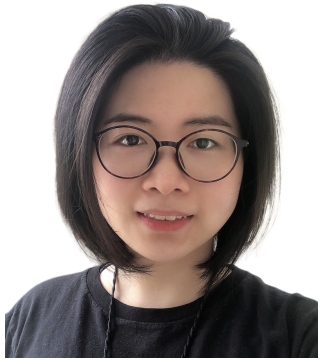
Calibrated Optimal Decision-Making with Multiple Data Sources and Limited Outcome



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August 12, 2021

Introduction

Personalized optimal decision making has attracted increasing attention.

- Developing an individualized treatment rule for patients to optimize expected clinical outcomes of interest [Medicine];
- Offering customized incentives to increase sales and level of engagement [Economics];
- Designing a personalized advertisement recommendation system to raise the click rates [Marketing].

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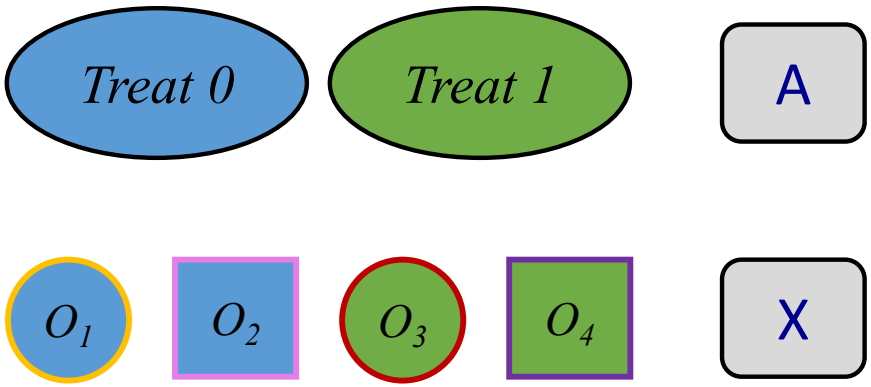
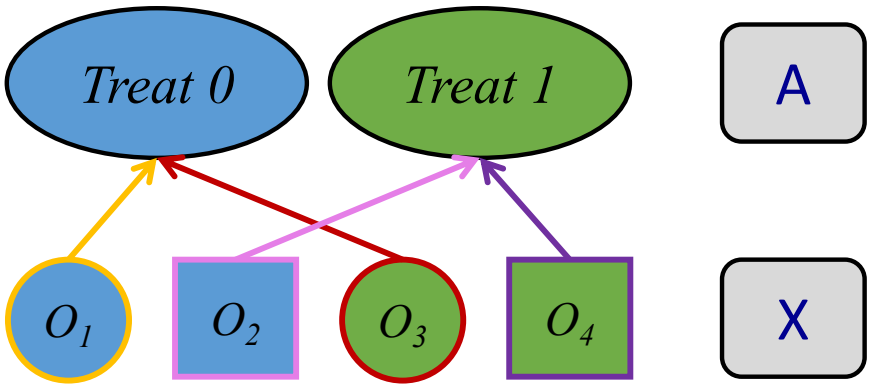
General Setup for Finding the Optimal Decision Rule

Consider assigning individuals with covariates X to some treatments A.



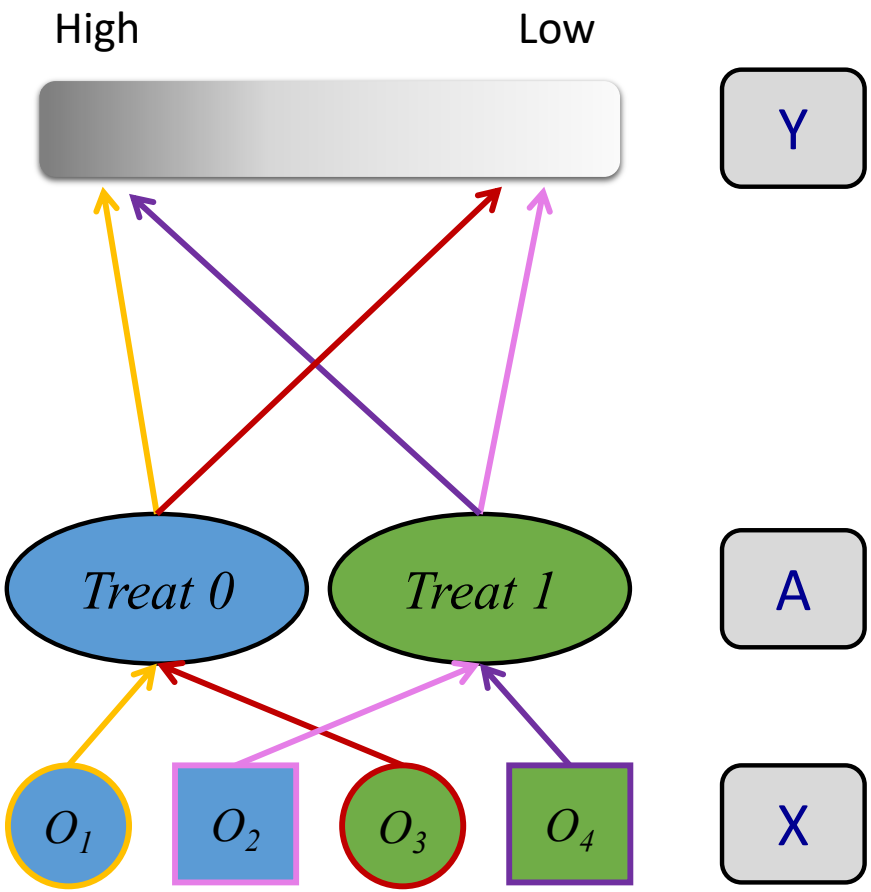
General Setup for Finding the Optimal Decision Rule

Treatments may be assigned randomly or following some clinical advices.



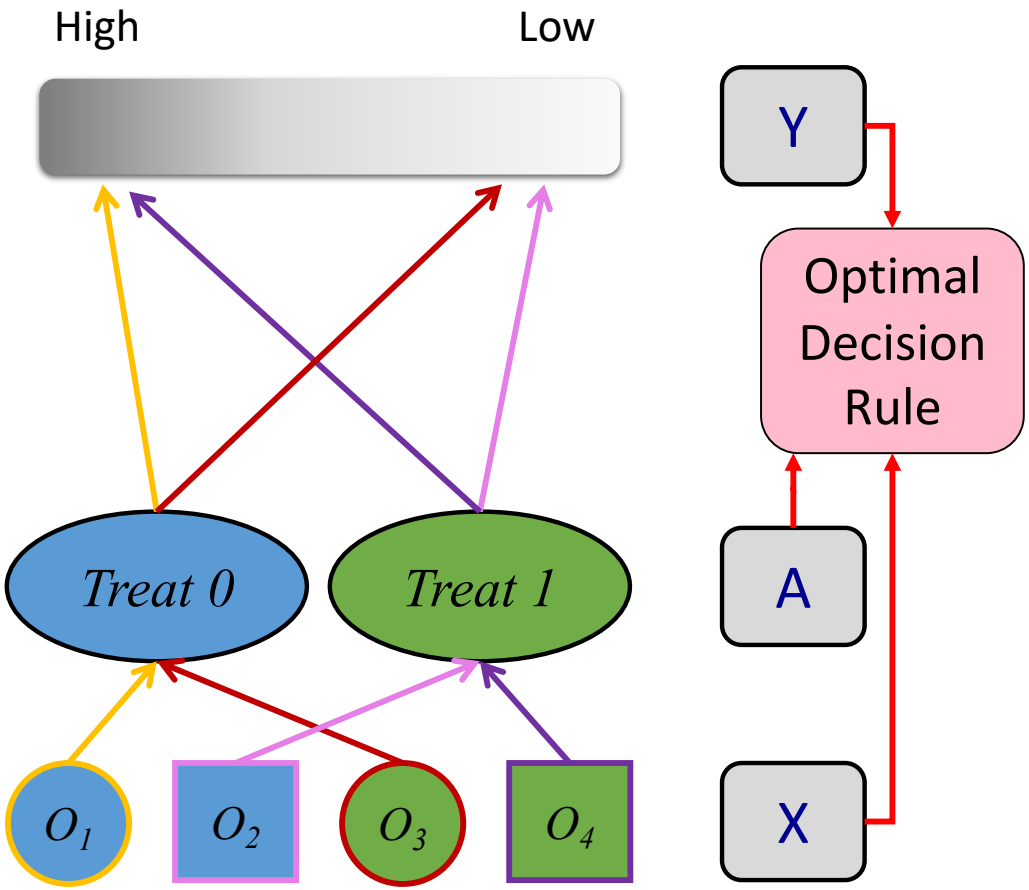
General Setup for Finding the Optimal Decision Rule

The outcome Y can be observed after A is given. Due to individuals' heterogeneity in Y to different A, there may not exist a unified best decision.



