Online Supplement for “Optimal Treatment Allocations Accounting for Population Differences”

Wei Zhang[1], Zhiwei Zhang[2,*], and Aiyi Liu[3]

[1]State Key Laboratory of Mathematical Sciences, Academy of Mathematics and Systems Science, Chinese Academy of Sciences, Beijing, China

[2]Biostatistics Innovation Group, Gilead Sciences, Foster City, California, USA

[3]Biostatistics and Bioinformatics Branch, Division of Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland, USA

*zhiwei.zhang6@gilead.com

A. Proofs of Lemma 1 and Theorem 1

A.1. Proof of Lemma 1

We follow the approach of Bickel et al. (1993) to derive the efficient influence function for Δ^* under the randomization assumption in Section 2.1. To this end, we think of the observed data $\{(W_i, A_i, Y_i), i = 1, \cdots, n\}$ and $\{(W_i^*), i = 1, \cdots, n^*\}$ as independent copies of $\{O^\circ = (Z, W^\circ, A^\circ, Y^\circ)\}$, where Z is an indicator of trial participation ($Z = 1$ if in the trial and $Z = 0$ otherwise), $W^\circ = ZW + (1 - Z)W^*$, $A^\circ = ZA$, and $Y^\circ = ZY$. The joint density of O° (with respect to some σ-finite measure) is given by

$$f_{O^\circ}(o) = f_{O^\circ}(z, w, a, y) = f^\circ(w)\{1 - e^\circ(w)\}^{1-z}\left[e^\circ(w)\mathrm{pr}(A = a|W = w) f_a(y|w)\right]^z,$$

where $f^\circ(w)$ is the density of $W^\circ = w$, $e^\circ(w) = \mathrm{pr}(Z = 1|W^\circ = w)$, and $f_a(y|w)$ is the conditional density of $(Y^\circ = y|Z = 1, W^\circ = w, A^\circ = a) = (Y = y|W = w, A = a)$. Note that no assumptions are imposed on the distribution of the observed data. Then we consider a regular parametric submodel

$$f^\circ(w;\theta)\{1-e^\circ(w;\theta)\}^{1-z}\{e^\circ(w;\theta)\mathrm{pr}(A=a|W=w)f_a(y|w;\theta)\}^z,$$

which is equal to the true distribution when $\theta=\theta_0$. The corresponding score for θ at θ_0 is derived as

$$\begin{aligned} s_{O^\circ}(o;\theta_0) &= s_{O^\circ}(z,w,a,y;\theta_0) \\ &= s^\circ(w,\theta_0)+\frac{\dot e^\circ(w;\theta_0)\{z-e^\circ(w,\theta_0)\}}{e^\circ(w,\theta_0)\{1-e^\circ(w,\theta_0)\}}+zas_1(y|w;\theta_0)+z(1-a)s_0(y|w;\theta_0), \end{aligned}$$

where $s^\circ(w,\theta)=\partial\log f^\circ(w;\theta)/\partial\theta$, $s_a(y|w;\theta)=\partial\log f_a(y|w;\theta)/\partial\theta$ $(a=0,1)$, and $\dot e^\circ(w;\theta)=\partial e^\circ(w;\theta)/\partial\theta$. Based on this, the tangent space for the nonparametric model for O is given by

$$\mathscr{T}^{\mathrm{tr}}_{\mathrm{CDR}}=\{b_1(w)+b_2(w)\{z-e^\circ(w)\}+zah_1(y|w)+z(1-a)h_0(y|w)\},$$

where $b_1(w)$ is an arbitrary function such that $\mathrm{E}\{b_1(W^\circ)\}=0$ and $\mathrm{var}\{b_1(W^\circ)\}<\infty$, $b_2(w)$ is an arbitrary function such that $\mathrm{var}\{b_2(W^\circ)\}<\infty$, $h_a(y|w)(a=0,1)$ satisfies the constraint $\mathrm{E}\{h_a(Y|W)|A=a,W=w\}=0$ for all w.

