# Estimating Causal Effects with Error-Prone Exposures Using Control Variates

ENAR 2024 Spring Meeting

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# Roadmap

Motivation

Problem setting

The control variates method

Simulation study: brief snapshot

Discussion

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- Effect of early ART initiation on 1-year post-initiation risk of suffering an AIDs-defining event

In observational studies, it is often difficult/expensive to obtain accurate measurements of the exposure $A$

- Time of initiation often transcribed/recalled incorrectly
    - Particularly when derived from electronic health records / self-reported

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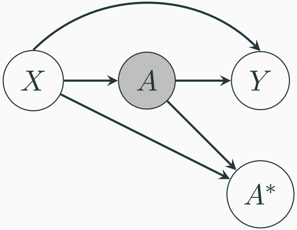

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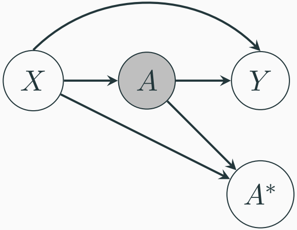

Growing literature on the perils of exposure measurement error in causal inference (Valeri 2021)

- Using $A^*$ in place of $A$ tends to produce biased effect estimates
- Difficult to correct for this bias without information on the measurement error mechanism
    - Requires *design-based* approaches that collect supplemental data

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    - Typically referred to as a *double sampling* study design (Hidiroglou 2001) or *validation study*
    - Usually infeasible to validate *every* subject (otherwise, would be no need for this talk)
- The subset of data with gold-standard measurements is typically referred to as the *validation data*
    - Intuition: provides complete information for a subset of data, and provides insight into measurement error mechanism

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**(b)** Validation dataset

# Assumptions

Make the standard causal inference assumptions: **consistency**, **positivity** and **unconfoundedness**

Additionally, assume the validation data is obtained completely at random: $S \perp\!\!\!\perp (Y, A, A^*, \boldsymbol{X})$

- Can be enforced by design in EHR data settings
- This can be relaxed to allow for more flexible validation sampling schemes/study designs

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Our approach is adapted from Yang and Ding (2019)

- **Idea**: Improve the efficiency of an initial unbiased (but inefficient) estimator of $\tau$ by **augmenting** it with a variance reduction term formed from the full data

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### Step 1: obtain validation data only estimator

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Validation data only estimate: $\hat{\tau}_{\text{val}}$

### Step 2: construct the control variate

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Error-prone estimate: $\hat{\tau}^{\text{e.p.}}_{\text{main}}$

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Error-prone estimate: $\hat{\tau}^{\text{e.p.}}_{\text{val}}$

### Step 3: Compute the variance reduction term

Obtain $\hat{\Gamma} = \widehat{\text{Cov}}(\hat{\tau}_{\text{val}}, \hat{\tau}^{\text{e.p.}}_{\text{main}} - \hat{\tau}^{\text{e.p.}}_{\text{val}})$ and $\hat{V} = \widehat{\text{Var}}(\hat{\tau}^{\text{e.p.}}_{\text{main}} - \hat{\tau}^{\text{e.p.}}_{\text{val}})$

### Step 4: Form the final estimator

Obtain final estimate: $\hat{\tau}_{\text{CV}} = \hat{\tau}_{\text{val}} - \hat{\Gamma}\hat{V}^{-1}(\hat{\tau}^{\text{e.p.}}_{\text{main}} - \hat{\tau}^{\text{e.p.}}_{\text{val}})$

# Control variates method: properties

**Efficiency gain**: $\mathsf{Var}(\hat{\tau}_{\mathsf{CV}}) = \mathsf{Var}(\hat{\tau}_{\mathsf{val}}) - \Gamma^2/V$, where

- $\Gamma$ is the covariance between $\hat{\tau}_{\mathsf{val}}$ and the control variate
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**Flexible estimation of nuisance models**:

- $\hat{\tau}_{\mathsf{CV}} \xrightarrow{p} \tau$ at $\sqrt{n}$ rates
- Even if the nuisance models are estimated with ML methods that themselves have slower rates of convergence
    - Common property of “doubly-robust” estimators

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The control variates method is **flexible** – can account for...

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The control variates method is **flexible** – can account for...

- More general validation data sampling schemes / account for multiple study sites
- Simultaneous error in the outcome of interest
- Other causal estimands
    - E.g. **local average treatment effects** if one has access to an instrumental variable

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# Brief snapshot of simulation study

Compared the control variates estimator to

- An oracle estimator (know $A$ for the entire dataset, estimate $\tau$ with AIPW) and a naive estimator that uses $A^*$ in place of $A$
- A validation data only estimator
- Multiple imputation
  - Standard method for performing causal inference with error-prone exposures

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# Brief snapshot of simulation study

Compared performances of each estimator under:

- Varying degrees of **exposure misclassification**
- Two different **sampling schemes** for the validation data
  1. Obtained completely at random
  2. Obtained conditionally (on $\boldsymbol{X}$) at random
- Varying the **relative size** of the validation data, $\mathbb{P}(S = 1)$
  - For this talk, $\mathbb{P}(S = 1) = 0.3$

