

Supplementary Materials

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A Notations and Assumptions

A.1 Notations

- **Sample size.** For each $t = 1, \dots, T$, n_t is the number of subjects in Stage t . The cumulative sample size up to Stage t is denoted by $N_t = \sum_{s=1}^t n_s$. We set $N = N_T$ for notational simplicity.

X_{it} denotes subject i 's covariate information. We partition the covariate sample space $\mathcal{X}$ into m pre-specified non-overlapping subgroups, denoted as $\{\mathcal{S}_j\}_{j=1}^m$. We use $\mathbb{1}_{(X_{it} \in \mathcal{S}_j)}$ to indicate whether X_{it} belongs to subgroup j . Furthermore, we denote the number of subjects enrolled in subgroup j at Stage t as $n_{tj} = \sum_{i=1}^{n_t} \mathbb{1}_{(X_{it} \in \mathcal{S}_j)}$. The cumulative sample size for group j up to Stage t is $N_{tj} = \sum_{s=1}^t n_{sj}$. Finally, $N_j = N_{Tj}$ is the total number of subjects enrolled in subgroup j .

- **Treatment and potential outcomes.** In Stage t , $D_{it} \in \{0, 1\}$ denotes the treatment assignment status for subject i , and $i = 1, \dots, n_t$. The observed outcome is denoted by $Y_{it} \in \mathbb{R}$. We define $Y_{it}(d)$ as the potential outcome we would have observed if subject i receives treatment d at Stage t , for $d \in \{0, 1\}$.
- **Conditional moments.** We define the conditional moments and variances of the potential outcomes as

$$\begin{aligned}\mu_{j,c}(d) &= \mathbb{E}[Y_{it}(d)^c | X_{it} \in \mathcal{S}_j], \quad \text{for } c > 0 \text{ and } d = 0, 1, \\ \sigma_j(d)^2 &= \mu_{j,2}(d) - \mu_{j,1}(d)^2 = \mathbb{V}[Y_{it}(d) | X_{it} \in \mathcal{S}_j], \quad \text{for } d = 0, 1.\end{aligned}$$

- **Filtration.** We let $\mathcal{H}_0$ be the trivial sigma-algebra, and for $t = 1, 2, \dots, T$, $\mathcal{H}_t$ is the sigma-algebra formed by $(X_{is}, D_{is}, Y_{is})_{1 \leq i \leq n_s, 1 \leq s \leq t}$.
- **Actual treatment allocation.** The phrase ‘‘actual treatment allocation’’ will refer to the empirical treatment assignment frequencies. To be specific,

$$\hat{e}_{tj} = \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is}}{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)}}.$$

We also adopt the notation

$$\hat{e}_j = \hat{e}_{Tj}$$

for the RAR design, to emphasize that the above is the actual treatment probability in group j at the end of the experiment. The vector collecting all $\hat{e}_j$ will be denoted by $\hat{\mathbf{e}}$:

$$\hat{\mathbf{e}} = (\hat{e}_1, \dots, \hat{e}_m) = (\hat{e}_{T1}, \dots, \hat{e}_{Tm}).$$

- **Actual enrichment proportion.** Similarly, for adaptive enrichment designs, we define “actual enrichment proportion” as

$$\hat{p}_{tj} = \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)}}{\sum_{s=1}^t n_s} = \frac{\sum_{s=1}^t n_{sj}}{\sum_{s=1}^t n_s},$$

and

$$\hat{p}_j = \hat{p}_{Tj}$$

is the actual enrichment proportion at the end of the experiment. The vector $\hat{\mathbf{p}}$ collects all $\hat{p}_j$:

$$\hat{\mathbf{p}} = (\hat{p}_1, \dots, \hat{p}_m) = (\hat{p}_{T1}, \dots, \hat{p}_{Tm}).$$

- **Optimized treatment allocation.** We use the phrases “optimized treatment allocation” and “optimized subgroup enrichment proportion” to refer to the allocation rule obtained by solving the optimization problems in Sections 4.1 and 5.1 at Stage t , which are denoted by

$$\hat{\mathbf{e}}_t^* = (\hat{e}_{t1}^*, \dots, \hat{e}_{tm}^*), \quad \text{and} \quad \hat{\mathbf{p}}_t^* = (\hat{p}_{t1}^*, \dots, \hat{p}_{tm}^*).$$

For example, in the RAR design, treatment is assigned based on the above allocation rule as $\mathbb{P}(D_{it} = 1 | X_{it} \in \mathcal{S}_j, \mathcal{H}_{t-1}) = \hat{e}_{tj}^*$.

- **Oracle treatment allocation and oracle enrichment proportion.** Finally, we define the “oracle treatment allocation” and “oracle enrichment proportion” as

$$\mathbf{e}^* = (e_1^*, \dots, e_m^*), \quad \text{and} \quad \mathbf{p} = (p_1^*, \dots, p_m^*).$$

- **Population treatment effects.** We define the population subgroup treatment effect as τ_j :

$$\tau_j = \mathbb{E}[Y_{it}(1) | X_{it} \in \mathcal{S}_j] - \mathbb{E}[Y_{it}(0) | X_{it} \in \mathcal{S}_j], \quad \text{for } j = 1, 2, \dots, m.$$

- **Stage t treatment effect estimator.** The subgroup treatment effect estimator at Stage t is denoted by $\hat{\tau}_{tj}$, for $t = 1, \dots, T$, $j = 1, \dots, m$:

$$\hat{\tau}_{tj} = \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} Y_{is}}{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is}} - \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (1 - D_{is}) Y_{is}}{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (1 - D_{is})}.$$

- **Final-stage treatment effect estimator.** For notational simplicity, we drop the subscript T in $\hat{\tau}_{Tj}$, which is the estimated subgroup treatment effect at the end of the experiment. In

other words:

$$\hat{\tau}_j = \hat{\tau}_{Tj} = \frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} D_{it} Y_{it}}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} D_{it}} - \frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it}) Y_{it}}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it})}.$$

In the main manuscript, to distinguish between the two different designs, we denote the final-stage estimator for RAR design as $\hat{\tau}_j^{\text{RAR}}$ and the final estimator for adaptive enrichment design as $\hat{\tau}_j^{\text{AE}}$.

- **Best subgroup index.** j^* indicates the subgroup with the largest estimated treatment effect:

$$j^* = \operatorname{argmax}_{1 \leq j \leq m} \hat{\tau}_j^{\text{RAR}}$$

under the RAR design, or

$$j^* = \operatorname{argmax}_{1 \leq j \leq m} \hat{\tau}_j^{\text{AE}}$$

under the adaptive enrichment design.

- **Asymptotic variances.** As the asymptotic variance of the estimated subgroup treatment effects depend on the treatment probability (or the enrichment proportion), we define

$$\mathbb{V}_j(e) = \frac{\sigma_j(1)^2}{p_j e} + \frac{\sigma_j(0)^2}{p_j (1 - e)},$$

for the RAR design. Similarly, let

$$\mathbb{V}_j(p) = \frac{\sigma_j(1)^2}{p e_j} + \frac{\sigma_j(0)^2}{p (1 - e_j)},$$

for the enrichment design.

- **Variance estimator.** Their estimates are

$$\hat{\mathbb{V}}_{tj}(e) = \frac{\hat{\sigma}_{tj}(1)^2}{\hat{p}_{tj} e} + \frac{\hat{\sigma}_{tj}(0)^2}{\hat{p}_{tj} (1 - e)}, \quad \hat{\mathbb{V}}_{tj}(p) = \frac{\hat{\sigma}_{tj}(1)^2}{p \hat{e}_{tj}} + \frac{\hat{\sigma}_{tj}(0)^2}{p (1 - \hat{e}_{tj})},$$

respectively.

A.2 List of assumptions

Assumption 1 (Finite moments).

The potential outcomes $Y_{it}(d)$ have bounded fourth moments: $\mathbb{E}[|Y_{it}(d)|^4] \leq c < \infty$ for $d = 0, 1$ and some constant c .

Assumption 2 (Subgroup treatment effects).

There are total $m \geq 2$ subgroups, and the subgroup treatment effects can be monotonically ordered as $\tau_1 > \tau_2 > \dots > \tau_m$.

Assumption 3 (Subgroup proportions and treatment assignment probabilities).

(i) For the response-adaptive randomization (RAR) design, the subgroup proportions $p_1, \dots, p_m$ are bounded away from 0 by a positive constant, that is, there exists a constant $\delta \in (0, 1)$ such that $p_j \geq \delta$ for all j . (ii) For the adaptive enrichment (AE) design, The subgroup treatment assignment probabilities $e_1, \dots, e_m$ are bounded away from 0 and 1, that is, there exists a constant $\delta \in (0, 1/2)$ such that $\delta \leq e_j \leq 1 - \delta$ for all $j = 1, 2, \dots, m$.

Assumption 4 (Asymptotic regime).

(i) A fully adaptive design corresponds to $T \rightarrow \infty$ and $n_t = 1$ (or a fixed constant). (ii) A multi-stage design corresponds to $N \rightarrow \infty$, and T is fixed.

B Proofs of Results in Section 5

B.1 Proof of Remark 1 in Section 5.1

Proof. First, we want to show the following equalities hold:

(i) For the adaptive enrichment design:

$$G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{p}) = G(\mathcal{S}_1, \mathcal{S}_k, \mathbf{p}), \text{ for } j, k = 2, \dots, m, j \neq k. \quad (1)$$

(ii) For the RAR design:

$$G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{e}) = G(\mathcal{S}_1, \mathcal{S}_k, \mathbf{e}), \text{ for } j, k = 2, \dots, m, j \neq k.$$

In what follows, we provide the proof under the RAR design. The proof of the adaptive enrichment design follows the similar procedures. From Section H.2.1, we obtain the rate function under the RAR design as $G(\mathcal{S}_1, \mathcal{S}_j; \mathbf{e}) = \frac{(\tau_j - \tau_1)^2}{\mathbb{V}_1(\mathbf{e}_1) + \mathbb{V}_j(\mathbf{e}_j)}$. And the original optimization problem is

$$\begin{aligned} & \max_{\mathbf{e}} \min_{2 \leq j \leq m} G(\mathcal{S}_1, \mathcal{S}_j; \mathbf{e}), \\ & \text{s.t. } \sum_{l=1}^m p_l e_l \leq c_1, \\ & c_2 \leq e_l \leq 1 - c_2, \quad l = 1, \dots, m. \end{aligned}$$

The original optimization problem can be expressed via the epigraph representation:

$$\begin{aligned} & \max_{\mathbf{e}} z, \\ & \text{s.t. } G(\mathcal{S}_1, \mathcal{S}_j; \mathbf{e}) \geq z, \quad j = 2, \dots, m, \\ & \sum_{l=1}^m p_l e_l \leq c_1, \quad 0 < c_1 < 1, \\ & c_2 \leq e_l \leq 1 - c_2, \quad l = 1, \dots, m, \quad c > 0. \end{aligned}$$

The Lagrangian associated with the above problem is

$$L(\mathbf{e}, \boldsymbol{\lambda}, \gamma, \boldsymbol{\alpha}, \boldsymbol{\beta}, z) = z + \sum_{j=2}^m \lambda_j (G(\mathcal{S}_1, \mathcal{S}_j; \mathbf{e}) - z) + \gamma (c_1 - \sum_{l=1}^m p_l e_l) + \sum_{l=1}^m \alpha_l (e_l - c_2) + \sum_{l=1}^m \beta_l (1 - c_2 - e_l).$$

From the KKT conditions:

$$\begin{aligned} \lambda_j (G(\mathcal{S}_1, \mathcal{S}_j; \mathbf{e}) - z) &= 0, \\ \lambda_k (G(\mathcal{S}_1, \mathcal{S}_k; \mathbf{e}) - z) &= 0, \end{aligned}$$

when $\lambda_j \neq 0$, $\lambda_k \neq 0$, $j \neq k$,

$$G(\mathcal{S}_1, \mathcal{S}_j; \mathbf{e}) - z = 0, \quad j = 2, \dots, m.$$

Similarly,

$$G(\mathcal{S}_1, \mathcal{S}_k; \mathbf{e}) - z = 0, \quad k \neq j, k = 2, \dots, m.$$

Therefore, we conclude our proof by showing $G(\mathcal{S}_1, \mathcal{S}_j; \mathbf{e}) = G(\mathcal{S}_1, \mathcal{S}_k; \mathbf{e})$, for $j, k = 2, \dots, m$, $j \neq k$.

By Eq (1), we have

$$\begin{aligned} G(\mathcal{S}_1, \mathcal{S}_j; \mathbf{p}) &= G(\mathcal{S}_1, \mathcal{S}_k; \mathbf{p}), \\ \frac{(\tau_j - \tau_1)^2}{\mathbb{V}_1(p_1) + \mathbb{V}_j(p_j)} &= \frac{(\tau_k - \tau_1)^2}{\mathbb{V}_1(p_1) + \mathbb{V}_k(p_k)}. \end{aligned}$$

Therefore,

$$\frac{(\tau_j - \tau_1)^2}{\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)} + \frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1-e_j)}} = \frac{(\tau_k - \tau_1)^2}{\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)} + \frac{\sigma_k(1)^2}{p_k e_k} + \frac{\sigma_k(1)^2}{p_k(1-e_k)}}.$$

Let $\sigma_j^2 = \sigma_j(1)^2/e_j + \sigma_j(0)^2/(1-e_j)$.

$$\frac{(\tau_j - \tau_1)^2}{\frac{\sigma_1^2}{p_1} + \frac{\sigma_j^2}{p_j}} = \frac{(\tau_k - \tau_1)^2}{\frac{\sigma_1^2}{p_1} + \frac{\sigma_k^2}{p_k}}.$$

We want to simplify the above equality by showing the following holds:

$$\frac{(\tau_k - \tau_1)^2}{\sigma_k^2/p_k} = \frac{(\tau_j - \tau_1)^2}{\sigma_j^2/p_j} + R_n, \quad (2)$$

where $R_n = \frac{(\tau_j - \tau_1)^2}{\sigma_j^2/p_j} \cdot \frac{\frac{1}{A_k} - \frac{1}{A_j}}{\frac{1}{A_1} + \frac{1}{A_j}}$, $\frac{1}{A_k} - \frac{1}{A_j} = \frac{1}{\frac{\sigma_k(1)^2}{p_k e_k} + \frac{\sigma_k(0)^2}{p_k(1-e_k)}} - \frac{1}{\frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1-e_j)}}$, and $\frac{1}{A_1} = \frac{1}{\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)}}$.

We assume $R_n = 0$ by assuming $\frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1} = 0$.

To show Eq (2) holds, first, by Eq (1),

$$\frac{(\tau_j - \tau_1)^2}{\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)} + \frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1-e_j)}} = \frac{(\tau_k - \tau_1)^2}{\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)} + \frac{\sigma_k(1)^2}{p_k e_k} + \frac{\sigma_k(0)^2}{p_k(1-e_k)}}.$$

$$\text{Let } A_1 = \frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)}, A_j = \frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1-e_j)}, A_k = \frac{\sigma_k(1)^2}{p_k e_k} + \frac{\sigma_k(0)^2}{p_k(1-e_k)},$$

$$\begin{aligned} \frac{(\tau_j - \tau_1)^2}{A_1 + A_j} &= \frac{(\tau_k - \tau_1)^2}{A_1 + A_k}, \\ (\tau_j - \tau_1)^2 \frac{1}{(A_1 + A_j)} &= (\tau_k - \tau_1)^2 \frac{1}{(A_1 + A_k)}, \\ (\tau_j - \tau_1)^2 \frac{1}{(\frac{1}{A_1} + \frac{1}{A_j}) A_1 A_j} &= (\tau_k - \tau_1)^2 \frac{1}{(\frac{1}{A_1} + \frac{1}{A_k}) A_1 A_k}, \\ (\frac{1}{A_1} + \frac{1}{A_j}) A_1 A_j (\tau_j - \tau_1)^2 &= (\frac{1}{A_1} + \frac{1}{A_k}) A_1 A_k (\tau_j - \tau_1)^2, \\ \frac{A_j (\tau_k - \tau_1)^2}{A_k (\tau_j - \tau_1)^2} &= \frac{\frac{1}{A_1} + \frac{1}{A_k}}{\frac{1}{A_1} + \frac{1}{A_j}}, \\ \frac{(\frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1-e_j)}) \cdot (\tau_k - \tau_1)^2}{(\frac{\sigma_k(1)^2}{p_k e_k} + \frac{\sigma_k(0)^2}{p_k(1-e_k)}) \cdot (\tau_j - \tau_1)^2} &= \frac{\frac{1}{A_1} + \frac{1}{A_k}}{\frac{1}{A_1} + \frac{1}{A_j}}, \\ \frac{(\tau_k - \tau_1)^2 \cdot \sigma_j^2 \cdot \frac{1}{p_j}}{(\tau_j - \tau_1)^2 \cdot \sigma_k^2 \cdot \frac{1}{p_k}} &= \frac{\frac{1}{A_1} + \frac{1}{A_k}}{\frac{1}{A_1} + \frac{1}{A_j}}, \\ \frac{(\tau_k - \tau_1)^2}{\sigma_k^2/p_k} &= \frac{(\tau_j - \tau_1)^2}{\sigma_j^2/p_j} \cdot \frac{\frac{1}{A_1} + \frac{1}{A_k}}{\frac{1}{A_1} + \frac{1}{A_j}}, \\ \frac{(\tau_k - \tau_1)^2}{\sigma_k^2/p_k} &= \frac{(\tau_j - \tau_1)^2}{\sigma_j^2/p_j} \cdot \left(1 + \frac{\frac{1}{A_k} - \frac{1}{A_j}}{\frac{1}{A_1} + \frac{1}{A_j}}\right), \\ \frac{(\tau_k - \tau_1)^2}{\sigma_k^2/p_k} &= \frac{(\tau_j - \tau_1)^2}{\sigma_j^2/p_j} + \underbrace{\frac{(\tau_j - \tau_1)^2}{\sigma_j^2/p_j} \cdot \frac{\frac{1}{A_k} - \frac{1}{A_j}}{\frac{1}{A_1} + \frac{1}{A_j}}}_{R_n}, \end{aligned}$$

$$\begin{aligned} \text{where } \frac{1}{A_k} - \frac{1}{A_j} &= \frac{1}{\frac{\sigma_k(1)^2}{p_k e_k} + \frac{\sigma_k(0)^2}{p_k(1-e_k)}} - \frac{1}{\frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1-e_j)}}, \\ \frac{1}{A_1} &= \frac{1}{\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)}}. \end{aligned}$$

Therefore, to set $R_n = 0$, we can let $\frac{1}{A_1} \rightarrow \infty$ by letting $\frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1} = 0$.

