Multiply Robust Federated Estimation of Targeted Average Treatment Effects

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Promises of distributed research networks

- OHDSI
- PCORNET
- FDA Sentinel
- 4CE
- …

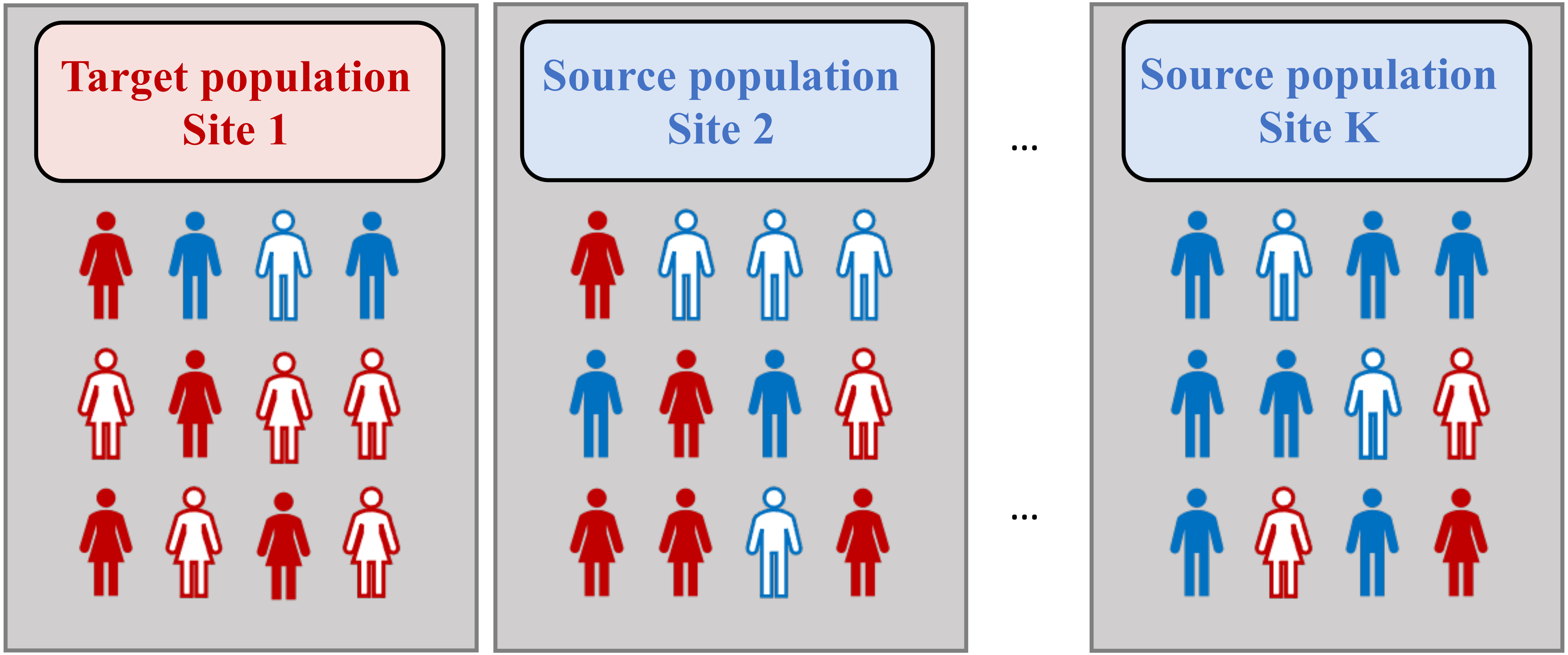
Promises of distributed research networks

