Shrinkage Estimation for Causal Inference and Experimental Design

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Introductions

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- Research interests
  - Causal inference, experimental design (this talk)
  - Voting, elections, political methodology

Outline

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  - Researcher controls treatment assignment $\Longrightarrow$
  - (Almost) no assumptions needed for unbiased treatment effect estimation!

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- Sometimes, cannot (ethically) run an RCT, e.g. smoking
- Even when you can, RCTs are typically too small to get a precise estimate for every effect we want...
  - Expensive to run! $\Longrightarrow$ few individuals recruited
  - May need an answer rapidly
  - What about effects on small subgroups?

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  - Often large, cheap, and representative! But...
  - No randomization $\Longrightarrow$ treated and untreated units differ $\Longrightarrow$ confounding bias!
    - Ex: Doctors give a drug to sicker patients
    - Ex: Healthier and wealthier people opt into a vaccine

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Overall goals

Can we use ODBs to...

- *obtain better causal estimates by combining ODB causal estimates with those obtained from RCTs?*
- *design prospective experiments to be more accurate?*

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  - Causal inference (Kallus et al., 2018; Ghassami et al., 2022; Mooij et al., 2016)
- Notable uptick in methodological work since roughly 2020 (Oberst et al., 2022; Yang et al., 2023; Cheng and Cai, 2021; Chen et al., 2021; Lin and Evans, 2023).

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Potential Outcomes Framework

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- Causal quantity we are interested in is

$$\tau_i = Y_i(1) - Y_i(0)$$

Causal Estimands

- **Fundamental Problem of Causal Inference**
  - Each unit has a treatment status $Z_i \in \{0, 1\}$, and we observe

$$Y_i = Z_i Y_i(1) + (1 - Z_i) Y_i(0).$$

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  - Hence: cannot observe both $Y_i(0)$ and $Y_i(1)$ simultaneously!
- Typically settle for:
  - **Average treatment effect (ATE):**

$$\mathbb{E}(Y(1) - Y(0)), \qquad \text{or}$$

  - **Conditional average treatment effect (CATE):**

$$\mathbb{E}(Y(1) - Y(0) \mid X \in \mathcal{X}).$$

Our Problem: Notation

- Observational data: n_o units sampled from

$$\Big(\underbrace{Y_i(0), Y_i(1)}_{\text{potential outcomes}}, \underbrace{X_i}_{\text{covariates}}, \underbrace{Z_i}_{\text{treatment indicators}}\Big) \stackrel{\text{iid}}{\sim} F_O.$$

- Experimental data: sample n_r units via

$$(Y_i(0), Y_i(1), X_i, Z_i) \stackrel{\text{iid}}{\sim} F_R.$$

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Assume strata $k = 1, \ldots, K$. Stratum k defined by set of covariates values $\mathcal{X}_k$. Define variables: $S_i = k \iff X_i \in \mathcal{X}_k$.

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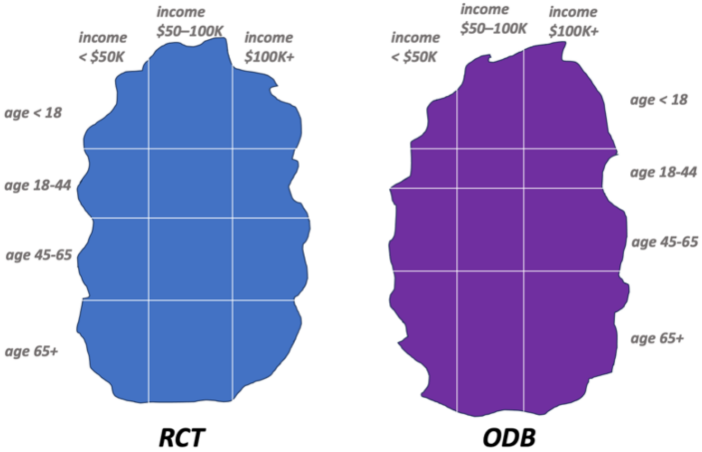

Figure 1: Example stratification of RCT and ODB with 12 strata.