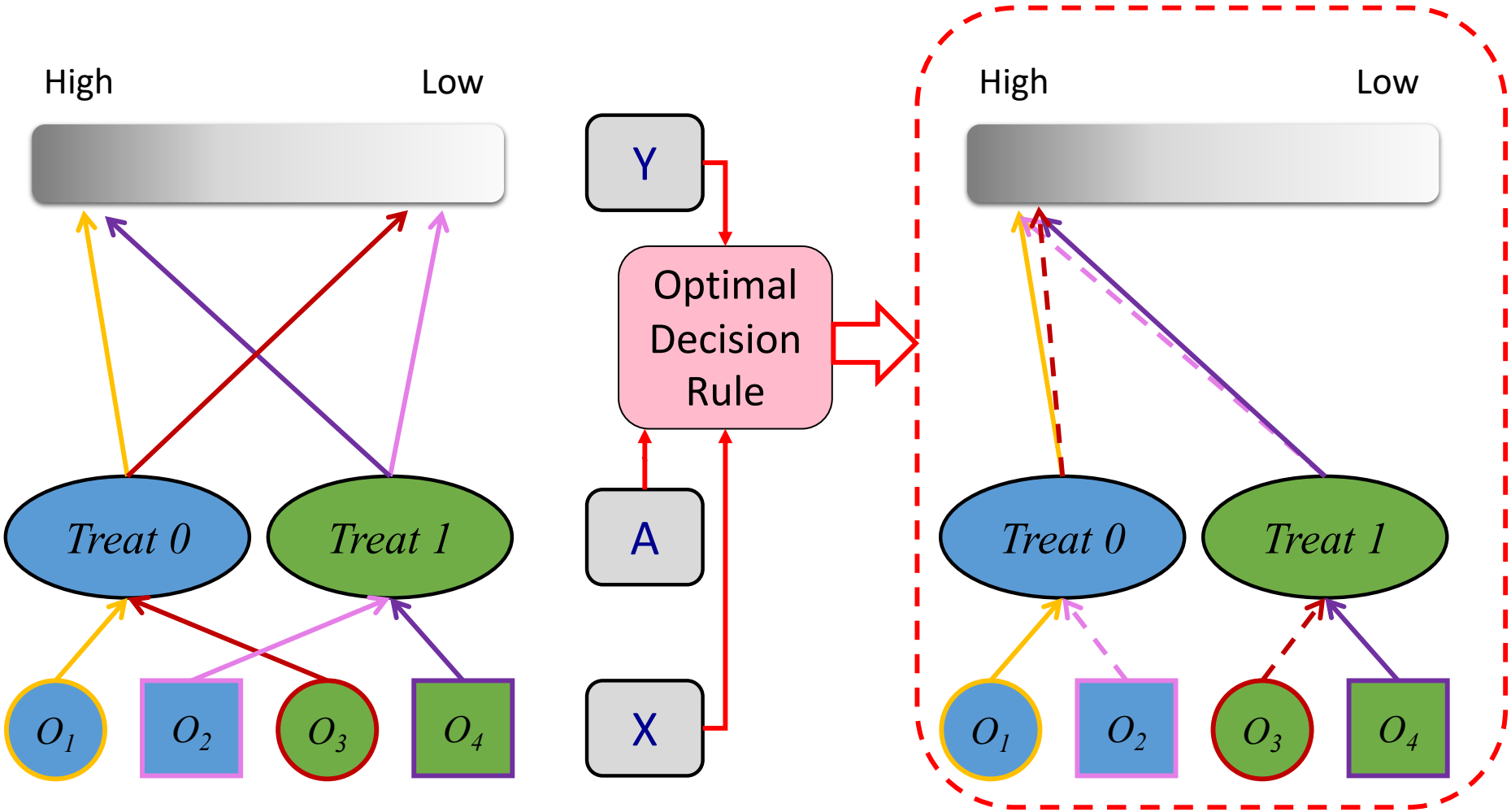
General Setup for Finding the Optimal Decision Rule

The goal is to learn the optimal decision rule (ODR) that maximizes the mean outcome from either randomized trials or observational studies.



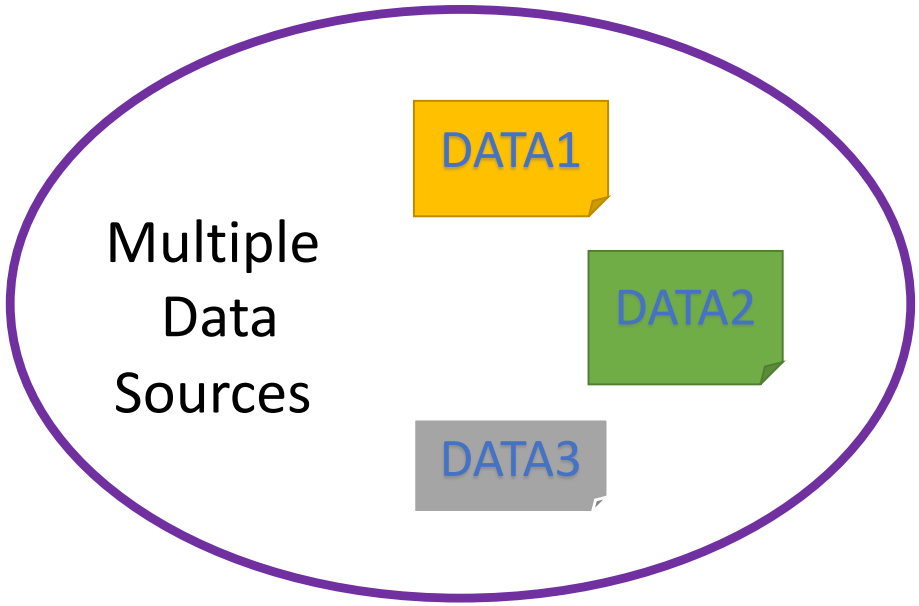
General Setup for Finding the Optimal Decision Rule

Using ODR, we aim to assign future individuals with the best treatment option according to their covariates.



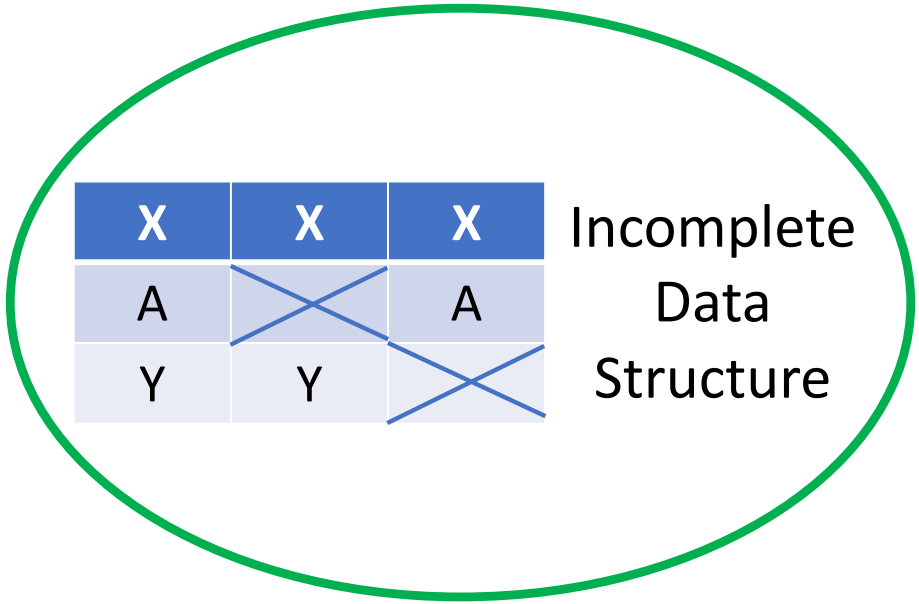
Real World Problems are Complicated...

Multiple datasets from different sources, such as a primary sample of interest and other auxiliary datasets.



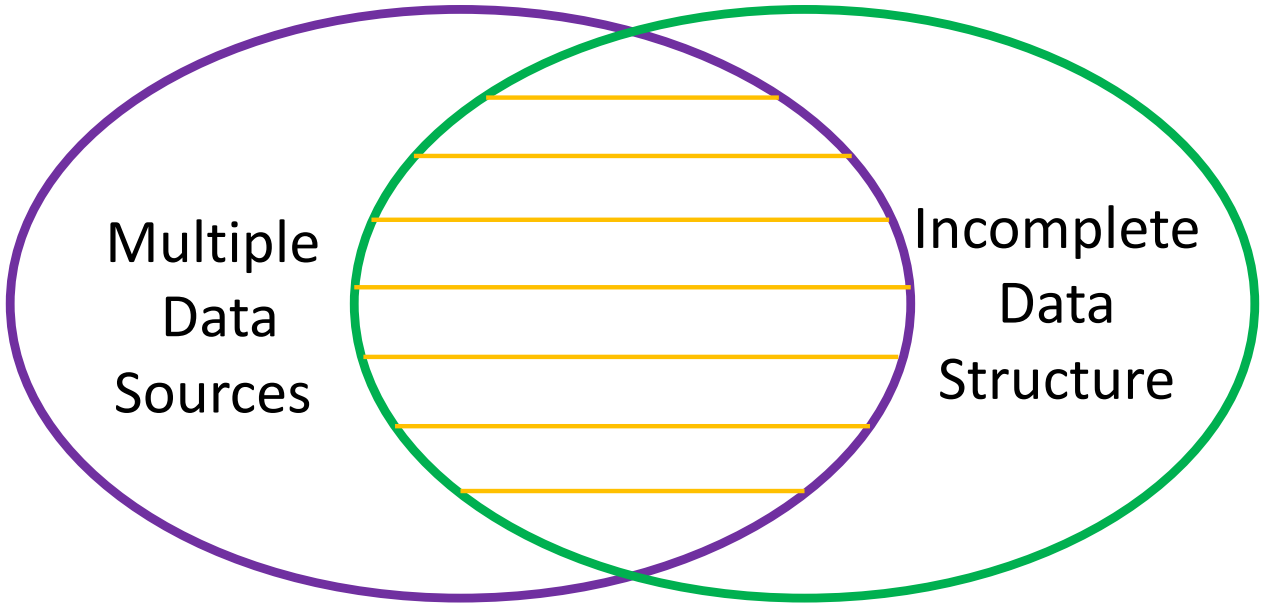
Real World Problems are Complicated...

The data structure can be incomplete due to contamination, short experiment duration, etc.



Real World Problems are Complicated...

Focus on the challenging intersection: optimal decision making with multiple data sources and incomplete data structure.