Lastly, by Eq (2), we have

$$\frac{(\tau_j - \tau_1)^2}{\frac{\sigma_j^2}{p_j}} = \frac{(\tau_k - \tau_1)^2}{\frac{\sigma_k^2}{p_k}}.$$

As a result, one can derive the optimal enrichment proportions as

$$p_j^* = \frac{\beta_j}{\sum_{j=1}^m \beta_j}, \quad \beta_j = \begin{cases} \sigma_j^2 / (\tau_j - \tau_1)^2 & j \neq 1, \\ \sigma_j \sqrt{\sum_{l \neq 1} \beta_l^2 / \sigma_l^2} & j = 1. \end{cases}$$

□

C Proofs of Results in Section 6.2

C.1 Revisit theoretical results in Section 6.2

In this section, we prove the results in Section 6.2 of the main manuscript. We first provide a useful lemma (Lemma 1 in the main manuscript), which justifies consistent estimation of moments of potential outcomes under very mild assumptions. In particular, we will only need to assume that the treatment probabilities are bounded away from zero and one, and that the subgroup proportions are bounded away from zero. Therefore, the consistency result applies to both the proposed RAR and AE designs, as the treatment probabilities and the subgroup proportions are bounded away from zero and one by our design strategy (see the optimization problems A and C for justification of this statement).

Lemma C.1. *Assume Assumption 1 holds. Let $\mathbf{p}_{tj} = \mathbb{P}(X_{it} \in \mathcal{S}_j | \mathcal{H}_{t-1})$ be the subgroup proportions, and $\mathbf{e}_{tj} = \mathbb{P}(D_{it} = 1 | X_{it} \in \mathcal{S}_j, \mathcal{H}_{t-1})$ be the treatment probabilities. Assume there exists some $\delta \in (0, 1/2)$ such that for all $j = 1, 2, \dots, m$ and $t = 1, 2, \dots$,*

$$\mathbf{p}_{tj} \geq \delta, \text{ and } \delta \leq \mathbf{e}_{tj} \leq 1 - \delta.$$

Then for any $j = 1, 2, \dots, m$, and any t satisfying $N_t \rightarrow \infty$,

$$\begin{aligned} \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} Y_{is}^c}{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is}} &= \mu_{j,c}(1) + O_p\left(\frac{1}{\sqrt{N_t}}\right), \\ \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (1 - D_{is}) Y_{is}^c}{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (1 - D_{is})} &= \mu_{j,c}(0) + O_p\left(\frac{1}{\sqrt{N_t}}\right). \end{aligned}$$

We make two remarks. First, $\mathbf{p}_{tj} = p_j$ and $\mathbf{e}_{tj} = \hat{e}_{tj}^*$ in the RAR design, and $\mathbf{p}_{tj} = \hat{p}_{tj}^*$ and $\mathbf{e}_{tj} = e_j$ in the AE design. Second, the above lemma encompasses two asymptotic regimes. For a multi-stage design (i.e., T fixed), the consistency holds for any fixed $t = 1, 2, \dots, T$, provided that $n_t \rightarrow \infty$ for each stage. On the other hand, a fully adaptive design corresponds to $n_t = 1$ (or a

fixed constant) for all t , in which case the consistency result applies as $t \rightarrow \infty$.

The algorithms we proposed in the main paper requires solving the optimized treatment allocation in the RAR design (or the optimized subgroup proportion in the AE design), for which an important ingredient is the estimated variance. Building on Lemma C.1, we show the consistency of $\widehat{\mathbb{V}}_{tj}(\cdot)$.

Corollary C.1. *Let $\delta \in (0, 1/2)$ be some constant. Assume Assumptions 1 and 3 hold,*

$$\begin{aligned} \text{RAR design:} \quad & \sup_{\delta \leq e \leq 1-\delta} \left| \widehat{\mathbb{V}}_{tj}(e) - \mathbb{V}_j(e) \right| = O_p \left(\frac{1}{\sqrt{N_t}} \right), \\ \text{AE design:} \quad & \sup_{\delta \leq p \leq 1-\delta} \left| \widehat{\mathbb{V}}_{tj}(p) - \mathbb{V}_j(p) \right| = O_p \left(\frac{1}{\sqrt{N_t}} \right), \end{aligned}$$

for $j = 1, 2, \dots, m$.

Recall that at each stage, we rank the estimated subgroup treatment effects using the “order statistics” notation: $\widehat{\tau}_{t,(1)} \geq \widehat{\tau}_{t,(2)} \geq \dots \widehat{\tau}_{t,(m)}$. (To be very precise, the ranking should also be indexed by t , as it may change at each stage; that is, a more precise notation would be $\widehat{\tau}_{t,(1)t} \geq \widehat{\tau}_{t,(2)t} \geq \dots \geq \widehat{\tau}_{t,(m)t}$. We drop the further subscript for the ranking as it is too cumbersome). Another corollary following Lemma C.1 is that the estimated subgroup treatment effects are consistent:

Corollary C.2. *Assume Assumptions 1 and 3 hold. Then for both RAR and AE designs,*

$$\widehat{\tau}_{tj} - \tau_j = O_p \left(\frac{1}{\sqrt{N_t}} \right), \quad j = 1, \dots, m,$$

If Assumption 2 also holds, then as $t \rightarrow \infty$,

$$\mathbb{P}(\widehat{\tau}_{t,(j)} = \tau_j) \rightarrow 1, \quad \mathbb{P}(\tau_{(j)} = \tau_j) \rightarrow 1.$$

Next, we break Theorem 1 in the main manuscript into two lemmas to illustrate the convergence of the optimized treatment allocation (or enrichment proportion) and the convergence of the actual treatment allocation (or enrichment proportion) to the oracle rules,

First, we prove that the optimized allocation rule achieves the oracle allocation asymptotically. Since the solution to the oracle optimization problems may not be unique, we denote by $\mathcal{E}^*$ the set of oracle allocation rules.

Lemma C.2. *Consider the RAR design, and assume Assumptions 1-3 hold. Let $\mathcal{E}^*$ be the solution(s) to Problem A, and $\widehat{\mathcal{E}}^*$ be the optimized treatment allocations solved from the sample analog of Problem A. Then for any $\delta > 0$, and any t satisfying $N_{t-1} \rightarrow \infty$,*

$$\mathbb{P} \left(\sup_{\widehat{e}_t^* \in \widehat{\mathcal{E}}^*} \inf_{e^* \in \mathcal{E}^*} \|\widehat{e}_t^* - e^*\| \leq \delta \right) \rightarrow 1.$$

Consider the AE design, and assume Assumptions 1-3 hold. Let $\mathcal{P}^*$ be the solution(s) to Problem C, and $\hat{\mathcal{P}}^*$ be the optimized treatment allocations solved from the sample analog of Problem C. Then for any $\delta > 0$, and any t satisfying $N_{t-1} \rightarrow \infty$,

$$\mathbb{P}\left(\sup_{\hat{\mathbf{p}}_t^* \in \hat{\mathcal{P}}^*} \inf_{\mathbf{p}^* \in \mathcal{P}^*} \|\hat{\mathbf{p}}_t^* - \mathbf{p}^*\| \leq \delta\right) \rightarrow 1.$$

Second, we prove that the actual allocation rule achieves the oracle allocation asymptotically. Here, we assume that the optimization problems admit unique solutions. Such an assumption is quite mild and innocuous because whenever the optimization problems deliver multiple solutions, the researcher can always choose one by employing some additional criteria. More discussions can be found in Section 6.2 in the main manuscript.

Lemma C.3. *Consider the RAR design, and assume Assumptions 1-3 hold. Further assume that the solution to the oracle problem A is unique. Let $\delta > 0$ be an arbitrary constant. Then for the fully adaptive design or the multi-stage design (assuming $n_1/N \rightarrow 0$),*

$$\mathbb{P}(\|\hat{\mathbf{e}} - \mathbf{e}^*\| \leq \delta) \rightarrow 1.$$

Consider the AE design, and assume Assumptions 1-3 hold. Further assume that the solution to the oracle problem C is unique. Let $\delta > 0$ be an arbitrary constant. Then for the fully adaptive design or the multi-stage design (assuming $n_1/N \rightarrow 0$),

$$\mathbb{P}(\|\hat{\mathbf{p}} - \mathbf{p}^*\| \leq \delta) \rightarrow 1.$$

We remark that Lemma C.3 hold for the multi-stage setting when n_1/N tends to 0. If n_1 is a non-vanishing fraction of N , that is, if $n_1/N \rightarrow c > 0$, the actual treatment allocation in each stage should be calibrated based on each stage's sample size; see the form of $\tilde{\mathbf{e}}_t$ in Section 4.3. Similarly, for the adaptive enrichment design, the actual enrichment proportion should be calibrated as in Section 5.2.

C.2 Proof of Lemma C.1

Proof. In what follows, we provide the proof of Lemma C.1, which is the same as Lemma 1 in Section 6.2 in the main manuscript.

We let $N_t = \sum_{s=1}^t n_s$. To start, we write

$$\hat{\mu}_{tj,c}(1) = \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} Y_{is}^c}{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is}},$$

and therefore

$$\hat{\mu}_{tj,c}(1) - \mu_{j,c}(1) = \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} (Y_{is}(1)^c - \mu_{j,c}(1))}{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is}}.$$

Consider the denominator first. We further rewrite it as

$$\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} = \sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (D_{is} - \mathfrak{e}_{sj}) + \sum_{s=1}^t \mathfrak{e}_{sj} \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)}.$$

It is straightforward to verify that

$$\mathbb{E} \left[\sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (D_{is} - \mathfrak{e}_{sj}) \middle| \mathcal{H}_{s-1} \right] = 0.$$

As a result,

$$\begin{aligned} \mathbb{V} \left[\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (D_{is} - \mathfrak{e}_{sj}) \right] &= \sum_{s=1}^t \mathbb{V} \left[\sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (D_{is} - \mathfrak{e}_{sj}) \right] \\ &= \sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{E} \left[\mathbb{1}_{(X_{is} \in \mathcal{S}_j)} \mathfrak{e}_{sj} (1 - \mathfrak{e}_{sj}) \right] \leq \delta(1 - \delta) N_t = O(\sqrt{N_t}), \end{aligned}$$

where the second equality follows from total variance decomposition by conditioning on $\mathcal{H}_{s-1}$ and X_{is} . On the other hand,

$$\sum_{s=1}^t \mathfrak{e}_{sj} \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} = \sum_{s=1}^t \mathfrak{e}_{sj} \sum_{i=1}^{n_s} (\mathbb{1}_{(X_{is} \in \mathcal{S}_j)} - \mathfrak{p}_{sj}) + \underbrace{\sum_{s=1}^t n_s \mathfrak{e}_{sj} \mathfrak{p}_{sj}}_{\geq \delta^2 N_t},$$

and by variance calculation, the first term on the rhs is of order $O_p(\sqrt{N_t})$. To summarize, the denominator satisfies

$$\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} \asymp_p N_t.$$

Now consider the numerator. We notice that

$$\mathbb{E} \left[\sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} (Y_{is}(1)^c - \mu_{j,c}(1)) \middle| \mathcal{H}_{s-1} \right] = 0.$$

As a result,

$$\begin{aligned} \mathbb{V} \left[\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} (Y_{is}(1)^c - \mu_{j,c}(1)) \right] &= \sum_{s=1}^t \mathbb{V} \left[\sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} (Y_{is}(1)^c - \mu_{j,c}(1)) \right] \\ &= \sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{E} \left[\mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} \mathbb{V}[Y_{is}(1)^c | X_{is} \in \mathcal{S}_j] \right] \leq \mu_{j,4}(1) \sum_{s=1}^t \sum_{i=1}^{n_s} \mathbb{E} [\mathfrak{p}_{sj} \mathfrak{e}_{sj}] \\ &\lesssim N_t. \end{aligned}$$

The third equality is the result of the law of iterated expectation by conditioning on $\mathcal{H}_{s-1}$. To conclude, we have shown that term (I) satisfies

$$\hat{\mu}_{tj,c}(1) - \mu_{j,c}(1) = \frac{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} (Y_{is}(1)^c - \mu_{j,c}(1))}{\sum_{s=1}^t \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_j)} D_{is}} = O_p \left(\frac{1}{\sqrt{N_t}} \right).$$

The same proof strategy applies to showing the consistency of $\hat{\mu}_{tj,c}(0)$. $\square$

C.3 Proof of Corollary C.1

Proof. In what follows, we provide the proof of Corollary C.1, which is the same as Corollary 1 in Section 6.2 in the main manuscript.

Here, we prove the result for the RAR design. The proof for the AE design follows the similar procedure. To start, we notice that

$$\begin{aligned} \hat{\mathbb{V}}_{tj}(e) - \mathbb{V}_j(e) &= \frac{1}{\hat{p}_{tj}e} \left(\hat{\sigma}_{tj}(1)^2 - \sigma_j(1)^2 \right) - \frac{\sigma_j(1)^2}{e} \frac{\hat{p}_{tj} - p_j}{\hat{p}_{tj}p_j} \\ &\quad + \frac{1}{\hat{p}_{tj}(1-e)} \left(\hat{\sigma}_{tj}(0)^2 - \sigma_j(0)^2 \right) - \frac{\sigma_j(0)^2}{1-e} \frac{\hat{p}_{tj} - p_j}{\hat{p}_{tj}p_j}. \end{aligned}$$

Thanks to Lemma C.1, we have that

$$\hat{\sigma}_{tj}(1)^2 - \sigma_j(1)^2 = O_p \left(\frac{1}{\sqrt{N_t}} \right), \quad \hat{\sigma}_{tj}(0)^2 - \sigma_j(0)^2 = O_p \left(\frac{1}{\sqrt{N_t}} \right), \quad N_t = \sum_{s=1}^t n_s.$$

For the RAR design, X_{is} are independently and identically distributed across both $i = 1, 2, \dots, n_s$ and $s = 1, 2, \dots$. Therefore, standard variance computation suggests that

$$\hat{p}_{tj} - p_j = O_p \left(\frac{1}{\sqrt{N_t}} \right).$$

This closes the proof. $\square$

C.4 Proof of Corollary C.2

Proof. Corollary C.2 is the same as Corollary 2 in Section 6.2 in the main manuscript. This corollary follows directly from Lemma C.1. $\square$

C.5 Proof of Lemma C.2

Proof. Here, we show the consistency of the optimized treatment allocation under our proposed RAR design. The proof for the optimized enrichment proportion under the proposed AE design follows similar procedures.