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2. Under F_R,

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3. For $k = 1, \ldots, K$, have

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

   Assume **“transportability”** of CATEs across datasets.
   Denote as $\boldsymbol{\tau} = (\tau_1, \ldots, \tau_K) \in \mathbb{R}^K$ the vector of CATEs

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2. Assumptions and Set-Up
3. Estimators to Combine Data
   - SURE-Based Procedures
   - Using a Hierarchical Model
4. Application to the WHI

Setup

Collect our estimators into vectors:

$$\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} = (\hat{\tau}_{r1}, \ldots, \hat{\tau}_{rK}), \quad \hat{\boldsymbol{\tau}}_{\boldsymbol{o}} = (\hat{\tau}_{o1}, \ldots, \hat{\tau}_{oK}) \in \mathbb{R}^K$$

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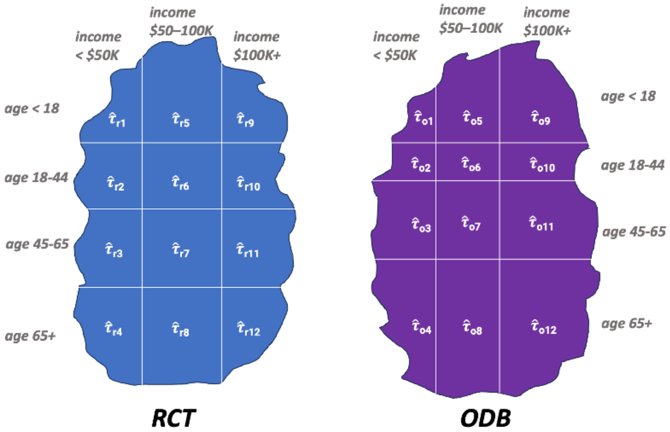

Figure 2: Causal estimates by stratum.

- Under mild conditions, we have

$$\hat{\tau}_r \sim N\left(\tau, \Sigma_r\right), \qquad \hat{\tau}_o \sim \left(\tau + \xi, \Sigma_o\right)$$

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- Seek to design estimator $\hat{\boldsymbol{\tau}} = f(\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}, \hat{\boldsymbol{\tau}}_{\boldsymbol{o}})$ to minimize expected squared error loss:

$$\mathcal{L}(\hat{\boldsymbol{\tau}}, \boldsymbol{\tau}) = \sum_{k=1}^{K} (\hat{\tau}_k - \tau_k)^2.$$

Useful Prior Work

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  - a normal, unbiased estimator (like $\hat{\tau}_r$), and
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  - a normal, unbiased estimator (like $\hat{\tau}_r$), and
  - a biased estimator (like $\hat{\tau}_o$)
- **Key ideas**
  - Take convex combinations of components of $\hat{\tau}_r$ and $\hat{\tau}_o$.
  - Bias-variance tradeoff: estimators can stabilize high-variance $\hat{\tau}_r$ by introducing some bias with shrinkage toward $\hat{\tau}_o$

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Stein's Unbiased Risk Estimate (SURE): foundational result in the shrinkage estimation literature.

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Upshot: when weighting between between (normal) estimator $\hat{\theta}_1$ and another estimator $\hat{\theta}_2$: SURE is an unbiased estimator of the *estimation error*, even if parameter θ is unknown!

Utility: gives us an objective function! To design estimators, a common tactic (Li et al., 1985; Xie et al., 2012) is to

1. posit a method to do the weighting
2. derive exact functional form by minimizing SURE

A Generalized Version of SURE (I)

Theorem (Estimator Risk)

Suppose we have $\boldsymbol{U} \sim \mathcal{N}(\boldsymbol{\theta}, \Sigma)$, *random* $\boldsymbol{B}$, *and* $\mathcal{L}(\boldsymbol{\theta}, \boldsymbol{v}) = (\boldsymbol{v} - \boldsymbol{\theta})^{\mathsf{T}}(\boldsymbol{v} - \boldsymbol{\theta})$ *where* $\Sigma = diag(\sigma_1^2, , \ldots, \sigma_k^2)$.