- *OHDSI*
- *PCORNET*
- *FDA Sentinel*
- *4CE*
- *…*

✓ Enhance generalizability

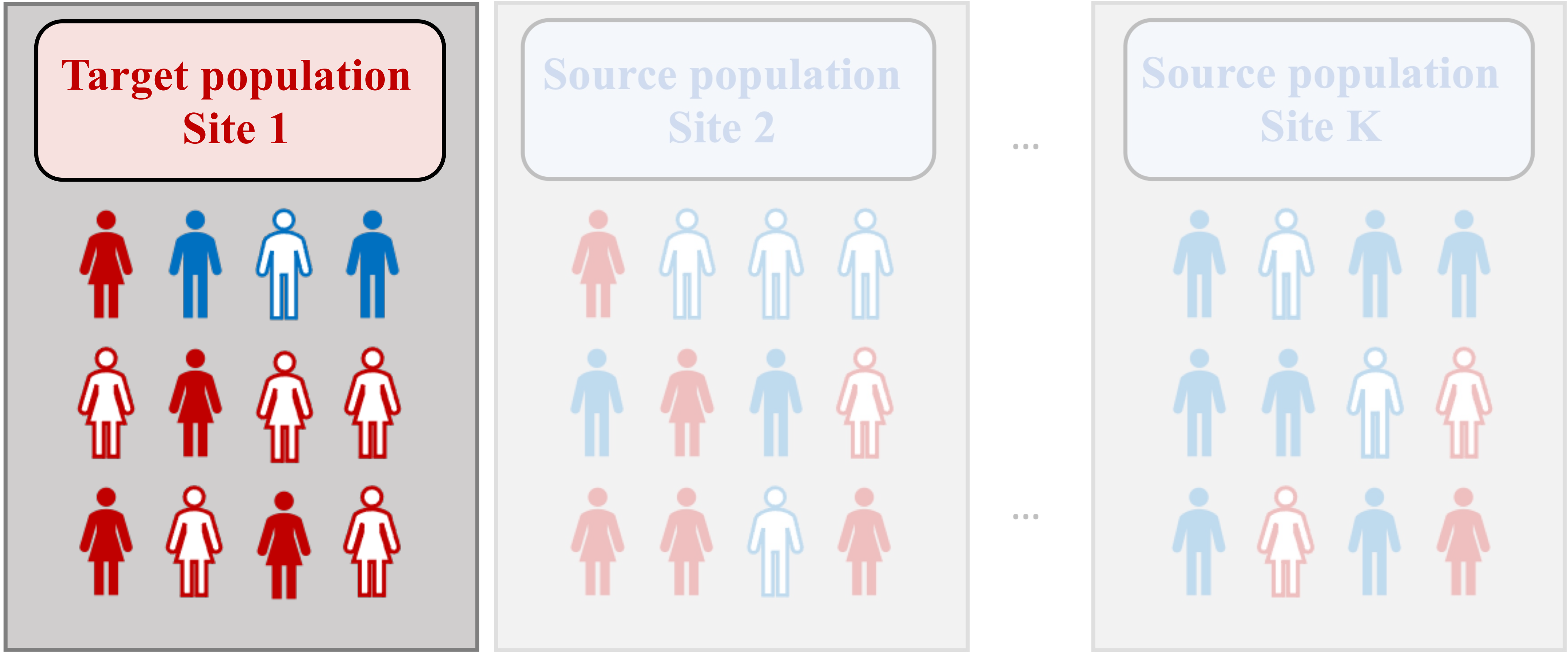
✓ Accelerate decision-making

✓ Study underrepresented populations, rare diseases, and exposures



Question we seek to answer

In multi-source settings, how can we make optimal use of available data to make causal inferences for a target population of interest?