Let $f(\mathbf{e}) = \min_{2 \leq j \leq m} \frac{(\tau_j - \tau_1)^2}{\mathbb{V}_1(e_1) + \mathbb{V}_j(e_j)}$ be the oracle objective function, then the original optimization problem can be written as

$$\max_{\mathbf{e}} f(\mathbf{e}), \quad \text{s.t.} \quad \sum_{j=1}^m p_j e_j \leq c_1, \quad c_2 \leq e_j \leq 1 - c_2, \quad j = 1, \dots, m.$$

For notational simplicity, let $\mathcal{E}$ be the set of candidate allocation rules (i.e., all allocation rules satisfying the constraints). Similarly, we let $\hat{f}_t(\mathbf{e})$ be the estimated objective function, that is,

$$\hat{f}_t(\mathbf{e}) = \min_{2 \leq j \leq m} \frac{(\hat{\tau}_{t-1,(j)} - \hat{\tau}_{t-1,(1)})^2}{\hat{\mathbb{V}}_{t-1,(1)}(e_1) + \hat{\mathbb{V}}_{t-1,(j)}(e_j)}.$$

We solve the following optimization problem:

$$\max_{\mathbf{e}} \hat{f}_t(\mathbf{e}), \quad \text{s.t.} \quad \sum_{j=1}^m p_j e_j \leq c_1, \quad c_2 \leq e_j \leq 1 - c_2, \quad j = 1, \dots, m.$$

We denote the set of maximizers to the above optimization problem as $\hat{\mathcal{E}}^*$. Lastly, let the δ -enlargement of $\mathcal{E}^*$ be $\mathcal{E}^* + B_\delta$, where B_δ is the Euclidean ball centered at the origin with radius δ : $\mathcal{E}^* + B_\delta = \{\mathbf{e} + \mathbf{u} : \mathbf{e} \in \mathcal{E}^*, \|\mathbf{u}\| = \delta\}$.

We now collect a few useful observations. First, because $f(\mathbf{e})$ is a continuous function and $\mathcal{E}$ is compact, the set of maximizers, $\mathcal{E}^*$, is nonempty. For $\delta > 0$, we define

$$\varepsilon = \sup_{\mathbf{e} \in \mathcal{E}} f(\mathbf{e}) - \sup_{\mathbf{e} \notin \mathcal{E}^* + B_\delta} f(\mathbf{e}).$$

Notice that the above is strictly positive. Consider the event

$$A_t(\varepsilon/3) : \sup_{\mathbf{e} \in \mathcal{E}} |\hat{f}_t(\mathbf{e}) - f(\mathbf{e})| \leq \varepsilon/3.$$

Next, for an arbitrary $\mathbf{e} \notin \mathcal{E}^* + B_\delta$, we have $f(\mathbf{e}) \leq \max_{\mathbf{e} \in \mathcal{E}} f(\mathbf{e}) - \varepsilon$. Therefore, for such $\mathbf{e}$, the event $A_t(\varepsilon/3)$ implies that

$$\hat{f}_t(\mathbf{e}) \leq f(\mathbf{e}) + \frac{\varepsilon}{3} < \max_{\mathbf{e} \in \mathcal{E}} f(\mathbf{e}) - \varepsilon + \frac{\varepsilon}{3}.$$

In addition, because $|\max_{\mathbf{e} \in \mathcal{E}} f(\mathbf{e}) - \max_{\mathbf{e} \in \mathcal{E}} \hat{f}_t(\mathbf{e})| \leq \varepsilon/3$ under the event $A_t(\varepsilon/3)$,

$$\hat{f}_t(\mathbf{e}) \leq f(\mathbf{e}) + \frac{\varepsilon}{3} < \max_{\mathbf{e} \in \mathcal{E}} f(\mathbf{e}) - \frac{2}{3}\varepsilon \leq \max_{\mathbf{e} \in \mathcal{E}} \hat{f}_t(\mathbf{e}) - \frac{1}{3}\varepsilon.$$

The above inequalities show that

$$A_t(\varepsilon/3) \Rightarrow \hat{\mathcal{E}}^* \subseteq \mathcal{E}^* + B_\delta.$$

Finally, we notice that $\sup_{e \in \mathcal{E}} |\hat{f}_t(e) - f(e)| = o_p(1)$ due to Lemma C.1, Corollary C.1, and Corollary C.2. $\square$

C.6 Proof of Theorem 1 in Section 6.2

Proof. Theorem 1 in the main manuscript contains two sets of theoretical results. The first set of results shows the consistency of the optimized treatment allocation and the optimized enrichment proportion. The second set of results shows the consistency of the actual treatment allocation and the optimized enrichment proportion.

The proof for the first set of results can be found in the proof of Lemma C.2. In what follows, we prove the second set of results in Theorem 1 (Lemma C.3 in the Supplementary Materials). We will provide the proof under the RAR design, as the proof for the AE design follows similar procedures.

We notice that

$$\begin{aligned} \hat{e}_j = \hat{e}_{Tj} &= \frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} D_{it}}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)}} \\ &= \underbrace{\frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} (D_{it} - \hat{e}_{tj}^*)}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)}}}_{\text{(I)}} + \underbrace{\frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} \hat{e}_{tj}^*}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)}}}_{\text{(II)}}. \end{aligned}$$

By our assumption, it is easy to verify that

$$\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} = Np_j + O_p(\sqrt{N}) \asymp N.$$

With variance calculation, the numerator of (I) has the order $O_p(\sqrt{N})$:

$$\mathbb{V} \left[\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} (D_{it} - \hat{e}_{tj}^*) \right] = \sum_{t=1}^T \sum_{i=1}^{n_t} \mathbb{E} \left[\mathbb{V}[\mathbf{1}_{(X_{it} \in \mathcal{S}_j)} (D_{it} - \hat{e}_{tj}^*) | \mathcal{H}_{t-1}] \right] \lesssim p_j N.$$

As a result,

$$\text{(I)} = \frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} (D_{it} - \hat{e}_{tj}^*)}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)}} = O_p \left(\frac{1}{\sqrt{N}} \right).$$

Now consider term (II). We further write it as

$$\begin{aligned} \text{(II)} &= \frac{\sum_{t=1}^T \sum_{i=1}^{n_t} (\mathbf{1}_{(X_{it} \in \mathcal{S}_j)} - p_j) \hat{e}_{tj}^*}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)}} + \frac{p_j N}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)}} \frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \hat{e}_{tj}^*}{N} \\ &= O_p \left(\frac{1}{\sqrt{N}} \right) + (1 + o_p(1)) \frac{\sum_{t=1}^T n_t \hat{e}_{tj}^*}{N}. \end{aligned}$$

For the multi-stage design, T is fixed, and $n_t \rightarrow \infty$ for all t . From Lemma C.2, one has

$$\sup_{2 \leq t \leq T} |\widehat{e}_{tj}^* - e_j^*| = o_p(1).$$

On the other hand, for the first stage, $\widehat{e}_{1j}^*$ is nonrandom and equals to some constant c . Therefore, term (II) satisfies

$$\frac{\sum_{t=1}^T \sum_{i=1}^{n_t} n_t \widehat{e}_{tj}^*}{N} = \frac{n_1}{N} \widehat{e}_{1j}^* + \frac{1}{N} \sum_{t=2}^T n_t \widehat{e}_{tj}^* = \frac{n_1}{N} c + \frac{1}{N} \sum_{t=2}^T n_t e_j^* + o_p(1).$$

The above will converge to e_j^* provided that $n_1/N \rightarrow 0$. We remark that in the multi-stage setting, n_1 could be a non-vanishing fraction of N . In this case, we replace $\widehat{e}_{tj}^*$ with $\widetilde{e}_{tj}$, which is the calibrated treatment assignment probability based on each stage's sample size. The calibration procedure can be found in Section 4 in the main manuscript.

Now consider the fully adaptive design, where $n_t = 1$ (or a fixed constant) for all t . From Lemma C.2, we have that $\widehat{e}_{tj}^* = e_j^* + o_p(1)$ as $t \rightarrow \infty$. Then for any subsequence of $1, 2, \dots$, there is a further subsequence along which the convergence of $\widehat{e}_{tj}^*$ is almost sure. This can be used to show that

$$\frac{\sum_{t=1}^T n_t \widehat{e}_{tj}^*}{N} = \frac{\sum_{t=1}^T \widehat{e}_{tj}^*}{T} = e_j^* + o_p(1),$$

which closes the proof. $\square$

C.7 Proof of Theorem 2 in Section 6.2

Proof. As the proof for the AE design follows similar procedures to the RAR designs. In that follows, we shall only provide the proof for the RAR design. Recall that the treatment effect estimator takes the form

$$\widehat{\tau}_j^{\text{RAR}} = \frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} D_{it} Y_{it}}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} D_{it}} - \frac{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it}) Y_{it}}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it})}.$$

In addition, the treatment effect for group j takes the form

$$\tau_j = \mathbb{E}[Y_{it}(1)|X_{it} \in \mathcal{S}_j] - \mathbb{E}[Y_{it}(0)|X_{it} \in \mathcal{S}_j] := \mu_{j,1}(1) - \mu_{j,1}(0),$$

where we denote the two conditional expectations on the rhs by $\mu_{j,1}(1)$ and $\mu_{j,1}(0)$, respectively. Then

$$\sqrt{N}(\widehat{\tau}_j^{\text{RAR}} - \tau_j) = \frac{\sqrt{N} \sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} D_{it} (Y_{it}(1) - \mu_{j,1}(1))}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbf{1}_{(X_{it} \in \mathcal{S}_j)} D_{it}}$$

$$- \frac{\sqrt{N} \sum_{t=1}^T \sum_{i=1}^{n_t} \mathbb{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it}) (Y_{it}(0) - \mu_{j,1}(0))}{\sum_{t=1}^T \sum_{i=1}^{n_t} \mathbb{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it})}.$$

By Theorem 1 in the main manuscript, the denominators satisfy

$$\frac{1}{N} \sum_{t=1}^T \sum_{i=1}^{n_t} \mathbb{1}_{(X_{it} \in \mathcal{S}_j)} D_{it} \rightarrow_p p_j e_j^*, \quad \frac{1}{N} \sum_{t=1}^T \sum_{i=1}^{n_t} \mathbb{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it}) \rightarrow_p p_j (1 - e_j^*).$$

Therefore, to prove the asymptotic normality result, it suffices to study

$$\begin{aligned} (\text{I}) &:= \frac{1}{p_j e_j^*} \frac{1}{\sqrt{N}} \sum_{t=1}^T \sum_{i=1}^{n_t} \mathbb{1}_{(X_{it} \in \mathcal{S}_j)} D_{it} (Y_{it}(1) - \mu_{j,1}(1)) \\ &\quad - \frac{1}{p_j (1 - e_j^*)} \frac{1}{\sqrt{N}} \sum_{t=1}^T \sum_{i=1}^{n_t} \mathbb{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it}) (Y_{it}(0) - \mu_{j,1}(0)). \end{aligned}$$

We define the following filtration:

$$\mathcal{H}_{i,1} = \sigma\{(X_{\ell 1}, D_{\ell 1}, Y_{\ell 1}) : 1 \leq \ell \leq i\}, \quad \mathcal{H}_{i,t} = \sigma\{(X_{\ell t}, D_{\ell t}, Y_{\ell t}) : 1 \leq \ell \leq i\} \cup \mathcal{H}_{n_{t-1}, t-1}.$$

For notational convenience, we set $\mathcal{H}_{0,1}$ to the trivial σ -algebra, and $\mathcal{H}_{0,t} = \mathcal{H}_{n_{t-1}, t-1}$. Then it is easy to see that (I) is the average of a martingale difference sequence with respect to the filtration $(\mathcal{H})_{1 \leq i \leq n_t, 1 \leq t \leq T}$. We first compute the (conditional) variance:

$$\begin{aligned} &\mathbb{V} \left[\frac{\mathbb{1}_{(X_{it} \in \mathcal{S}_j)} D_{it} (Y_{it}(1) - \mu_{j,1}(1))}{p_j e_j^*} - \frac{\mathbb{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it}) (Y_{it}(0) - \mu_{j,1}(0))}{p_j (1 - e_j^*)} \middle| \mathcal{H}_{i-1,t} \right] \\ &= \frac{\widehat{e}_{tj}^*}{p_j (e_j^*)^2} \sigma_j(1)^2 + \frac{1 - \widehat{e}_{tj}^*}{p_j (1 - e_j^*)^2} \sigma_j(0)^2, \end{aligned}$$

where $\sigma_j(1)^2$ and $\sigma_j(0)^2$ are the conditional variances of $Y_{it}(1)$ and $Y_{it}(0)$ within subgroup j . To be more specific, the above can be obtained by further conditioning on X_{it} and the total variance decomposition formula. By Lemma C.2, we have

$$\begin{aligned} &\frac{1}{N} \sum_{t=1}^T \sum_{i=1}^{n_t} \mathbb{V} \left[\frac{\mathbb{1}_{(X_{it} \in \mathcal{S}_j)} D_{it} (Y_{it}(1) - \mu_{j,1}(1))}{p_j e_j^*} - \frac{\mathbb{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it}) (Y_{it}(0) - \mu_{j,1}(0))}{p_j (1 - e_j^*)} \middle| \mathcal{H}_{i-1,t} \right] \\ &= \frac{1}{N} \sum_{t=1}^T \sum_{i=1}^{n_t} \left(\frac{\widehat{e}_{tj}^*}{p_j (e_j^*)^2} \sigma_j(1)^2 + \frac{1 - \widehat{e}_{tj}^*}{p_j (1 - e_j^*)^2} \sigma_j(0)^2 \right) \rightarrow_p \frac{1}{p_j e_j^*} \sigma_j(1)^2 + \frac{1}{p_j (1 - e_j^*)} \sigma_j(0)^2. \end{aligned}$$

In particular, the last step builds on the observation that

$$\frac{1}{N} \sum_{t=1}^T n_t \widehat{e}_{tj}^* \rightarrow_p e_j^*.$$

See the proof of Theorem 1 for details. Given our assumption on finite fourth moments of the potential outcomes, it is also straightforward to verify Lindeberg's condition by computing

$$\mathbb{E} \left[\left(\frac{\mathbb{1}_{(X_{it} \in \mathcal{S}_j)} D_{it} (Y_{it}(1) - \mu_{j,1}(1))}{p_j e_j^*} - \frac{\mathbb{1}_{(X_{it} \in \mathcal{S}_j)} (1 - D_{it}) (Y_{it}(0) - \mu_{j,1}(0))}{p_j (1 - e_j^*)} \right)^4 \middle| \mathcal{H}_{i-1,t} \right] \lesssim 1,$$

since e_j^* and p_j^* are bounded away from zero and one. By applying the martingale central limit theorem (Theorem 3.2 in [Hall and Heyde \(1980\)](#)),

$$\sqrt{N}(\hat{\tau}_j^{\text{RAR}} - \tau_j) \xrightarrow{\mathcal{D}} \mathcal{N} \left(0, \frac{\mathbb{V}[Y_{it}(1) | X_{it} \in \mathcal{S}_j]}{p_j e_j^*} + \frac{\mathbb{V}[Y_{it}(0) | X_{it} \in \mathcal{S}_j]}{p_j (1 - e_j^*)} \right).$$

Consistency of the variance estimator follows from Lemma [C.1](#). $\square$

D Proofs of Results in Section 6.3

D.1 List of lemmas

Recall that we use $\hat{\tau}_j(\hat{\mathbf{e}}_j)$ to denote the estimated subgroup treatment effect under the actual treatment allocation $\hat{\mathbf{e}}_j$, and $\hat{\tau}_j(\hat{\mathbf{p}}_j)$ to denote the estimated subgroup treatment effect under the actual enrichment proportion $\hat{\mathbf{p}}_j$. We further remark that under our proposed RAR design, $\mathbf{e}_j = e_j^*$, for $j = 1, \dots, m$. Under the complete randomization design, in the presence of cost constraint, we set $\mathbf{e}_j = c_1$, for $j = 1, \dots, m$. Under our proposed AE design, $\mathbf{p}_j = p_j^*$.

