Shrinkage Estimation for Causal Inference and Experimental Design

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Motivating Setting

Randomized Controlled Trials (RCT)

- Researcher controls assignment to treatment

Observational Databases (ODB)

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- "Unbiased but imprecise"

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  - Confounding $\implies$ unverifiable assumptions for unbiasedness
  - Large, often inexpensive.
- "Precise, but biased"

Our Approach

We consider two problems:

- **How to design shrinkage estimators to merge ODB and RCT data?**
- **How to improve experimental design using shrinkers?**

Outline

Central Role of Stratification

- Work in a stratified setting, with K strata.
  - Characterize heterogeneity in treatment effect
  - Arise from subject matter expertise, modern ML method, etc.
- Each unit i in RCT + ODB has associated stratum indicator $S_i \in \{1, \ldots, K\}$
- (Unobserved) Conditional avg. stratum treatment effects:

$$\tau_{rk} = \mathbb{E}_R \left(Y_i(1) - Y_i(0) \mid S_i = k \right)$$
$$\tau_{ok} = \mathbb{E}_O \left(Y_i(1) - Y_i(0) \mid S_i = k \right)$$

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Transportability of CATEs: For $k = 1, \ldots, K$, treatment effects $\tau_{ok} = \tau_{rk}$, and we call their common value τ_k.
Define $\boldsymbol{\tau} = (\tau_1, \ldots, \tau_K)^{\mathsf{T}}$.

Setup

- Collect our estimators into vectors:

$$\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} = \left(\hat{\tau}_{r1}, \ldots, \hat{\tau}_{rK}\right), \qquad \hat{\boldsymbol{\tau}}_{\boldsymbol{o}} = \left(\hat{\tau}_{o1}, \ldots, \hat{\tau}_{oK}\right).$$

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- Under mild conditions, we have

$$\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} \sim N\left(\boldsymbol{\tau}, \Sigma_r\right), \quad \hat{\boldsymbol{\tau}}_{\boldsymbol{o}} \sim \left(\boldsymbol{\tau} + \boldsymbol{\xi}, \Sigma_o\right)$$

for bias $\boldsymbol{\xi}$ and covariance matrices Σ_r and Σ_o

  - $\Sigma_r = \mathrm{diag}(\sigma^2_{r1}, \ldots, \sigma^2_{rK})$ is estimable from the data
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  for bias $\boldsymbol{\xi}$ and covariance matrices Σ_r and Σ_o
  - $\Sigma_r = \mathrm{diag}(\sigma_{r1}^2, \ldots, \sigma_{rK}^2)$ is estimable from the data
  - $\boldsymbol{\xi}$ cannot be estimated
- Seek to design shrinkage estimator $\hat{\boldsymbol{\tau}} = f(\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}, \hat{\boldsymbol{\tau}}_{\boldsymbol{o}})$ to minimize expected (weighted) squared error loss,

$$\mathcal{L}(\hat{\boldsymbol{\tau}}, \boldsymbol{\tau}) = \sum_k w_k \left(\hat{\tau}_k - \tau_k\right)^2.$$

Useful Prior Work

- **Shrinkage estimation**: a rich literature stretching back to multivariate normal mean estimation work of Stein (1956)
- Green and Strawderman (1991) and Green et al. (2005) propose estimators for shrinkage between ...
  - a normal, unbiased estimator (like $\hat{\tau}_r$), and
  - a biased estimator (like $\hat{\tau}_o$)

Outline

A Recipe for Estimators

1. Posit a structure for the shrinkage estimator

$$f(\hat{\tau}_{\boldsymbol{r}}, \hat{\tau}_{\boldsymbol{o}}) = \hat{\tau}_{\boldsymbol{r}} - \boldsymbol{g}(\hat{\tau}_{\boldsymbol{r}}, \hat{\tau}_{\boldsymbol{o}})$$

for any differentiable g satisfying $E(||\boldsymbol{g}||^2) < \infty$.

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   for any differentiable g satisfying $E(||\boldsymbol{g}||^2) < \infty$.