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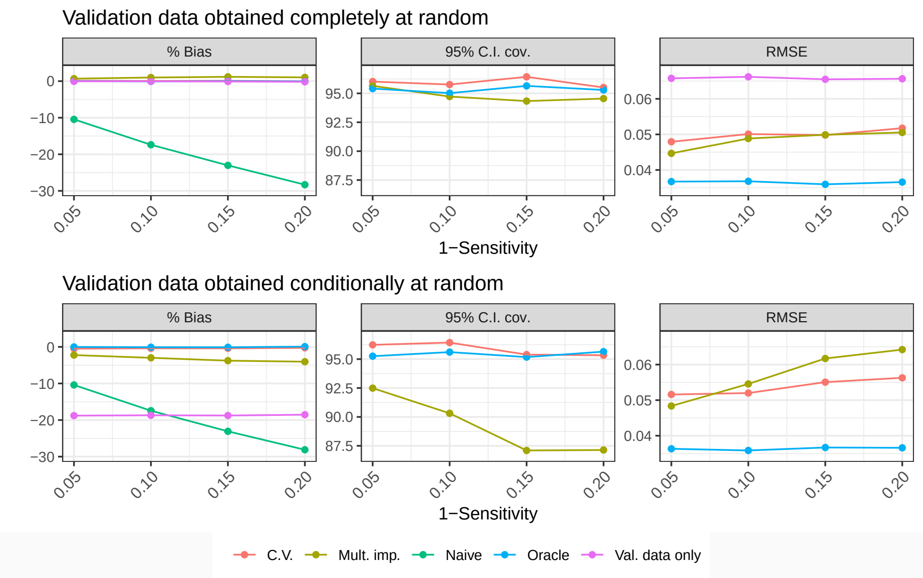

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    - with some additional theoretical properties commonly associated with traditional “doubly-robust” estimators

⚠ The control variates method isn’t appropriate for every measurement error problem

- Requires the availability of /ability to obtain a validation dataset
- As always, care should be taken to assess the plausibility of the causal assumptions

Thank you!

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Working paper coming soon!

# References

Dahabreh, I. J., Robertson, S. E., Tchetgen, E. J., Stuart, E. A., and Hernán, M. A. (2019). Generalizing causal inferences from individuals in randomized trials to all trial-eligible individuals. *Biometrics*, 75(2):685–694.

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# Variance Reduction

Notice

$$\begin{aligned}\mathsf{Var}(\hat{\tau}_{\mathsf{CV}}) &= \mathsf{Var}(\hat{\tau}_{\mathsf{val}}) + b^2\mathsf{Var}(\hat{\tau}_{\mathsf{main,ep}} - \hat{\tau}_{\mathsf{val,ep}}) - 2b\mathsf{Cov}(\hat{\tau}_{\mathsf{val}}, \hat{\tau}_{\mathsf{main,ep}} - \hat{\tau}_{\mathsf{val,ep}}) \\ &= \mathsf{Var}(\hat{\tau}_{\mathsf{val}}) + b^2 V - 2b\Gamma\end{aligned}$$

Minimzing with respect to $b$ yields

$$b = \Gamma V^{-1}$$

Implying with this choice of $b$,

$$\mathsf{Var}(\hat{\tau}_{\mathsf{CV}}) = \mathsf{Var}(\hat{\tau}_{\mathsf{val}}) - \Gamma^2 V^{-1}$$

Back to control variates slide

# Covariate-dependent selection

Back to main CV method

In many realistic scenarios, validation data won't just be a random draw from main dataset

- When that's the case, naively implementing C.V. method will actually *add* bias
- Intuition is that $\hat{\tau}_{\text{val,e.p.}} \overset{p}{\not\to} \hat{\tau}_{\text{main,e.p.}}$ when $\boldsymbol{X} \not\perp\!\!\!\perp S$ (distributions of effect modifiers are different)
- On top of that, our validation-data only estimator $\hat{\tau}_{\text{val}}$ will be subject to *external validity bias*

This implies we need to explore ways to

- Adjust $\hat{\tau}_{\text{val}}$ so that it targets the ATE in the population of interest
- Adjust $\hat{\tau}_{\text{val,e.p.}}$ in the same manner

# Covariate-dependent selection

In the 2 study *generalizability* setting, Dahabreh et al. (2019) and Zeng et al. (2023) have proposed the following doubly-robust estimator for $\tau$:

$$\hat{\psi}_a = \sum_{i=1}^{n} \left[ \frac{I(A_i = a, S_i = 1)(Y_i - \hat{\mu}_a(\boldsymbol{X}_i))}{\hat{\rho}(\boldsymbol{X}_i)\hat{\pi}_a(\boldsymbol{X}_i)} + \hat{\mu}_a(\boldsymbol{X}_i) \right]$$

- $\hat{\rho}(\boldsymbol{X}_i)$ is estimated probability of "selection" into val. data
- $\hat{\mu}_a(\boldsymbol{X}_i) = \hat{\mathbb{E}}(Y|\boldsymbol{X}_i, A = a, S = 1)$, $\hat{\pi}_a(\boldsymbol{X}_i) = \hat{\mathbb{P}}(A_i = a|\boldsymbol{X}_i, S_i = 1)$
- $\hat{\tau}$ is obtained by taking the difference $\hat{\psi}_1 - \hat{\psi}_0$

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3. Under the earlier causal assumptions, will have

$$\sqrt{n_{\text{val}}}\begin{pmatrix} \hat{\tau}_{\text{val}} - \tau \\ \hat{\tau}_{\text{main,ep}} - \hat{\tau}_{\text{val,ep}} \end{pmatrix} \xrightarrow{D} N\left(\mathbf{0}, \mathbf{\Sigma}\right), \quad \mathbf{\Sigma} = \begin{pmatrix} v & \Gamma \\ \Gamma & V \end{pmatrix}$$

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setting $b = \Gamma V^{-1}$ so that $\text{Var}(\hat{\tau}_{\text{CV}}) \leq \text{Var}(\hat{\tau}_{\text{val}})$ Finding $b$