Motivation Case: Sepsis in Intensive Care Units (ICU)

In the MIMIC-III clinical database (Goldberger et al. 2000, Johnson et al. 2016, Biseda et al. 2020),

- thousands of patients in ICUs of the Beth Israel Deaconess Medical Center between 2001 and 2012,
- with 11 covariates (X) including age (years), gender (0=female, 1=male), admission weights (kg), Glasgow Coma Score (GCS), ...
- are treated with different medical supervision (A) such as vasopressor,
- and followed up for their mortality due to sepsis (Y).
- Some intermediate outcomes (M) (also known as surrogacies or proximal outcomes) after the treatment was given can be observed, such as the total urine output and the cumulated net of metabolism.

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Similar information is also recorded in the eICU collaborative research database (Goldberger et al. 2000, Pollard et al. 2018).

- It contains over 200,000 admissions to ICUs across the United States between 2014 and 2015,
- with records of covariates (X), medical supervision (A), and intermediate outcomes (M) as in the MIMIC-III dataset.
- However, the outcome of interest, i.e., the mortality due to sepsis (Y), was unrecorded.
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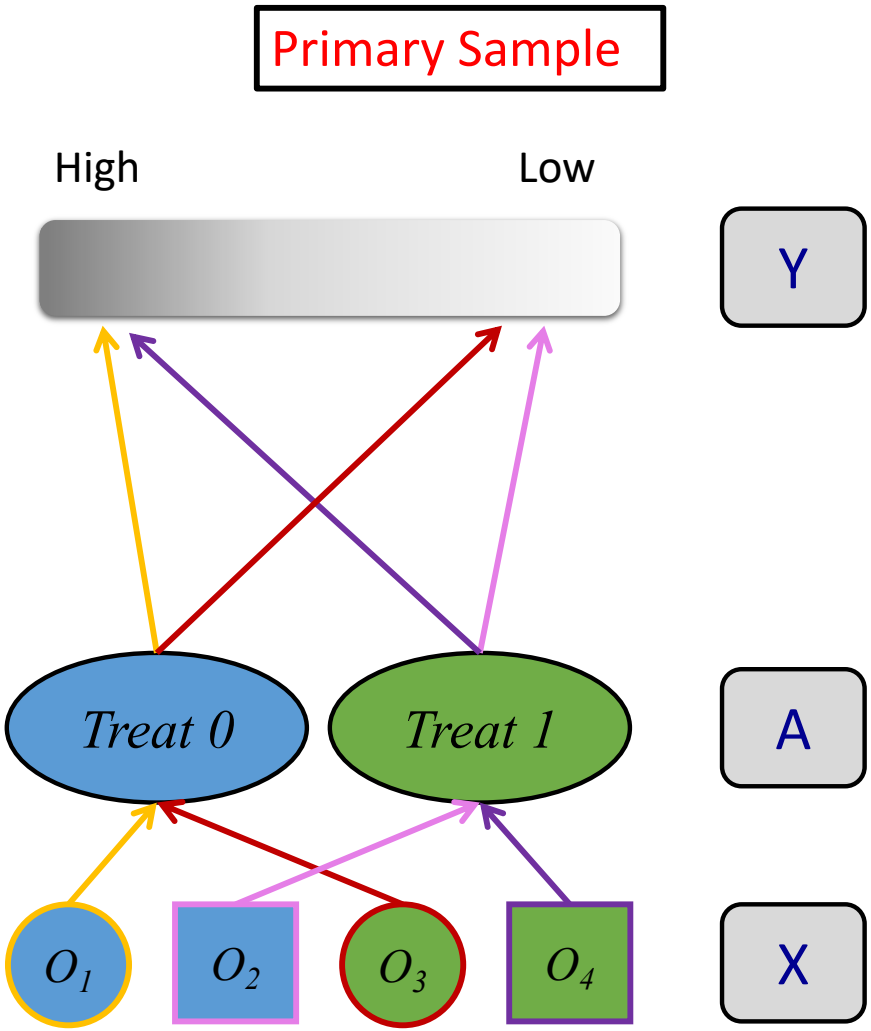
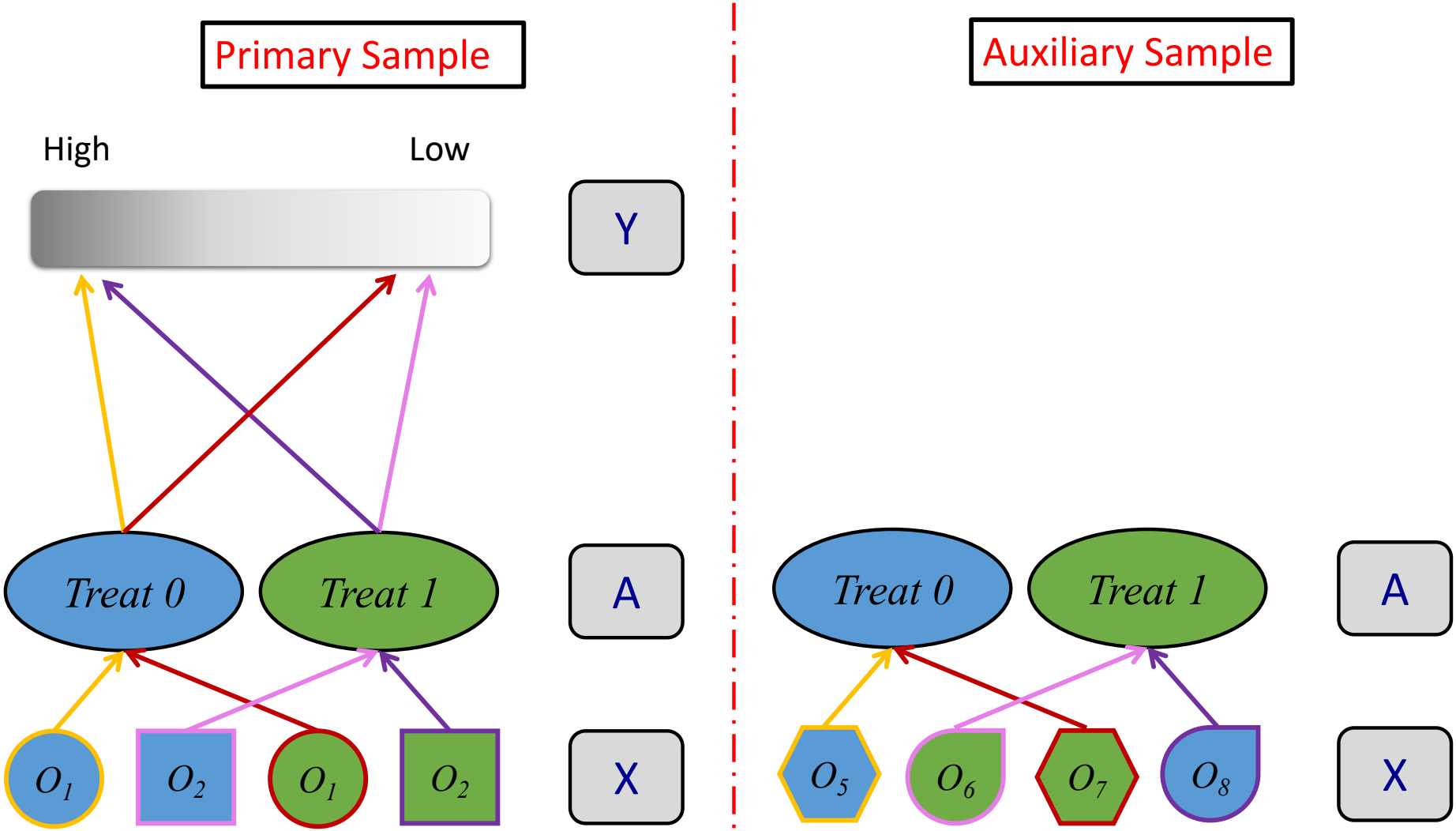
Summary of Data Structure

View the MIMIC-III as the primary sample containing general setup for ODR.