2. Following common precedent (Li et al., 1985; Xie et al., 2012), minimize unbiased risk estimate,

$$\text{URE} = \frac{1}{K}\left(\text{Tr}\left(\Sigma_r \boldsymbol{W}\right) + \sum_{k=1}^{K} w_k \left(g_k^2(\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}, \hat{\boldsymbol{\tau}}_{\boldsymbol{o}}) - 2\sigma_{rk}^2 \frac{\partial g_k(\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}, \hat{\boldsymbol{\tau}}_{\boldsymbol{o}})}{\hat{\tau}_{rk}}\right)\right)$$

   over hyperparameters to obtain the estimator.

Case 1: Common Shrinkage Factor

We consider shrinkage estimators which share a common shrinkage factor λ across components. Denote generic estimator as

$$\boldsymbol{\kappa}(\lambda, \hat{\boldsymbol{\tau}}_{\boldsymbol{r}}, \hat{\boldsymbol{\tau}}_{\boldsymbol{o}}) = \hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \lambda(\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{o}}) \, .$$

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Then, URE evaluates to

$$\mathrm{URE}(\lambda) = \mathrm{Tr}\left(\Sigma_r \boldsymbol{W}\right) + \lambda^2 \left(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}}\right)^{\mathsf{T}} \boldsymbol{W} \left(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}}\right) - 2\lambda \mathrm{Tr}(\Sigma_r \boldsymbol{W})$$

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which has minimizer in λ,

$$\lambda_1^{\mathrm{URE}} = \frac{\mathrm{Tr}(\Sigma_r \boldsymbol{W})}{\left(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}}\right)^{\mathsf{T}} \boldsymbol{W} \left(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}}\right)}\,.$$

Useful Properties of λ_1^{URE} (I)

1. Define

$$\boldsymbol{\kappa}_1 = \hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \lambda_1^{\text{URE}} \left(\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{o}} \right)$$

Lemma ($\boldsymbol{\kappa}_1$ Risk Guarantee)

Suppose $4 \max_k w_k \sigma_{rk}^2 < \sum_k w_k \sigma_{rk}^2$. *Then* $\boldsymbol{\kappa}_1$ *has risk strictly less than that of* $\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}$.

- Requires a dimension of at least $K = 5$.
- May require substantially larger K if high heteroscedasticity or non-uniform weights.

Useful Properties of λ_1^{URE} (II)

2. Its positive part analogue,

$$\boldsymbol{\kappa}_{1+} = \hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \left\{ \lambda_1^{\text{URE}} \right\}_{[0,1]} \left(\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{o}} \right) ,$$

where

$$\{u\}_{[0,1]} = \min(\max(u, 0), 1) ,$$

satisfies the following notion of optimality:

Useful Properties of λ_1^{URE} (III)

Theorem ($\boldsymbol{\kappa}_{1+}$ Asymptotic Risk)

Suppose

$$\limsup_{K\to\infty} \frac{1}{K}\sum_k w_k^2\sigma_{rk}^2\xi_k^2 < \infty\,, \quad \limsup_{K\to\infty} \frac{1}{K}\sum_k w_k^2\sigma_{rk}^2\sigma_{ok}^2 < \infty\,,$$

$$\text{and} \quad \limsup_{K\to\infty} \frac{1}{K}\sum_k w_k^2\sigma_{rk}^4 < \infty\,.$$

Then, in the limit $K \to \infty$, $\boldsymbol{\kappa}_{1+}$ has the lowest risk among all estimators with a shared shrinkage factor across components.

Case 2: Variance-Weighted Shrinkage Factor

This procedure is general purpose. For example, may instead want an estimator that shrinks each component proportionally to σ^2_{rk}.