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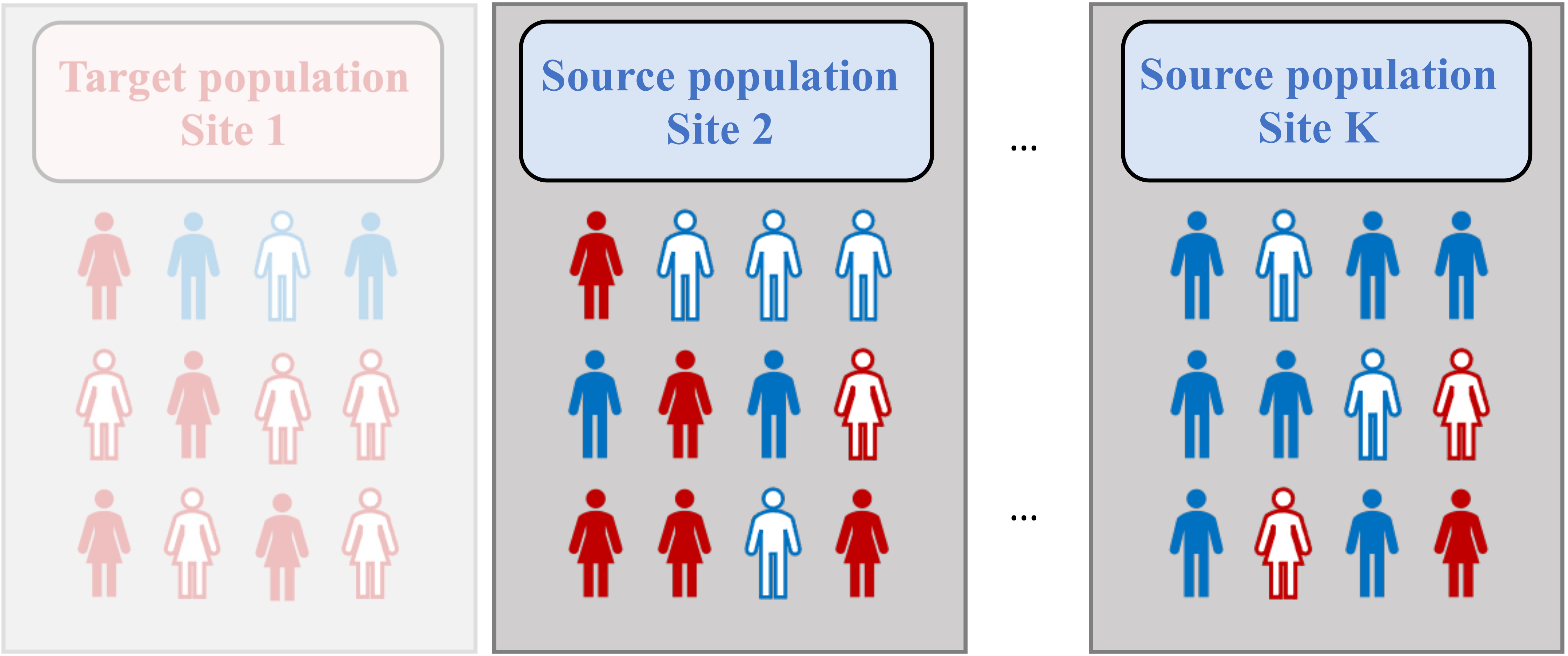

