# Federated Causal Inference: Multi-Source ATE Estimation beyond Meta-Analysis

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# Motivation

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- Goal of causal inference: measure the (average) impact of a treatment on an outcome

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    - Economics and social sciences: impact of studies on future earnings in developing countries? (Duflo, Glennerster, and Kremer, 2007)
    - Public Health & Economy: evaluating drugs efficacy. French social security reimburses drugs based on their proven efficacy. (French Health Authority, 2024)

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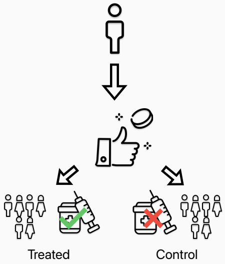

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  $\rightarrow$ Multisource approach: several RCTs are better than 1!

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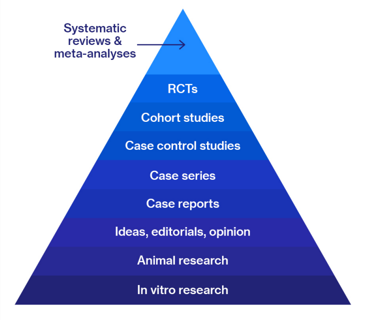

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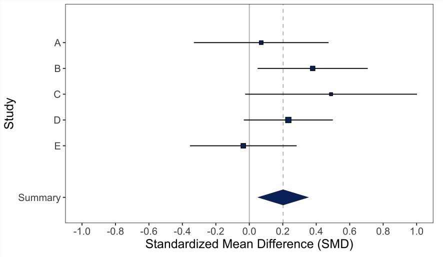

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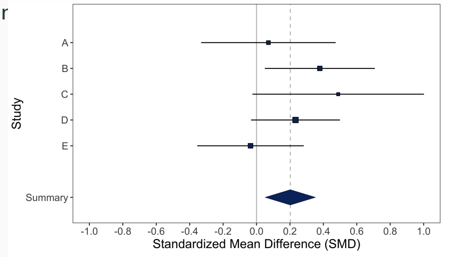

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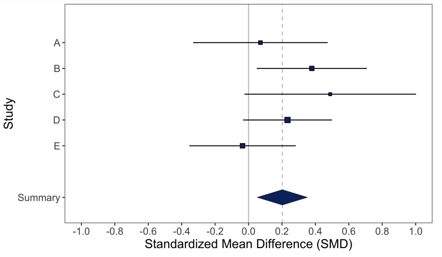

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    - Aggregates estimated causal effects from published summary statistics of multiple studies
    - Increased statistical power and more precise estimates
    - Keeps the data decentralized
    - Limits: no direct access of individual observations $\Longrightarrow$ face important challenges in presence of heterogeneity between the studies

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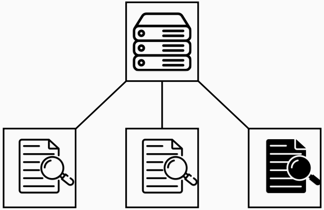

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  - Study and compare (bias and asymptotic variances) Meta-Analysis, One-Shot federated and Gradient Descent federated estimators of ATE
  - Compare their robustness to several heterogeneity scenarios

# Introduction to Causal Inference

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| Obs. | Covariates | | | Treatment | Outcome | Potential Outcomes | |
|---|---|---|---|---|---|---|---|
| $i$ | $X_1$ | $X_2$ | $X_3$ | $W$ | $Y$ | $Y^{(1)}$ | $Y^{(0)}$ |
| 1 | 2.3 | 1.5 | M | 1 | 3.2 | 3.2 | ?? |
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measured as a risk difference:

$$\tau = \mathbb{E}\left(Y_i(1) - Y_i(0)\right)$$

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(a) Unconfoundedness: $W_i \perp\!\!\!\perp \{Y_i(1), Y_i(0)\}$

RCTs: $W_i \sim \mathcal{B}(p_i), \implies W_i \perp\!\!\!\perp X_i$

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(b) Consistency: $Y_i = W_i Y_i(1) + (1 - W_i) Y_i(0)$

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**Unbiased ATE estimation:**

- Difference-in-Means:
$\hat{\tau}_{\mathrm{DM}} = \overline{Y_{|W=1}} - \overline{Y_{|W=0}}$

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| 1 | 2.3 | 1.5 | M | 1 | 3.2 | 3.2 | $\widehat{2.4}$ |
| 2 | 2.2 | 3.1 | F | 0 | 2.8 | $\widehat{3.5}$ | 2.8 |
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| $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ |
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- Covariate-adjusted G-Formula:
  $\hat{\tau}_{\mathrm{G}} = \frac{1}{n}\sum_{i=1}^{n}\left(\hat{\mu}_1(X_i) - \hat{\mu}_0(X_i)\right)$

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  $\hat{\tau}_{\mathrm{DM}} = \overline{Y_{|W=1}} - \overline{Y_{|W=0}}$
- Linearly-adjusted G-Formula:
  $\hat{\tau}_{\mathrm{OLS}} = \frac{1}{n}\sum_{i=1}^{n}\left(X_i\hat{\beta}^{(1)} - X_i\hat{\beta}^{(0)}\right)$

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  with $\hat{\beta}^{(w)}$ the OLS regressor learned on individuals with $W = w$.

