Efficient machine learning for causal effects

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Outline

Quick Note on Efficiency

Efficiency refers to *statistical* efficiency of an estimator

- Low mean squared error

Cross-fitting procedures are not *computationally* efficient

Notation

Y_i: observed outcome of interest for individual i

X_i: observed exposure or treatment of interest

$Y_i(x)$: potential outcome under exposure set to x

Z_i: covariate(s)

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Motivating Problem

Our collaborators want us to help them address what the difference in the risk of atherosclerotic cardiovascular disease (Y) had been if everyone was given statins ($x = 1$) compared to if no one was given statins ($x = 0$)?

$$\psi = E[Y(x = 1)] - E[Y(x = 0)]$$

They are planning on collecting some observational (non-investigator randomized) data to address this.

Identification

Identifiability Assumptions

Need to determine under what assumptions the average causal effect is *identifiable*

One set of identifiability assumptions

- Causal consistency
- Conditional exchangeability
- Positivity

Causal Consistency

An assumption regarding the potential outcomes observed

- We are able to observe at least one for some individuals

For X can write as

$$Y_i = Y_i(x) \text{ if } x = X_i$$

or as the treatment-variation irrelevance analog

$$Y_i = Y_i(x, b) \text{ for all } b \in B$$

where b could be versions of statins (e.g., 10mg vs 100mg)

Conditional Exchangeability

Synonyms

- No unmeasured confounding
- Potential outcomes of ASCVD are conditionally independent of statin use
- No unmeasured common causes of statins and ASCVD

Requires substantive knowledge outside of the data

- Directed Acyclic Graph
- Single-World Intervention Graph

Positivity

Conditional exchangeability requires that the probability for all values of statins to be non-zero in all strata of the confounders

$$\text{if } \Pr(Z = z) > 0 \text{ then } \Pr(X = x | Z = z) > 0$$

Positivity violations

- Some individuals never have access to statins
- Example: statins for children under 18 without inherited hypercholesterolemia

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Estimation

Motivating Problem

After discussion with our collaborators, the following covariates are determined to be confounders:

- Age
- Low-density lipoprotein (LDL)
- American Heart Association's ASCVD risk scores
- Diabetes

Model-free Causal Inference

When Z is low-dimensional

- No model is required
- Directly apply the non-parametric g-formula
- Unlikely in practice

Our Z includes continuous covariates (LDL, ASCVD risk scores)

- Model-free is not an option

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High-Dimensional Data

High-dimensional data

- Continuous Z or more strata of z than n
  - LDL can range from less than 100 to more than 190
- Sparse data in comparison to data dimension

How can we make progress?

- Categorize
  - E.g., LDL as $<$140, 140-159, 160-189, 190$+$
- Model

Categorize

Model

Model is an *a priori* restriction on the distribution of the data

- Parametric model restricts to a parametric distribution
- Not necessary for identification
- Adds information not in the data

Two processes can choose to model (nuisance models)

- exposure-model: $\Pr(X|Z;\alpha) = \pi(Z;\alpha)$
- outcome-model: $\Pr(Y|X = x, Z;\beta) = m_x(Z;\beta)$

No Model Misspecification

Addition of information via a model is not free

- Requires the addition of assumption on model specification
- True density is within model's ($\mathcal{M}$) class of densities
- exposure-model: $\Pr(X|Z) \in \mathcal{M}_\alpha$
- outcome-model: $\Pr(Y|X,Z) \in \mathcal{M}_\beta$

Implications

- Suggests use of flexible models

Doubly Robust Estimators

Clever combination of $\pi(Z; \alpha)$ and $m_x(Z; \beta)$

- Consistent as long as one model is correct
- Two chances for parametric model

Common doubly-robust estimators

- Augmented inverse probability weighting
- Targeted maximum likelihood estimation

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Machine Learning

Data-adaptive estimators (machine learning)

- Less restrictive than parametric modeling
  - Capture wider class of densities
- May be more reasonable to believe flexible enough model
  - Or that model is sufficiently close