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$$\boldsymbol{\kappa}(\boldsymbol{U}, \boldsymbol{B}) = \boldsymbol{U} - \boldsymbol{g}(\boldsymbol{U}, \boldsymbol{B})$$

where $\boldsymbol{g}(\boldsymbol{U}, \boldsymbol{B})$ *is a function of* $\boldsymbol{U}$ *and* $\boldsymbol{B}$ *that is differentiable, satisfying* $\mathbb{E}(||\boldsymbol{g}||^2) < \infty$,

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where $\boldsymbol{g}(\boldsymbol{U}, \boldsymbol{B})$ *is a function of* $\boldsymbol{U}$ *and* $\boldsymbol{B}$ *that is differentiable, satisfying* $\mathbb{E}(||\boldsymbol{g}||^2) < \infty$, *we have*

$$\mathbb{E}\left(||\boldsymbol{\theta} - \boldsymbol{\kappa}(\boldsymbol{U}, \boldsymbol{B})||_2^2\right) = Tr(\Sigma) + \mathbb{E}\left(\sum_{k=1}^{K} g_k^2(\boldsymbol{U}, \boldsymbol{B}) - 2\sigma_k^2 \frac{\partial g_k(\boldsymbol{U}, \boldsymbol{B})}{\partial U_k}\right).$$

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From this theorem, obtain a generalization of Stein's Unbiased Risk Estimate (Stein, 1981),

$$\text{SURE}(\boldsymbol{\theta}, \boldsymbol{\kappa}(\boldsymbol{Z}, \boldsymbol{Y})) = \text{Tr}\,(\Sigma) + \sum_{k=1}^{K} g_k^2(\boldsymbol{U}, \boldsymbol{B}) - 2\sigma_k^2 \frac{\partial g_k(\boldsymbol{U}, \boldsymbol{B})}{\partial U_k}\,.$$

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In keeping with the literature, a simple procedure:

1. Posit a structure for the shrinkage estimator
2. Derive a functional form by minimizing SURE

Case 1: Common Shrinkage Factor

We consider shrinkage estimators which share a common shrinkage λ factor across components. Denote a 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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which has minimizer in λ,

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

A Note on λ_1^{SURE}

The true risk-minimizing shrinkage weight is given by

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λ_1^{SURE} substitutes $(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})^\mathsf{T} (\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})$ for its own expectation,

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

Useful Property of λ_1^{SURE}

Define

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

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

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

$\boldsymbol{\kappa}_1$ admits a testable condition under which it is guaranteed to reduce risk relative to $\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}$.

Lemma ($\boldsymbol{\kappa}_{1+}$ Risk Guarantee)

Suppose $4 \max_k \sigma_{rk}^2 < \sum_k \sigma_{rk}^2$. Then $\boldsymbol{\kappa}_{1+}$ has risk strictly less than that of $\hat{\boldsymbol{\tau}}_{\boldsymbol{r}}$.

- Requires a dimension of at least $K = 4$.
- May require substantially larger K if high heteroscedasticity or non-uniform weights.