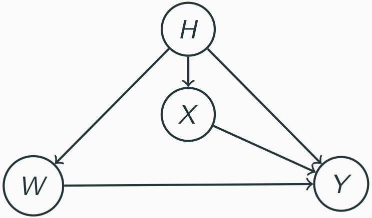
Refs.: U.S. Food and Drug Administration, 2023, European Medicines Agency, 2024, Tsiatis et al., 2008, Benkeser et al., 2021, Lin, 2013, Wager, 2020, Lei and Ding, 2021, Van Lancker, Bretz, and Dukes, 2024

Main Motivation: $\mathbb{V}(\hat{\tau}_{\mathrm{OLS}}) \leq \mathbb{V}(\hat{\tau}_{\mathrm{DM}})$ even when $\mu_1$ and $\mu_0$ are not linear functions!

# Multisource Causal Framework

- **Multisource** inference goal: estimate the impact of $W$ on $Y$ given $X$ describing a population, split across $K$ studies.
- Data is decentralized:

| Source | Obs. | Covariates | | | Treatment | Outcomes |
|---|---|---|---|---|---|---|
| $H$ | $i$ | $X_1$ | $X_2$ | $X_3$ | $W$ | $Y$ |
| 1 | 1 | 2.3 | 1.5 | M | 1 | 3.2 |
| 1 | 2 | 2.2 | 3.1 | F | 0 | 2.8 |
| $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ |
| 2 | 1 | 4.5 | 5.0 | F | 1 | 4.1 |
| $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ |
| $K$ | 1 | 3.7 | 2.0 | F | 0 | 2.8 |
| $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ | $\vdots$ |
| $K$ | $n_K$ | 2.5 | 1.7 | M | 0 | 3.2 |

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$$\tau = \mathbb{E}\left(\mathbb{E}\left(Y^{(1)} - Y^{(0)} \mid H\right)\right)$$

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|---|---|---|---|---|---|---|---|
| $H$ | $i$ | $X_1$ | $X_2$ | $X_3$ | $W$ | $Y$ | $\mathbb{P}(W_i)$ |
| 1 | 1 | 2.3 | 1.5 | M | 1 | 3.2 | $p_1$ |
| 1 | 2 | 2.2 | 3.1 | F | 0 | 2.8 | $p_1$ |
| ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ |
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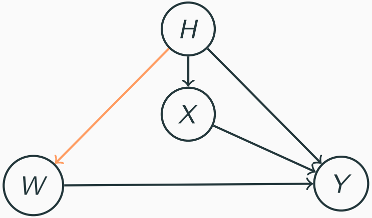
Heterogeneity in **treatment allocation**

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| $H$ | $i$ | $X_1$ | $X_2$ | $X_3$ | $W$ | $Y$ | $\mathcal{D}$ |
| 1 | 1 | 2.3 | 1.5 | M | 1 | 3.2 | $\mathcal{D}_1$ |
| 1 | 2 | 2.2 | 3.1 | F | 0 | 2.8 | $\mathcal{D}_1$ |
| ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ |
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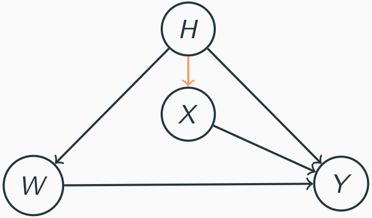
Heterogeneity in **covariates distribution**

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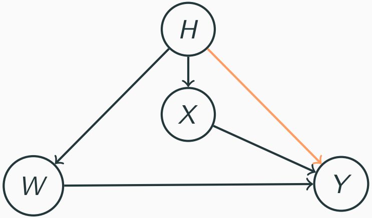
| $H$ | $i$ | $X_1$ | $X_2$ | $X_3$ | $W$ | $Y$ | + cste |
| 1 | 1 | 2.3 | 1.5 | M | 1 | 3.2 | $h_1$ |
| 1 | 2 | 2.2 | 3.1 | F | 0 | 2.8 | $h_1$ |
| ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ |
| 2 | 1 | 4.5 | 5.0 | F | 1 | 4.1 | $h_2$ |
| ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ |
| $K$ | 1 | 3.7 | 2.0 | F | 0 | 2.8 | $h_3$ |
| ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ | ⋮ |
| $K$ | $n_K$ | 2.5 | 1.7 | M | 0 | 3.2 | $h_3$ |

Heterogeneity in **center effects**




**ATE**:

$$\tau = \mathbb{E}\left(\mathbb{E}\left(Y^{(1)} - Y^{(0)} \mid H\right)\right)$$

$\rightarrow$ How to estimate $\tau$?