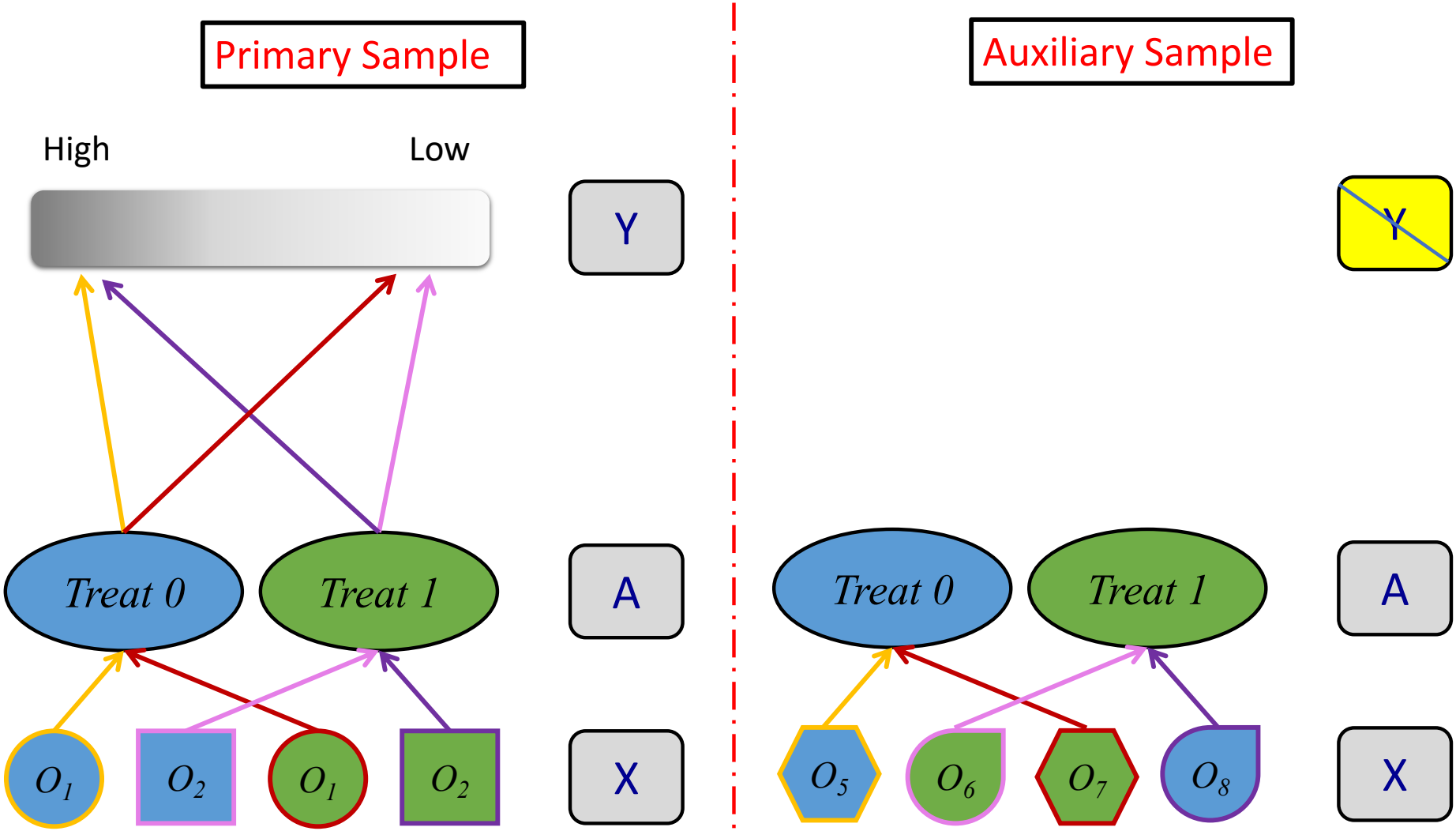
Summary of Data Structure

View the eICU data as the auxiliary sample from a different source.



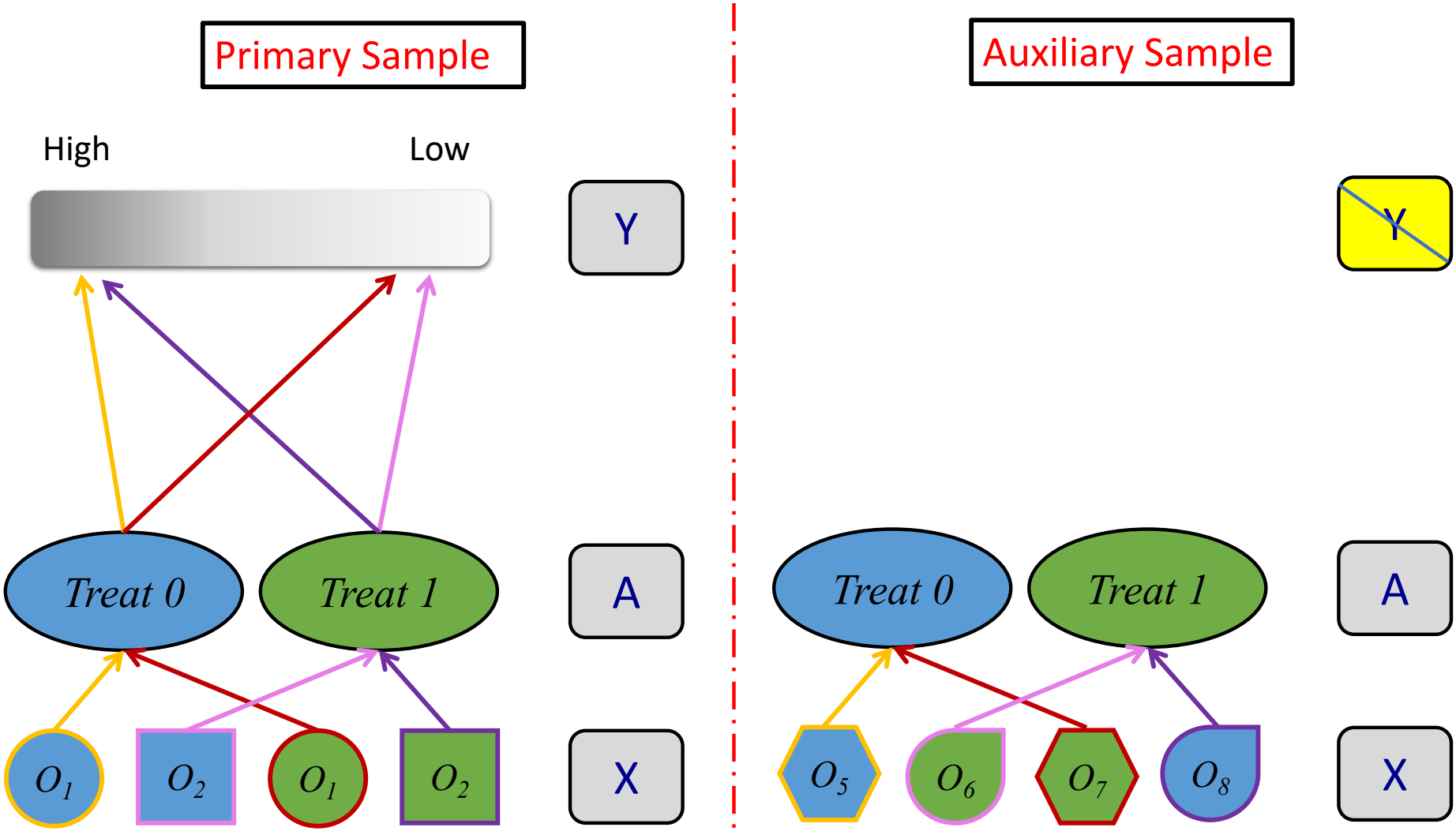
Summary of Data Structure

The outcome of interest is limited and only recorded in the primary sample.



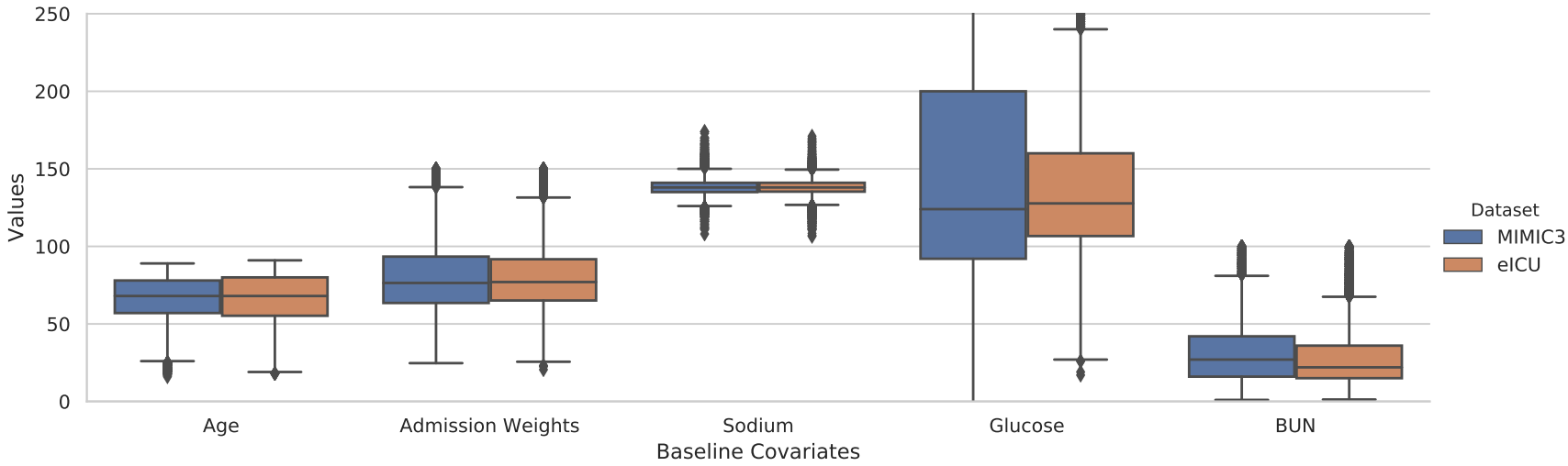
Challenges in Developing the ODR in the ICU datasets

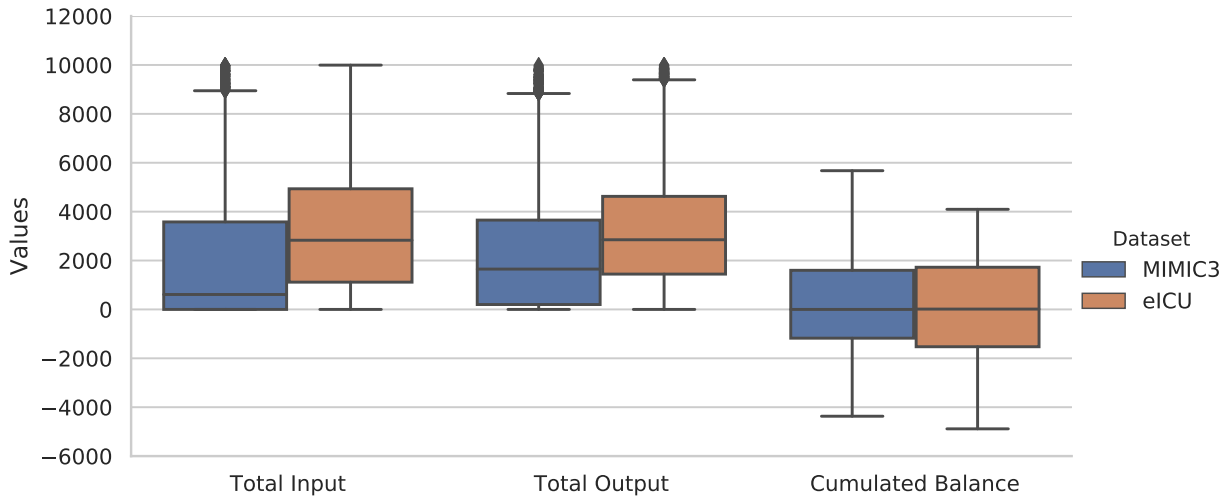
Challenge 1. Two samples cannot be combined directly due to the limited outcome.



