Generalizable Recommendation to a Target Population by Leveraging Randomized and Observational Studies

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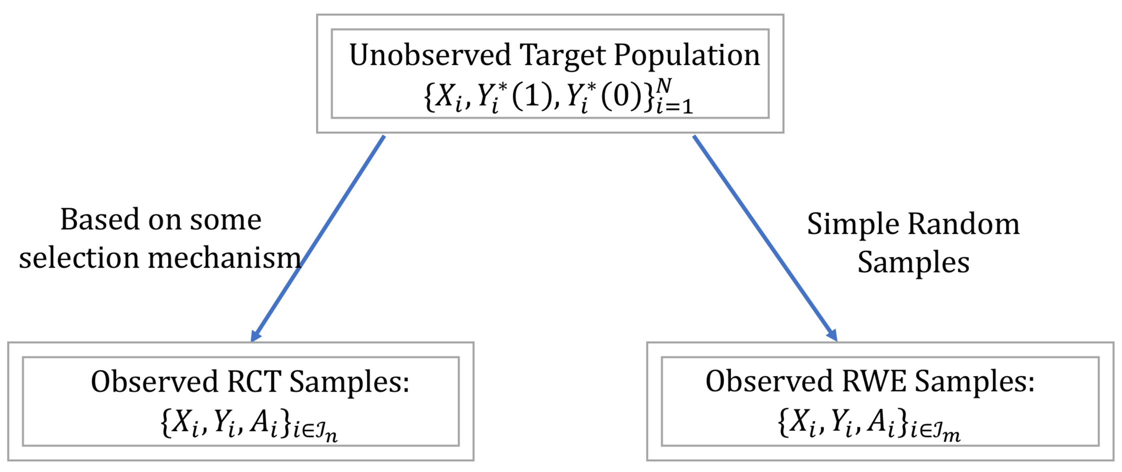
Abstract

- Personalized medicine focuses on the recommendation of treatment to patients based on their individual characteristics. The golden standard is to use randomized clinical trials (RCT).
- Comparing with the complex non-linear decision rules, clinicians are interested in parsimonious decision rules (e.g., linear or decision tree rules) which are more interpretable.
- This work is to give generalizable recommendations to the target population by use the information from RCT and real world evidence (RWE).