Lemma D.1. *Under Assumptions [1-3](#), there exist some positive constants $C_1, \dots, C_m$ such that, under an RAR design, the correct selection probability is lower bounded by:*

$$\mathbb{P}(\hat{\tau}_1(\hat{\mathbf{e}}_1) \geq \max_{2 \leq j \leq m} \hat{\tau}_j(\hat{\mathbf{e}}_j)) \geq 1 - C_1 \exp \left(- \frac{(\tau_1 - \tau_2)^2 cN}{8\mathbb{V}_1(\mathbf{e}_1)m} \right) - \sum_{j=2}^m C_j \exp \left(- \frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2\mathbb{V}_j(\mathbf{e}_j)m} \right).$$

Under an AE design, the correct selection probability is lower bounded by:

$$\mathbb{P}(\hat{\tau}_1(\hat{\mathbf{p}}_1) \geq \max_{2 \leq j \leq m} \hat{\tau}_j(\hat{\mathbf{p}}_j)) \geq 1 - C_1 \exp \left(- \frac{(\tau_1 - \tau_2)^2 cN}{8\mathbb{V}_1(\mathbf{p}_1)m} \right) - \sum_{j=2}^m C_j \exp \left(- \frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2\mathbb{V}_j(\mathbf{p}_j)m} \right).$$

D.2 Proof of Lemma [D.1](#)

Proof. In what follows, we provide the proof under the RAR design. The proof for the AE design follows similar procedures. Denote $\hat{\tau}_j^r$ as the estimated causal effect of subgroup j under sample size r . Following Corollary [C.2](#), the correct selection event can be expressed as

$$\mathcal{E} := \bigcap_{r=n_1}^N \left\{ \left\{ \hat{\tau}_1^r \geq \frac{\tau_1 + \tau_2}{2} \right\} \cap \left\{ \bigcap_{j \neq 1} \left\{ \hat{\tau}_j^r \leq \frac{\tau_1 + \tau_2}{2} \right\} \right\} \right\},$$

$$:= \bigcap_{r=n_1}^N \left\{ \left\{ \hat{\tau}_1^r \geq \tau_1 - \frac{\tau_1 - \tau_2}{2} \right\} \cap \left\{ \bigcap_{j \neq 1} \left\{ \hat{\tau}_j^r \leq \tau_j + \tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2} \right\} \right\} \right\}.$$

The correct selection probability can be characterized as

$$\begin{aligned} & 1 - \mathbb{P}(\hat{\tau}_1(\hat{\mathbf{e}}_1) \leq \max_{j=2, \dots, m} \hat{\tau}_j(\hat{\mathbf{e}}_j)) \\ & \geq 1 - \mathbb{P}(\mathcal{E}^c) \\ & \geq 1 - \sum_{r=n_1}^N \left[\mathbb{P}\left(\hat{\tau}_1^r < \tau_1 - \frac{\tau_1 - \tau_2}{2}\right) + \sum_{j=2}^m \mathbb{P}\left(\hat{\tau}_1^r > \tau_j + \tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2}\right) \right], \\ & \geq 1 - \left[\sum_{r=n_1}^{\infty} \mathbb{P}\left(\hat{\tau}_1^r < \tau_1 - \frac{\tau_1 - \tau_2}{2}\right) + \sum_{j=2}^m \sum_{r=n_1}^{\infty} \mathbb{P}\left(\hat{\tau}_1^r > \tau_j + \tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2}\right) \right], \\ & \geq 1 - \left[\sum_{r=n_1}^{\infty} \exp\left(-\frac{(\tau_1 - \tau_2)^2 r}{8\mathbb{V}_1(\mathbf{e}_1)}\right) + \sum_{j=2}^m \sum_{r=n_1}^{\infty} \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2 r}{2\mathbb{V}_j(\mathbf{e}_j)}\right) \right], \\ & \geq 1 - \left[\frac{\exp\left(-\frac{(\tau_1 - \tau_2)^2 n_1}{8\mathbb{V}_1(\mathbf{e}_1)m}\right)}{1 - \exp\left(-\frac{(\tau_1 - \tau_2)^2 (n_1 + n_2 - n_1)}{8\mathbb{V}_1(\mathbf{e}_1)}\right)} + \sum_{j=2}^m \frac{\exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2 n_1}{2\mathbb{V}_j(\mathbf{e}_j)m}\right)}{1 - \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2 (n_1 + n_2 - n_1)}{2\mathbb{V}_j(\mathbf{e}_j)}\right)} \right], \\ & = 1 - \left[C'_1 \exp\left(-\frac{(\tau_1 - \tau_2)^2 cN}{8\mathbb{V}_1(\mathbf{e}_1)m}\right) + \sum_{j=2}^m C'_j \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2 cN}{2\mathbb{V}_j(\mathbf{e}_j)m}\right) \right], \end{aligned}$$

where

$$\begin{aligned} C_1 &= \frac{1}{1 - \exp\left(-\frac{(\tau_1 - \tau_2)^2 (n_1 + n_2 - n_1)}{8\mathbb{V}_1(\mathbf{e}_1)}\right)} = \frac{1}{1 - \exp\left(-\frac{(\tau_1 - \tau_2)^2}{8\mathbb{V}_1(\mathbf{e}_1)}\right)}, \\ C_j &= \frac{1}{1 - \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2 (n_1 + n_2 - n_1)}{2\mathbb{V}_j(\mathbf{e}_j)}\right)} = \frac{1}{1 - \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2\mathbb{V}_j(\mathbf{e}_j)}\right)}, \end{aligned}$$

In the fully adaptive setting, we let $n_1 + n_2 - n_1 = 1$. Similarly, under the AE design, the correct selection probability is lower bounded by

$$\begin{aligned} 1 - \mathbb{P}(\hat{\tau}_1(\hat{\mathbf{p}}_1) \leq \max_{j=2, \dots, m} \hat{\tau}_j(\hat{\mathbf{p}}_j)) & \geq 1 - \left[C'_1 \exp\left(-\frac{(\tau_1 - \tau_2)^2 cN}{8\mathbb{V}_1(\mathbf{p}_1)m}\right) + \sum_{j=2}^m C'_j \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2 cN}{2\mathbb{V}_j(\mathbf{p}_j)m}\right) \right], \\ C'_1 &= \frac{1}{1 - \exp\left(-\frac{(\tau_1 - \tau_2)^2 cN}{8\mathbb{V}_1(\mathbf{p}_1)}\right)} = \frac{1}{1 - \exp\left(-\frac{(\tau_1 - \tau_2)^2}{8\mathbb{V}_1(\mathbf{p}_1)}\right)}, \\ C'_j &= \frac{1}{1 - \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2\mathbb{V}_j(\mathbf{p}_j)}\right)} = \frac{1}{1 - \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2\mathbb{V}_j(\mathbf{p}_j)}\right)}. \end{aligned}$$

□

D.3 Proof of Proposition 1 in Section 6.3

Proof. Following Lemma D.1, we can show that under our proposed design:

$$\begin{aligned} & \frac{1}{N} \log (1 - \mathbb{P}(\hat{\tau}_1(\hat{e}_1) \geq \max_{2 \leq j \leq m} \hat{\tau}_j(\hat{e}_j))) \\ & \leq -\frac{(\tau_1 - \tau_2)^2 c}{8\mathbb{V}_1(e_1^*)m} + \frac{1}{N} \log \left(1 + \exp \left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2\mathbb{V}_j(e_j^*)m} + \frac{(\tau_1 - \tau_2)^2 n_1}{8\mathbb{V}_1(e_1^*)m} \right) \right). \end{aligned}$$

Under the complete randomization design:

$$\begin{aligned} & \frac{1}{N} \log (1 - \mathbb{P}(\hat{\tau}_1(\hat{e}_1^{\text{CR}}) \geq \max_{2 \leq j \leq m} \hat{\tau}_j(\hat{e}_j^{\text{CR}}))) \\ & \leq -\frac{(\tau_1 - \tau_2)^2 c}{8\mathbb{V}_1(c_1)m} + \frac{1}{N} \log \left(1 + \exp \left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2\mathbb{V}_j(c_1)m} + \frac{(\tau_1 - \tau_2)^2 n_1}{8\mathbb{V}_1(c_1)m} \right) \right). \end{aligned}$$

When $N \rightarrow \infty$, we have

$$\lim_{N \rightarrow \infty} \frac{1}{N} \log (1 - \mathbb{P}(\hat{\tau}_1(\hat{e}_1) \geq \max_{2 \leq j \leq m} \hat{\tau}_j(\hat{e}_j))) = -\frac{(\tau_1 - \tau_2)^2 c}{8\mathbb{V}_1(e_1^*)m},$$

and

$$\lim_{N \rightarrow \infty} \frac{1}{N} \log (1 - \mathbb{P}(\hat{\tau}_1(\hat{e}_1^{\text{CR}}) \geq \max_{2 \leq j \leq m} \hat{\tau}_j(\hat{e}_j^{\text{CR}}))) = -\frac{(\tau_1 - \tau_2)^2 c}{8\mathbb{V}_1(c_1)m}.$$

To be consistent with the notation in the main manuscript, we replace $\hat{\tau}_j(\hat{e}_j)$ with $\hat{\tau}_j^{\text{RAR}}$ and replace $\hat{\tau}_j(\hat{e}_j^{\text{CR}})$ with $\hat{\tau}_j^{\text{CR}}$, for $j = 1, \dots, m$. As e_1^* maximizes the rate function under our design, we conclude our proof by establish the following inequality:

$$\lim_{N \rightarrow \infty} \frac{1}{N} \log (1 - \mathbb{P}(\hat{\tau}_1^{\text{RAR}} \geq \max_{2 \leq j \leq m} \hat{\tau}_j^{\text{RAR}})) \leq \lim_{N \rightarrow \infty} \frac{1}{N} \log (1 - \mathbb{P}(\hat{\tau}_1^{\text{CR}} \geq \max_{2 \leq j \leq m} \hat{\tau}_j^{\text{CR}})).$$

□

D.4 Proof of Proposition 2 in Section 6.3

Proof. Assume $\sigma_j(1)^2 = \sigma_j(0)^2$, $\sigma_1(1)^2 = \dots = \sigma_m(1)^2$, and $p_1 = p_2 = \dots = p_m$, for $j = 1, \dots, m$,

$$\begin{aligned} \mathbb{V}^{\text{Proposed}} &= \frac{1}{p_j e_j^*} + \frac{1}{p_j (1 - e_j^*)} = \frac{1}{p_j e_j^* (1 - e_j^*)}, \\ \mathbb{V}^{\text{CR}} &= \frac{1}{p_j \cdot c_1} + \frac{1}{p_j \cdot c_1} = \frac{1}{p_j \cdot c_1 \cdot c_1}. \end{aligned}$$

$$\text{When } \frac{\mathbb{V}^{\text{CR}}}{\mathbb{V}^{\text{Proposed}}} = \frac{\frac{1}{p_j \cdot c_1 \cdot c_1}}{\frac{1}{p_j e_j^* (1 - e_j^*)}} \geq 1,$$

$$\begin{aligned}\frac{1}{p_j \cdot c_1 \cdot c_1} &\geq \frac{1}{p_j e_j^* (1 - e_j^*)}, \\ \frac{1}{c_1^2} &\geq \frac{1}{e_j^* (1 - e_j^*)}\end{aligned}$$

From the rate function equality in the proof of Remark 1 (Section B.1), we obtain

$$\begin{aligned}\frac{(\tau_1 - \tau_2)^2}{\frac{1}{e_1} + \frac{1}{(1-e_1)} + \frac{1}{e_2} + \frac{1}{(1-e_2)}} &= \frac{(\tau_1 - \tau_3)^2}{\frac{1}{e_1} + \frac{1}{(1-e_1)} + \frac{1}{e_3} + \frac{1}{(1-e_3)}}, \\ \frac{(\tau_1 - \tau_2)^2}{\frac{1}{e_1(1-e_1)} + \frac{1}{e_2(1-e_2)}} &= \frac{(\tau_1 - \tau_3)^2}{\frac{1}{e_1(1-e_1)} + \frac{1}{e_3(1-e_3)}}, \\ \frac{(\tau_1 - \tau_2)^2}{(\tau_1 - \tau_3)^2} &= \frac{\frac{1}{e_1(1-e_1)} + \frac{1}{e_2(1-e_2)}}{\frac{1}{e_1(1-e_1)} + \frac{1}{e_3(1-e_3)}},\end{aligned}$$

As a result,

$$\begin{aligned}\mathbb{V}^{\text{CR}} &\geq \mathbb{V}^{\text{Proposed}} \text{ when } \frac{1}{c_1^2} \geq \frac{1}{e_j^* (1 - e_j^*)} \\ \text{that is } \frac{1}{c_1^2} &\geq (\tau_j - \tau_1)^2 - \frac{1}{e_1^* (1 - e_1^*)}\end{aligned}$$

□

D.5 Proof of Proposition 3 in Section 6.3

Proof. To reach a correct selection probability level of $1 - \varepsilon$, we have,

$$1 - \varepsilon \geq 1 - C_1 \exp\left(-\frac{(\tau_1 - \tau_2)^2 c N}{8 \mathbb{V}_1(e_1^*) m}\right) - \sum_{j=2}^m C_j \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2 \mathbb{V}_j(e_j^*) m}\right).$$

As $N \rightarrow \infty$,

$$\begin{aligned}\varepsilon &= C_1 \exp\left(-\frac{(\tau_1 - \tau_2)^2 c N}{8 \mathbb{V}_1(e_1^*) m}\right), \\ \frac{1}{N} \log \varepsilon \cdot \mathbb{V}_1(e_1) &= -(\tau_1 - \tau_2)^2, \\ \frac{1}{N} \log \varepsilon \cdot \left(\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1 (1 - e_1)}\right) &= -(\tau_1 - \tau_2)^2.\end{aligned}$$

We assume $\sigma_j(1)^2 = \sigma_j(0)^2$. Under the complete randomization design,

$$\frac{1}{N} \log \varepsilon \cdot \left(\frac{\sigma_1(1)^2}{p_1 \cdot c_1} + \frac{\sigma_1(0)^2}{p_1 \cdot c_1}\right) = -(\tau_1 - \tau_2)^2,$$

$$\begin{aligned}\frac{1}{N} \log \varepsilon \cdot \left(\frac{2\sigma_1(1)^2}{p_1 \cdot c_1} \right) &= -(\tau_1 - \tau_2)^2, \\ \frac{1}{N^{\frac{1}{2}}} \cdot |\log \varepsilon \cdot C|^{1/2} &= (\tau_1 - \tau_2).\end{aligned}$$

We want to show that under our proposed design,

$$\begin{aligned}\frac{1}{N} \log \varepsilon \cdot \left(\frac{\sigma_1(1)^2}{p_1 \cdot e_1^*} + \frac{\sigma_1(1)^2}{p_1 \cdot (1 - e_1^*)} \right) &= -(\tau_1 - \tau_2)^2, \\ \frac{1}{N^{\frac{2}{3}}} |\log \varepsilon \cdot C'|^{1/2} &= \tau_1 - \tau_2,\end{aligned}$$

by showing $e_1^* = C'(\tau_1 - \tau_2)^{1/2}$.

In what follows, we first derive the closed-form expression of e_1^* under a simplified setting. Assume $\sigma_j(1)^2 = \sigma_j(0)^2$,

$$\sigma_j^2(e_j) = \frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1 - e_j)} = \frac{\sigma_j(1)^2}{p_j e_j(1 - e_j)}.$$

First, we derive optimal treatment allocation for subgroup $j \neq 1$. Using the first-order optimality condition in the proof of Remark 1 in Section B.1, we obtain $G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{e}) = G(\mathcal{S}_1, \mathcal{S}_k, \mathbf{e})$:

$$\begin{aligned}\frac{(\tau_j - \tau_1)^2}{\mathbb{V}_1(e_1) + \mathbb{V}_j(e_j)} &= \frac{(\tau_k - \tau_1)^2}{\mathbb{V}_1(e_1) + \mathbb{V}_k(e_k)}, \\ \frac{(\tau_j - \tau_1)^2}{\frac{\sigma_1(1)^2}{p_1 e_1(1 - e_1)} + \frac{\sigma_j(1)^2}{p_j e_j(1 - e_j)}} &= \frac{(\tau_k - \tau_1)^2}{\frac{\sigma_1(1)^2}{p_1 e_1(1 - e_1)} + \frac{\sigma_k(1)^2}{p_k e_k(1 - e_k)}}.\end{aligned}$$

Assume $\frac{\sigma_1(1)^2}{p_1 e_1(1 - e_1)} \ll \frac{\sigma_j(1)^2}{p_j e_j(1 - e_j)}$, $j \neq 1$,

$$\begin{aligned}\frac{(\tau_j - \tau_1)^2}{\frac{\sigma_j(1)^2}{p_j e_j(1 - e_j)}} &= \frac{(\tau_k - \tau_1)^2}{\frac{\sigma_k(1)^2}{p_k e_k(1 - e_k)}}, \\ \frac{(\tau_j - \tau_1)^2}{(\tau_k - \tau_1)^2} &= \frac{\frac{\sigma_j(1)^2}{p_j e_j(1 - e_j)}}{\frac{\sigma_k(1)^2}{p_k e_k(1 - e_k)}} = \frac{\sigma_j(1)^2}{p_j e_j(1 - e_j)} \cdot \frac{p_k e_k(1 - e_k)}{\sigma_k(1)^2}, \\ \frac{e_j(1 - e_j)}{e_k(1 - e_k)} &= \frac{p_k(\tau_k - \tau_1)^2 / \sigma_k(1)^2}{p_j(\tau_j - \tau_1)^2 / \sigma_j(1)^2}.\end{aligned} \tag{3}$$

One can compute e_j^* as

$$\begin{aligned}e_j^2 - e_j + \frac{\sigma_j(1)^2}{p_j(\tau_j - \tau_1)^2} &= 0, \\ e_j^* &= \frac{1}{2} \pm \frac{1}{2} \sqrt{1 - 4 \frac{\sigma_j(1)^2}{p_j(\tau_j - \tau_1)^2}}, \quad j \neq 1.\end{aligned}$$

Second, we derive the optimal treatment allocation for subgroup 1. Using the first-order optimality condition $\sum_{j=2}^m \frac{\partial G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{e}) / \partial e_1}{\partial G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{e}) / \partial e_j} = 1$.