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

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

and its positive-part improvement,

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

Simulated Data Visualization

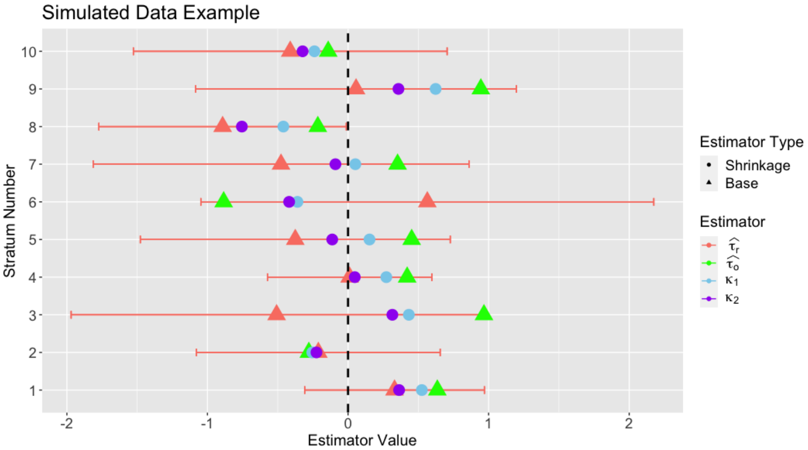

Figure 3: Simulated shrinkage between $\hat{\tau}_r$ and $\hat{\tau}_o$ with ten strata. 90% confidence intervals for $\hat{\tau}_r$ in red, with κ_{1+} and κ_{2+} shown in circles.

Outline

1. Problem Background
2. Assumptions and Set-Up
3. Estimators to Combine Data
   - SURE-Based Procedures
   - Using a Hierarchical Model
4. Application to the WHI

Alternative Approach: Hierarchical Model

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Simple model generalizing one introduced in Green and Strawderman (1991):

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$$\begin{aligned}
\boldsymbol{\tau} &\sim \mathcal{N}\left(0, \eta^2 \boldsymbol{I}_K\right), \\
\boldsymbol{\xi} &\sim \mathcal{N}\left(0, \gamma^2 \boldsymbol{I}_K\right), \\
\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} \mid \boldsymbol{\tau} &\sim \mathcal{N}\left(\boldsymbol{\tau}, \Sigma_r\right), \text{ and} \\
\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} \mid \boldsymbol{\tau}, \boldsymbol{\xi} &\sim \mathcal{N}\left(\boldsymbol{\tau} + \boldsymbol{\xi}, \Sigma_o\right).
\end{aligned} \tag{1}$$

for **unknown** hyperparameters η^2 and γ^2, but **known** covariance matrices Σ_r, Σ_o.

Estimator Form

Bayesian stats: compute **posterior mean** of $\boldsymbol{\tau}$ under Model 1:

$$\psi_k(\eta^2,\gamma^2) = \underbrace{\left(\frac{\eta^2\left(\gamma^2+\sigma_{ok}^2+\sigma_{rk}^2\right)}{\sigma_{rk}^2\left(\gamma^2+\sigma_{ok}^2\right)+\eta^2\left(\gamma^2+\sigma_{ok}^2+\sigma_{rk}^2\right)}\right)}_{\boldsymbol{a_k}(\boldsymbol{\eta}^2,\boldsymbol{\gamma}^2)\text{: aggregate shrinkage toward zero}} \times \left(\underbrace{\frac{\left(\gamma^2+\sigma_{ok}^2\right)}{\gamma^2+\sigma_{ok}^2+\sigma_{rk}^2}}_{\substack{\boldsymbol{\lambda_k}(\boldsymbol{\eta}^2,\boldsymbol{\gamma}^2)\text{:}\\ \text{data-driven weight}}}\hat{\tau}_{rk} + \underbrace{\frac{\sigma_{rk}^2}{\gamma^2+\sigma_{ok}^2+\sigma_{rk}^2}}_{1-\boldsymbol{\lambda_k}(\boldsymbol{\eta}^2,\boldsymbol{\gamma}^2)}\hat{\tau}_{ok}\right). \tag{2}$$

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This is the **double-shrinkage** property: take a data-driven convex combo of $\boldsymbol{\hat{\tau}_r}$ and $\boldsymbol{\hat{\tau}_o}$ and then a Stein-like shrinakge toward zero.

MLE Version of the Estimator

To construct a usable estimator, need estimates of η^2, γ^2.

