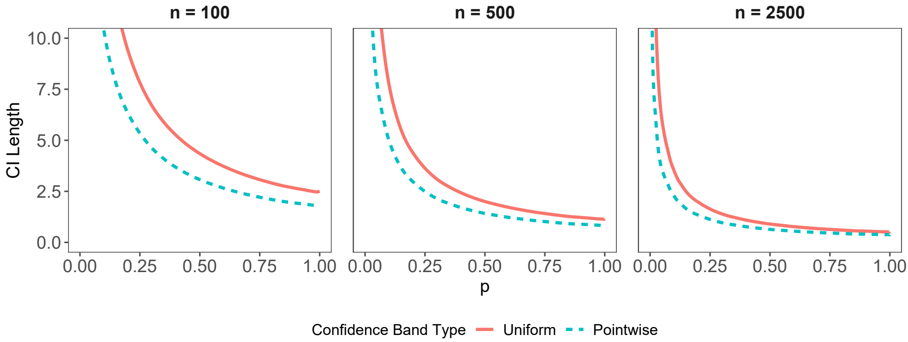
where $\{\beta_0^*(\alpha), \beta_1^*(\alpha)\}$ are the solution to:

$$\underset{\beta_0,\beta_1\in\mathbb{R}_+^2}{\text{argmin}} \int_0^1 \beta_0 + \beta_1\sqrt{t}\; dt \quad \text{subject to} \quad \mathbb{P}\left(W(t) \leq \beta_0 + \beta_1\sqrt{t},\ \forall t \in [0,1] \right) \geq 1-\alpha.$$

Simulation Studies

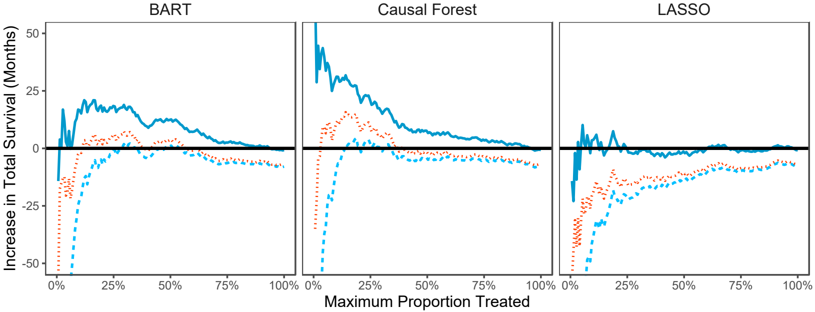
- A data generating process from the ACIC

ML algorithm	Uniform			Pointwise		
	$n = 100$	$n = 500$	$n = 2500$	$n = 100$	$n = 500$	$n = 2500$
BART	96.1%	96.0%	95.2%	87.2%	76.5%	70.3%
Causal Forest	96.0%	95.3%	95.7%	83.7%	77.1%	71.9%
LASSO	95.8%	95.6%	95.6%	84.1%	76.0%	69.8%



Empirical Application

- Clinical trial data on late-stage prostate cancer ($n_1 = 125$, $n_0 = 127$)
- Outcome: total survival in months, Treatment: estrogen
- Sample-split (40% train., 60% eval.), ATE estimate -0.3 month



ML algorithm	Estimated proportion of exceptional responders	Estimated GATES	90% uniform confidence band
Causal Forest	18.8%	27.2	$(4.45, \infty)$
BART	32.2%	18.1	$(2.12, \infty)$
LASSO	91.2%	1.35	$(-6.26, \infty)$

Concluding Remarks

- Causal machine learning (ML) is rapidly becoming popular
  - estimation of heterogeneous treatment effects
  - development of individualized treatment rules
- Safe deployment of causal ML requires uncertainty quantification
- Subgroup identification with statistical performance guarantees
  - Does not assume that ML algorithms are accurate
  - Computationally efficient (no resampling)
  - Applicable to any complex causal ML algorithms
  - Good small sample performance
- Open source software: evalITR: Evaluating Individualized Treatment Rules at CRAN `https://CRAN.R-project.org/package=evalITR`
- More information: `https://imai.fas.harvard.edu/research/`