Challenges in Developing the ODR in the ICU datasets

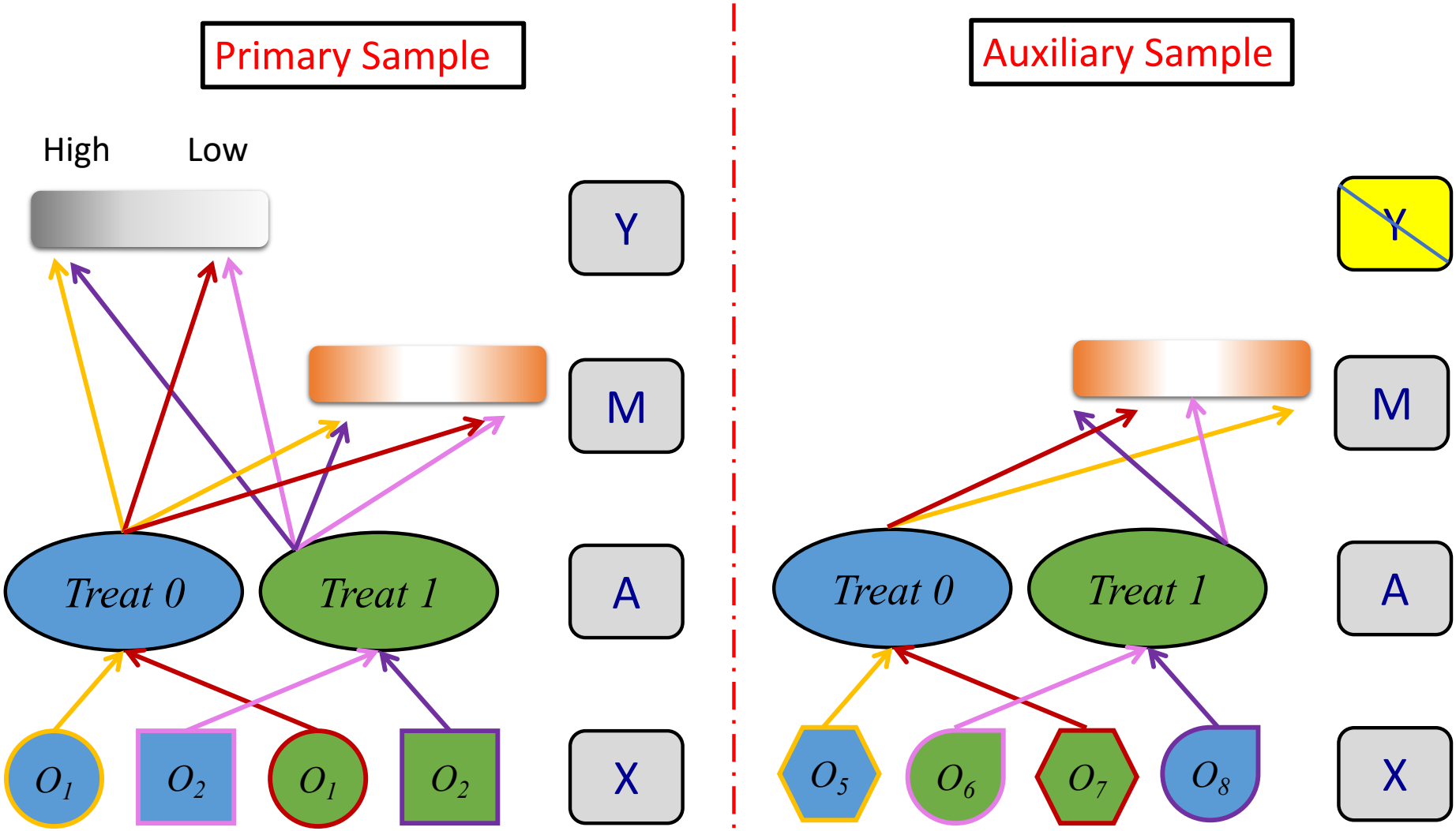
Challenge 2. Two samples show certain heterogeneity such as different probability distributions.





Main Idea

Recall the intermediate outcomes are available in both samples.



Main Idea

Connect the shared common information in multiple data sources, through a calibration technique to address two challenges together.

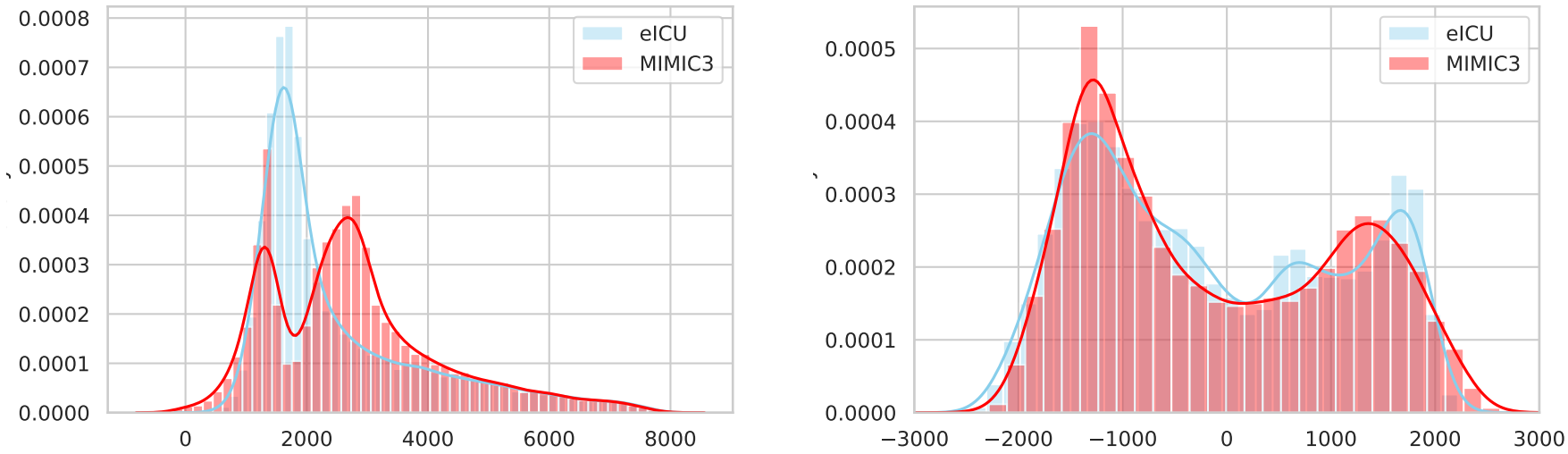


Figure 1: The density plots for the conditional mean of two intermediate outcomes in the MIMIC-III data and the eICU data. Left: for the total output. Right: for the cumulated balance.

Related Works

- Use multiple data sources to estimate the average treatment effect (Yang & Ding 2019, Athey et al. 2020, Kallus & Mao 2020):
  - Considered two samples are from the same population and link them together through a missing data framework.
  - Note the MIMIC III and eICU data show their heterogeneity.
- Derive robust ODR to account for heterogeneity in multiple data sources (Shi et al. 2018b, Mo et al. 2020):
  - Developed a single ODR that can work for multiple treatments.
  - They do not utilize auxiliary data sources.
- We are interested in improving the efficiency of the ODR for the limited outcome observed in the primary sample only, by leveraging available auxiliary data sources.

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Overview of Calibrated ODR (CODR)

- First work on developing ODR from multiple data sources with the limited outcome;
- Propose a mild and testable assumption on the conditional means of M given X and A, to avoid specification of the missing mechanism;
- Develop a new calibration technique by doubly robust estimators for the conditional mean of outcomes (i.e., the value function) of a class of decision rules;
- Our proposed calibrated value estimator is shown to be consistent, asymptotically normal, and more efficient than that obtained using the primary sample solely.
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Statistical Framework

For simplicity of exposition, we consider a study with two data sources.

E: a primary sample of interest with sample size N_E.

- X_E: r-dimensional individual's baseline covariates.
- $A_E \in \{0, 1\}$: the treatment an individual receives.
- M_E: s-dimensional intermediate outcomes.
- Y_E: primary outcome of interest.

U: an auxiliary sample with sample size N_U.

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- However, primary outcome of interest is not available.

Denote $t = N_E/N_U$ as the sample ratio between the primary sample and the auxiliary sample, and $0 < t < +\infty$.

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Assumptions under CODR

Define the potential outcomes $Y_E^*(0)$ and $Y_E^*(1)$ as the primary outcome that would be observed after treatment 0 or 1, respectively. Define the potential intermediate outcomes $\{M_E^*(0), M_E^*(1)\}$ and $\{M_U^*(0), M_U^*(1)\}$ similarly.

- (A1). Stable Unit Treatment Value Assumption (SUTVA):

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Y_E &= A_E Y_E^\star(1) + (1 - A_E) Y_E^\star(0); \\
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\{Y_E^*(0), Y_E^*(1), M_E^*(0), M_E^*(1)\} &\perp\!\!\!\perp A_E \mid X_E; \\
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Assumptions under CODR

Let the propensity score function as $\pi_E(x) = \mathrm{Pr}(A_E = 1|X_E = x)$ for the primary sample and $\pi_U(x) = \mathrm{Pr}(A_U = 1|X_U = x)$ for the auxiliary sample.