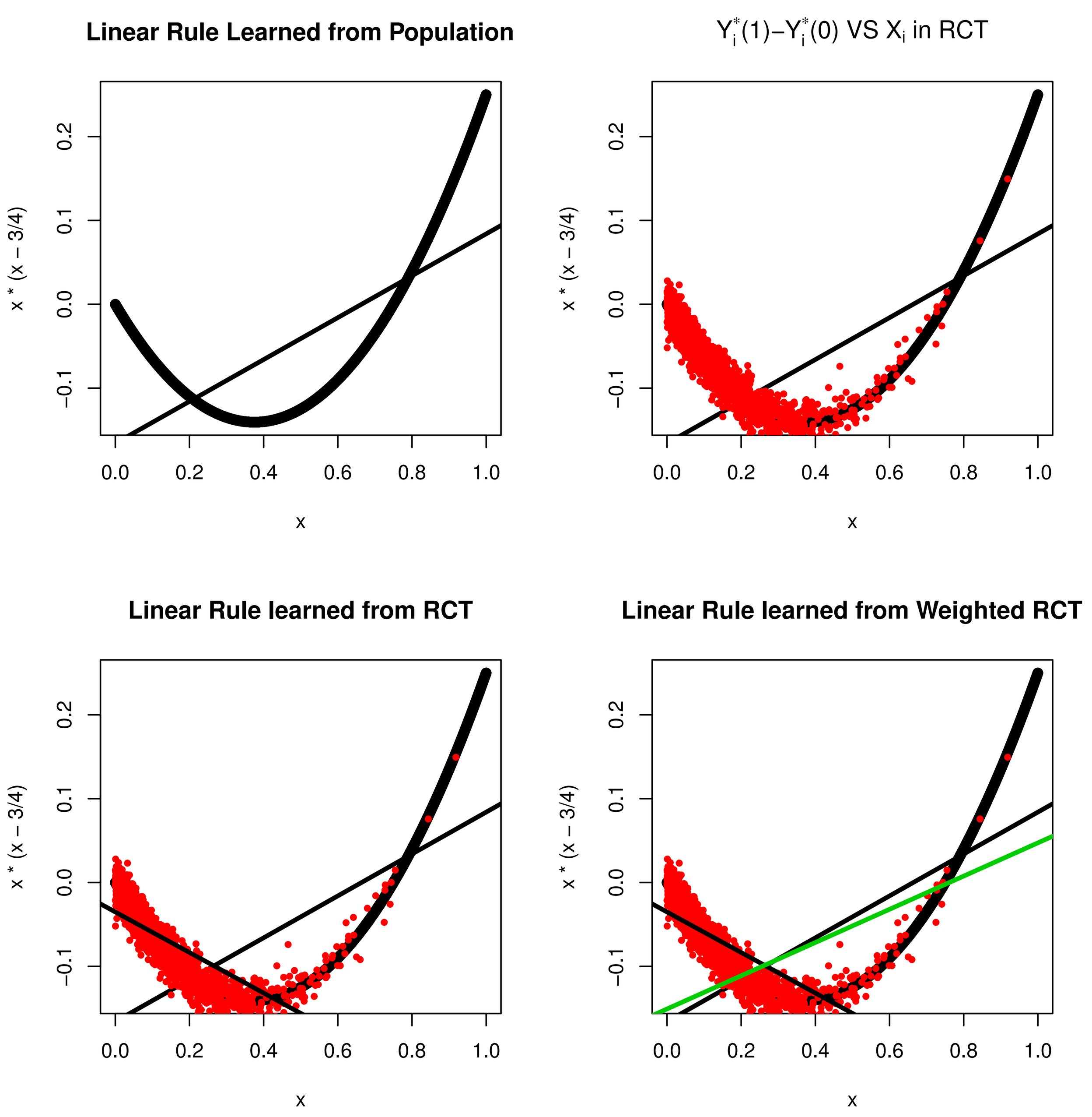
Data Sources Illustration



Issues

- There may exist unmeasured confounders affecting treatment and outcomes in RWE.
- There is selection bias in RCT (i.e., people's characteristics distribution in RCT may be very different from the target population), can a parsimonious optimal rule derived from it really be the optimal rule to the target population?

Selection Bias in RCT



Main Objectives

1. Estimate transferring weights to correct covariate distribution in RCT.
2. Use the weights abotained above to learn interpretable decision rules which have better generalizability to the target population.

Methods

- Notations: treatment $A \in \mathcal{A} = \{0, 1\}$, covariates $X \in \mathbf{R}^p$, potential outcomes $Y^*(0), Y^*(1) \in \mathbf{R}$, target population size N, index set of RCT samples $\mathcal{I}_n$ with size n, index set of RWE samples $\mathcal{I}_m$ with size m. $\delta_i = 1$ means the ith individual is in RWE, and $\widetilde{\delta}_i = 1$ means the ith individual is in RCT.
- Assume the covariate distribution in RWE is the same as that in the target population. Thus $\frac{1}{m}\sum_{i\in\mathcal{I}_m} X_i$ would be an unbiased estimator of $E(X)$, the covariate expectation in the target population.
- Note that $E\Big\{\frac{\widetilde{\delta}_i X_i}{P(\widetilde{\delta}_i=1|X_i)}\Big\} = E\Big\{E\Big\{\frac{\widetilde{\delta}_i X_i}{P(\widetilde{\delta}_i=1|X_i)}\Big|X_i\Big\}\Big\} = E(X_i)$,
- Goal: to find transferring weights $\widetilde{w}_i := \frac{1}{P(\widetilde{\delta}_i=1|X_i)}$.