$$\begin{aligned}\frac{\partial G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{e})}{\partial e_1} &= -(\tau_j - \tau_1)^2 \left(\mathbb{V}_1(e_1) + \mathbb{V}_j(e_j) \right)^{-2} \cdot \left(\frac{-\sigma_1(1)^2}{p_1 e_1^2} + \frac{\sigma_1(1)^2}{p_1(1-e_1)^2} \right), \\ \frac{\partial G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{e})}{\partial e_j} &= -(\tau_j - \tau_1)^2 \left(\mathbb{V}_1(e_1) + \mathbb{V}_j(e_j) \right)^{-2} \cdot \left(\frac{-\sigma_j(1)^2}{p_j e_j^2} + \frac{\sigma_j(1)^2}{p_j(1-e_j)^2} \right).\end{aligned}$$

$$\begin{aligned}\sum_{j=2}^m \left\{ \frac{\partial G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{e}) / \partial e_1}{\partial G(\mathcal{S}_1, \mathcal{S}_j, \mathbf{e}) / \partial e_j} \right\} &= \sum_{j=2}^m \left\{ \left(\frac{-\sigma_1(1)^2}{p_1 e_1^2} + \frac{\sigma_1(1)^2}{p_1(1-e_1)^2} \right) / \left(\frac{-\sigma_j(1)^2}{p_j e_j^2} + \frac{\sigma_j(1)^2}{p_j(1-e_j)^2} \right) \right\}, \\ &= \sum_{j=2}^m \left\{ \left(\frac{\sigma_1(1)^2(2e_1-1)}{p_1 e_1^2(1-e_1)^2} \right) / \left(\frac{\sigma_j(1)^2(2e_j-1)}{p_j e_j^2(1-e_j)^2} \right) \right\} = 1,\end{aligned}$$

Therefore,

$$\begin{aligned}1 &= \left(\frac{\sigma_1(1)^2(2e_1-1)}{p_1 e_1^2(1-e_1)^2} \right) \cdot \sum_{j=2}^d \frac{p_j e_j^2(1-e_j)^2}{\sigma_j(1)^2(2e_j-1)}, \\ \frac{p_1 e_1^2(1-e_1)^2}{\sigma_1(1)^2(2e_1-1)} &= \sum_{j=2}^m \frac{p_j e_j^2(1-e_j)^2}{\sigma_j(1)^2(2e_j-1)}.\end{aligned}$$

Let $a = p_1$, $b = \sigma_1(1)^2$, $d = \sum_{j=2}^m \frac{p_j e_j^2(1-e_j)^2}{\sigma_j(1)^2(2e_j-1)}$,

$$\frac{a e_1^2(1-e_1)^2}{b(2e_1-1)} = d,$$

$$\text{Let } c = \frac{bd}{a},$$

$$e_1^4 - 2e_1^3 + e_1^2 - 2c \cdot e_1 + c = 0,$$

$$e_1^* = -\frac{-2}{4} \pm S \pm \frac{1}{2} \sqrt{-4S^2 - 2p \pm \frac{q}{S}},$$

$$\text{where } p = \frac{-1}{2}, \quad q = -2c,$$

$$S = \frac{1}{2} \sqrt{-\frac{2}{3}(-\frac{1}{2}) + \frac{1}{3}(Q + \frac{\Delta_0}{Q})},$$

$$Q = \left(\frac{\Delta_1 + \sqrt{\Delta_1^2 - 4\Delta_0^3}}{2} \right)^{1/3},$$

$$\Delta_0 = 1, \quad \Delta_1 = 2 + 108c.$$

$$e_1^* = \frac{1}{2} \pm S \pm \frac{1}{2} \sqrt{-4S^2 + 1 \pm \frac{-2c}{S}},$$

$$S = \frac{1}{2} \sqrt{\frac{1}{3} + \frac{1}{3}(Q + \frac{1}{Q})}, \quad Q = \left(\frac{(2 + 108c) + \sqrt{(2 + 108c)^2 - 4}}{2} \right)^{1/3}$$

Therefore, $e_1^* = C'(\tau_2 - \tau_1)^{\frac{1}{2}}$. As a result,

$$\begin{aligned}\frac{1}{N}|\log \varepsilon \cdot C'| \cdot (\tau_1 - \tau_2)^{\frac{1}{2}} &= (\tau_1 - \tau_2)^2, \\ \frac{1}{N^{\frac{2}{3}}}|\log \varepsilon \cdot C'| &= \tau_1 - \tau_2,\end{aligned}$$

We conclude the proof by showing that under the complete randomization design,

$$N \geq \frac{1}{(\tau_1 - \tau_2)^2} \cdot |C \cdot \log(\varepsilon) \cdot \sigma_1(1)^2|.$$

Under our proposed RAR design,

$$N \geq \frac{1}{(\tau_1 - \tau_2)^2} \cdot |C' \cdot \log(\varepsilon) \cdot \sigma_1(1)^2|^{3/4},$$

for some positive constants $C < \infty$ and $C' < \infty$. □

D.6 Additional theoretical insights for Section 6.3

In this section, we provide additional theoretical results for Section 6.3 under more general settings. In Proposition D.1, we provide an efficiency comparison with complete randomization under two subgroups. Here, different from Proposition 2 in the main manuscript, we neither assume $\sigma_j(1)^2 = \sigma_j(0)^2$ nor require $c_1 < 0.5$.

Proposition D.1 (Efficiency comparison under two subgroups). *Assume there are two subgroups (1) with equal subgroup proportions, $p_1 = p_2$, and (2) are under the cost constraint, $p_1 e_1 + p_2 e_2 < 0.5$. We can obtain the oracle treatment allocations:*

$$\begin{cases} e_1^* &= \frac{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2}}{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}, \\ e_2^* &= \frac{\sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}. \end{cases}$$

Let $\sigma_1(0)^2 = c_1 \sigma_1(1)^2$, $\sigma_2(0)^2 = c_2 \sigma_2(1)^2$, assume $\sigma_1(1)^2 = \sigma_2(1)^2$ and $c_1 > 1, c_2 > 1$,

$$\begin{cases} \mathbb{V}_1(e_1^*) \leq \mathbb{V}_1(1/2) \text{ and } \mathbb{V}_2(e_2^*) \geq \mathbb{V}_2(1/2), & \text{if } c_1 \geq c_2; \\ \mathbb{V}_1(e_1^*) > \mathbb{V}_1(1/2) \text{ and } \mathbb{V}_2(e_2^*) < \mathbb{V}_2(1/2), & \text{if } c_1 < c_2. \end{cases}$$

Proposition D.1 shows the efficiency trade-off under two subgroups and in the presence of the cost constraint. Intuitively, the result suggests that not all the subgroups will simultaneously have efficiency gain. For example, when subgroup 1 has a larger variance in the control arm than subgroup 2, subgroup 1 achieves efficiency gain compared to the complete randomization design, while subgroup 2 does not have efficiency gain. Otherwise, the complete randomization achieves higher

estimation efficiency. Proposition D.1 highlights the role of subgroup variances in our proposed design. Unlike complete randomization, our design strategy simultaneously incorporates the variances of all the subgroups when deciding the treatment allocation for the best subgroup. In Remark D.1, we provide more insights on the efficiency trade-off through a simulation.

Remark D.1 (Efficiency comparison under three subgroups). *We consider three subgroups and assume (1) $p_1 = p_2 = p_3$, (2) $p_1 e_1 + p_2 e_2 + p_3 e_3 \leq 0.3$. The treatment allocation under our proposed design strategy can be found by solving the following equations:*

$$\begin{cases} e_1 + e_2 + e_3 = 1, \\ \frac{1}{\frac{-\sigma_2(1)^2}{e_2^2} + \frac{-\sigma_2(0)^2}{(1-e_2)^2}} + \frac{1}{\frac{-\sigma_3(1)^2}{e_3^2} + \frac{-\sigma_3(0)^2}{(1-e_3)^2}} = \frac{1}{\frac{-\sigma_1(1)^2}{e_1^2} + \frac{-\sigma_1(0)^2}{(1-e_1)^2}}, \\ \frac{(\tau_2 - \tau_1)^2}{\left(\frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1}\right) + \left(\frac{\sigma_2(1)^2}{e_2} + \frac{\sigma_2(0)^2}{1-e_2}\right)} = \frac{(\tau_3 - \tau_1)^2}{\left(\frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1}\right) + \left(\frac{\sigma_3(1)^2}{e_3} + \frac{\sigma_3(0)^2}{1-e_3}\right)}. \end{cases}$$

Because we impose the cost constraint, to make fair comparisons with the complete randomization, we now set $e_1 = e_2 = e_3 = 1/3$ in the complete randomization design. We fix $\tau_1 = 10$, $\sigma_j(1)^2 = 2$, $\sigma_j(0)^2 = 1$, for $j = 1, 2, 3$ and compare the asymptotic variances of our proposed design with the complete randomization design in the three subgroups. In Figure 1, we fix $\tau_1 - \tau_2 = 0.5$. In Figure 2, we set $\tau_1 - \tau_2 = 3$.

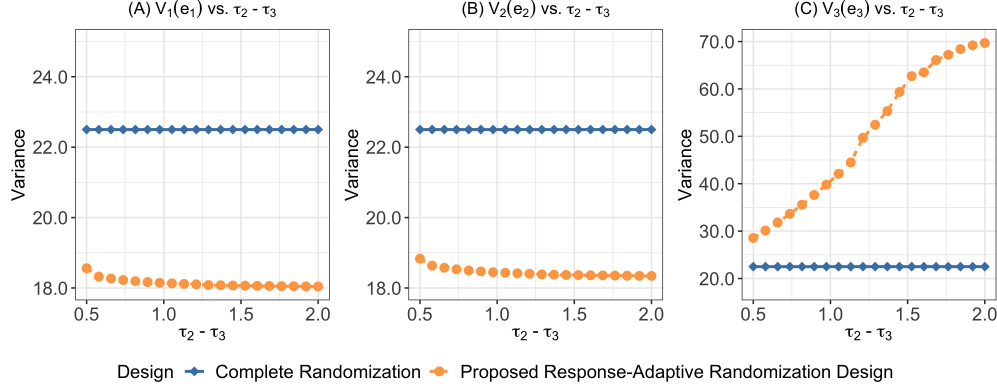


Figure 1: Efficiency trade-off with respect to the distance between τ_2 and τ_3 . We fix $\tau_1 = 10$, $\sigma_j(1)^2 = 2$, $\sigma_j(0)^2 = 1$, $j = 1, 2, 3$, and set $\tau_1 - \tau_2 = 0.5$. (A)–(C) show the asymptotic variance of subgroups 1 to 3, respectively

Remark D.1 aims to showcase the role of subgroup treatment effects in the efficiency comparison. Figure 1 demonstrates that when estimating the best subgroup treatment effect, the asymptotic variance under our proposed RAR design is always smaller than the complete randomization design (Figure 1(A) and 2(A)). However, when τ_j is far away from τ_1 , our proposed response-adaptive randomization design is less likely to have efficiency gain (Figure 1(C) and 2(C)).

Together, Proposition D.1 and Remark D.1 entail the efficiency trade-off between our proposed design and the complete randomization design. In Proposition D.2, we further provide the sample

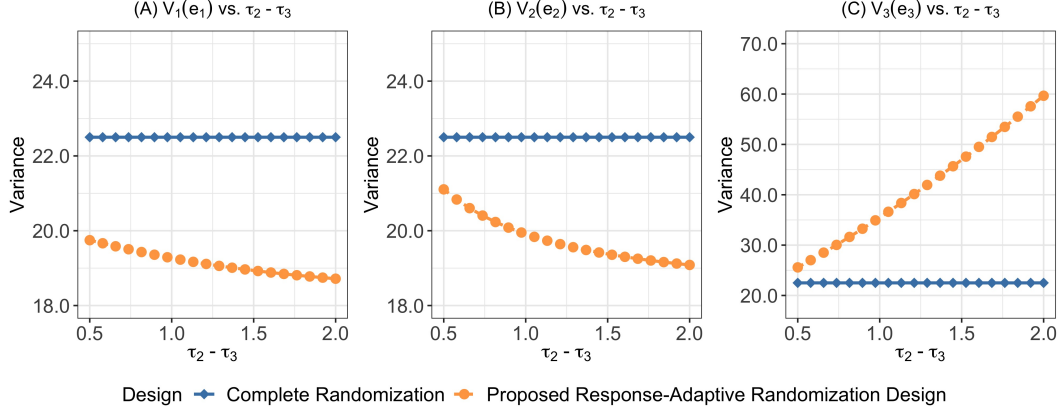


Figure 2: Efficiency trade-off with respect to the distance between τ_2 and τ_3 . We fix $\tau_1 = 10$, $\sigma_j(1)^2 = 2$, $\sigma_j(0)^2 = 1$, and $\tau_1 - \tau_2 = 3$. (A)–(C) show the asymptotic variance of the three subgroups respectively

size comparison in more general setting.

Proposition D.2 (Sample size comparison). *Suppose we aim to reach a correct selection probability of at least $1 - \varepsilon$.*

(i) *Complete randomization design: the required sample size is characterized as*

$$N \geq \frac{1}{(\tau_1 - \tau_2)^2} \cdot \left\lceil \frac{\log(\varepsilon)}{p_1} \right\rceil \cdot (2\sigma_1(1)^2 + 2\sigma_1(0)^2).$$

(ii) *Our proposed design without cost constraint: Suppose our optimization problem does not have cost constraint, we can obtain the oracle treatment allocation: $e_1^* = \frac{\sigma_1(1)}{\sigma_1(1) + \sigma_1(0)}$. The required sample size is characterized as*

$$N \geq \frac{1}{(\tau_1 - \tau_2)^2} \cdot \left\lceil \frac{\log(\varepsilon)}{p_1} \right\rceil \cdot (\sigma_1(1) + \sigma_1(0))^2.$$

(iii) *Our proposed design under cost constraint: Suppose there are two subgroups satisfying (1) $p_1 = p_2$ and (2) $p_1 e_1 + p_2 e_2 = 0.5$, we can obtain the oracle treatment allocation $e_1^* = (\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2}) / (\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2})$. The required sample size is characterized as*

$$N \geq \frac{1}{(\tau_1 - \tau_2)^2} \cdot \left\lceil \frac{\log(\varepsilon)}{p_1} \right\rceil \cdot \left(\sigma_1(1)^2 \cdot \frac{\sqrt{A} + \sqrt{B}}{\sqrt{A}} + \sigma_1(0)^2 \cdot \frac{\sqrt{A} + \sqrt{B}}{\sqrt{B}} \right),$$

where $A = \sigma_1(1)^2 + \sigma_2(0)^2$, $B = \sigma_1(0)^2 + \sigma_2(1)^2$.

Proposition D.2 conveys similar message as Proposition 3 in the main manuscript. It says that to reach a correct selection probability level of at least $1 - \varepsilon$, our proposed adaptive design strategy requires a smaller sample size compared to the complete randomization design.