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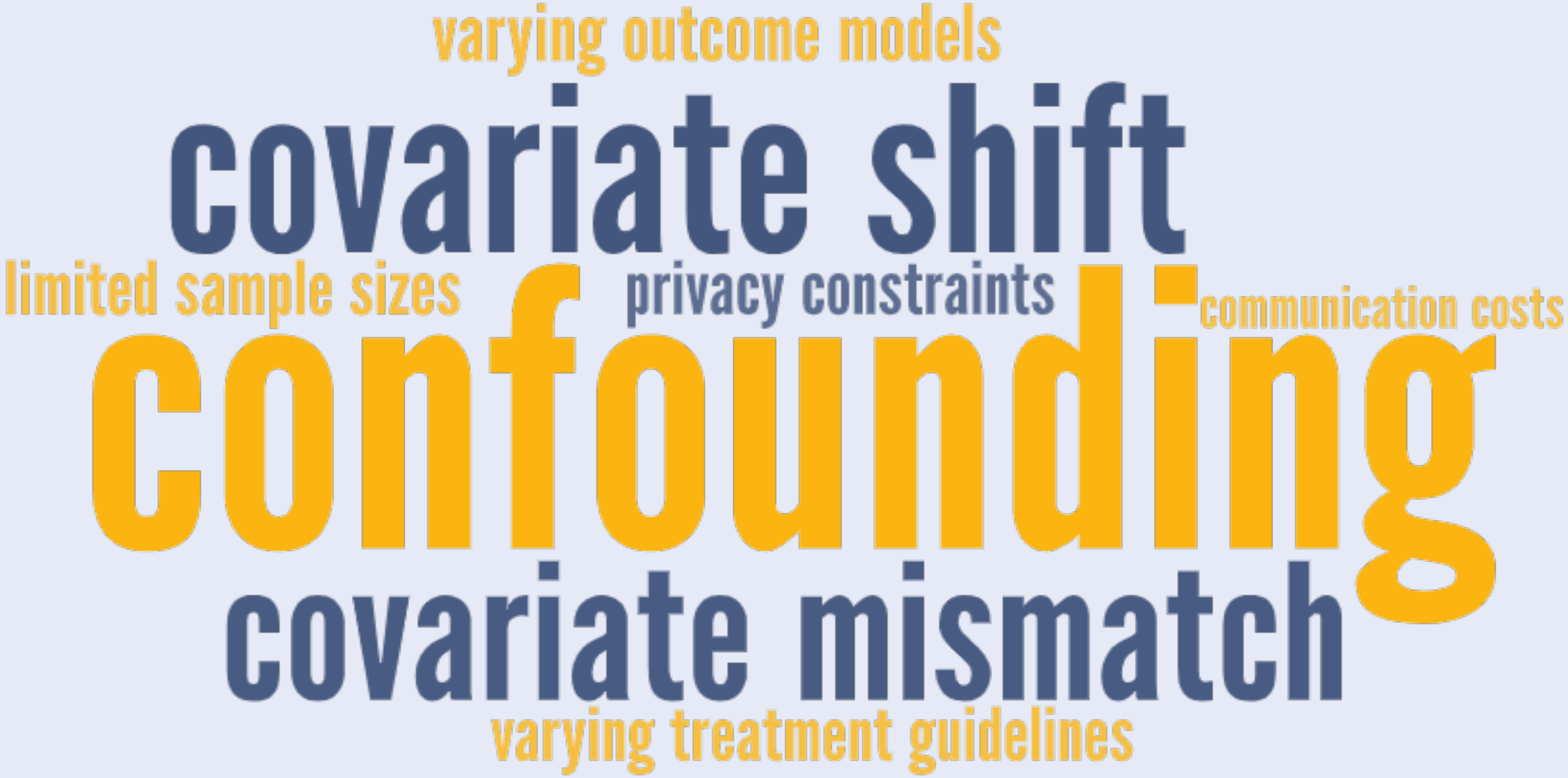
Under multiple real-world constraints:



Workflow

Identification

- Estimand
- Assumption

Site-specific Estimation

- Density Ratio Weighting
- Multiply Robust Estimation
- Covariate Mismatch

Federated Estimation

- Adaptive Ensemble

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Target Estimand

$$\Delta_T = \mu_{1,T} - \mu_{0,T}, \text{ where } \mu_{a,T} = E\{Y_i(a) | R_i = T\} \text{ for } a \in \{0,1\}$$

Target Population

Outcome

Site Indicator

Binary Treatment

Identification Assumptions

- Consistency
- Mean exchangeability over treatment in target population
- Mean exchangeability over treatment in source population
- Positivity of treatment in target population
- Positivity of treatment in source population
- Mean exchangeability over site selection
- Positivity of site selection

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Density Ratio Weighting

for adjusting covariate shift across sites

Existing methods
adjust for heterogeneity in covariate distributions (covariate shift) across
sites by the **inverse probability of selection weighting (IPSW)**

But
IPSW requires pooling target and source samples, which is often not possible due to **data privacy regulations**.

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IPSW requires pooling target and source samples, which is often not possible due to **data privacy regulations**.

We
consider a **density ratio weighting** approach, which offers equivalent estimation without the need for direct data pooling.

Multiply Robust Estimation

for multiple, different models across sites

Existing methods
require **common models** to be specified across sites.