Easy to solve for

$$\boldsymbol{\kappa}_2 = \boldsymbol{\kappa}(\lambda_2^{\text{URE}}, \hat{\boldsymbol{\tau}}_{\boldsymbol{r}}, \hat{\boldsymbol{\tau}}_{\boldsymbol{o}}) = \hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \frac{\text{Tr}(\Sigma_r^2 \boldsymbol{W})\Sigma_r}{(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})^{\mathsf{T}} \Sigma_r^2 \boldsymbol{W} (\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})} (\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{o}})$$

and its positive-part improvement,

$$\boldsymbol{\kappa}_{2+} = \hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \left\{ \frac{\text{Tr}(\Sigma_r^2 \boldsymbol{W})\Sigma_r}{(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})^{\mathsf{T}} \Sigma_r^2 \boldsymbol{W} (\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})} \right\}_{[0,1]} (\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{o}}) \ .$$

Simulated Data Visualization

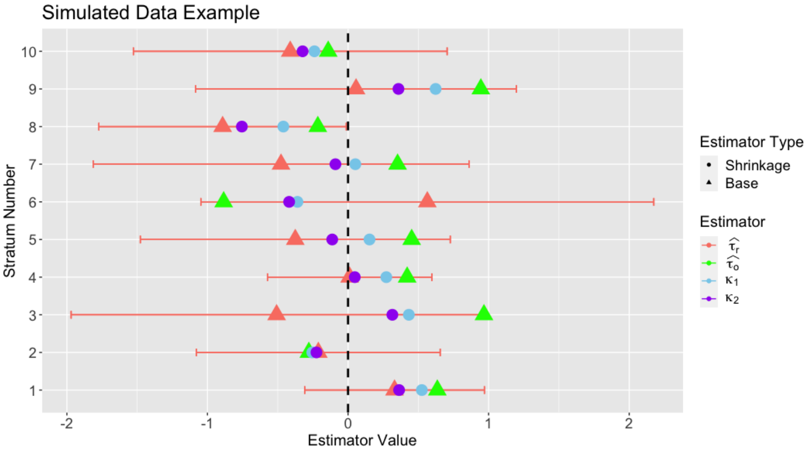

Figure 1: Simulated shrinkage between $\hat{\tau}_r$ and $\hat{\tau}_o$ with ten strata. 90% conf. sets for $\hat{\tau}_r$ in red, with κ_{1+} and κ_{2+} shown in circles.

Outline

A New Setting: Design

Can these insights inform the design of a **prospective** RCT?

- Observational study already completed, $\hat{\boldsymbol{\tau}}_{\boldsymbol{o}}$ obtained.
- Designing a prospective RCT of n_r units
- Want to use a shrinker to combine $\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}$ with $\hat{\boldsymbol{\tau}}_{\boldsymbol{o}}$. Design experiment to better complement ODB

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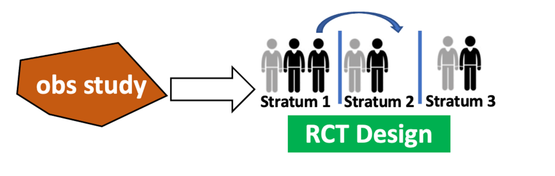
Goal: choose an RCT allocation of treated and control counts per stratum, $\boldsymbol{d} = \{(n_{rkt}, n_{rkc})\}_{k=1}^{K}$, s.t. $\sum_k n_{rkt} + n_{rkc} = n_r$:

- implies how to *recruit* ...
- and *assign* treatment



Estimator and Risk

We proceed with our estimator $\boldsymbol{\kappa}_{2+}$ from the prior section:

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Can compute this efficiently via numerical integration (Bao and Kan, 2013), as long as $\boldsymbol{V}$ and $\boldsymbol{\xi}$ are known.

1. Naïve Optimization Assuming $\xi = 0$

Under enhanced transportability assumption, can estimate $\hat{\boldsymbol{V}}$ using pilot estimates obtained from ODB:

$$\hat{\sigma}^2_{kt} = \widehat{\mathrm{var}}\left(Y(1) \mid S = k\right) \quad \text{and} \quad \hat{\sigma}^2_{kc} = \widehat{\mathrm{var}}\left(Y(0) \mid S = k\right) .$$

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Use a simple heuristic: assume $\xi = 0$.

Minimize $\mathcal{R}_2(\boldsymbol{d}, \hat{\boldsymbol{V}}, \xi = 0)$ over $\boldsymbol{d}$, via **greedy swap algorithm**.