Two Approaches to estimate Weights

1. Method of propensity score: Assume $\pi(X_i;\alpha) := P(\widetilde{\delta}_i = 1|X_i;\alpha) = \frac{exp(\alpha^\intercal X_i)}{1+exp(\alpha^\intercal X_i)}$, where $\alpha \in \mathbf{R}^p$, so we can get the maximum likelihood estimator

$$\begin{aligned}\hat{\alpha} =&\arg\max_{\alpha} \sum_{i=1}^N \{\widetilde{\delta}_i \log \pi(x_i;\alpha) + (1-\widetilde{\delta}_i)\log(1-\pi(x_i;\alpha))\}\\ =&\arg\max_{\alpha} \sum_{i=1}^N \{\widetilde{\delta}_i(\alpha^\intercal x_i) - \log(1+\exp(\alpha^\intercal x_i))\}\\ \approx&\arg\max_{\alpha} \Big\{\sum_{i=1}^N \widetilde{\delta}_i(\alpha^\intercal x_i) - \sum_{i\in\mathcal{I}_m}\frac{N}{m}\log(1+\exp(\alpha^\intercal x_i))\Big\}.\end{aligned}$$

2. Method of estimating equations:

$$\frac{1}{N}\sum_{i=1}^N \frac{\widetilde{\delta}_i X_i}{P(\widetilde{\delta}_i = 1|X_i;\alpha)} = \frac{1}{m}\sum_{i\in\mathcal{I}_m} X_i,$$

where $P(\widetilde{\delta}_i = 1|X_i;\alpha)$ is modeled same as in the above (1). So we can solve p equations to get $\hat{\alpha}$.

Decision Rules Larning with the Weights

1. Linear Decision Rules:
   - Target population parameter: $\beta_N^* = \arg\min_\beta \sum_{i=1}^N \{Y_i^*(1) - Y_i^*(0) - X_i^\intercal\beta\}^2$
   - Add $\widetilde{w}_i$ into least square loss function:

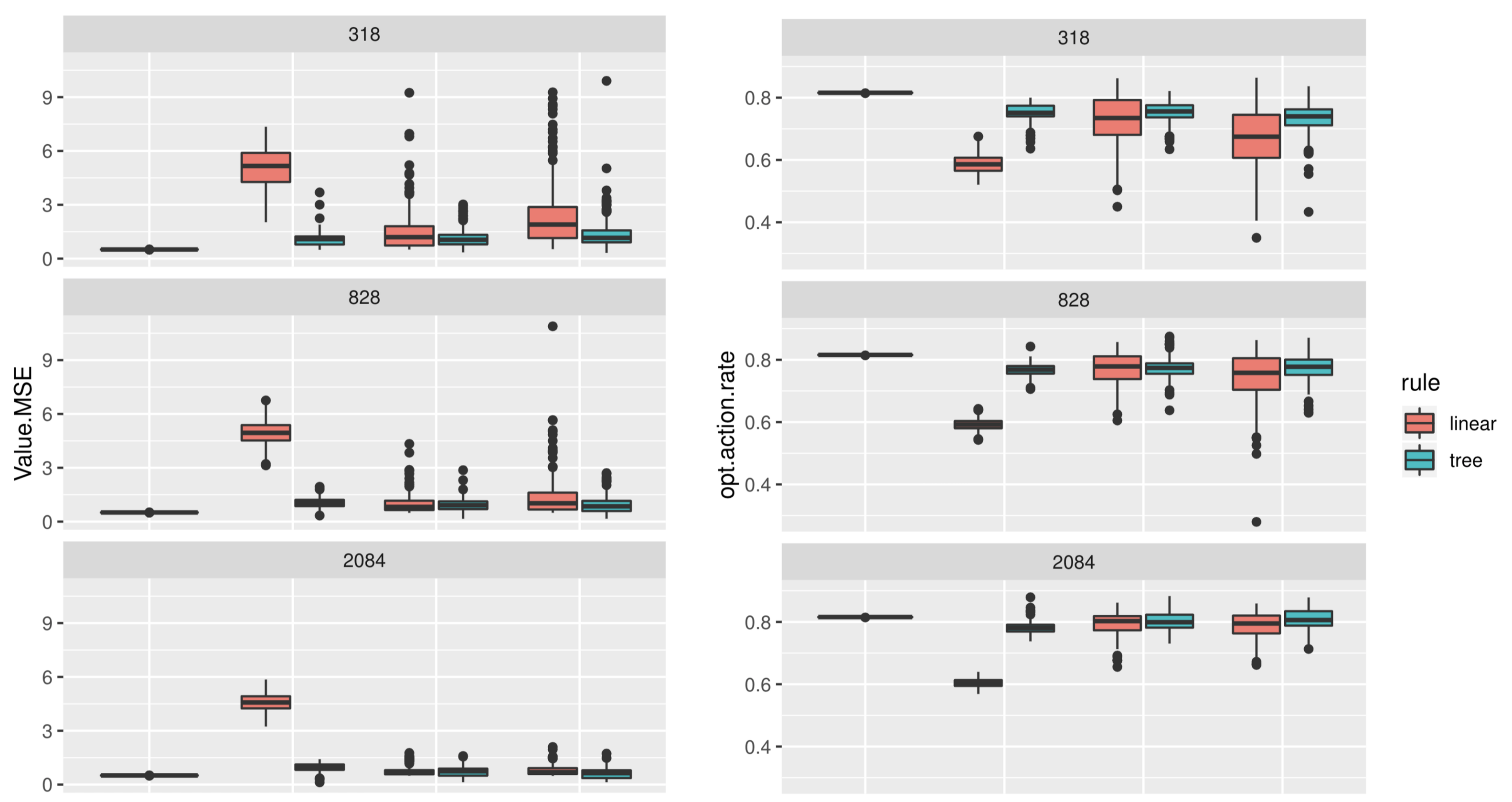
$$\hat{\beta}^* = \arg\min_\beta \sum_{i\in\mathcal{I}_n} \widetilde{w}_i\{\widehat{Y}_i^* - X_i^\intercal\beta\}^2,$$