Problems in Application

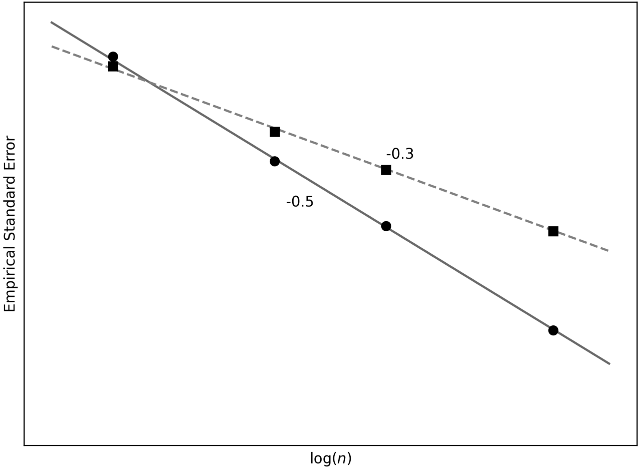
1. Convergence
2. Complexity

Convergence

Remainder term goes to zero as function of n

- *Not* computational complexity issue
  - **NOT** when software says 'did not converge'
  - Inherent feature of the estimators
- How fast standard error of estimators decreases with n
- For inference, root-n ($n^{-1/2}$) is desirable
  - Parametric models meet this criteria
  - Data-adaptive likely don't
- Slower than $n^{-1/2}$ may result in invalid inference
  - Estimated variance is too small
  - Implies greater certainty than true

Convergence



Convergence and AIPW

AIPW can allow for slower convergence

- Under the assumption that both models are correct
  - Second-order bias is a product of the approximation errors
  - Only need at least $n^{-1/4}$ for both models

- Wider range of models can be validly used with AIPW
  - Comes at cost of double-robustness
  - Becomes more akin to **double-susceptible**
  - Maybe okay if we use flexible models?

Complexity

Restrictions on the complexity of a model

- Allows borrowing of information across observations
- Restricted to Donsker class

Why restricting to Donsker is inappropriate

- Machine learning
  - Dimension allowed to increase with n
  - Exist in highly complex spaces

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Cross-fitting

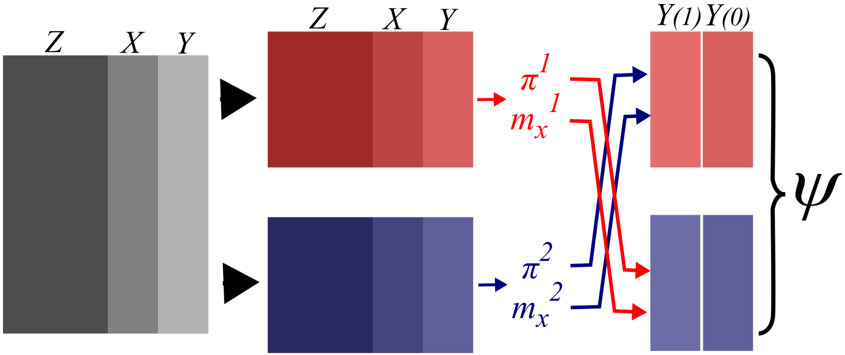
Approach to relax Donsker class restriction

- Estimate model in one split and predict in other split
- Since from different sample
  - Avoid the Donsker class restriction

Synonyms

- Sample splitting
- Double machine learning
- Cross-validated

Single Cross-fit



Single Cross-fit

Removes own-observation bias

- Best data-adaptive estimator memorizes the data
  - Highly predictive for the data
  - Poor out-of-sample performance
- Cross-fit prevents correlation between estimator and data
  - Without need for Donsker class

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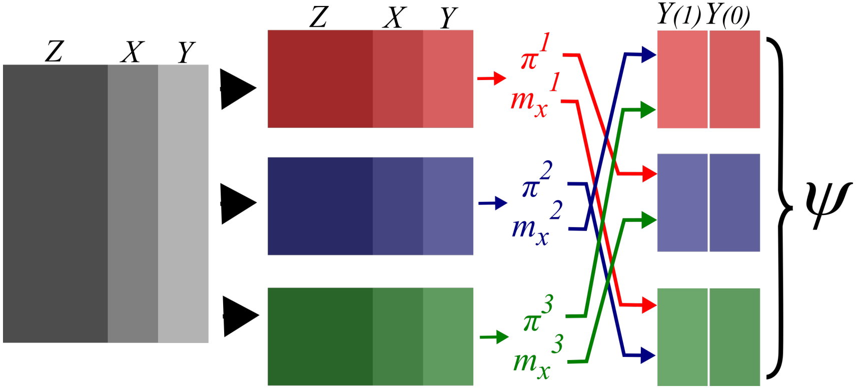
Double Cross-fit