- Swap units across strata, treatment statuses until no improvement in $\mathcal{R}_2(\boldsymbol{d}, \hat{\boldsymbol{V}}, 0)$
- Non-convexity: run from several starting points.

2. Heuristic Optimization Assuming Worst-Case Error Under Γ-Level Unmeasured Confounding

- Can take a more pessimistic approach using marginal sensitivity model of Tan (2006)
- For a user-chosen value of $\Gamma \geq 1$:
  - can obtain worst-case $\xi_k(\Gamma)$ using Zhao et al. (2019), and...
  - can obtain associated $\hat{\sigma}^2_{kt}$ and $\hat{\sigma}^2_{kc}$.

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posit a value of $\Gamma \implies$

collect results into $\boldsymbol{V}_\Gamma$ and $\boldsymbol{\xi}_\Gamma \implies$

run greedy algorithm on $\mathcal{R}_2(\boldsymbol{d}, \boldsymbol{V}_\Gamma, \boldsymbol{\xi}_\Gamma)$ instead of $\mathcal{R}_2(\boldsymbol{d}, \hat{\boldsymbol{V}}, 0)$

Outline

WHI Overview

Dataset Overview

- Study of postmenopausal women initiated in 1991
- RCT of hormone therapy (HT) w/ 16k enrollees
- ODB w/ 50k comparable enrollees

Consider the effect of HT on coronary heart disease (CHD)

Results

Subgroup Variable(s)	# of Strata	Loss as % of $\hat{\tau}_r$ Loss	
		κ_{1+}	κ_{2+}
Cardiovascular disease (CVD)	2	37.6%	<u>36.9%</u>
Age	3	37.3%	<u>30.1%</u>
Solar	5	29.4%	<u>23.5%</u>
Age, CVD	6	<u>38.0%</u>	38.2%
CVD, Solar	10	<u>30.6%</u>	32.5%
Age, Solar	15	<u>22.4%</u>	23.0%
Age, CVD, Solar	30	<u>50.3%</u>	<u>50.3%</u>

Table 1: Empirical avg. loss using bootstrap samples of size 1,000 from RCT.

Designs

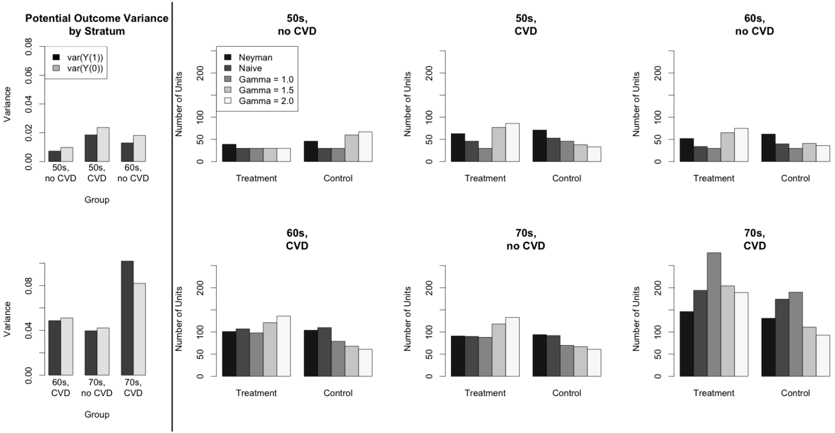

Figure 2: Allocations of $n_r = 1,000$ units in WHI with strata defined by history of CVD and age, under different design heuristics.

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- Guillaume Basse
- Mike Baiocchi
- Art Owen
- Luke Miratrix

Inference paper out in Biometrics
Design paper available at arXiv:2204.06687

Thanks!