   where $\widehat{Y}_i^* = \frac{A_iY_i}{P(A_i=1|X_i)} - \frac{(1-A_i)Y_i}{1-P(A_i=1|X_i)}$.

2. Decision Tree Rule:
   - Define the policy D : dom $X \rightarrow \{0,1\}$ and the value of the policy D as $V(D) = E_D(Y) = E[Y^*\{D(X)\}]$ over the target population. To maximize $V(D)$ is equivalent to $\min_D \sum_{i\in\mathcal{I}_n} \frac{|\widetilde{R}_i|}{\pi(A_i,X_i)} I[\{(2A_i-1)\text{sign}(\widetilde{R}_i)+1\}/2 \neq D(X_i)]$ [Wang et al., 2016], where $\widetilde{R}_i = Y_i - \widehat{R}_i$, and the predicted $\widehat{R}_i$ is fitted by outcomes Y_i only on X_i, and $\pi(A_i, X_i)$ is the probability of taking action A_i.
   - Add $\widetilde{w}_i$ into the loss function: $\min_D \sum_{i\in\mathcal{I}_n} \frac{\widetilde{w}_i|\widetilde{R}_i|}{\pi(A_i,X_i)} I[\{(2A_i-1)\text{sign}(\widetilde{R}_i)+1\}/2 \neq D(X_i)]$.

Simulation Results

- Generative model: $Y_i = 1 + X_{i1} + A_i\beta\widetilde{X}_i + \epsilon_i$, where $N = 10^6$, $\widetilde{X}_i = (\cos(1)-\frac{1}{2},\ \cos(X_{i1})-\frac{1}{2},\ \cos(X_{i2})-\frac{1}{2},\ \cos(X_{i3})-\frac{1}{2})^\intercal$, $X_i = (X_{i1}, X_{i2}, X_{i3})^\intercal \sim N(\mathbf{1}, I_3)$, $A_i \sim$ Bernoulli(0.5), $\beta = (1,2,3,4)$, $\epsilon_i \sim N(0, 0.5^2)$, $i = 1,\cdots,N$ independently . Let $\alpha = (\alpha_1, 1, -2, 1)$.



References

[Wang et al., 2016] Wang, Y., Wu, P., Liu, Y., Weng, C., and Zeng, D. (2016). Learning optimal individualized treatment rules from electronic health record data. In *2016 IEEE International Conference on Healthcare Informatics (ICHI)*, pages 65–71. IEEE.