- (A3). Positivity: $0 < \pi_E(x) < 1$ for all $x \in \mathbb{X}_E$, and $0 < \pi_U(x) < 1$ for all $x \in \mathbb{X}_U$.
- (A4). Comparable Intermediate Outcomes (CIO) Assumption:

$$\mathrm{E}(M_E|X_E = x, A_E = a) = \mathrm{E}(M_U|X_U = x, A_U = a),$$

for all $x \in \mathbb{X}_E \cup \mathbb{X}_U$ and for all $a \in \{0, 1\}$.

This assumption is the minimum requirement to combine data sources from different populations, and is testable based on two samples. (A4) automatically holds when the data sources are from the same population.

Assumptions under CODR

Let the propensity score function as $\pi_E(x) = \mathrm{Pr}(A_E = 1|X_E = x)$ for the primary sample and $\pi_U(x) = \mathrm{Pr}(A_U = 1|X_U = x)$ for the auxiliary sample.

- (A3). Positivity: $0 < \pi_E(x) < 1$ for all $x \in \mathbb{X}_E$, and $0 < \pi_U(x) < 1$ for all $x \in \mathbb{X}_U$.
- (A4). Comparable Intermediate Outcomes (CIO) Assumption:

$$\mathrm{E}(M_E|X_E = x, A_E = a) = \mathrm{E}(M_U|X_U = x, A_U = a),$$

for all $x \in \mathbb{X}_E \cup \mathbb{X}_U$ and for all $a \in \{0, 1\}$.

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Statistical Framework

- Decision Rule $d(\cdot)$ is a deterministic function that maps $\mathbb{X}_E$ to $\{0, 1\}$.
- Value function under $d(\cdot)$ is $V(d) = \mathrm{E}\{Y^*(d)\}$, where $Y_E^*(d) = Y_E^*(0)\{1 - d(X_E)\} + Y_E^*(1)d(X_E)$ is the potential outcome under $d(\cdot)$ that would be observed if an individual had received a treatment according to $d(\cdot)$.
- Optimal Decision Rule (ODR) is to maximize the value function over the primary sample among a class of decision rules of interest as $d^{opt}(\cdot) = \arg\min_{d(\cdot)} V(d)$.

Table 1: The data structure of the two samples under CODR.

Sample	X	A	M	Y	ODR for Y	ODR for M
Primary	✓	✓	✓	✓	✓	✓
Auxiliary	✓	✓	✓	×	×	✓

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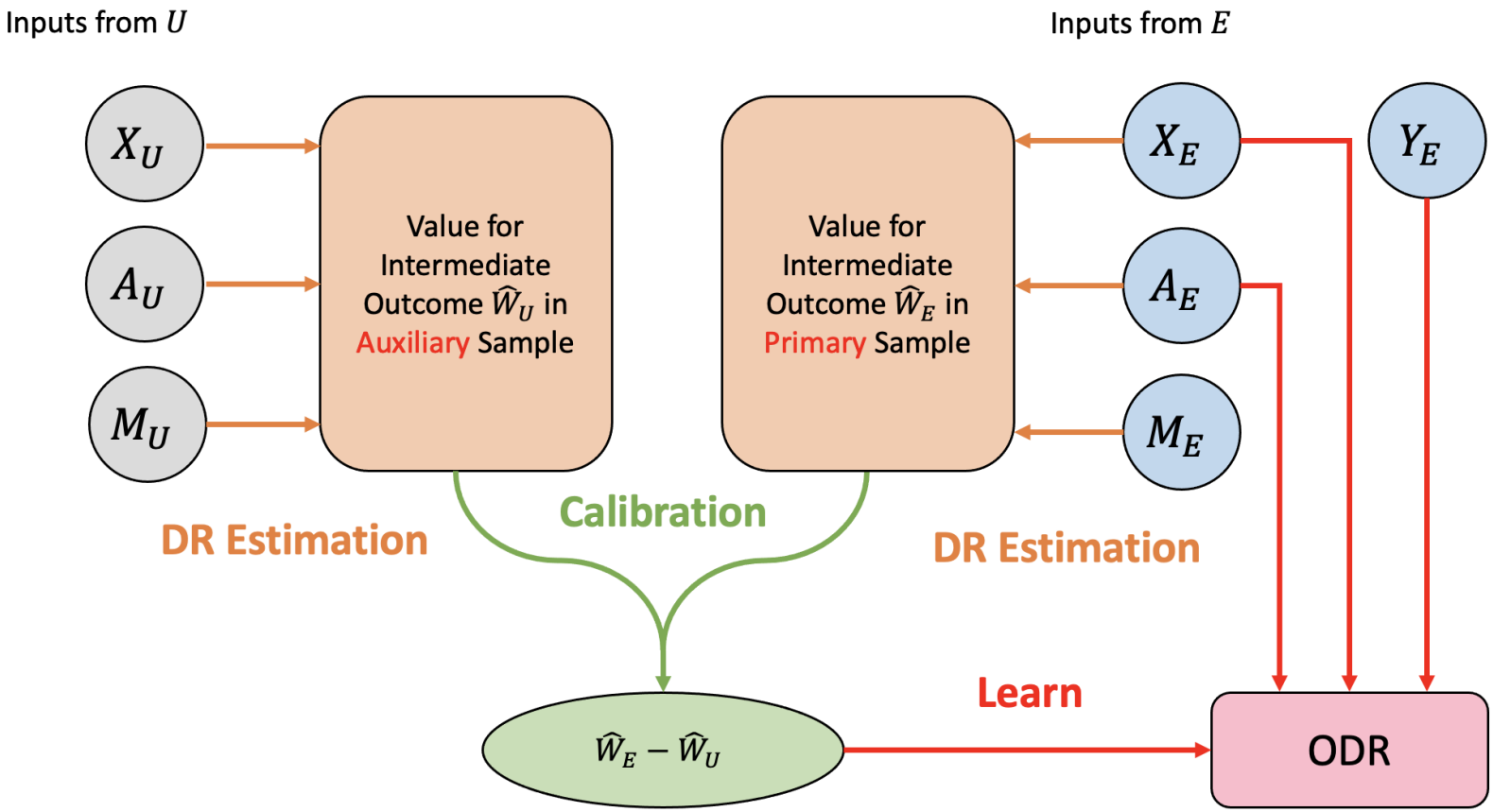
Auxiliary	✓	✓	✓	×	×	✓

Architecture of the Proposed CODR

Lemma 1 (Equal Value Function for Intermediate Outcomes)

Under assumptions (A1) - (A4) and homogeneous baseline covariates $(X_E \sim X_U)$, $W(d) \equiv \mathrm{E}\{M_E^*(d)\} = \mathrm{E}\{M_U^*(d)\}$.



Step 1. Doubly Robust (DR) Estimation

DR Estimator for Intermediate Outcomes

$$\widehat{W}_E(d) = \frac{1}{N_E}\sum_{i=1}^{N_E} \frac{\mathbb{I}\{A_{E,i} = d(X_{E,i})\}}{A_{E,i}\widehat{\pi}_E(X_{E,i}) + (1-A_{E,i})\{1-\widehat{\pi}_E(X_{E,i})\}}[M_{E,i} - \widehat{\theta}\{X_{E,i}, A_{E,i} = d(X_{E,i})\}]$$
$$+ \widehat{\theta}\{X_{E,i}, A_{E,i} = d(X_{E,i})\},$$
$$\widehat{W}_U(d) = \frac{1}{N_U}\sum_{i=1}^{N_U} \frac{\mathbb{I}\{A_{U,i} = d(X_{U,i})\}}{A_{U,i}\widehat{\pi}_U(X_{U,i}) + (1-A_{U,i})\{1-\widehat{\pi}_U(X_{U,i})\}}[M_{U,i} - \widehat{\theta}\{X_{U,i}, A_{U,i} = d(X_{U,i})\}]$$
$$+ \widehat{\theta}\{X_{U,i}, A_{U,i} = d(X_{U,i})\},$$

where $\widehat{W}_E(d)$ and $\widehat{W}_U(d)$ are $s \times 1$ vectors, $\widehat{\pi}_E$ and $\widehat{\pi}_U$ are the estimators of the propensity score functions, and $\widehat{\theta}(x,a)$ is the estimated conditional mean for $\theta(x,a) \equiv \mathsf{E}(M_E|X_E = x, A_E = a) = \mathsf{E}(M_U|X_U = x, A_U = a)$ based on two samples under (A4).

Step 2. Calibration – Mean Zero Value Difference Vector

With regular conditions, we can show

$$\sqrt{N_E}\Big\{\widehat{W}_E(d) - W(d)\Big\} \xrightarrow{D} N_s\Big\{\mathbf{0}_s, \Sigma_E(d)\Big\},$$
$$\sqrt{N_U}\Big\{\widehat{W}_U(d) - W(d)\Big\} \xrightarrow{D} N_s\Big\{\mathbf{0}_s, \Sigma_U(d)\Big\},$$

where $\mathbf{0}_s$ is the s-dimensional zero vector, Σ_E and Σ_U are $s \times s$ matrices presenting the asymptotic covariance matrices for two samples.

Lemma 2

Assume (A1)-(A4) hold. With regular conditions and $T \equiv \lim_{N_E \to +\infty} t \in (0, +\infty)$, we have

$$\sqrt{N_E}\Big\{\widehat{W}_E(d) - \widehat{W}_U(d)\Big\} \xrightarrow{D} N_s\Big\{\mathbf{0}_s, \Sigma_M(d)\Big\},$$

where $\Sigma_M(d) = \Sigma_E(d) + T\Sigma_U(d)$ is a $s \times s$ asymptotic covariance matrix.

Step 2. Calibration – Calibrated Value Estimator

DR Estimator for Primary Outcome in the Primary Sample

$$\widehat{V}_E(d) = \frac{1}{N_E}\sum_{i=1}^{N_E} \frac{\mathbb{I}\{A_{E,i} = d(X_{E,i})\}[Y_{E,i} - \widehat{\mu}_E\{X_{E,i}, A_{E,i} = d(X_{E,i})\}]}{A_{E,i}\widehat{\pi}_E(X_{E,i}) + (1 - A_{E,i})\{1 - \widehat{\pi}_E(X_{E,i})\}} + \widehat{\mu}_E\{X_{E,i}, A_{E,i} = d(X_{E,i})\},$$

where $\widehat{\mu}_E(x, a)$ is the estimator for $\mathbb{E}(Y_E|X_E = x, A_E = a)$.