D.6.1 Proof of Proposition D.1 in Section D.6

Proof. Assume there are two subgroups and $p_1 = p_2 = 1/2$. The optimization problem becomes

$$\max_{e_1, e_2} \frac{(\tau_2 - \tau_1)^2}{2\left(\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)} + \frac{\sigma_2(1)^2}{p_2 e_2} + \frac{\sigma_2(0)^2}{p_2(1-e_2)}\right)}$$

Assume there exists the cost constraint: $p_1 e_1 + p_2 e_2 = 0.5$; given $p_1 = p_2$, $e_2 = 1 - e_1$.

$$\max_{e_1} \frac{(\tau_2 - \tau_1)^2}{2\left(\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1-e_1)} + \frac{\sigma_2(1)^2}{p_1(1-e_1)} + \frac{\sigma_2(0)^2}{p_1 e_1}\right)}.$$

Let

$$\begin{aligned} \frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1} + \frac{\sigma_2(1)^2}{1-e_1} + \frac{\sigma_2(0)^2}{e_1} &= \frac{\sigma_1(1)^2 + \sigma_2(0)^2}{e_1} + \frac{\sigma_1(0)^2 + \sigma_2(1)^2}{1-e_1}, \\ \text{Let } A &= \sigma_1(1)^2 + \sigma_2(0)^2, \\ B &= \sigma_1(0)^2 + \sigma_2(1)^2. \end{aligned}$$

Take derivative of the denominator with respect to e_1 , we obtain

$$\begin{aligned} \frac{A}{e_1^2} &= \frac{B}{(1-e_1)^2}, \\ B e_1^2 &= A(1-e_1)^2, \\ \sqrt{B} e_1 &= \sqrt{A}(1-e_1), \\ (\sqrt{B} + \sqrt{A}) e_1 &= \sqrt{A}. \end{aligned}$$

Therefore,

$$e_1^* = \frac{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2}}{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}$$

The variance of subgroup 1 under our proposed design is

$$\mathbb{V}(e_1^*) = \frac{\sigma_1(1)^2}{\frac{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2}}{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}} + \frac{\sigma_1(0)^2}{\frac{\sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}}$$

When $\mathbb{V}_1(e_1^*) \leq \mathbb{V}_1(1/2)$,

$$\begin{aligned} \frac{\sigma_1(1)^2}{\frac{\sqrt{A}}{\sqrt{A} + \sqrt{B}}} + \frac{\sigma_1(0)^2}{\frac{\sqrt{B}}{\sqrt{A} + \sqrt{B}}} &\leq \frac{\sigma_1(1)^2}{1/2} + \frac{\sigma_1(0)^2}{1/2}, \\ \sigma_1(1)^2 \left(\frac{\sqrt{A} + \sqrt{B}}{\sqrt{A}} - 2 \right) + \sigma_1(0)^2 \left(\frac{\sqrt{A} + \sqrt{B}}{\sqrt{B}} - 2 \right) &\leq 0, \end{aligned}$$

$$\begin{aligned} \sigma_1(1)^2 \left(\frac{\sqrt{A} + \sqrt{B} - 2\sqrt{A}}{\sqrt{A}} \right) + \sigma_1(0)^2 \left(\frac{\sqrt{A} + \sqrt{B} - 2\sqrt{B}}{\sqrt{B}} \right) &\leq 0, \\ \sigma_1(1)^2 \left(\frac{\sqrt{B} - \sqrt{A}}{\sqrt{A}} \right) &\leq \sigma_1(0)^2 \left(\frac{\sqrt{B} - \sqrt{A}}{\sqrt{B}} \right), \\ \text{if } \sqrt{B} &> \sqrt{A}, \end{aligned}$$

$$\mathbb{V}_1(e_1^*) < \mathbb{V}_1(1/2) \text{ when } \frac{\sigma_1(1)^2}{\sigma_1(0)^2} < \frac{\sqrt{A}}{\sqrt{B}} = \frac{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2}}{\sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}.$$

Assume $\sigma_1(0)^2 = c_1\sigma_1(1)^2$, $\sigma_2(0)^2 = c_2\sigma_2(1)^2$,

$$\frac{1}{c_1} < \frac{\sqrt{\sigma_1(1)^2 + c_2\sigma_2(1)^2}}{\sqrt{c_1\sigma_1(1)^2 + \sigma_2(1)^2}}.$$

Further assume $\sigma_1(1)^2 = \sigma_2(1)^2$, if $\sqrt{c_1\sigma_1(1)^2 + \sigma_1(1)^2} > \sqrt{\sigma_1(1)^2 + c_2\sigma_1(1)^2}$, that is, when $c_1 > c_2$,

$$\begin{aligned} \frac{1}{c_1} &< \frac{\sqrt{\sigma_1(1)^2 + c_2\sigma_1(1)^2}}{\sqrt{c_1\sigma_1(1)^2 + \sigma_1(1)^2}} = \frac{\sqrt{1 + c_2}}{\sqrt{1 + c_1}}, \\ \mathbb{V}_1(e_1^*) &< \mathbb{V}_1(1/2) \text{ when } c_1 > \frac{\sqrt{1 + c_1}}{\sqrt{1 + c_2}}. \end{aligned}$$

□

D.6.2 Proof of Remark D.1 in Section D.6

Proof. The optimization problem in Remark 2 is

$$\begin{aligned} \max_{\mathbf{e}} \quad & z \\ \text{s.t.} \quad & e_1 + e_2 + e_3 \leq 1, \\ & \frac{(\tau_2 - \tau_1)^2}{2(\mathbb{V}_1(e_1) + \mathbb{V}_2(e_2))} - z \geq 0, \\ & \frac{(\tau_3 - \tau_1)^2}{2(\mathbb{V}_1(e_1) + \mathbb{V}_3(e_3))} - z \geq 0. \end{aligned}$$

The primal problem is

$$\begin{aligned} \max_{\mathbf{e}} \min_{z, \boldsymbol{\lambda}} \quad & f(z, \boldsymbol{\lambda}, \mathbf{e}) \\ = \quad & z + \lambda_1(1 - e_1 - e_2 - e_3) + \lambda_2 \left(\frac{(\tau_2 - \tau_1)^2}{2(\mathbb{V}_1(e_1) + \mathbb{V}_2(e_2))} - z \right) + \lambda_3 \left(\frac{(\tau_3 - \tau_1)^2}{2(\mathbb{V}_1(e_1) + \mathbb{V}_3(e_3))} - z \right). \end{aligned}$$

The KKT conditions are

$$\frac{\partial f(z, \boldsymbol{\lambda}, \mathbf{e})}{\partial e_1} = -\lambda_1 + \lambda_2 \frac{\partial G(e_1, e_2)}{\partial e_1} + \lambda_3 \frac{\partial G(e_1, e_3)}{\partial e_1} = 0,$$

$$\begin{aligned}
\frac{\partial f(z, \boldsymbol{\lambda}, \mathbf{e})}{\partial e_2} &= -\lambda_1 + \lambda_2 \frac{\partial G(e_1, e_2)}{\partial e_2} = 0, \\
\frac{\partial f(z, \boldsymbol{\lambda}, \mathbf{e})}{\partial e_3} &= -\lambda_1 + \lambda_2 \frac{\partial G(e_1, e_3)}{\partial e_3} = 0, \\
\lambda_1(1 - e_1 - e_2 - e_3) &= 0, \\
\lambda_2\left(\frac{(\tau_2 - \tau_1)^2}{2(\mathbb{V}_1(e_1) + \mathbb{V}_2(e_2))} - z\right) &= 0, \\
\lambda_3\left(\frac{(\tau_2 - \tau_1)^2}{2(\mathbb{V}_1(e_1) + \mathbb{V}_3(e_3))} - z\right) &= 0.
\end{aligned}$$

We consider the case when $\lambda_1 > 0$, $\lambda_2 > 0$, and $\lambda_3 > 0$. We obtain

$$\begin{cases}
e_1 + e_2 + e_3 = 1, \\
\frac{\partial G(e_1, e_2)/\partial e_1}{\partial G(e_1, e_2)/\partial e_2} + \frac{\partial G(e_1, e_3)/\partial e_1}{\partial G(e_1, e_3)/\partial e_3} = 1, \\
G(e_1, e_2) = G(e_1, e_3).
\end{cases}$$

$$\begin{aligned}
\frac{\partial G(e_1, e_2)}{\partial e_1} &= \frac{-(\tau_2 - \tau_1)^2}{2} (\mathbb{V}_1(e_1) + \mathbb{V}_2(e_2))^{-2} \cdot \left(\frac{-\sigma_1(1)^2}{e_1^2} + \frac{-\sigma_1(0)^2}{(1-e_1)^2} \right), \\
\frac{\partial G(e_1, e_2)}{\partial e_2} &= \frac{-(\tau_2 - \tau_1)^2}{2} (\mathbb{V}_1(e_1) + \mathbb{V}_2(e_2))^{-2} \cdot \left(\frac{-\sigma_2(1)^2}{e_2^2} + \frac{-\sigma_2(0)^2}{(1-e_2)^2} \right), \\
\frac{\partial G(e_1, e_2)/\partial e_1}{\partial G(e_1, e_2)/\partial e_2} &= \frac{\left(\frac{-\sigma_1(1)^2}{e_1^2} + \frac{-\sigma_1(0)^2}{(1-e_1)^2} \right)}{\left(\frac{-\sigma_2(1)^2}{e_2^2} + \frac{-\sigma_2(0)^2}{(1-e_2)^2} \right)}.
\end{aligned}$$

Therefore, $\frac{\partial G(e_1, e_2)/\partial e_1}{\partial G(e_1, e_2)/\partial e_2} + \frac{\partial G(e_1, e_3)/\partial e_1}{\partial G(e_1, e_3)/\partial e_3} = 1$ is equivalent to

$$\begin{aligned}
&\frac{\left(\frac{-\sigma_1(1)^2}{e_1^2} + \frac{-\sigma_1(0)^2}{(1-e_1)^2} \right)}{\left(\frac{-\sigma_2(1)^2}{e_2^2} + \frac{-\sigma_2(0)^2}{(1-e_2)^2} \right)} + \frac{\left(\frac{-\sigma_1(1)^2}{e_1^2} + \frac{-\sigma_1(0)^2}{(1-e_1)^2} \right)}{\left(\frac{-\sigma_3(1)^2}{e_3^2} + \frac{-\sigma_3(0)^2}{(1-e_3)^2} \right)} = 1, \\
&\frac{1}{\left(\frac{-\sigma_2(1)^2}{e_2^2} + \frac{-\sigma_2(0)^2}{(1-e_2)^2} \right)} + \frac{1}{\left(\frac{-\sigma_3(1)^2}{e_3^2} + \frac{-\sigma_3(0)^2}{(1-e_3)^2} \right)} = \frac{1}{\left(\frac{-\sigma_1(1)^2}{e_1^2} + \frac{-\sigma_1(0)^2}{(1-e_1)^2} \right)}.
\end{aligned}$$

Lastly,

$$\frac{(\tau_2 - \tau_1)^2}{\left(\frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1} \right) + \left(\frac{\sigma_2(1)^2}{e_2} + \frac{\sigma_2(0)^2}{1-e_2} \right)} = \frac{(\tau_3 - \tau_1)^2}{\left(\frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1} \right) + \left(\frac{\sigma_3(1)^2}{e_3} + \frac{\sigma_3(0)^2}{1-e_3} \right)}.$$

One can find e_j^* 's by solving

$$\left\{ \begin{array}{l} e_1 + e_2 + e_3 = 1, \\ \frac{1}{\left(\frac{-\sigma_2(1)^2}{e_2^2} + \frac{-\sigma_2(0)^2}{(1-e_2)^2}\right)} + \frac{1}{\left(\frac{-\sigma_3(1)^2}{e_3^2} + \frac{-\sigma_3(0)^2}{(1-e_3)^2}\right)} = \frac{1}{\left(\frac{-\sigma_1(1)^2}{e_1^2} + \frac{-\sigma_1(0)^2}{(1-e_1)^2}\right)}, \\ \frac{(\tau_2 - \tau_1)^2}{\left(\frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1}\right) + \left(\frac{\sigma_2(1)^2}{e_2} + \frac{\sigma_2(0)^2}{1-e_2}\right)} = \frac{(\tau_3 - \tau_1)^2}{\left(\frac{\sigma_1(1)^2}{e_1} + \frac{\sigma_1(0)^2}{1-e_1}\right) + \left(\frac{\sigma_3(1)^2}{e_3} + \frac{\sigma_3(0)^2}{1-e_3}\right)}. \end{array} \right.$$

□

D.6.3 Proof of Proposition D.2 in Section D.6

Proof. To reach a correct selection probability level of $1 - \varepsilon$, we have, we have

$$1 - \varepsilon = 1 - C_1 \exp\left(-\frac{(\tau_1 - \tau_2)^2 cN}{8\mathbb{V}_1(e_1^*)m}\right) - \sum_{j=2}^m C_j \exp\left(-\frac{(\tau_2 - \tau_j + \frac{\tau_1 - \tau_2}{2})^2}{2\mathbb{V}_j(e_j^*)m}\right).$$

As $N \rightarrow \infty$,

$$\begin{aligned} \varepsilon &= C_1 \exp\left(-\frac{(\tau_1 - \tau_2)^2 cN}{8\mathbb{V}_1(e_1^*)m}\right), \\ \frac{1}{N} \log \varepsilon \cdot \mathbb{V}_1(e_1) &= -(\tau_1 - \tau_2)^2, \\ \frac{1}{N} \log \varepsilon \cdot \left(\frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1 - e_1)}\right) &= -(\tau_1 - \tau_2)^2. \end{aligned}$$

(1) Under the complete randomization design,

$$\begin{aligned} \frac{1}{N} \log \varepsilon \cdot \left(\frac{\sigma_1(1)^2}{p_1 \cdot \frac{1}{2}} + \frac{\sigma_1(0)^2}{p_1 \cdot \frac{1}{2}}\right) &= -(\tau_1 - \tau_2)^2, \\ \frac{1}{N^{\frac{1}{2}}} \cdot \sqrt{-\log \varepsilon} \cdot \sqrt{\frac{2\sigma_1(1)^2 + 2\sigma_1(0)^2}{p_1}} &= \tau_1 - \tau_2. \end{aligned}$$

(2) Under an unconstrained setting,

$$\begin{aligned} \frac{1}{N} \log \delta \cdot \left(\frac{\sigma_1(1)^2}{p_1 \cdot \frac{\sigma_1(1)}{\sigma_1(1) + \sigma_1(0)}} + \frac{\sigma_1(0)^2}{p_1 \cdot \frac{\sigma_1(0)}{\sigma_1(1) + \sigma_1(0)}}\right) &= -(\tau_1 - \tau_2)^2, \\ \frac{1}{N^{1/2}} \sqrt{-\log \delta} \cdot \sqrt{\frac{(\sigma_1(1) + \sigma_1(0))^2}{p_1}} &= \tau_1 - \tau_2. \end{aligned}$$

We observe $2\sigma_1(1)^2 + 2\sigma_1(0)^2 \geq \sigma_1(1) + \sigma_1(0) + 2\sigma_1(1)\sigma_1(0)$ because

$$\sigma_1(1)^2 + \sigma_1(0)^2 \geq 2\sigma_1(1)\sigma_1(0),$$

$$\frac{\sigma_1(1)}{\sigma_1(0)} + \frac{\sigma_1(0)}{\sigma_1(1)} \geq 2.$$

(3) Under a constrained setting, when there are two subgroups, in the presence of cost constraint, $p_1 e_1 + p_2 e_2 = 0.5$ and $p_1 = p_2$,

$$\begin{aligned} & \frac{1}{N} \log \varepsilon \cdot \left(\frac{\sigma_1(1)^2}{p_1 \cdot \frac{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2}}{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}} + \frac{\sigma_1(0)^2}{p_1 \cdot \frac{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2}}{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}} \right) = -(\tau_1 - \tau_2)^2, \\ & \frac{1}{N^{1/2}} \sqrt{-\log \varepsilon} \\ & \cdot \sqrt{\frac{\sigma_1(1)^2}{p_1} \cdot \frac{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2}}} + \frac{\sigma_1(0)^2}{p_1} \cdot \frac{\sqrt{\sigma_1(1)^2 + \sigma_2(0)^2} + \sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}{\sqrt{\sigma_1(0)^2 + \sigma_2(1)^2}}} \\ & = \tau_1 - \tau_2. \end{aligned}$$

□

E Additional simulation results

In the first set of additional simulations, we follow a similar simulation setup as in Section 7 of the main manuscript. Here, we consider the fully adaptive experiments when the first stage sample size is small. We set $n_1 = 50$, and $N \in \{400, \dots, 2000\}$. In Figure 3, we provide the simulation results for the RAR design. In Figure 4, we provide the simulation results for the adaptive enrichment design. These two figures demonstrate that even when the first stage sample size is rather small, our proposed designs still have robust performance compared to the other designs. More concretely, our proposed designs achieve the same level of correct selection probability with a smaller sample size and have a smaller bias in estimating the best subgroup treatment effect.

In the second set of additional simulations, we aim to investigate the behavior of the actual treatment allocation in fully adaptive experiments. To illustrate that the actual treatment allocation converges to the oracle treatment allocation, we provide the simulation results in Figure 5. Here, we plot the trajectories of the actual treatment allocation under the fully adaptive setting across experimental stages. Figure 5 shows that as the number of experimental stages increases, the actual treatment assignment probability converges to the oracle. The simulation results in Figure 5 further verify the theoretical results presented in Theorem 1 in the main manuscript.

F An additional synthetic case study

CYP2D6 (cytochrome P450 2D6)-substrate drugs are commonly prescribed for treating major depressive disorder (MDD), yet MDD patients may respond differently to CYP2D6-substrate drugs due to patients' heterogeneous metabolic behavior (Ayano, 2016). The heterogeneous metabolic

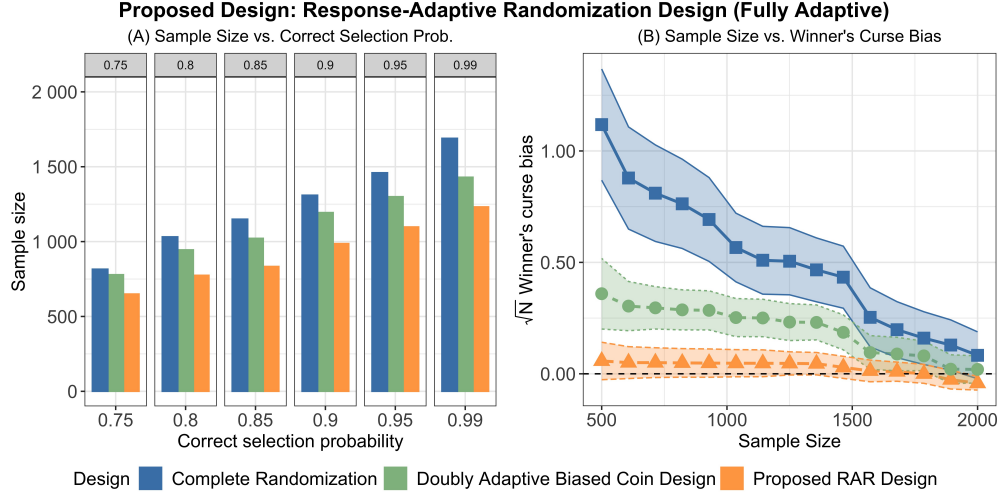


Figure 3: Comparison of the proposed response-adaptive randomization design, the complete randomization design, and the doubly adaptive biased coin design under the fully adaptive setting when the first stage sample size is small ($n_1 = 50$). (A) shows the sample size comparison under various correct selection probability levels. (B) shows the $\sqrt{N}$ -scaled winner's curse bias comparison with respect to different sample sizes.