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Appendices

Practical Considerations

- **Variance estimation:** In practice, Σ_r not known. Must be estimated from data.
- **Propensity score adjustment**
  - No unconfoundedness $\implies$ propensity score adjustment can't remove all bias
  - If ODB is large, adjusting will typically be good practice. We suggest stabilized IPTW adjustments.
- **Sensitivity analysis**
  - Marginal sensitivity model of Tan (2006) summarizes degree of unmeasured confounding by a single value, $\Gamma \geq 1$
  - Can "reverse engineer" implied confounding value Γ_{imp} when using a shrinker, via work of Zhao et al. (2019)
  - Evaluate Γ_{imp} to obtain a ✓ or ✗ for using shrinker

A Note on λ_1^{URE}

The true risk-minimizing shrinkage weight is given by

$$\lambda_{\mathrm{opt}} = \frac{\mathrm{Tr}(\Sigma_r \boldsymbol{W})}{\mathrm{Tr}(\Sigma_r \boldsymbol{W}) + \mathrm{Tr}(\Sigma_o \boldsymbol{W}) + \underbrace{\xi^{\mathsf{T}} \boldsymbol{W}^2 \xi}_{\text{Not estimable from data}}},$$

but observe that

$$E\left((\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})^{\mathsf{T}} \boldsymbol{W} (\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}}) \right) = \mathrm{Tr}(\Sigma_r \boldsymbol{W}) + \mathrm{Tr}(\Sigma_o \boldsymbol{W}) + \xi^{\mathsf{T}} \boldsymbol{W}^2 \xi \, .$$

λ_1^{URE} substitutes the quadratic form for its expectation,

$$\lambda_1^{\mathrm{URE}} = \frac{\mathrm{Tr}(\Sigma_r \boldsymbol{W})}{(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})^{\mathsf{T}} \boldsymbol{W} (\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})} \, .$$

Guardrails

Simplicity of Algorithm 2 makes it easy to impose guardrails $\Longrightarrow$ for any invalid design, just set objective value to ∞.

Recommend simple guardrails for designs:

1. **Sample size**: to retain CLT, enforce

$$\min_k n_{rkt} \geq SS_{\min}, \quad \min_k n_{rkc} \geq SS_{\min}$$

2. **Detachability**: for default design $\tilde{\boldsymbol{d}} = \{\tilde{n}_{rkt}, \tilde{n}_{rkc}\}_k$ and tolerance parameter $\delta_d \geq 1$, enforce

$$\sum_k \frac{\hat{\sigma}^2_{kt}}{n'_{rkt}} + \frac{\hat{\sigma}^2_{kc}}{n'_{rkc}} \geq \delta_d \sum_k \frac{\hat{\sigma}^2_{kt}}{\tilde{n}_{rkt}} + \frac{\hat{\sigma}^2_{kc}}{\tilde{n}_{rkc}},$$

for any proposed design $\boldsymbol{d'} = \{n'_{rkt}, n'_{rkc}\}_k$.

3. **Risk reduction**: for proposed $\boldsymbol{d'} = \{n'_{rkt}, n'_{rkc}\}_k$, enforce

$$4 \max_k \left(\frac{\hat{\sigma}^2_{kt}}{n'_{rkt}} + \frac{\hat{\sigma}^2_{kc}}{n'_{rkc}} \right)^2 > \sum_k \left(\frac{\hat{\sigma}^2_{kt}}{n'_{rkt}} + \frac{\hat{\sigma}^2_{kc}}{n'_{rkc}} \right)^2.$$

Application to the WHI

- Split RCT data into "gold" and "silver" subsets
- Gold dataset: used to obtain "gold standard" estimates of stratum treatment effects
- Repeat $1,000$ times:
  - Draw bootstrap samples:
    - $1,000$ RCT units (from silver data)
    - Observational sample (50K units)
  - Compute L_2 loss for $\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}, \boldsymbol{\kappa}_{1+}, \boldsymbol{\kappa}_{2+}, \boldsymbol{\delta}_1, \boldsymbol{\delta}_2$.
- Average loss over draws

Stratification Variables

Stratify on two variables from WHI protocol (Roehm, 2015):
Age + **CVD** (history of cardiovascular disease)

Also include a variable unassociated with potential outcomes:
Langley (solar irradiance)