# Federated Causal Inferences: estimation strategies

$k = 1$  $\hat{\tau}_1$

$k = 2$  $\hat{\tau}_2$

$\vdots$

$k = K$  $\hat{\tau}_K$

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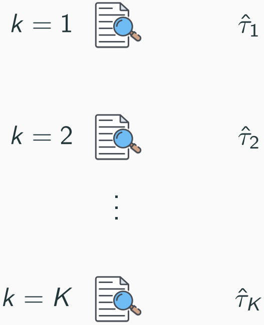
**Global estimates of the treatment effect**:

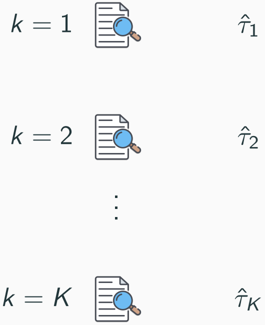
# Federated Causal Inferences: estimation strategies




**Global estimates of the treatment effect**:

- **Meta-analysis**: average-weighted aggregation of local estimates $\rightarrow \hat{\tau} = \sum_{k=1}^{K} w_k \hat{\tau}_k$

# Federated Causal Inferences: estimation strategies

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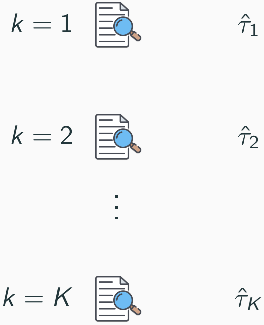


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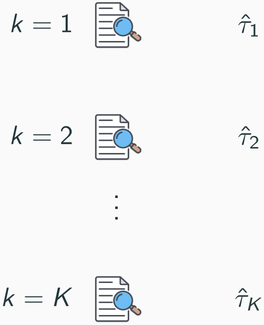


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- Federated estimation:
  a. Learn the parameters for the outcome and/or propensity score models
  b. Build a global estimate $\hat{\tau}$ from these models (e.g., G-Formula, IPW, AIPW).

# Multi-sources ATE Estimation

# Federated ATE estimation in linear outcome modelling

- Denote $X_k^{(w)}$ (resp. $Y_k^{(w)}$) the covariates matrix (resp. outcome vector) of study $k$ under treatment arm $w$

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$\rightarrow$ Goal: estimate $\tau := \mathbb{E}\left(\mathbb{E}(Y_i^{(1)} - Y_i^{(0)} \mid H_i)\right) = c^{(1)} - c^{(0)} + \mathbb{E}(\mathbb{E}(X_i \mid H_i))(\beta^{(1)} - \beta^{(0)})$.

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**Local causality assumptions**:

- Consistency: $\forall i, Y_i = W_i Y_i^{(1)} + (1 - W_i) Y_i^{(0)}$
- Positivity: $\forall x \in \mathcal{X}, \exists \eta > 0$ s.t. $\eta \leq \mathbb{P}(W_i = 1 \,|\, X_i = x) \leq 1 - \eta$
- Unconfoundedness: $W_i \perp\!\!\!\perp \{Y_i^{(1)}, Y_i^{(0)}\} \,|\, X_i, H_i$

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**Regression assumptions**:

- $\forall (k, w), \mathbb{E}(X_k^\top \varepsilon(w)) = 0, \mathbb{V}\left(\varepsilon(w) \mid X_k\right) = \sigma^2,$
- Local Full Rank: $\text{rank}(X_k^\top X_k) = d$

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**Pool G-Formula estimator:**

$$\hat{\tau} = \frac{1}{n}\sum_{i=1}^{n}(\hat{\mu}_1(X) - \hat{\mu}_0(X)) = \frac{1}{n}\sum_{i=1}^{n} X_i(\hat{\theta}^{(1)}_{\text{pool}} - \hat{\theta}^{(0)}_{\text{pool}})$$