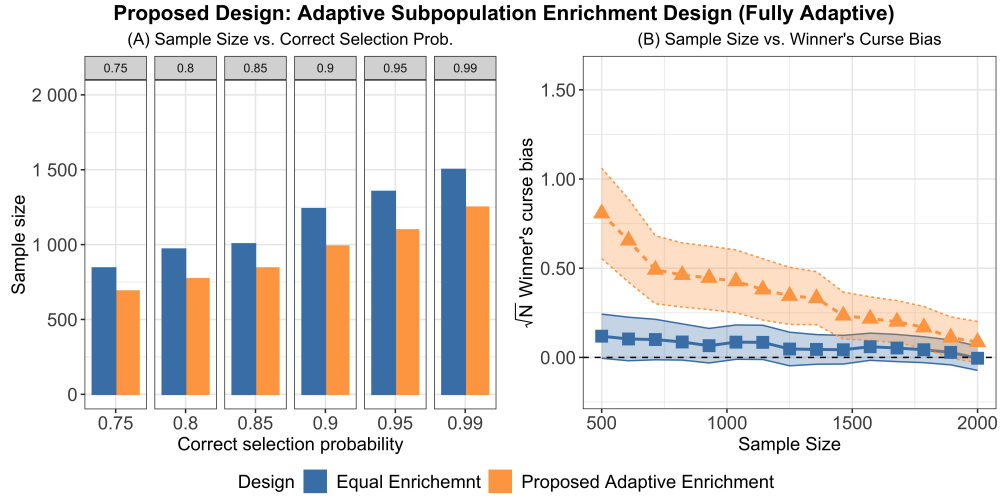


Figure 4: Comparison of the proposed adaptive subgroup enrichment design and the equal enrichment design under the fully adaptive setting when the first stage sample size is small ($n_1 = 50$). (A) shows the sample size comparison under various correct selection probability levels. (B) shows the $\sqrt{N}$ -scaled winner's curse bias comparison with respect to different sample sizes.

behavior is related to the CYP2D6 enzyme, which catalyzes the metabolism of CYP2D6-substrate drugs, and this enzyme is encoded by the *CYP2D6* gene (Ruaño et al., 2013). With the presence of polymorphisms in the *CYP2D6* gene, the side effects of taking CYP2D6-substrate drugs might be prominent (Rafaniello et al., 2018; Arafa and Atteia, 2018). In this case, a genetically-guided therapy that prescribes CYP2D6-substrate drugs based on the *CYP2D6* gene could potentially provide a more precise and beneficial treatment for MDD patients. In this study, we use synthetic

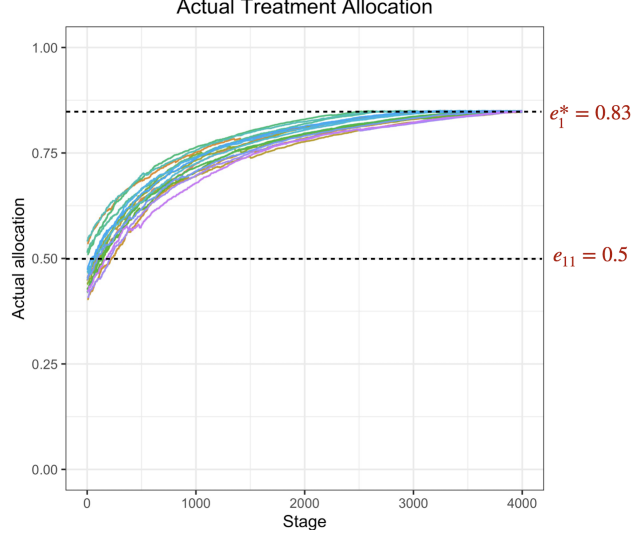


Figure 5: The change of actual treatment allocation under the fully adaptive design with respect to experimental stages across 20 Monte Carlo iterations, where $t = 1, \dots, 2000$, $n_1 = 1000$, $N = 5000$. We set $\tau_1 - \tau_2 = 0.5$.

data from CYP-GUIDES (Cytochrome Psychotropic Genotyping Under Investigation for Decision Support) trial (Ruaño et al., 2021) to investigate which MDD patient subgroup would benefit the most from the genetically-guided therapy.

The original trial is conducted at the Institute of Living at Hartford Hospital, consisting of 1459 patients that are genotyped for *CYP2D6* (Tortora et al., 2020). In this study, there are two considered therapies: (1) the standard therapy ($D = 0$), which does not rely on *CYP2D6* functional status; (2) the genetically-guided therapy ($D = 1$), in which the drugs are prescribed based on *CYP2D6* functional status. More specifically, for the genetically-guided therapy, patients who have abnormal *CYP2D6* function are proscribed medications metabolized by the *CYP2D6* enzyme. The outcome of interest is the length of stay in the hospital, measured by hours. The shorter the length of stay, the more beneficial the therapy is. In addition, we consider six patient age subgroups: (1) 18-20; (2) 21-30; (3) 31-40; (4) 41-50; (5) 51-60; (6) > 60 .

We assume that patients are administered sequentially, and physicians treat one patient at a time. We adaptively revise the probability of applying genetically-guided therapy. To initialize the experiment, we enroll $n_1 = 100$ patients in the first stage. We randomly sample $n_t = 1$ patient in the following stages, where $t = 2, \dots, 200$. To generate synthetic outcomes, for example, if patient A's outcome under the genetically-guided therapy is not observed in the original data, we would match patient A with patient B who shares similar baseline characteristics but is treated by the genetically-guided therapy. Then we use the matched patient's outcome as the outcome we would have observed for patient A under the genetically-guided therapy. We compare three adaptive experiment strategies: (1) our proposed response-adaptive randomization design, (2) the complete randomization design, and (3) the doubly adaptive biased coin design. We then evaluate the treatment effect of the genetically-guided therapy in each patient age subgroup. The results

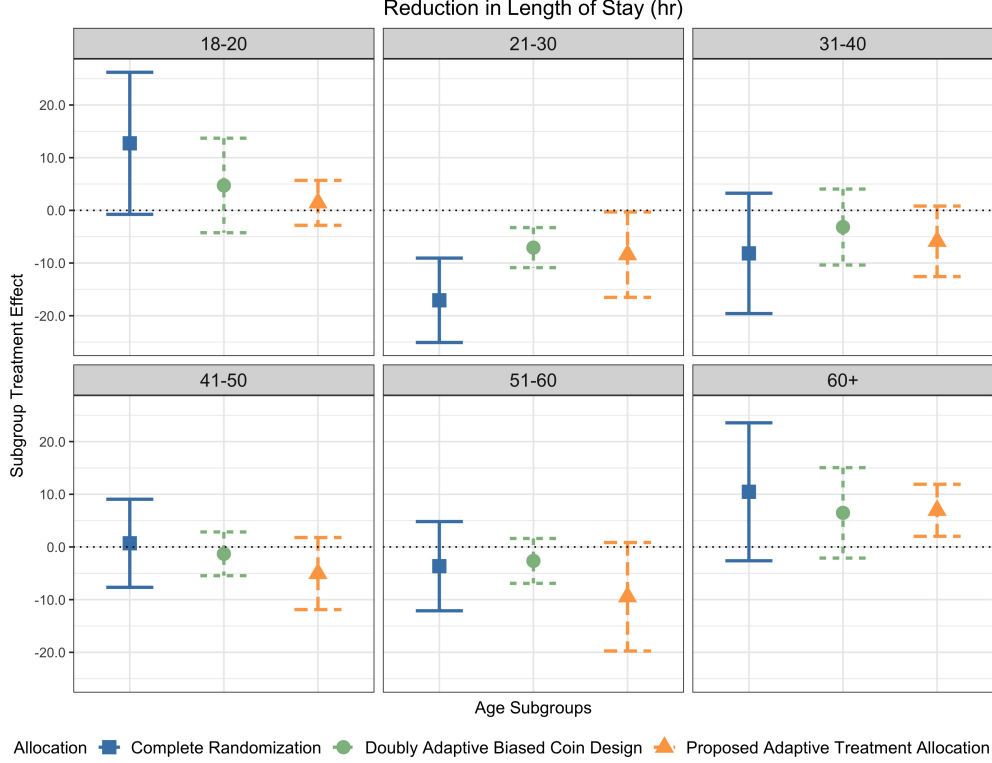


Figure 6: The estimated treatment effects in the six age subgroups under the complete randomization design, the doubly adaptive biased coin design, and our proposed response-adaptive randomization design. The initialization stage includes $n_1 = 100$ patients. In the following stages, we have $n_t = 1$, where $t = 2, \dots, 200$.

are summarized in Figure 6.

Figure 6 demonstrates that the genetically-guided therapy reduces the length of stay the most in patients who are older than 60 under our proposed response-adaptive randomization design. Compared to the other two designs, our proposed response-adaptive randomization design estimates the treatment effects in the age group older than 60 and the age group 18-20 with high efficiency. Our response-adaptive randomization design does not have significant efficiency gains in the other age subgroups, which verifies the theoretical results in Proposition 1. This case study's results suggest that prescribing drugs for MDD patients based on individual CYP2D6 functional status could potentially deliver more informed medical treatments and thus better improve patients' welfare, especially for patients who are older than 60.

G Extensions of our proposed methodology

G.1 Extension to subgroups with exact or near ties

When conducting adaptive experiments, experimenters may have the prior belief that the best subgroup may have exact ties or near ties with other subgroups, that is $\tau_1 \geq \dots \geq \tau_m$. In this

scenario, we propose to merge the tied subgroups in the course of the experiments and select the “merged best subgroup” at the end of the experiments.

To describe our proposal, we first introduce some additional notation. We denote the exact tie set of τ_1 as $\mathcal{A}_T = \{j : \tau_1 = \tau_j, j = 1, \dots, m\}$, and the near tie set of τ_1 as $\mathcal{A}_N = \{j : \tau_1 - \tau_j = O(N^{-1/2}), j = 1, \dots, m\}$ following the definition in [Hall and Miller \(2010\)](#) and [Claggett et al. \(2014\)](#). The near tie set captures the subgroups of which the treatment effects lie in the $\sqrt{N}$ -local neighborhood of τ_1 . We denote the merged best subgroup as $\mathcal{S}_{[p]}$, $[p] = \{1, \dots, p\}$. The population treatment effect under the merged best subgroup is defined as $\tau_{[p]} = \mathbb{E}[Y_{it}(1) - Y_{it}(0) | X_{it} \in \cup_{j \in [p]} \mathcal{S}_j]$. For $\delta \in (0, 1)$, we impose two assumptions on the merged best subgroup: (1) “tie-breaking assumption,” which says that there exists a positive integer $p_0 \leq m$ where

$$p_0 = \arg \min \{p : N^\delta \cdot \min_{j \notin [p]} (\tau_{[p]} - \tau_j) \rightarrow +\infty, p = 1, \dots, m, \delta \in (0, 1)\}, \quad (4)$$

and (2) “subgroup heredity assumption,” which says that the merged subgroup “inherits” the nice properties from its parents subgroups, that is

$$\tau_{[p]} - \tau_{p+1} > N^{-1/2-\varepsilon}, p = 1, \dots, p_0,$$

for some small positive constant ε . The first assumption implies that there exists p_0 such that the subgroup treatment effect $\tau_{[p_0]}$ computed from the merged top p_0 subgroups will break the tie with τ_{p_0+1} . In addition, one can think of δ as a tuning parameter that controls the “extent” of near ties. The second assumption implies that the subgroup treatment effect from the best-merged subgroup is distinguishable from τ_{p+1} , meaning the $\tau_{[p_0]}$ remains to be the largest treatment effect.

In what follows, we shall illustrate our subgroup merging procedure. After Stage 1, we initialize the tie set as

$$\mathcal{A}_1 = \{j : \hat{\tau}_{1j} = \arg \max_{1 \leq j \leq m} \hat{\tau}_{1j}\}.$$

From Stage 2 and onwards, $t \geq 2$, we identify the near tie set as

$$\mathcal{A}_t = \{j : \hat{\tau}_{\mathcal{A}_{t-1}} - b_{L,t} \leq \hat{\tau}_j \leq \hat{\tau}_{\mathcal{A}_{t-1}} + b_{R,t}, j \notin \mathcal{A}_{t-1}, j = 1, \dots, m\} \cup \mathcal{A}_{t-1},$$

where $b_{L,t}$ and $b_{R,t}$ are tuning parameters with $b_{L,t} - b_{R,t} = O(N^{-\delta})$, $\delta \in (0, 1/2)$. We use the subscript t to denote the data-adaptive choice of b_L and b_R in each stage t . After identifying the near tie set for Stage t , we merge subgroups belong to $\mathcal{A}_t$, compute the merged subgroup treatment effect

$$\hat{\tau}_{\mathcal{A}_t} = \frac{\sum_{j \in \mathcal{A}_t} \{\hat{\tau}_{tj} \sum_{s=1}^t N_{sj}\}}{\sum_{j \in \mathcal{A}_t} \sum_{s=1}^t N_{sj}},$$

and update the estimated variance $\hat{\mathbb{V}}_{\mathcal{A}_t}$.

G.2 Extension to augmented inverse propensity score weighting estimator

In this section, we shall discuss the extension of our proposed adaptive experiment strategy to the augmented inverse propensity score weighting (AIPW) estimator in the context of the response-adaptive randomization design.

Stage 1. *Enroll subjects from all the considered subgroups. Then randomly assign subjects in each subgroup to the treatment arm with a pre-specified propensity score, $e_{1j} = \frac{1}{2}$, $j = 1, \dots, m$.*

Stage 1 of our design serves as an exploration stage, in which we obtain initial estimates of the subgroup treatment effects $\hat{\tau}_{1j}$ and their standard errors $\hat{V}_{1j}$ as

$$\begin{aligned}\hat{\tau}_{1j} &= \frac{\sum_{i=1}^{n_1} \mathbf{1}_{(X_{i1} \in \mathcal{S}_j)} \cdot \hat{\varphi}_{1j}(X_{i1})}{\sum_{i=1}^{n_1} \mathbf{1}_{(X_{i1} \in \mathcal{S}_j)}}, \\ \hat{V}_{1j} &= \frac{\sum_{i=1}^{n_1} \mathbf{1}_{(X_{i1} \in \mathcal{S}_j)} \left(\hat{\varphi}_{1j}(X_{i1}) - \hat{\tau}_{1j} \right)^2}{\sum_{i=1}^{n_1} \mathbf{1}_{(X_{i1} \in \mathcal{S}_j)}}, \\ \text{where } \hat{\varphi}_{1j}(X_{i1}) &= \frac{D_{i1}(Y_{i1} - \hat{\mu}_1(X_{i1}))}{\sum_{i=1}^{n_1} \mathbf{1}_{(X_{i1} \in \mathcal{S}_j)} D_{i1} / \sum_{i=1}^{n_1} \mathbf{1}_{(X_{i1} \in \mathcal{S}_j)}} + \hat{\mu}_1(X_{i1}) \\ &\quad - \frac{(1 - D_{i1})(Y_{i1} - \hat{\mu}_0(X_{i1}))}{\sum_{i=1}^{n_1} \mathbf{1}_{(X_{i1} \in \mathcal{S}_j)} (1 - D_{i1}) / \sum_{i=1}^{n_1} \mathbf{1}_{(X_{i1} \in \mathcal{S}_j)}} - \hat{\mu}_0(X_{i1}),\end{aligned}$$

and $\hat{\mu}_d(X_{i1}) = \hat{\mathbb{E}}[Y_{i1} | D_{i1} = d, X_{i1} \in \mathcal{S}_j]$, $d \in \{0, 1\}$.