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Maximum Likelihood: Observing that

$$\mathcal{L}(\eta^2, \gamma^2) \propto \prod_k \left(\eta^2 + \sigma_{rk}^2\right)^{-1/2} e^{-\frac{\hat{\tau}_{rk}^2}{2\left(\eta^2+\sigma_{rk}^2\right)}} \times \prod_k \left(\eta^2 + \gamma^2 + \sigma_{ok}^2\right)^{-1/2} e^{-\frac{\hat{\tau}_{ok}^2}{2\left(\eta^2+\gamma^2+\sigma_{ok}^2\right)}}.$$

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We can numerically optimize to obtain the estimates

$$(\hat{\eta}^2_{\text{mle}}, \hat{\gamma}^2_{\text{mle}}) = \max_{\eta^2, \gamma^2 \geq 0} \log\left(\mathcal{L}(\eta^2, \gamma^2)\right) .$$

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Definition (Robust EB Confidence Intervals (EBCIs))

The robust EBCI for ψ_k, the causal effect estimate obtained from any version of double-shrinkage estimators, is

$$\psi_k \pm cva(c_k)\hat{a}_k \sqrt{\left(\hat{\lambda}_k^2 \sigma_{rk}^2 + (1-\hat{\lambda}_k)^2 \sigma_{ok}^2\right)},$$

where $\hat{a}_k$ and $\hat{\lambda}_k$ are the shrinkage factors, and $cva(c_k)$ is an inflation factor whose form is given in Armstrong et al. (2020).

Outline

WHI Overview

Dataset Overview

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

Application to the WHI

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  - Compute squared error loss for $\hat{\tau}_r, \hat{\psi}_{\text{mle}}, \kappa_{1+}, \kappa_{2+}, \delta_1, \delta_2$.

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- Average loss over draws

Choice of Stratification Variables

Stratify on:

- two variables from WHI protocol:
  age + history of cardiovascular disease (Roehm, 2015).
- a variable unassociated with treatment effect:
  solar irradiance ("sun") $\Longrightarrow$ uncorrelated with outcome

Results

Subgroup Variable(s)	# of Strata	Loss as % of $\hat{\tau}_r$ Loss				
		$\hat{\psi}_{\text{mle}}$	κ_{1+}	κ_{2+}	δ_1	δ_2
CVD	2	**16%**	36%	36%	100%	100%
Age	3	**16%**	37%	30%	62%	73%
Sun	5	**9%**	28%	22%	40%	52%
CVD, Age	6	**21%**	39%	42%	38%	82%
CVD, Sun	10	**17%**	34%	36%	30%	87%
Age, Sun	15	**8%**	22%	21%	23%	43%
Age, CVD, Sun	30	**20%**	51%	51%	50%	78%

Further Work: Design

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

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- implies how to *recruit* ...
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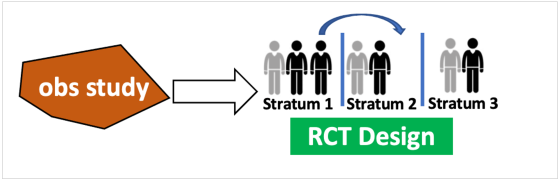

Current & Future Work

- Current work
  - **Applied project**: air pollution and mortality. Synthesizing evidence from Medicare claims database with Medicare Current Beneficiary Survey using these estimators.
  - **Design methods**: extending to online & adaptive designs

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  - **Applied project**: air pollution and mortality. Synthesizing evidence from Medicare claims database with Medicare Current Beneficiary Survey using these estimators.
  - **Design methods**: extending to online & adaptive designs
- Future work
  - **ML approaches**: shrinkage between flexible *functional* estimates of CATEs $\hat{\tau}_{\boldsymbol{r}}(x)$ and $\hat{\tau}_{\boldsymbol{o}}(x)$
  - **Inference:** are shorter confidence intervals possible?

Acknowledgments

Thank you to my collaborators on this work:

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

The papers...

- *SURE-based procedure* paper available in Biometrics.
- *Hierarchical model* paper available at arXiv:2309.06727.
- *Design* paper available in Electronic Journal of Statistics.

Thanks!