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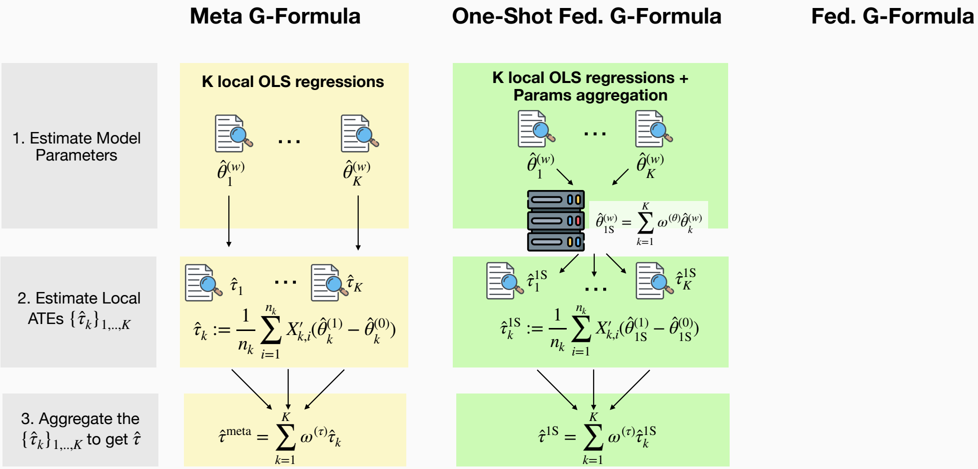
$\rightarrow$ Problem: we do not have access to the pooled dataset !

$\rightarrow$ Need to consider other estimation strategies for $\hat{\tau}$.

# Meta vs. (One Shot) Federated G-Formula

| | Meta G-Formula | One-Shot Fed. G-Formula | Fed. G-Formula |
|---|---|---|---|
| 1. Estimate Model Parameters | **K local OLS regressions**<br>$\hat{\theta}_1^{(w)}$ ... $\hat{\theta}_K^{(w)}$ | | |
| 2. Estimate Local ATEs $\{\hat{\tau}_k\}_{1,..,K}$ | $\hat{\tau}_1$ ... $\hat{\tau}_K$<br>$\hat{\tau}_k := \frac{1}{n_k} \sum_{i=1}^{n_k} X'_{k,i}(\hat{\theta}_k^{(1)} - \hat{\theta}_k^{(0)})$ | | |
| 3. Aggregate the $\{\hat{\tau}_k\}_{1,..,K}$ to get $\hat{\tau}$ | $\hat{\tau}^{\text{meta}} = \sum_{k=1}^{K} \omega^{(\tau)} \hat{\tau}_k$ | | |

# Meta vs. (One Shot) Federated G-Formula



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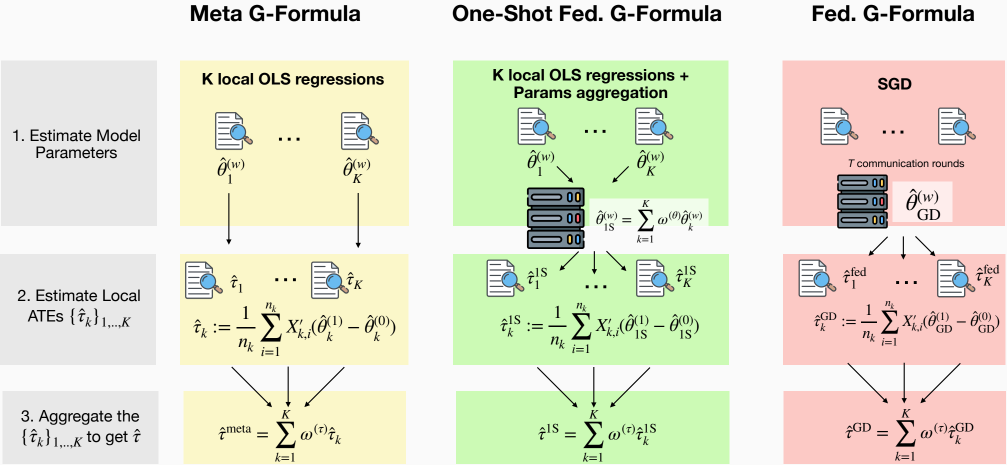

# Comparison of the Estimators

## Homogeneous setting

# Asymptotic Variances

Homogeneous population setting:

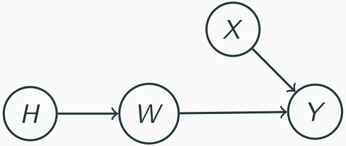


**Figure 1:** Graphical model: $K$ RCTs

$\implies \forall\{k, i\}, W_{k,i} \sim \mathcal{B}(p_k)$, different treatment allocation schemes.