But
it is beneficial for investigators at different sites to incorporate **site-specific knowledge** when specifying candidate models.

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it is beneficial for investigators at different sites to incorporate **site-specific knowledge** when specifying candidate models.

We
We relax this requirement by adopting a **multiply robust** estimator, allowing investigators in each site to propose **multiple, different outcome and treatment models**.

Covariate Mismatch

adjusted by a new nuisance function $\tau_{a,k}$

Existing methods
assume **a common set of observed covariates**.

But
assumption rarely met due to **variations in local practices**, e.g., differing data collection standards and coding practices.

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We
We introduce a **new nuisance function $\tau_{a,k}$** which projects all site-specific estimates of conditional outcomes to a common hyperplane defined by shared effect modifiers across sites.

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Federated Estimation
by an adaptive ensemble method

Existing methods
- Target only
- Sample size weighting (SS)
- Inverse variance weighting (IVW)
- …

But
preventing **negative transfer** is critical when there are multiple, potentially biased source sites.

Federated Estimation
by an adaptive ensemble method

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- Target only
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- …

But
preventing **negative transfer** is critical when there are multiple, potentially biased source sites.

We
We combine all site-specific estimates by an **adaptive ensemble** method; control for bias due to non-transportable site estimates while achieving **optimal efficiency**.

Treatment effect of percutaneous coronary intervention (PCI) on length of hospital stay for acute myocardial infarction (AMI) patients

- Target state: Maine
- Source states: 48 other continental states
- Coarsened covariates: Demographics
- Additional covariates: Comorbidities

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Estimator	Est.	(CI)
Target	−7.63	(−11.45 −3.81)
SS	−9.93	(−15.29 −4.56)
IVW	−8.94	(−9.47 −8.41)
AIPW−L1	−7.84	(−9.60 −6.09)
MR−L1	−7.49	(−9.82 −5.16)

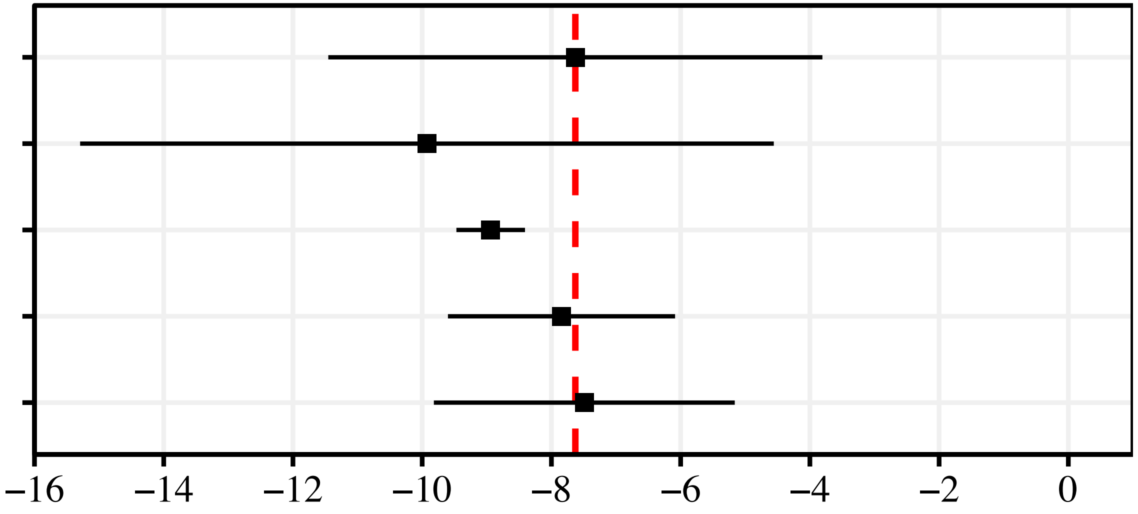

Figure: Estimates of PCI treatment effect in Maine with covariate mismatch in patient comorbidities