With regular conditions, we can show

$$\sqrt{N_E}\Big\{\widehat{V}_E(d) - V(d)\Big\} \xrightarrow{D} N\Big\{0, \sigma_Y^2(d)\Big\}, \tag{1}$$

where $\sigma_Y^2(d)$ is the asymptotic variance given any $d(\cdot)$.

Step 2. Calibration – Calibrated Value Estimator (cont.)

Based on (1) and Lemma 2, we have

$$\sqrt{N_E}\begin{bmatrix}\widehat{V}_E(d)-V(d)\\ \widehat{W}_E(d)-\widehat{W}_U(d)\end{bmatrix}\xrightarrow{D}N_{s+1}\left\{\mathbf{0}_{s+1},\begin{bmatrix}\sigma_Y^2(d),\boldsymbol{\rho}(d)^\top\\ \boldsymbol{\rho}(d),\Sigma_M(d)\end{bmatrix}\right\},\quad \forall d(\cdot),$$

where $\boldsymbol{\rho}(d)$ is the $s\times 1$ asymptotic covariance vector.

Calibrated Value Estimator

$$\widehat{V}(d)=\widehat{V}_E(d)-\widehat{\boldsymbol{\rho}}(d)^\top\widehat{\Sigma}_M^{-1}(d)\{\widehat{W}_E(d)-\widehat{W}_U(d)\},$$

where $\widehat{\boldsymbol{\rho}}(d)$ is the estimator for $\boldsymbol{\rho}(d)$, and $\widehat{\Sigma}_M(d)$ is the estimator for $\Sigma_M(d)$.

Step 3. Learn the ODR from Calibrated Value Estimator

Calibrated Optimal Decision Rule (CODR)

The CODR is found to optimize the calibrated value estimator within a pre-specified class of decision rules Π as $\widehat{d} = \arg\max_{d \in \Pi} \widehat{V}(d)$, with the corresponding estimated value function as $\widehat{V}(\widehat{d})$.

- Class of decision rules: Vapnik-Chervonenkis (VC) Class: Π has a finite VC-dimension and is countable, such as finite-depth decision trees, generalized linear rules, and threshold rules.
- Estimation models: the propensity score function π and the conditional mean μ can be estimated through any parametric or nonparametric model.

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- Estimation models: the propensity score function π and the conditional mean μ can be estimated through any parametric or nonparametric model.

Theoretical Properties

Theorem 1 (Consistency)

Under (A1)-(A7), (i) $\widehat{\sigma}_Y^2(d) = \sigma_Y^2(d) + o_p(1)$; (ii) $\widehat{\boldsymbol{\rho}}(d) = \boldsymbol{\rho}(d) + o_p(1)$; (iii) $\widehat{\Sigma}_M(d) = \Sigma_M(d) + o_p(1)$; (iv) $\widehat{V}(d) = V(d) + o_p(1)$.

Theorem 2 (Asymptotic Distribution)

Suppose $\{d^{opt}, \widehat{d}\} \in \Pi$. Under assumptions (A1)-(A8), we have

$$\sqrt{N_E}\Big\{\widehat{V}(\widehat{d}) - V(d^{opt})\Big\} \xrightarrow{D} N\Big\{0, \sigma^2(d^{opt})\Big\},$$

where $\sigma^2(d^{opt}) = \sigma_Y^2(d^{opt}) - \boldsymbol{\rho}(d^{opt})^\top \Sigma_M^{-1}(d^{opt})\boldsymbol{\rho}(d^{opt})$.

Remark: When Y is correlated with one of the selected M, i.e., $\boldsymbol{\rho}(d^{opt})$ is a non-zero vector, the asymptotic variance of the calibrated value estimator is strictly smaller than that based on the primary sample solely. The proposed CODR is more efficient by integrating different data sources.

Simulation Studies

Data generated from

$$A \overset{I.I.D.}{\sim} \text{Bernoulli}\{\pi(X)\}, \quad X^{(1)}, \cdots, X^{(r)} \overset{I.I.D.}{\sim} \text{Uniform}[-2, 2],$$
$$M = U^M(X) + AC^M(X) + \epsilon^M, \quad Y = U^Y(X) + AC^Y(X) + \epsilon^Y,$$

where $\text{logit}\{\pi(X)\} = 0.4 + 0.2X^{(1)} - 0.2X^{(2)}$, $\epsilon^M \overset{I.I.D.}{\sim} N(0, 1/3)$ in the primary sample while $\epsilon^M \overset{I.I.D.}{\sim} \text{Uniform}[-1, 1]$ in the auxiliary sample, and $\epsilon^Y \overset{I.I.D.}{\sim} N(0, 1)$.

Scenario 1 (decision tree):

$$\begin{cases} U^M(X) = X^{(1)} + 2X^{(2)}, C^M(X) = X^{(1)} \times X^{(2)}; \\ U^Y(X) = 2X^{(1)} + X^{(2)}, C^Y(X) = 2X^{(1)} \times X^{(2)}. \end{cases}$$

Scenario 2 (linear rule):

$$\begin{cases} U^M(X) = X^{(1)} + 2X^{(2)}, C^M(X) = X^{(1)} - X^{(2)}; \\ U^Y(X) = 2X^{(1)} + X^{(2)}, C^Y(X) = 2\{X^{(2)} - X^{(1)}\}. \end{cases}$$

Simulation Studies

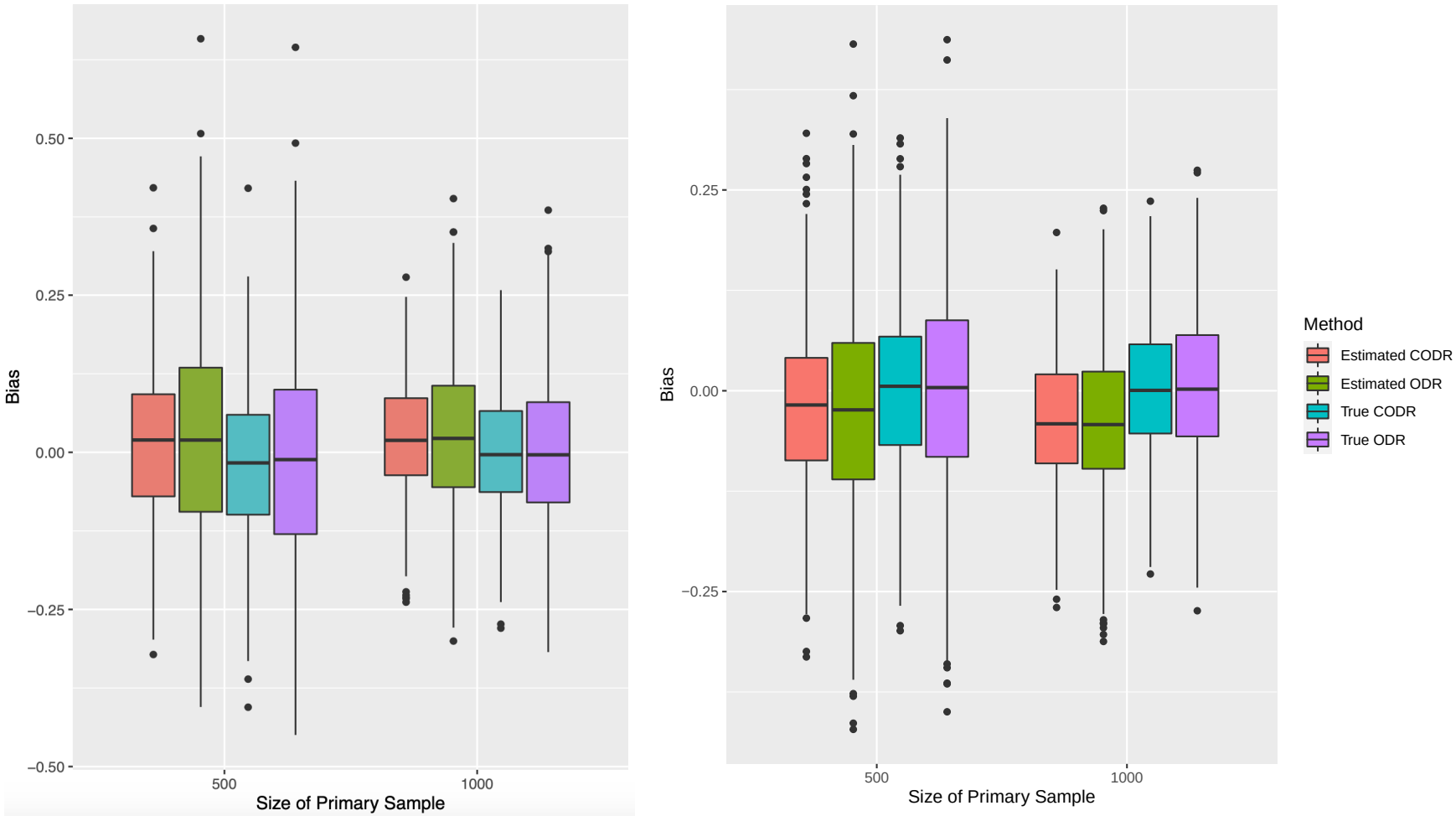

Figure 2: The box-plot of the biases of the estimated values under different methods. Left: for Scenario 1. Right: for Scenario 2.