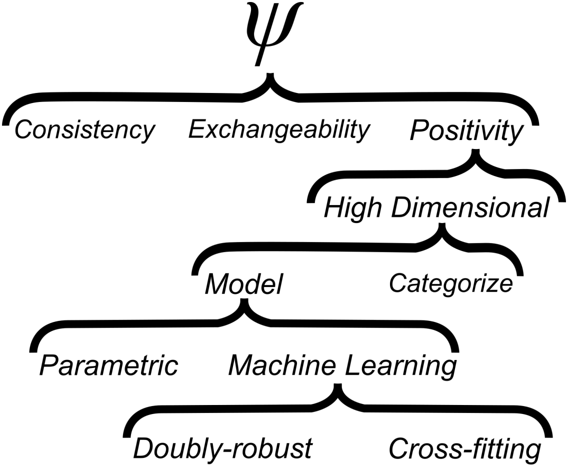
Double Cross-fit

Removes own-observation bias & non-linearity

- Cross-fit prevents correlation between estimator and data
  - Without need for Donsker class

- Further de-couples data and estimators
  - Compared to single cross-fit

Looking Back...



Simulations

Data Generation

Average Causal Effect of Statins on ASCVD

- Age, low-density lipoprotein, ASCVD risk scores, diabetes
- 2000 reps with $n = 3000$