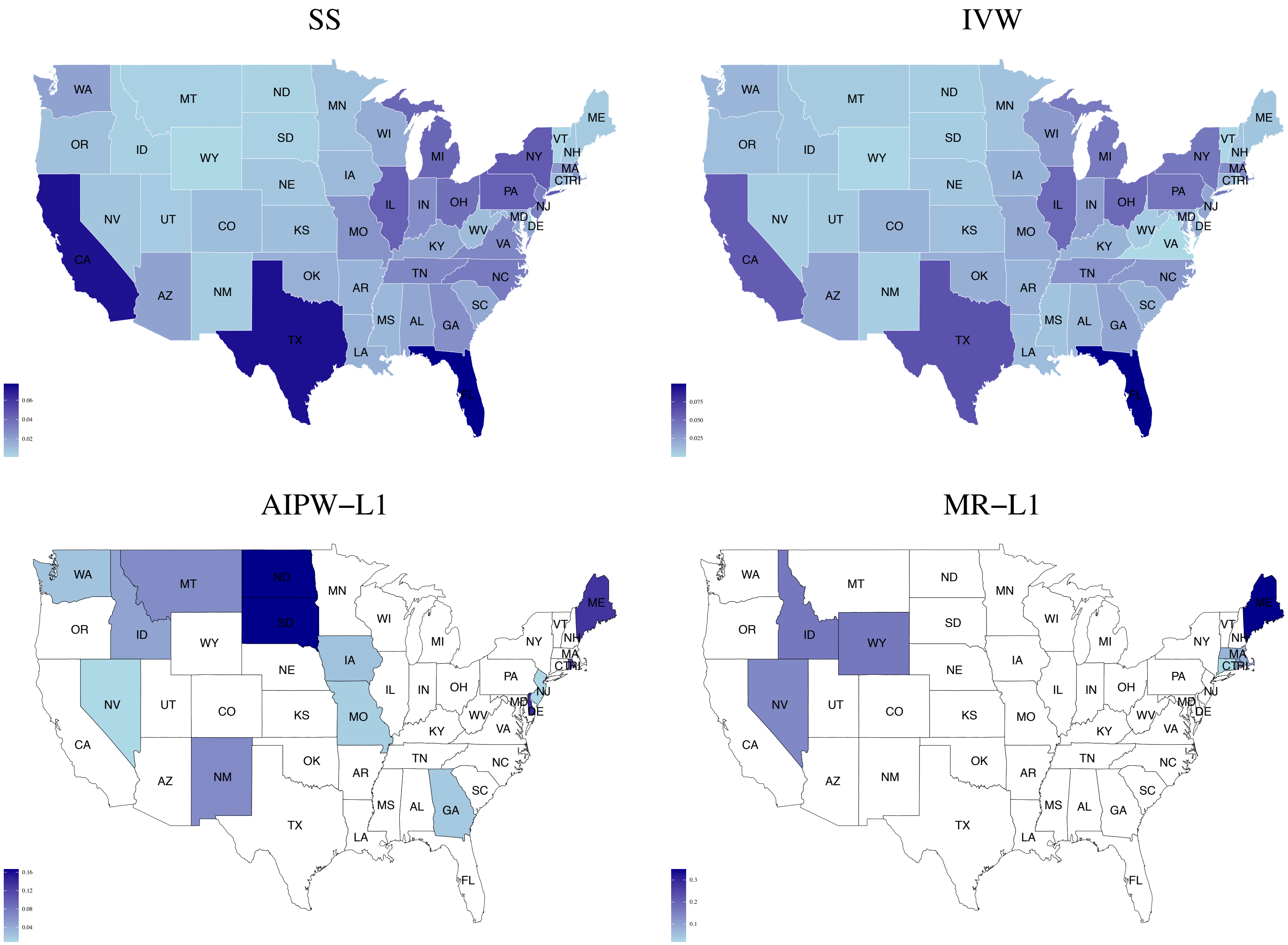

Figure: Federation weights across states for the PCI treatment effect in Maine with four federated estimators

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Paper: https://arxiv.org/abs/2309.12600

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