Stage t , for $t = 2, \dots, T - 1$. *Obtain $\hat{e}_t^*$ by solving the sample analog of Problem B, that is*

$$\hat{e}_t^* = \arg \max_e \left\{ z : \sum_{j=1}^m \hat{p}_{t,(j)} e_j \leq c_1, \quad c_2 \leq e_j \leq 1 - c_2, \quad \min_{2 \leq j \leq m} \frac{(\hat{\tau}_{t-1,(j)} - \hat{\tau}_{t-1,(1)})^2}{2(\hat{V}_{t-1,(1)}(e_1) + \hat{V}_{t-1,(j)}(e_j))} - z \geq 0 \right\}, \quad (5)$$

where

$$\begin{aligned}\hat{\tau}_{t-1,(j)} &= \frac{1}{\sum_{s=1}^{t-1} \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_{(j)})}} \sum_{s=1}^{t-1} \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_{(j)})} \cdot \hat{\varphi}_{sj}(X_{is}), \\ \hat{V}_{t-1,(j)}(e_j) &= \frac{1}{\sum_{s=1}^{t-1} \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_{(j)})}} \sum_{s=1}^{t-1} \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_{(j)})} \left(\hat{\varphi}_{sj}(X_{is}) - \hat{\tau}_{t-1,(j)} \right)^2, \\ \text{and } \hat{\varphi}_{sj}(X_{is}) &= \frac{D_{is}(Y_{is} - \hat{\mu}_1(X_{is}))}{\sum_{s=1}^{t-1} \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_{(j)})} D_{is} / \sum_{s=1}^{t-1} \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_{(j)})}} + \hat{\mu}_1(X_{is}) \\ &\quad - \frac{(1 - D_{is})(Y_{is} - \hat{\mu}_0(X_{is}))}{\sum_{s=1}^{t-1} \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_{(j)})} (1 - D_{is}) / \sum_{s=1}^{t-1} \sum_{i=1}^{n_s} \mathbf{1}_{(X_{is} \in \mathcal{S}_{(j)})}} - \hat{\mu}_0(X_{is}),\end{aligned}$$

where $\hat{\mu}_d(X_{is}) = \hat{\mathbb{E}}[Y_{is} | D_{is} = d, X_{is} \in \mathcal{S}_j]$, $d \in \{0, 1\}$. Calculate the calibrated treatment assignment

probability $\tilde{e}_t^*$ based on $\hat{e}_t^*$. For $n_{t,j} > 0$,

$$\tilde{e}_{t,(j)}^* = \frac{1}{n_{tj}} \left((\hat{e}_{t,(j)}^* \sum_{s=1}^t n_{s,(j)}) - \sum_{s=1}^{t-1} n_{s,(j)} \tilde{e}_{s,(j)}^* \right), \text{ for } j = 1, \dots, m.$$

Assign treatment with probability $\tilde{e}_{t,(j)}^*$.

Statistical inference after Stage T . Construct the final subgroup treatment effect estimator along with its standard error:

$$\begin{aligned} \hat{\tau}_j &= \frac{1}{\sum_{s=1}^T \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)}} \sum_{s=1}^T \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} \cdot \hat{\varphi}_{sj}(X_{is}), \\ \hat{V}_j &= \frac{1}{\sum_{s=1}^T \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)}} \sum_{s=1}^T \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} \left(\hat{\varphi}_{sj}(X_{is}) - \hat{\tau}_j \right)^2, \\ \text{and } \hat{\varphi}_{sj}(X_{is}) &= \frac{D_{is}(Y_{is} - \hat{\mu}_1(X_{is}))}{\sum_{s=1}^T \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} D_{is} / \sum_{s=1}^T \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)}} + \hat{\mu}_1(X_{is}) \\ &\quad - \frac{(1 - D_{is})(Y_{is} - \hat{\mu}_0(X_{is}))}{\sum_{s=1}^T \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)} (1 - D_{is}) / \sum_{s=1}^T \sum_{i=1}^{n_s} \mathbb{1}_{(X_{is} \in \mathcal{S}_j)}} - \hat{\mu}_0(X_{is}), \end{aligned}$$

where $\hat{\mu}_d(X_{is}) = \hat{\mathbb{E}}[Y_{is} | D_{is} = d, X_{is} \in \mathcal{S}_j]$, $d \in \{0, 1\}$. Then, identify the best subgroup as the one exhibiting the maximal treatment effect size:

$$j^* = \operatorname{argmax}_{1 \leq j \leq m} \hat{\tau}_j.$$

Lastly, construct a two-sided level- α confidence interval for the selected best subgroup as

$$\left[\hat{\tau}_{j^*} \pm \Phi^{-1}(1 - \alpha/2) \cdot \sqrt{\hat{V}_{j^*}/N} \right].$$

H Motivation of our design objective under large and moderate deviation principles

In this section, we provide some justifications for our design objective function under large and moderate deviation principles.

H.1 Overview

The adoption of the large deviation principles requires distributional assumptions on the outcome variables, and it allows finer probabilistic characterization of the rare event of $\hat{\tau}_1 \leq \max_{2 \leq j \leq m} \hat{\tau}_j$ when τ_1 and τ_2 differ by a constant. Take Gaussian outcome variables for example, the large deviation principle sets $a_N = N$ for Eq (1) in the main manuscript. Then, with the Gartner-Ellis

Theorem (Dembo and Zeitouni, 2009, ch.2.3), see Section H.2.1 for derivation, we obtain:

$$\begin{aligned} \lim_{N \rightarrow \infty} \frac{1}{N} \log \left(1 - \mathbb{P}(\hat{\tau}_1 \geq \max_{2 \leq j \leq m} \hat{\tau}_j) \right) &= - \min_{2 \leq j \leq m} G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j), \\ G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j) &= \frac{(\tau_j - \tau_1)^2}{2(\mathbb{V}_1(e_1, p_1) + \mathbb{V}_j(e_j, p_j))}, \end{aligned} \quad (6)$$

where $\mathbb{V}_j(e_j, p_j)$ represents the variance of $\hat{\tau}_j$, for $j = 1, \dots, p$. When the outcome distribution deviates from the Gaussian distribution, say binary outcome, we show in Section H.2.2 that the binominal rate function is lower bounded by the Gaussian rate function. Therefore, maximizing the Gaussian rate function potentially provides a conservative solution when outcome variables follow binary distributions.

In contrast, when the distance between τ_1 and τ_2 is small, the moderate deviation principle kicks in. Due to this small distance, it's not feasible to scale the log of false selection probability with $1/N$. Instead, under the moderate deviation principle, we work with $a_N/N \rightarrow 0$ and $a_N \rightarrow \infty$. The benefit is that the moderate deviation principle no longer puts restrictions on the outcome distribution, and it instead only requires mild moment conditions. In Section H.3, by Cramér theorem (Section VIII.2 in Petrov (1975)), we reach

$$\begin{aligned} \lim_{N \rightarrow \infty} \frac{1}{a_N} \log \left(1 - \mathbb{P}(\hat{\tau}_1 \geq \max_{2 \leq j \leq m} \hat{\tau}_j) \right) &= - \min_{2 \leq j \leq m} G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j), \\ G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j) &= \frac{(\tau_j - \tau_1)^2}{2(\mathbb{V}_1(e_1, p_1) + \mathbb{V}_j(e_j, p_j))}. \end{aligned} \quad (7)$$

Lastly, we note that both the large and moderate deviation principles serve as motivations for our design objectives, focusing on the rate function. Our design neither requires the outcome distribution to follow any particular distribution nor requires τ_1 and τ_2 to be very close.

H.2 Motivation under large deviation principles

H.2.1 Rate function under Gaussian distribution

The large deviation principle quantifies the exponential rate at which the probabilities of certain rare events decay as some parameter (often related to the size of the system or the number of observations) goes to infinity. In our context, when the treatment effect estimators follow the Gaussian distributions, the probability of incorrect selection is

$$\mathbb{P}[\hat{\tau}_1 \leq \max_{2 \leq j \leq m} \hat{\tau}_j] = 1 - \mathbb{P}[\hat{\tau}_1 \geq \max_{2 \leq j \leq m} \hat{\tau}_j].$$

The incorrect selection probability can be bounded by

$$\max_{2 \leq j \leq m} \mathbb{P}[\hat{\tau}_1 \leq \hat{\tau}_j] \leq \mathbb{P}[\hat{\tau}_1 \leq \max_{2 \leq j \leq m} \hat{\tau}_j] \leq (m-1) \cdot \max_{2 \leq j \leq m} \mathbb{P}[\hat{\tau}_1 \leq \hat{\tau}_j], \quad (8)$$

where the second inequality follows from the union bound. By the large deviation theory (Dembo and Zeitouni, 2009), there exists a rate function $G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j)$, such that

$$\lim_{N \rightarrow \infty} \frac{1}{N} \log \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \hat{\tau}_j] \right) = -G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j), \quad j = 2, \dots, m.$$

For both sides of Eq (8), take logarithm and divide by N ,

$$\begin{aligned} & \frac{1}{N} \log \max_{2 \leq j \leq m} \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \hat{\tau}_j] \right) \\ & \leq \frac{1}{N} \log \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \max_{2 \leq j \leq m} \hat{\tau}_j] \right) \\ & \leq \frac{1}{N} \log \left((m-1) \cdot \max_{2 \leq j \leq m} \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \hat{\tau}_j] \right) \right) \\ & = \frac{1}{N} \log (m-1) + \frac{1}{N} \log \left(\max_{2 \leq j \leq m} \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \hat{\tau}_j] \right) \right). \end{aligned}$$

As $\max_{2 \leq j \leq m} \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \hat{\tau}_j] \right)$ is equivalent to $\exp \left(-\min_{2 \leq j \leq m} G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j) \right)$, we obtain

$$\begin{aligned} & -\min_{2 \leq j \leq m} G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j) \\ & \leq \frac{1}{N} \log \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \max_{2 \leq j \leq m} \hat{\tau}_j] \right) \\ & \leq \frac{\log (m-1)}{N} - \min_{2 \leq j \leq m} G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j). \end{aligned}$$

As a result, when the number of subgroups is fixed and the sample size tends to infinity,

$$\lim_{N \rightarrow \infty} \frac{1}{N} \log \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \max_{2 \leq j \leq m} \hat{\tau}_j] \right) = -\min_{2 \leq j \leq m} G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j).$$

As we adopted the IPW estimator for estimating the subgroup average treatment effect, the rate function has a specific form with

$$G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j) = \frac{(\tau_j - \tau_1)^2}{2(\mathbb{V}_1(e_1, p_1) + \mathbb{V}_j(e_j, p_j))}, \quad (9)$$

$$\mathbb{V}_1(e_1, p_1) = \frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1 - e_1)}, \quad \mathbb{V}_j(e_j, p_j) = \frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1 - e_j)}. \quad (10)$$

The above equations justify the Eq (3) and Eq (9) in the main manuscript.

We note that when the outcome variables follow Gaussian distributions, the IPW estimator with the estimated propensity score only converges to Gaussian distributions asymptotically. While we expect that large deviation results could be established for this estimator, as suggested by Shao (1997) in 'Self-normalized Large Deviation,' our manuscript does not delve into these nuances. Instead, we focus on how large deviation principles inform and motivate our design objectives.

H.2.2 Rate function under binary distribution

In this section, we shall provide the derivation of the rate function with binary outcomes under the large deviation principle, and a simulation study of rate function comparison under Gaussian and binary outcomes.

In this setup, for each subgroup j , assume under the treatment arm, the binary outcome is generated as $X \sim \text{Bernoulli}(p_1)$; under the control arm, the binary outcome is generated as $Y \sim \text{Bernoulli}(p_0)$. The subgroup ATE can be expressed as $\hat{\tau} = \bar{X} - \bar{Y}$. To derive the rate function of $\hat{\tau}$, we follow the steps:

- Derive moment generating function (MGF) $M_Z(t)$, where $Z = X - Y$.
- Derive rate function $I(Z)$ for random variable Z , where $I(Z) = \sup_t (tZ - \log M_Z(t))$;

(1) The MGFs for Bernoulli random variables X and Y are

$$M_X(t) = q_1 + p_1 e^t, \quad M_Y(t) = q_0 + p_0 e^t, \quad \text{where } q_1 = 1 - p_1, \quad q_0 = 1 - p_0.$$

The MGF for $Z = X - Y$ is

$$M_Z(t) = M_{X-Y}(t) = (q_1 + p_1 e^t) \cdot (q_0 + p_0 e^{-t}).$$

(2) The rate function for Z is

$$\begin{aligned} I(Z) &= \sup_t (tZ - \log M_Z(t)) \\ &= \sup_t [tZ - \log ((q_1 + p_1 e^t) \cdot (q_0 + p_0 e^{-t}))] \\ &= \sup_t f(t). \end{aligned}$$

First, we want to solve for t . Take derivative of $f(t)$ with respect to t :

$$\begin{aligned} \frac{\partial f(t)}{\partial t} &= Z - \frac{-q_1 p_0 e^{-t} + p_1 q_0 e^t}{q_1 q_0 + q_1 p_0 e^{-t} + p_1 q_0 e^t + p_1 p_0} = 0, \\ Z &= \frac{-q_1 p_0 e^{-t} + p_1 q_0 e^t}{q_1 q_0 + q_1 p_0 e^{-t} + p_1 q_0 e^t + p_1 p_0}, \\ Z q_1 p_0 e^{-t} + Z p_1 q_0 e^t + q_1 p_0 e^{-t} - p_1 q_0 e^t &= -Z q_1 q_0 - Z p_1 p_0, \\ e^{-t} (Z q_1 p_0 + q_1 p_0) + e^t (Z p_1 q_0 - p_1 q_0) &= -Z q_1 q_0 - Z p_1 p_0, \\ e^{-t} \cdot q_1 p_0 (Z + 1) + e^t \cdot p_1 q_0 (Z - 1) &= -Z q_1 q_0 - Z p_1 p_0. \end{aligned}$$

t^* can be solved via numerical method. Therefore,

$$I(Z) = t^* Z - \log [(q_1 + p_1 e^{t^*}) \cdot (q_0 + p_0 e^{-t^*})].$$

does not have a closed-form expression. We provide a comparison of large deviation rates with Gaussian outcome and binary outcome in Figure 7.

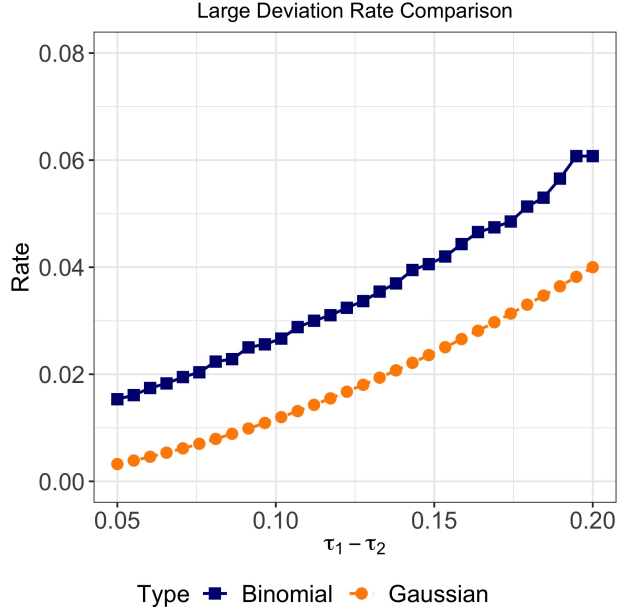


Figure 7: Comparison of large deviation rates

H.3 Justification of Eq (1) using moderation deviation principles

The same rate function can be deduced from the moderate deviation principle, and the moderate deviation results do not require the outcome variables to follow a Gaussian distribution. Nevertheless, they only apply to situations in which $\sqrt{N}(\tau_1 - \tau_j)$ is not “too large.” To be precise, we assume $\tau_1 - \tau_j = b_N c_j$, where $c_j > 0$, and b_N satisfies $b_N \rightarrow 0$ and $\sqrt{N}b_N \rightarrow \infty$. In addition, assume the moment-generating functions of the potential outcomes exist in a neighborhood of 0 (i.e., the Cramér condition holds). Then by Cramér theorem (see Section VIII.2 in [Petrov \(1975\)](#)),

$$\lim_{N \rightarrow \infty} \frac{1}{Nb_N^2} \log \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \hat{\tau}_j] \right) = -G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j).$$

Here, the rate function takes a similar form as in Section [H.2.1](#):

$$G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j) = \frac{c_j^2}{2(\mathbb{V}_1(e_1, p_1) + \mathbb{V}_1(e_j, p_j))},$$

$$\mathbb{V}_1(e_1, p_1) = \frac{\sigma_1(1)^2}{p_1 e_1} + \frac{\sigma_1(0)^2}{p_1(1 - e_1)}, \quad \mathbb{V}_j(e_j, p_j) = \frac{\sigma_j(1)^2}{p_j e_j} + \frac{\sigma_j(0)^2}{p_j(1 - e_j)}.$$

Therefore,

$$\lim_{N \rightarrow \infty} \frac{1}{Nb_N^2} \log \left(1 - \mathbb{P}[\hat{\tau}_1 \geq \max_{2 \leq j \leq m} \hat{\tau}_j] \right) = - \min_{2 \leq j \leq m} G(\mathcal{S}_1, \mathcal{S}_j; e_1, p_1, e_j, p_j).$$

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