Metrics

- Bias
- 95% Confidence interval coverage

Approaches

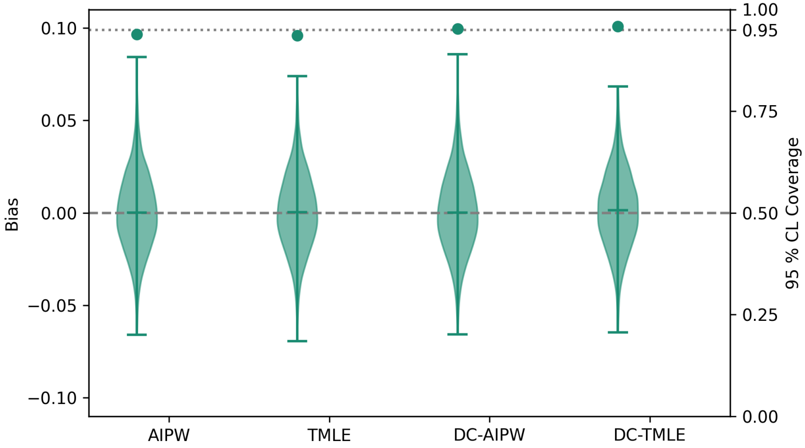
ACE estimators

- AIPW
- TMLE
- Double Cross-fit (DC-)AIPW
- DC-TMLE

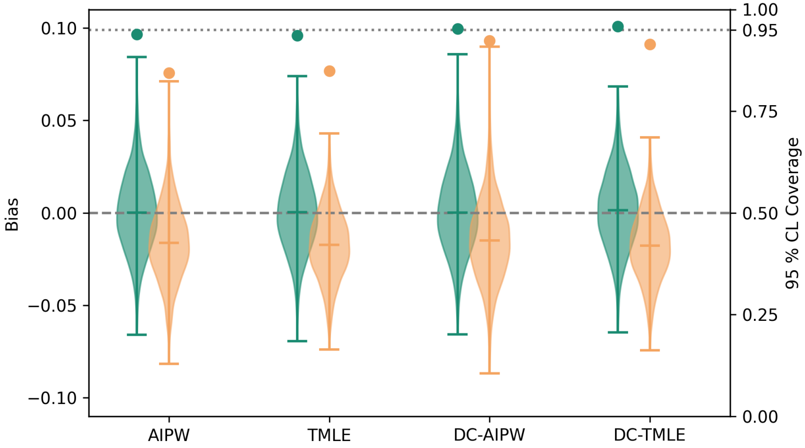
Nuisance model estimators

- Correct parametric model
- Main-effect parametric model
- Machine learning

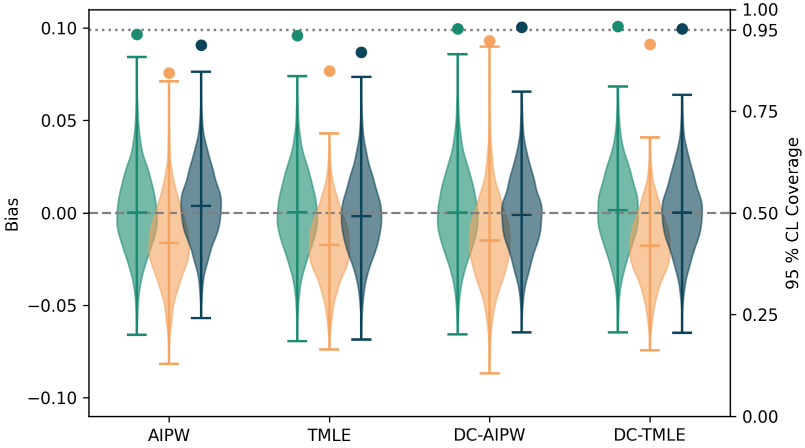
Simulation Results



Simulation Results



Simulation Results



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Implementation

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Partition versus Split

Split

- Observations grouped into non-overlapping, equal-sized groups
- Let s indicate the number of splits for a data set
  - $s = 2$ randomly splits observations into two groups

Partition

- A particular division of splits
- E.g., IDs 1,2,4 are in split 1 and IDs 3,5,6 are in split 2

Algorithm Pseudo-Code

Repeat for p different partitions

1. Partition data into s non-overlapping splits
2. For each s:
   - Estimate $\hat{\pi}^s(Z_i^s)$
   - Estimate $\hat{m}_x^s(Z_i^s)$
3. For each s:
   - Predict $\hat{\pi}^{\bar{s}}(Z_i^s)$
   - Predict $\hat{m}_x^{\bar{s}}(Z_i^s)$
   - Generate $\hat{Y}_i^*$
   - Estimate ψ^s
   - Estimate $Var(\psi^s)$
4. Estimate ψ^p as mean of $\hat{\psi}^s$
5. Estimate $Var(\psi^p)$ as mean of $\widehat{Var}(\hat{\psi}^s)$

Summarize all partitions with
$\hat{\psi} = \text{median}(\hat{\psi}^p)$; $\widehat{Var}(\hat{\psi})$

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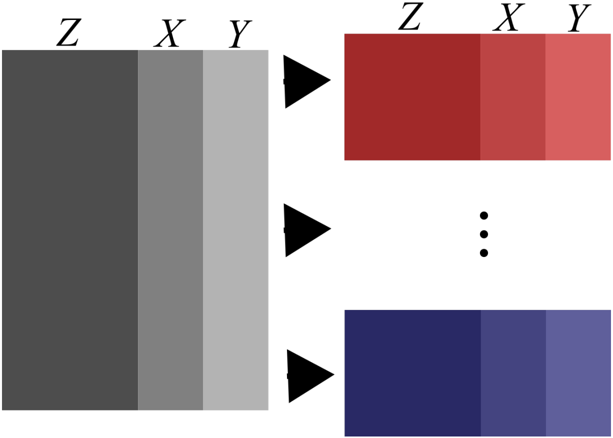
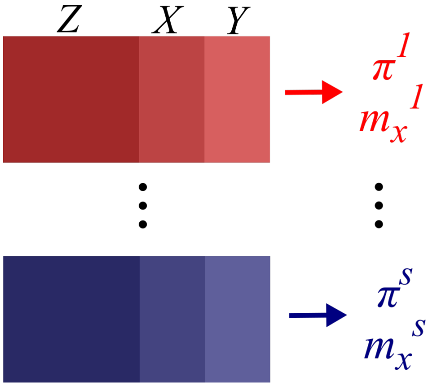
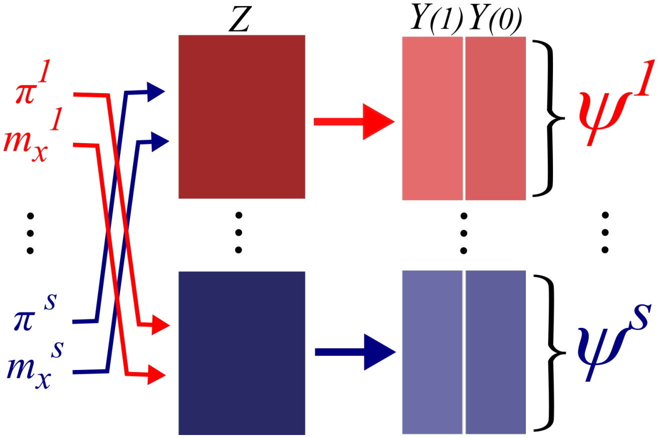
Step 1: Partition Data into Splits