Results

Subgroup Variable(s)	# of Strata	Avg. $\hat{\tau}_r$ Loss	Loss as % of RCT-Only Loss			
			κ_{1+}	κ_{2+}	δ_1	δ_2
Age	3	0.00064	40.1%	**34.3%**	63.3%	74.8%
Cardiovascular disease (CVD)	2	0.00149	40.6%	**39.6%**	100%	100%
Solar	5	0.00094	29.1%	**18.2%**	43.1%	52.9%
Age, CVD	6	0.00574	25.0%	**14.0%**	30.6%	85.6%
CVD, Solar	10	0.00803	**20.9%**	21.2%	21.0%	88.4%
Age, Solar	15	0.00398	31.2%	30.4%	**28.4%**	58.4%
Age, CVD, Solar	30	0.02901	15.8%	16.1%	**15.7%**	88.3%

Table 2: Empirical risk using bootstrap samples of size 1,000 from RCT data.

Simulations Set-Up (I)

- ODB has 20K units ($j \in \mathcal{O}$). RCT has 1,000 ($i \in \mathcal{E}$)
- Untreated potential outcomes $Y_\ell \in \{0,1\}$ for $\ell \in \mathcal{O} \cup \mathcal{E}$ sampled as indep. Bernoullis with

$$\Pr(Y_\ell(0) = 1 \mid \boldsymbol{x}_\ell) = \frac{1}{1 + e^{-\alpha - \beta^\mathsf{T} \boldsymbol{x}_\ell + \varepsilon_\ell}}, \quad \text{for } \beta = (1,1,1,1,1)^\mathsf{T}$$

for covariates $X_\ell \overset{\text{iid}}{\sim} \mathcal{N}(0, \boldsymbol{I}_5)$, α chosen s.t. mean is 10%.

- Treatment variables W_j for $j \in \mathcal{O}$ sampled via

$$\Pr(W_j = 1 \mid \boldsymbol{x}_j) = \frac{1}{1 + e^{-\gamma^\mathsf{T} \boldsymbol{x}_j}}, \quad \text{for } \gamma = (\sqrt{2}, \sqrt{2}, \sqrt{2}, 0, 0)^\mathsf{T}.$$

Simulations Set-Up (II)

- Treatment effects
  - Define $k = 1, \ldots, 12$ strata based on first + second covariate
  - Assign τ_k, stratum CATEs, via 3 treatment effect models:

$$\tau_k = T, \quad \tau_k = -T \times \frac{k}{K}, \quad \text{and} \quad \tau_k = T \times \left(\frac{k}{K}\right)^2$$

  - T chosen so that Cohen's D in ODB equals 0.5
- Simulation structure
  - Sample ODB data a single time. Correct via SIPW.
  - Compute RCT designs under different heuristics
  - Resample RCT units 5,000 times. For each sample, compute L_2 error in estimating $\boldsymbol{\tau}$ using $\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}, \boldsymbol{\kappa}_2$, and $\boldsymbol{\kappa}_{2+}$

Idealized Case: All Covariates Measured

Est	Trt	Eq.	Ney.	Naïve	Max Bias, Γ Value 1.0	1.1	1.2	1.5	Oracle
$\hat{\tau}_r$		100%	**87%**	91%	100%	96%	94%	94%	96%
κ_2	c	82%	48%	**44%**	52%	48%	47%	50%	42%
κ_{2+}		38%	28%	**26%**	26%	26%	26%	28%	23%
$\hat{\tau}_r$		100%	**89%**	92%	95%	94%	95%	97%	104%
κ_2	ℓ	93%	66%	58%	58%	**57%**	60%	64%	50%
κ_{2+}		59%	51%	45%	**43%**	45%	47%	49%	33%
$\hat{\tau}_r$		100%	**86%**	91%	95%	98%	94%	92%	91%
κ_2	q	81%	47%	**45%**	52%	52%	50%	48%	41%
κ_{2+}		37%	29%	**27%**	28%	28%	30%	29%	25%

Table 3: Risk over 5,000 iterations of $\hat{\tau}_r, \kappa_2$, and κ_{2+} in the case of no unmeasured confounding in the observational study. Risks are expressed as a percentage of the risk of $\hat{\tau}_r$ using an equally allocated experiment, for each of the three treatment effect models.