# Asymptotic Variances

Under an Homogeneous setting, all estimators are unbiased and:

| Estimator | Notation | $\mathbb{V}^\infty$ | Com. rounds | Com. cost |
|---|---|---|---|---|
| Meta-SW | $\hat{\tau}_{\text{Meta-SW}}$ | $\frac{\sigma^2}{n}\sum_{k=1}^{K}\frac{\rho_k}{p_k(1-p_k)}+\frac{1}{n}\lVert\beta^{(1)}-\beta^{(0)}\rVert_\Sigma^2$ | 1 | $O(1)$ |
| Meta-IVW | $\hat{\tau}_{\text{Meta-IVW}}$ | $\left(\sum_{k=1}^{K}(\sigma^2\frac{n\rho_k}{p_k(1-p_k)}+\frac{1}{n_k}\lVert\beta^{(1)}-\beta^{(0)}\rVert_\Sigma^2)^{-1}\right)^{-1}$ | 1 | $O(1)$ |
| 1S-SW | $\hat{\tau}_{\text{1S-SW}}$ | $V_{\text{pool}}$ | 2 | $O(d)$ |
| 1S-IVW | $\hat{\tau}_{\text{1S-IVW}}$ | $V_{\text{pool}}$ | 2 | $O(d^2)$ |
| GD | $\hat{\tau}_{\text{GD}}$ | $V_{\text{pool}}$ | $T+1$ | $O(Td)$ |
| Pool | $\hat{\tau}_{\text{pool}}$ | $V_{\text{pool}}=\frac{\sigma^2}{n}\frac{1}{p(1-p)}+\frac{1}{n}\lVert\beta^{(1)}-\beta^{(0)}\rVert_\Sigma^2$ | — | — |

with $\rho_k := \mathbb{P}(H_i = k) = \mathbb{E}(n_k)/n$ and $p = \sum_{k=1}^K \frac{n_k}{n} p_k$.

# Comparison of Variances - Homogeneous Setting

$$\begin{aligned}\mathbb{V}^{\infty}(\hat{\tau}_{\mathsf{pool}}) &= \mathbb{V}^{\infty}(\hat{\tau}_{\mathrm{GD}}) \\ &= \mathbb{V}^{\infty}(\hat{\tau}_{\mathrm{1S-SW}}) \\ &= \mathbb{V}^{\infty}(\hat{\tau}_{\mathrm{1S-IVW}})\end{aligned}$$

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# Comparison of Variances - Homogeneous Setting

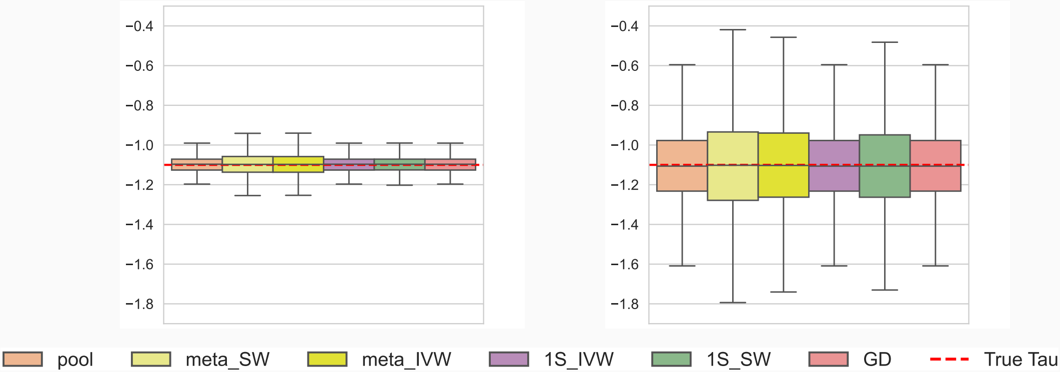
Parameters: $d = 10, K = 5$

**Large**

$\{n_k\}_k = 100 * d$, 3 studies have $p_k = 0.9$, 2 have $p_k = 0.1$

**Small**

$\{n_k\}_k = 5 * d$, 3 studies have $p_k = 0.65$, 2 have $p_k = 0.35$



# Comparison of the Estimators

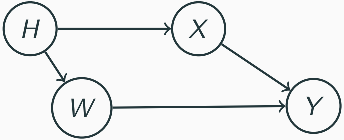
## Heterogeneous Distributions

# Comparison of Variances - Heterogeneity in $X$

Distributional Shift:

$$H \not\perp X \implies \mathcal{D}_k \neq \mathcal{D}_l \implies \tau_k \neq \tau_l$$

**Figure 1:** Graphical model for the heterogeneous distributions setting.

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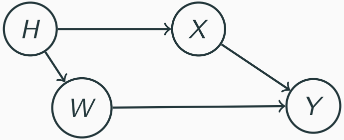


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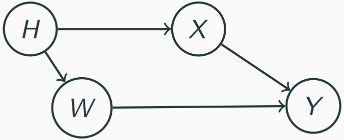