Step 2: Estimate Nuisance Models



Step 3: Estimate ψ^s



Step 3: Estimate ψ^s

Augmented Inverse Probability Weighting

$$\widehat{Y}_i^*(x) = \frac{I(X_i = x)Y_i}{\widehat{\pi}(Z_i)} + \frac{\widehat{m_x}(Z_i)(\widehat{\pi}(Z_i) - I(X_i = x))}{\widehat{\pi}(Z_i)}$$

Then calculate

$$\psi^s = \frac{1}{n_s} \sum_{i \in n_s} \widehat{Y}_i^*(x = 1) - \widehat{Y}_i^*(x = 0)$$

Step 4: Estimate ψ^p

Take the mean of all ψ^s

$$\hat{\psi}^p = \frac{1}{s} \sum_{i=1}^{s} \hat{\psi}^s$$

Step 5: Estimate $Var(\psi^p)$

Take the mean of all $Var(\psi^s)$

$$\widehat{Var}(\hat{\psi}^p) = \frac{1}{s} \sum_{i=1}^{s} \widehat{Var}(\hat{\psi}^s)$$

Repeat for p different partitions

Repeat previous steps for p times

Summarize all different partitions used via

$$\hat{\psi} = \text{median}(\hat{\psi}^p)$$

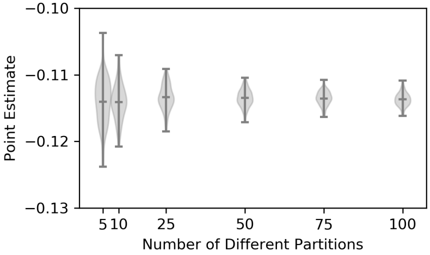
$$\widehat{Var}(\hat{\psi}) = \text{median}\left(\widehat{Var}(\hat{\psi}^p) + (\hat{\psi} - \hat{\psi}^p)^2\right)$$

- Median rather than mean since more stable to outliers

Why p Partitions?

Multiple splits

- Does not matter asymptotically
- For moderate n, $\hat{\psi}^p$ depends on the chosen split
  - Increases *statistical* efficiency
  - Decreases *computational* efficiency



Recommendations for Practical Application

1. Flexible library of learners
    - *k*-fold super-learner
    - Variety of models
        - Flexible regression, tree-based, gradient, etc.
    - Explore multiple tuning parameters
2. Doubly-robust estimator
3. Cross-fitting
4. Include transformations in data

Software

Python

- *zEpid*
  - https://github.com/pzivich/zEpid
  - v0.9.0+ Supports single and double cross-fit
  - Support for both AIPW and TMLE
- https://github.com/pzivich/publications-code

R

- https://github.com/yqzhong7/AIPW
- https://github.com/pzivich/publications-code

Conclusions

Conclusions

Machine learning is a useful tool for nuisance model specification

- Allow for flexible models
- Less concern over misspecification relative to parametric models
  - Captures wider set of densities
- Best benefit in my opinion
  - Allows us to devote time to other biases

> Epidemiology. 2021 Feb 2. doi: 10.1097/EDE.0000000000001332. Online ahead of print.

Machine learning for causal inference: on the use of cross-fit estimators

Paul N Zivich [1], Alexander Breskin

Affiliations + expand

PMID: 33591058 DOI: 10.1097/EDE.0000000000001332

Further Reading

Doubly-robust estimators generally

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Targeted maximum likelihood estimation

- Schuler & Rose, Targeted Maximum Likelihood Estimation for Causal Inference in Observational Studies. *American Journal of Epidemiology* 2017, 185:1 p65-67

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Further Reading

Machine Learning and Super learner

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- Keil & Edwards, You Are Smarter Than You Think: (Super) Machine Learning in Context. *European Journal of Epidemiology* 2018, 33:5 p437-440

Sample-splitting for machine learning

- Díaz, Machine learning in the estimation of causal effects: targeted minimum loss-based estimation and double/debiased machine learning, *Biostatistics* April 2020, 21:2 p353–358
- Chernozhukov et al., Double/debiased machine learning for treatment and structural parameters, *The Econometrics Journal* 2018 21, C1–C68
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- Newey & Robins, Cross-Fitting and Fast Remainder Rates for Semiparametric Estimation, *arXiv*:1801.09138

Machine learning for causal inference

- Naimi et al., Challenges in Obtaining Valid Causal Effect Estimates with Machine Learning Algorithms. *arXiv*:1711.07137

Acknowledgments

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