Realistic Case: Third Covariate Missing

Est	Trt	Eq.	Ney.	Naïve	Max Bias, Γ Value 1.0	1.1	1.2	1.5	Oracle
$\hat{\tau}_r$		100%	**90%**	90%	90%	92%	93%	95%	102%
κ_2	c	102%	81%	74%	**72%**	72%	72%	77%	69%
κ_{2+}		96%	80%	74%	**71%**	72%	72%	76%	67%
$\hat{\tau}_r$		100%	93%	**93%**	94%	95%	96%	96%	104%
κ_2	ℓ	102%	85%	77%	**75%**	76%	77%	79%	73%
κ_{2+}		98%	84%	77%	**75%**	76%	76%	79%	71%
$\hat{\tau}_r$		100%	**89%**	90%	93%	92%	91%	96%	96%
κ_2	q	101%	74%	69%	68%	68%	**67%**	73%	66%
κ_{2+}		88%	72%	67%	66%	66%	**65%**	71%	63%

Table 4: Risk over 5,000 iterations of $\hat{\tau}_r$, κ_2, and κ_{2+} under various experimental designs, in the case of unmeasured confounding in the observational study via failure to measure the third covariate.

1. Neyman Allocation

Using stronger form of Assumption 3 (shared variances), we can estimate from the ODB:

$$\hat{\sigma}^2_{kt} = \widehat{\mathrm{var}}\,(Y(1) \mid S = k) \qquad \text{and} \qquad \hat{\sigma}^2_{kc} = \widehat{\mathrm{var}}\,(Y(0) \mid S = k)\ .$$

Simplest design heuristic: use a Neyman allocation without a cost constraint, e.g.

$$n_{rkt} = \frac{n_r \cdot \hat{\sigma}^2_{kt}}{\sum_k \hat{\sigma}^2_{kt} + \hat{\sigma}^2_{kc}} \qquad \text{and} \qquad n_{rkc} = \frac{n_r \cdot \hat{\sigma}^2_{kc}}{\sum_k \hat{\sigma}^2_{kt} + \hat{\sigma}^2_{kc}}\ .$$

Optimizes over only the non-shrinkage portion of the risk, but reasonable in many practical settings.

Improving Interpretability of $\boldsymbol{\kappa}_{1+}$

- Recall: λ_1^{URE} can be interpreted as an estimate of

$$\lambda_{\mathsf{opt}} = \frac{\mathrm{Tr}(\Sigma_r \boldsymbol{W})}{\mathrm{Tr}(\Sigma_r \boldsymbol{W}) + \mathrm{Tr}(\Sigma_o \boldsymbol{W}) + \boldsymbol{\xi}^{\mathsf{T}} \boldsymbol{W}^2 \boldsymbol{\xi}},$$

  true MSE-minimizing weight on $\hat{\boldsymbol{\tau}}_{\boldsymbol{o}}$ in a convex combination
- We can use this idea to improve interpretability of $\boldsymbol{\kappa}_{1+}$!
- **Key idea**: frame in context of sensitivity model of Tan (2006)

Prior Work

- Marginal sensitivity model of Tan (2006) summarizes degree of unmeasured confounding by a single value, $\Gamma \geq 1$
  - Γ bounds odds ratio of treatment prob. conditional on potential outcomes + covariates vs. covariates only
  - Related to the famous model of Rosenbaum (1987), but extends to the setting of inverse probability weighting
- Zhao et al. (2019) derive valid confidence intervals for causal estimates under the set of models indexed by any choice of Γ
  - Implicitly maps Γ to a worst-case bias $\xi(\Gamma)$ and variance $\Sigma_O(\Gamma)$
  - Under some assumptions, allows us to obtain worst-case estimate of λ_{opt} as a function of Γ, which we call $\lambda(\Gamma)$