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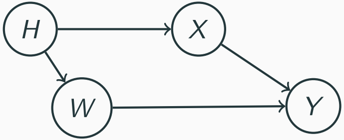


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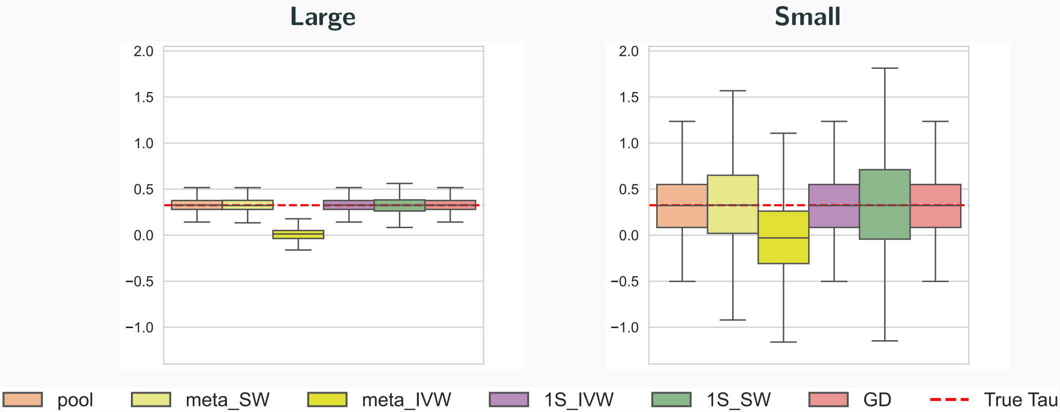
$$\mathbb{V}^{\infty}(\hat{\tau}_{\mathrm{pool}}) = \mathbb{V}^{\infty}(\hat{\tau}_{\mathrm{GD}}) = \mathbb{V}^{\infty}(\hat{\tau}_{\mathrm{1S-IVW}}) \leq \mathbb{V}^{\infty}(\hat{\tau}_{\mathrm{meta-SW}})$$

# Comparison of Variances - Heterogeneity in $X$

$$\forall k, X_k \sim \mathcal{N}(\mu_k, \Sigma_k)$$



# Comparison of the Estimators

## Presence of Center Effects

# Comparison of Variances - Heterogeneity through Center Effects

Presence of a constant (real-valued) effect of the center $k$ onto the outcome $Y$:

$$Y_{k,i}^{(w)} = c^{(w)} + \underline{h_k} + X_{k,i}\beta^{(w)} + \varepsilon_i(w)$$

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Studies may have different baselines in individual outcomes, from varying practices or organizational contexts (e.g. hospital specialized in oncology).

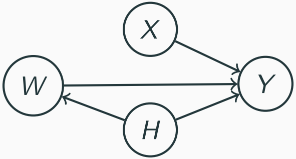


**Figure 1:** Graphical model for the center effects setting.

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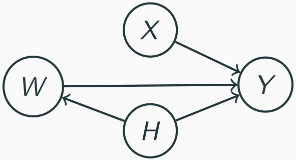


**Figure 1:** Graphical model for the center effects setting.

Caution: $H$ is now a confounder!

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Properties:

- All federated estimators are **biased** and need to be adjusted **except the metas** which naturally account for the center effects.

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Properties:

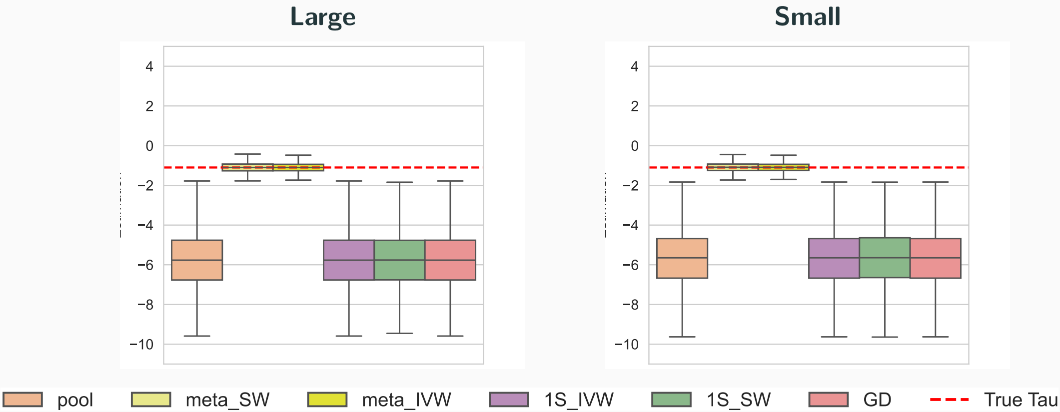
- All federated estimators are **biased** and need to be adjusted **except the metas** which naturally account for the center effects.