Real Data Analysis: ICU Datasets

Recall the MIMIC-III dataset as the primary sample and the eICU data as the auxiliary sample:

- There were $N_E = 10746$ sepsis patients (in MIMIC-III) treated in Israel during 2001 to 2012, and $N_U = 7402$ (in eICU) treated in the United States during 2014 to 2015.
- $r = 11$ Covariates X: age (years), gender (0=female), admission weights (kg), admission temperature (Celsius), Glasgow Coma Score (GCS), sodium amount (meq/L), glucose amount (mg/dL), blood urea nitrogen amount (BUN, mg/dL), creatinine amount (mg/dL), white blood cell count (WBC, E9/L), and total input amount (mL).
- The treatment A is coded as 1 if receiving the vasopressor, and 0 if receiving other medical supervision such as IV fluid resuscitation.
- $s = 2$ Intermediate Outcomes M: total urine output (mL) and cumulated balance (mL) of metabolism.
- The outcome of interest (Y_E) is 0 if a patient died due to sepsis and 1 if a patient is still alive, observed only in the primary sample.

Results

Table 2: The real data analysis under the proposed CODR method and the original ODR method based on the primary sample solely. All the decision rules are searched within the class of decision trees.

Sample Size	$N_E = 1000$		$N_E = 5000$		$N_E = 10746$	
Method	CODR	ODR	CODR	ODR	CODR	ODR
Estimated $\widehat{V}(\cdot)$	0.180	0.147	0.204	0.184	0.203	0.192
Estimated $\widehat{\sigma}$	0.0182	0.0199	0.0090	0.0097	0.0065	0.0068
Improved Efficiency	8.5%	/	7.2%	/	4.4%	/
# Treatment 0	545	460	2967	2671	5853	5478
# Treatment 1	455	540	2033	2329	4893	5268
Matching Rate	85.4%	/	87.5%	/	86.5%	/

Thank You!

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Estimation on Variances

Define the value functions for primary outcome at the individual level as

$$\widehat{v}_E^{(i)}(d) := \frac{\mathbb{I}\{A_{E,i} = d(X_{E,i})\}[Y_{E,i} - \widehat{\mu}_{E,i}]}{A_{E,i}\widehat{\pi}_E(X_{E,i}) + (1 - A_{E,i})\{1 - \widehat{\pi}_E(X_{E,i})\}} + \widehat{\mu}_{E,i},$$

in the primary sample, for $i \in \{1, \cdots, N_E\}$. Similarly, the value for the i-th individual in terms of intermediate outcomes are $\widehat{\boldsymbol{w}}_E^{(i)}(d)$ and $\widehat{\boldsymbol{w}}_U^{(i)}(d)$.

Estimators for $\sigma_Y^2(\cdot)$, $\boldsymbol{\rho}(\cdot)$ and $\Sigma_M(\cdot)$, where $z^{\otimes 2} = zz^\top$,

$$\widehat{\sigma}_Y^2(d) = \frac{1}{N_E}\sum_{i=1}^{N_E}\{\widehat{v}_E^{(i)}(d) - \widehat{V}_E(d)\}^2,$$

$$\widehat{\boldsymbol{\rho}}(d) = \frac{1}{N_E}\sum_{i=1}^{N_E}\left\{\widehat{v}_E^{(i)}(d) - \widehat{V}_E(d)\right\}\left\{\widehat{\boldsymbol{w}}_E^{(i)}(d) - \widehat{W}_E(d)\right\},$$

$$\widehat{\Sigma}_M(d) = \frac{1}{N_E}\sum_{i=1}^{N_E}\left\{\widehat{\boldsymbol{w}}_E^{(i)}(d) - \widehat{W}_E(d)\right\}^{\otimes 2} + t\frac{1}{N_U}\sum_{i=1}^{N_U}\left\{\widehat{\boldsymbol{w}}_U^{(i)}(d) - \widehat{W}_U(d)\right\}^{\otimes 2}.$$

CODR based on Finite-Depth Decision Trees

Calibrated Reward of the i-th Individual in the Primary Sample

$$\widehat{v}^{(i)}(d) = \widehat{v}_E^{(i)}(d) - \widehat{\boldsymbol{\rho}}(d)^\top \widehat{\Sigma}_M^{-1}(d)\{\widehat{\boldsymbol{w}}_E^{(i)}(d) - \widehat{W}_U(d)\}.$$

The estimators $\widehat{\boldsymbol{\rho}}(d)$ and $\widehat{\Sigma}_M^{-1}(d)$ are calculated using two samples based on (2). To address this difficulty, we propose an iterative algorithm:

- **Step 1:** Find the ODR based on the primary sample solely, i.e., $\widehat{d}_E$, as an initial decision rule.
- **Step 2:** Estimate $\rho(\cdot)$ and $\Sigma_M(\cdot)$ by plugging in $d = \widehat{d}_E$.
- **Step 3:** Search for the optimal decision tree within the class Π_1 to achieve a maximum overall calibrated reward, denoted as $\widehat{d}^{(1)}$.
- **Step 4:** Repeat steps 2 and 3 for $k = 1, \cdots, K$, by replacing the previous estimated decision tree $\widehat{d}^{(k-1)}$ ($\widehat{d}^{(0)} = \widehat{d}_E$) with the new estimated decision tree $\widehat{d}^{(k)}$ until it's convergent or achieves the maximum number of iterations K.

CODR based on Finite-Depth Decision Trees

Calibrated Reward of the i-th Individual in the Primary Sample

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CODR based on Finite-Depth Decision Trees

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$$\widehat{v}^{(i)}(d) = \widehat{v}_E^{(i)}(d) - \widehat{\boldsymbol{\rho}}(d)^\top \widehat{\Sigma}_M^{-1}(d)\{\widehat{\boldsymbol{w}}_E^{(i)}(d) - \widehat{W}_U(d)\}.$$

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Technical Assumptions

- (A5). The class of decision rules Π is a Vapnik-Chervonenkis Class.
- (A6). The supports are bounded.
- (A7). Rate double robustness for $\widehat{V}_E$, $\widehat{M}_E$, and $\widehat{M}_U$.
- (A8). Margin condition: there exist some constants $\gamma, \lambda > 0$ such that $\Pr\{0 < |\mathbb{E}(Y_E|X_E, A_E = 1) - \mathbb{E}(Y_E|X_E, A_E = 0)| \leq \xi\} = O(\xi^\gamma)$, where the big-$O$ term is uniform in $0 < \xi \leq \lambda$.

Extension of CODR to Heterogeneous Covariates

Let joint dataset as $\{X_i, A_i, M_i, R_i, R_iY_i\}_{i=1,\cdots,n}$ for $n = N_E + N_U$, where $R_i = 1$ if subject i is from primary sample and $R_i = 0$ if subject i is from auxiliary sample.

Posterior Sampling Probability

$$\begin{aligned} & P(R_i = 1 | X_i = x, A_i = a, M_i = m) \\ = & \frac{P(R_i = 1) f_E(x, a, m)}{P(R_i = 1) f_E(x, a, m) + P(R_i = 0) f_U(x, a, m)}, \end{aligned} \tag{2}$$

where $f_E(x, a, m)$ and $f_U(x, a, m)$ are the joint density function of $\{X_E, A_E, M_E\}$ in the primary sample and the joint density function of $\{X_U, A_U, M_U\}$ in the auxiliary sample, respectively.

Extension of CODR to Heterogeneous Covariates

Estimate the posterior sampling probability $r_i(x, a, m) \equiv P(R_i = 1 | X_i = x, A_i = a, M_i = m)$ as $\widehat{r}_i(x, a, m)$, and estimate the new propensity score function $P(A_i = 1 | X_i)$ as $\widehat{\pi}(X_i)$.

New DR estimators for intermediate outcomes

$$\widehat{W}_1(d) = \frac{1}{n}\sum_{i=1}^{n} \frac{R_i}{\widehat{r}_i\{X_i, d(X_i), M_i\}} \frac{\mathbb{I}\{A_i = d(X_i)\}}{A_i\widehat{\pi}(X_i) + (1 - A_i)\{1 - \widehat{\pi}(X_i)\}} [M_i - \widehat{\theta}\{X_i, A_i = d(X_i)\}] + \widehat{\theta}\{X_i, A_i = d(X_i)\},$$

$$\widehat{W}_0(d) = \frac{1}{n}\sum_{i=1}^{n} \frac{(1 - R_i)}{1 - \widehat{r}_i\{X_i, d(X_i), M_i\}} \frac{\mathbb{I}\{A_i = d(X_i)\}}{A_i\widehat{\pi}(X_i) + (1 - A_i)\{1 - \widehat{\pi}(X_i)\}} [M_i - \widehat{\theta}\{X_i, A_i = d(X_i)\}] + \widehat{\theta}\{X_i, A_i = d(X_i)\}.$$

Simulation Studies

Table 3: Empirical results of the proposed CODR method in comparison to the original ODR based on the primary sample solely under Scenario 1.

Method (Rule)	CODR (d^{opt})		CODR ($\widehat{d}$)		ODR (d^{opt})		ODR ($\widehat{d}_E$)	
$N_E =$	500	1000	500	1000	500	1000	500	1000
True $V(\cdot)$	0.999		0.958	0.976	0.999		0.978	0.984
$\widehat{V}(\cdot)$	0.982	0.994	1.015	1.018	0.987	0.999	1.030	1.022
$SD\{\widehat{V}(\cdot)\}$	0.119	0.090	0.119	0.090	0.162	0.115	0.162	0.116
E$\{\widehat{\sigma}\}$	0.126	0.094	0.125	0.094	0.166	0.117	0.166	0.117
Coverage	97.2%	95.2%	96.4%	96.2%	96.8%	95.0%	96.6%	94.6%
Improved	26.5%	21.7%	26.5%	22.4%	/	/	/	/
$\widehat{\boldsymbol{\rho}}(\cdot)$	7.83	7.79	7.84	7.79	/	/	/	/
$\widehat{\Sigma}_M(\cdot)$	10.33	12.45	10.36	12.47	/	/	/	/