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Appendices

A New Setting: Design

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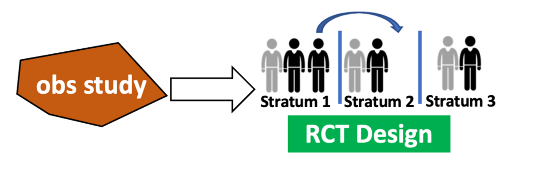

Estimator and Risk

We proceed with our estimator $\boldsymbol{\kappa}_1$ from the prior section:

$$\boldsymbol{\kappa}_1 = \hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \left(\frac{\mathrm{Tr}(\Sigma_r)}{(\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})^{\mathsf{T}} (\hat{\boldsymbol{\tau}}_{\boldsymbol{o}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{r}})} \right) (\hat{\boldsymbol{\tau}}_{\boldsymbol{r}} - \hat{\boldsymbol{\tau}}_{\boldsymbol{o}}) \ ,$$

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Optimize experimental design over $\mathcal{R}_1(\boldsymbol{d}, \boldsymbol{V}, \boldsymbol{\xi})$, the risk of $\boldsymbol{\kappa}_1$ under fixed $\hat{\boldsymbol{\tau}}_{\boldsymbol{o}}$, with

- design $\boldsymbol{d}$
- stratum potential outcome variances $\boldsymbol{V} = \{(\hat{\sigma}^2_{kt}, \hat{\sigma}^2_{kc})\}_{k=1}^{K}$
- bias vector $\boldsymbol{\xi}$.

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

Design Heuristics

Can estimate $\hat{\boldsymbol{V}}$ using pilot estimates obtained from ODB:

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

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Design heuristics:

1. **Naïve Optimization**: Assume $\xi = 0$ and minimize $\mathcal{R}_1(\boldsymbol{d}, \hat{\boldsymbol{V}}, \xi = 0)$ over $\boldsymbol{d}$, via **greedy swap algorithm**.
2. **Robust Optimization**: Under model of Tan (2006) and a user-chosen value of sensitivity $\Gamma \geq 1$, optimize the design $\boldsymbol{d}$ under worst-case bias

1. Neyman Allocation

Can estimate $\boldsymbol{V}$ using pilot estimates obtained from 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, 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.

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

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

$$
\begin{aligned}
\text{minimize} \quad & \mathcal{R}_2(\boldsymbol{d}, \boldsymbol{V}, \xi) \\
\text{subject to} \quad & \xi = 0, \boldsymbol{V} = \{(\hat{\sigma}^2_{kt}, \hat{\sigma}^2_{kc})\}_{k=1}^{K}, \\
& 0 < n_{rkt}, n_{rkc}, , \quad k = 1, \ldots, K, \\
& n_r = \sum_k n_{rkt} + n_{rkc} \, .
\end{aligned} \tag{3}
$$

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

2. 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 4 from several values of $\boldsymbol{d}_0$ and take minimum:

$$\begin{aligned}
&\texttt{Start with design } \boldsymbol{d}_0 = \{(n^{(0)}_{rkt}, n^{(0)}_{rkc})\}_k\,. \\
&\texttt{For iteration } j = 1, 2, \ldots : \\
&\quad \texttt{For each design } \boldsymbol{d}' \texttt{ in } \mathcal{D}_{j-1}\texttt{:} \\
&\qquad \texttt{Compute } \mathcal{R}_2(\boldsymbol{d'}, \boldsymbol{V}, 0))\,. \\
&\quad \texttt{Set } \boldsymbol{d_j} = \operatorname*{argmin}_{\boldsymbol{d'} \in \mathcal{D}_{j-1}} \mathcal{R}_2(\boldsymbol{d'}, \boldsymbol{V}, 0) \\
&\quad \texttt{If } \mathcal{R}_2(\boldsymbol{d_j}, \boldsymbol{V}, 0) >= \mathcal{R}_2(\boldsymbol{d_{j-1}}, \boldsymbol{V}, 0) \\
&\qquad \texttt{Return } d_{j-1}\,.
\end{aligned} \tag{4}$$

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

- Can take a more pessimistic approach again 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...
  - if outcome $Y_i \in \{0, 1\}$, can obtain associated $\hat{\sigma}^2_{kt}$ and $\hat{\sigma}^2_{kc}$.