Adjustment:

- Adjusted One-Shot estimators: share and aggregate only the covariates coefficients $\hat{\beta}_k$, while keeping the intercepts local
- Adjusted Gradient Descent: add $H$ variable into the datasets.

# Comparison of Variances - Heterogeneity through Center Effects

$$(h_1, h_2, h_3, h_4, h_5) = (1, .2, -1, 30, 2) \text{ and different } p_k$$



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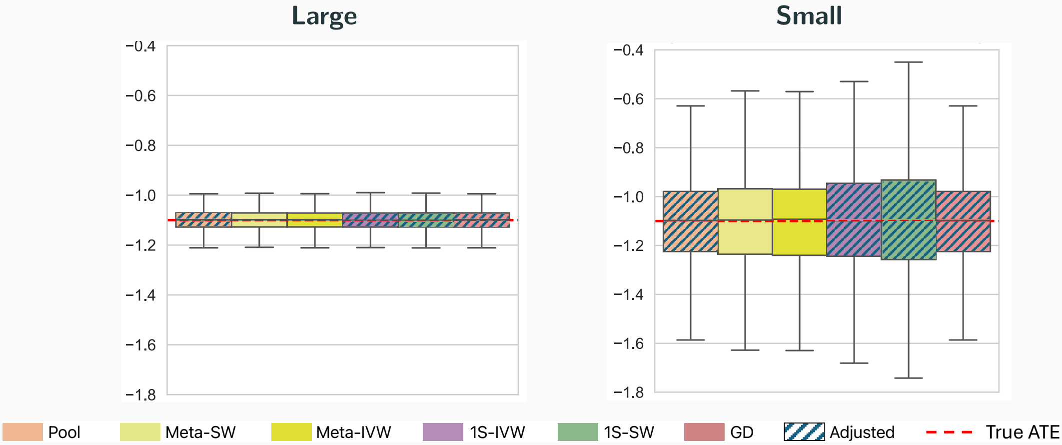
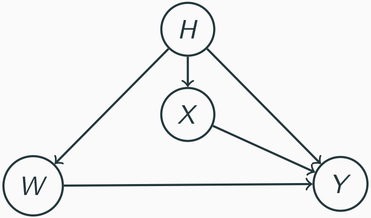


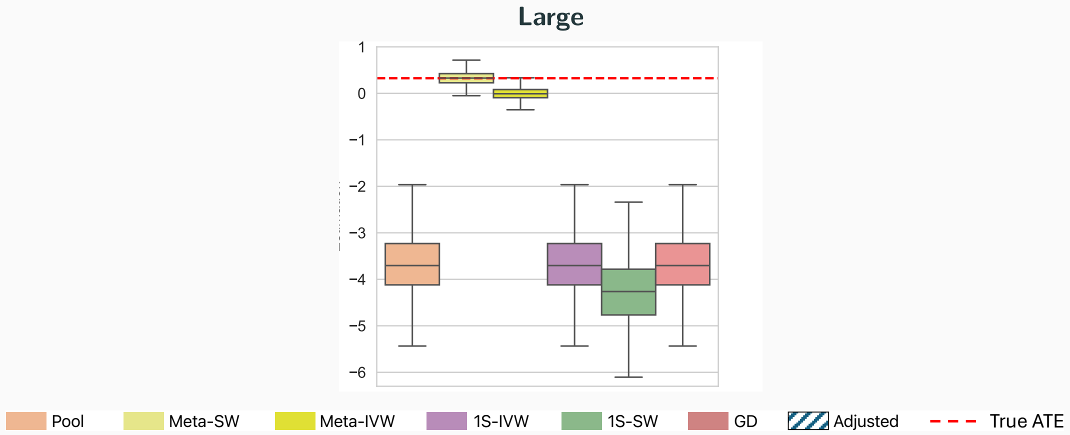
# Full Heterogeneity

Fully heterogeneous setting, realistic:



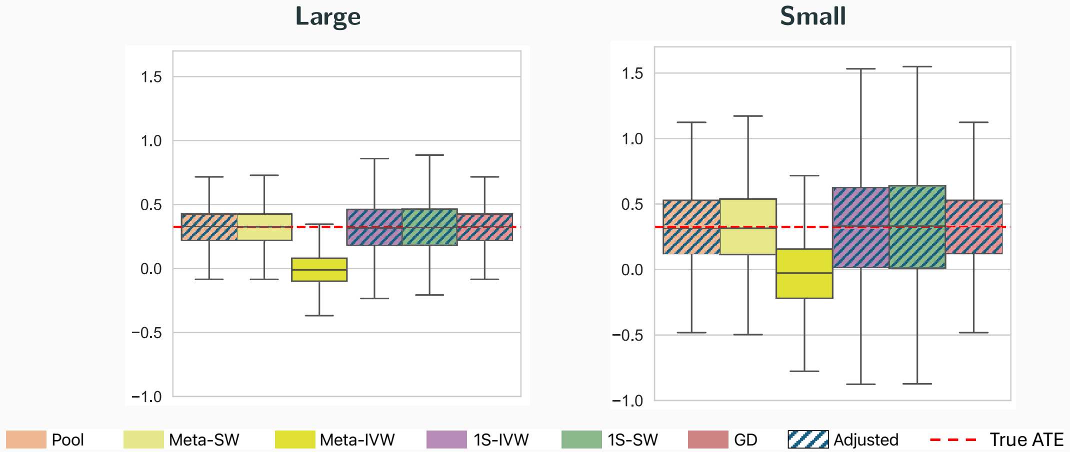
# Full Heterogeneity

Different $(h_k, p_k, \mu_k, \Sigma_k)$



# Full Heterogeneity

Different $h_k, p_k, \mu_k, \Sigma_k$



# Federated Causal Inferences: challenges

| | Meta-Analysis | One-Shot FL Learning | GD FL |
|---|---|---|---|
| + | • Easy to implement<br>• Private and low communications: 1 round<br>• Shares only summary statistics:<br>  ◦ Locally estimated ATEs $\{\hat{\tau}_k\}$<br>  ◦ Sample sizes $\{n_k\}$ or estimated variances $\{\hat{V}(\hat{\tau}_k)\}$ | • Easy to implement<br>• Private and low communications: 2 rounds<br>• Shares summary statistics:<br>  ◦ Sample sizes $\{n_k\}$ or empirical variance-covariance matrices $\{\hat{\Sigma}_k\}$ (can be costly when $d$ is large)<br>  ◦ Locally estimated ATEs with One-Shot federated outcome models $\{\hat{\tau}_k^{1\mathrm{S}}\}$ | • Flexible: (non-)parametric models, estimate <u>function</u> $\tau(X)$<br>• **Robust to locally small sample sizes** $(n_k^{(w)} < d)$<br>• **Robust to different treatment schemes**<br>• Private: using secure aggregation or differential privacy<br>• Accurate: learn from the pool dataset as if it was centralized |
| - | • Sensitive to imbalance in sample sizes<br>• No access to individual data: cannot detect and qualify heterogeneity<br>• The aggregation with lowest variance (IVW) yields a biased estimate under heterogeneity in distributions | • Not designed for heterogeneous settings | • Harder to implement in practice<br>• Heavy computations: compute $\nabla f(\hat{\theta})$ at each round |

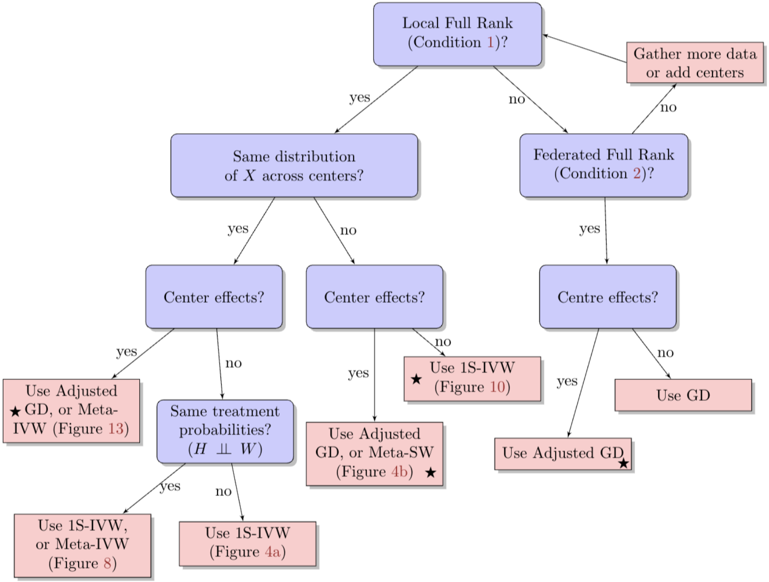



Figure 6: Decision Diagram for Practitionners. The sign ★ denotes scenarios where the DM estimator is biased.

# Perspectives

- Extend this work to **observational studies**.
- Quantify the bias and variances of the estimators in **finite sample sizes** settings.
- **Non-parametric** and non-linear approaches: federated random forests, neural networks, etc.
- Apply the **Differential-Privacy** framework to federated causal inferences.

# Scan my paper!

Thank you!

# References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