Relating the Models

- **Intuition**: larger Γ (confounding parameter) $\implies$ optimal weight λ_{opt} is smaller
- Let $\Gamma_{\text{imp}} = \sup\{\Gamma : \lambda(\Gamma) > \lambda_1^{\text{URE}}\}$
  - Largest value Γ for which the optimal shrinkage factor $\lambda(\Gamma)$ is greater than our shrinkage parameter λ_1^{URE}.
- Γ_{imp} can be used to evaluate level of shrinkage
  - If we believe true confounding level $\Gamma < \Gamma_{\text{imp}}$, then

    $$\lambda_1^{\text{URE}} \approx \lambda(\Gamma_{\text{imp}}) \leq \lambda_{\text{opt}} = \lambda(\Gamma)$$

    Hence the shrinkage level is conservative. ✓
  - If we believe $\Gamma > \Gamma_{\text{imp}}$, then estimator is overshrinking, relies too much on the observational estimate. X

1. Naïve Optimization Assuming $\xi = 0$ (I)

Using stronger Assumption 3 (shared var), can estimate from ODB:

$$\hat{\sigma}^2_{kt} = \widehat{\text{var}}\left(Y(1) \mid S = k\right) \qquad \text{and} \qquad \hat{\sigma}^2_{kc} = \widehat{\text{var}}\left(Y(0) \mid S = k\right) .$$

Define $\mathcal{R}_2(\boldsymbol{d}, \boldsymbol{V}, \boldsymbol{\xi}) = \mathcal{R}(\boldsymbol{\kappa}_2)$ analyzed under design $\boldsymbol{d}$, potential outcome variances $\boldsymbol{V} = \{(\hat{\sigma}^2_{kt}, \hat{\sigma}^2_{kt})\}_{k=1}^{K}$, and error $\boldsymbol{\xi}$.

Simple heuristic: assume $\boldsymbol{\xi} = 0$. Then solve:

$$\begin{aligned} \text{minimize} \quad & \mathcal{R}_2(\boldsymbol{d}, \boldsymbol{V}, \boldsymbol{\xi}) \\ \text{subject to} \quad & \boldsymbol{\xi} = 0, \boldsymbol{V} = \{(\hat{\sigma}^2_{kt}, \hat{\sigma}^2_{kc})\}_{k=1}^{K}, \\ & 0 < n_{rkt}, n_{rkc}, , \quad k = 1, \ldots, K, \\ & n_r = \sum_k n_{rkt} + n_{rkc} . \end{aligned} \tag{1}$$

But $\mathcal{R}_2(\boldsymbol{d}, \boldsymbol{V}, \boldsymbol{\xi})$ is not convex in the design $\boldsymbol{d}$...

1. Naïve Optimization Assuming $\xi = 0$ (II)

A practical approach: **greedy algorithm**. Define $\boldsymbol{d_j}$ as design on j^{th} iteration, and define

$$\mathcal{D}_j = \{\boldsymbol{d}' \mid \ \boldsymbol{d}' \text{ changes one unit across strata/treatment level from } \boldsymbol{d}_j\}.$$

Run Algorithm 2 from several values of $\boldsymbol{d}_0$ and take minimum:

$$\begin{aligned}
&\texttt{Start with design } \boldsymbol{d}_0 = \{(n^{(0)}_{rkt}, n^{(0)}_{rkc})\}_k. \\
&\texttt{For iteration } j = 1, 2, \ldots: \\
&\quad \texttt{For each design } \boldsymbol{d}' \texttt{ in } \mathcal{D}_{j-1}: \\
&\quad\quad \texttt{Compute } \mathcal{R}_2(\boldsymbol{d'}, \boldsymbol{V}, 0)). \\
&\quad \texttt{Set } \boldsymbol{d_j} = \operatorname*{argmin}_{\boldsymbol{d'} \in \mathcal{D}_{j-1}} \mathcal{R}_2(\boldsymbol{d'}, \boldsymbol{V}, 0) \\
&\quad \texttt{If } \mathcal{R}_2(\boldsymbol{d_j}, \boldsymbol{V}, 0) >= \mathcal{R}_2(\boldsymbol{d_{j-1}}, \boldsymbol{V}, 0) \\
&\quad\quad \texttt{Return } d_{j-1}.
\end{aligned} \tag{2}$$