$$\Gamma \implies$$

$$\boldsymbol{\xi}(\Gamma) \qquad \boldsymbol{V}(\Gamma) \implies$$

$$\mathcal{R}_2(\boldsymbol{d}, \boldsymbol{V}_\Gamma, \boldsymbol{\xi}_\Gamma) \qquad \mathcal{R}_2(\boldsymbol{d}, \boldsymbol{V}, 0)$$

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

- Can take a more pessimistic approach again using marginal sensitivity model of Tan (2006)
- Recall: for a user-chosen value of $\Gamma \geq 1$:
  - can obtain worst-case $\xi_k(\Gamma)$ using Zhao et al. (2019), and...
  - if outcome $Y_i \in \{0, 1\}$, can obtain associated $\hat{\sigma}^2_{kt}$ and $\hat{\sigma}^2_{kc}$.

posit a value of $\Gamma \Longrightarrow$

collect results into $\boldsymbol{V}(\Gamma)$ and $\boldsymbol{\xi}(\Gamma) \Longrightarrow$

run Algorithm 4 using $\mathcal{R}_2(\boldsymbol{d}, \boldsymbol{V}(\Gamma), \boldsymbol{\xi}(\Gamma))$ instead

Stratified WHI Study Design of $n_r = 1,000$ units

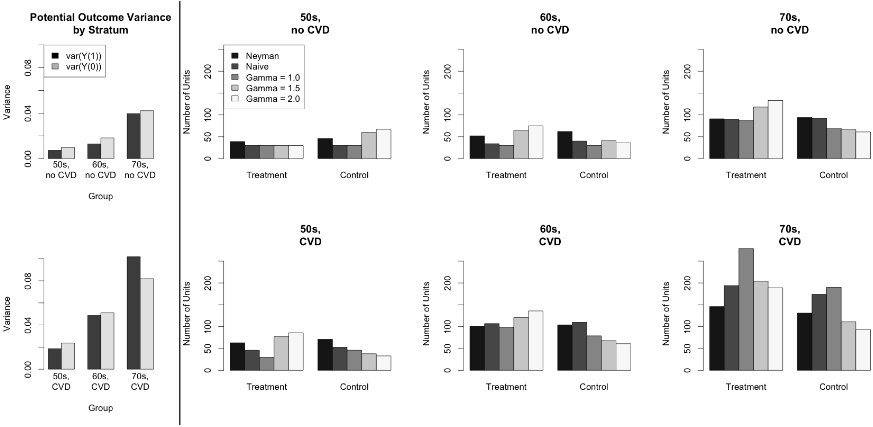

Figure 4: Allocations in WHI with strata defined by history of CVD and age, under different design heuristics.

Useful Properties of λ_1^{SURE} (I)

1. Define

$$\boldsymbol{\kappa}_1 = \hat{\boldsymbol{\tau}}_r - \lambda_1^{\text{SURE}} (\hat{\boldsymbol{\tau}}_r - \hat{\boldsymbol{\tau}}_o)$$

$\boldsymbol{\kappa}_1$ admits a testable condition under which it is guaranteed to reduce risk relative to $\hat{\boldsymbol{\tau}}_r$.

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 $\hat{\boldsymbol{\tau}}_r$.

- Requires a dimension of at least $K = 4$.
- May require substantially larger K if high heteroscedasticity or non-uniform weights.

Useful Properties of $\lambda_1^{\mathrm{SURE}}$ (II)

2. Its positive part analogue,

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

where

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

satisfies the following notion of optimality:

Useful Properties of λ_1^{SURE} (III)

Theorem (κ_{1+} Asymptotic Risk)

Suppose

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

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

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

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- **EB coverage** is a frequently-used weaker condition
  - Implies **average coverage**: under fixed τ, a $1-\alpha$ fraction of effects are covered with high probability in large samples
  - However, some outlying effects may <u>not</u> be covered with $1-\alpha$ probability across repeated samples of the data