Under the above parametric submodel, we can write the estimand Δ^* as a functional of f_{O°:

$$\Delta^*(\theta)=\frac{\iint y\{f_1(y|w;\theta)-f_0(y|w;\theta)\}\{1-e^\circ(w;\theta)\}f^\circ(w;\theta)dydw}{\int\{1-e^\circ(w;\theta)\}f^\circ(w;\theta)dw},$$

which implies that Δ^* is pathwise differentiable. It follows that

$$\begin{aligned} \frac{\partial\Delta^*(\theta)}{\partial\theta}\Big|_{\theta=\theta_0} &= \frac{\iint y\{s_1(y|w;\theta_0)f_1(y|w;\theta_0)-s_0(y|w;\theta_0)f_0(y|w;\theta_0)\}\{1-e^\circ(w;\theta_0)\}f^\circ(w;\theta_0)dydw}{\int\{1-e^\circ(w;\theta_0)\}f^\circ(w;\theta_0)dw} \\ &\quad-\frac{\iint y\{f_1(y|w;\theta_0)-f_0(y|w;\theta_0)\}\dot e^\circ(w;\theta_0)f^\circ(w;\theta_0)dydw}{\int\{1-e^\circ(w;\theta_0)\}f^\circ(w;\theta_0)dw} \\ &\quad+\frac{\iint y\{f_1(y|w;\theta_0)-f_0(y|w;\theta_0)\}\{1-e^\circ(w;\theta_0)\}s^\circ(w;\theta_0)f^\circ(w;\theta_0)dydw}{\int\{1-e^\circ(w;\theta_0)\}f^\circ(w;\theta_0)dw} \\ &\quad+\Delta^*\frac{\int\dot e^\circ(w;\theta_0)f^\circ(w;\theta_0)dw-\int\{1-e^\circ(w;\theta_0)\}s^\circ(w;\theta_0)f^\circ(w;\theta_0)dw}{\int\{1-e^\circ(w;\theta_0)\}f^\circ(w;\theta_0)dw}. \end{aligned}$$

Define

$$
\begin{aligned}
\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O) = {} & \frac{\{1-e^{\circ}(W^{\circ})\}\{\delta(W^{\circ})-\Delta^*\}}{1-\gamma} - \frac{\{\delta(W^{\circ})-\Delta^*\}\{Z-e^{\circ}(W^{\circ})\}}{1-\gamma} \\
& + \frac{ZA\{1-e^{\circ}(W)\}\{Y-m(1,W)\}}{(1-\gamma)p(W)e^{\circ}(W)} - \frac{Z(1-A)\{1-e^{\circ}(W)\}\{Y-m(0,W)\}}{(1-\gamma)\{1-p(W)\}e^{\circ}(W)} \\
= {} & \frac{(1-Z)\{\delta(W^{\circ})-\Delta^*\}}{1-\gamma} + \frac{ZA\{1-e^{\circ}(W)\}\{Y-m(1,W)\}}{(1-\gamma)p(W)e^{\circ}(W)} \\
& - \frac{Z(1-A)\{1-e^{\circ}(W)\}\{Y-m(0,W)\}}{(1-\gamma)\{1-p(W)\}e^{\circ}(W)} \\
= {} & \frac{(1-Z)\{\delta(W^{*})-\Delta^*\}}{1-\gamma} + \frac{ZAr(W)\{Y-m(1,W)\}}{\gamma p(W)} - \frac{Z(1-A)r(W)\{Y-m(0,W)\}}{\gamma\{1-p(W)\}},
\end{aligned}
$$

where $\gamma = \int e^{\circ}(w)f^{\circ}(w)dw = \mathrm{pr}(Z=1)$, $m(a,w) = \mathrm{E}(Y|A=a, W=w)$, $\delta(w) = m(1,w) - m(0,w)$, $p(w) = \mathrm{pr}(A=1|W=w)$, and $r(w)$ is the ratio of the conditional density of $(W^{\circ}=w \mid Z=0)$ to that of $(W^{\circ}=w \mid Z=1)$. Through some calculations, we can obtain that

$$
\left.\frac{\partial\Delta^*(\theta)}{\partial\theta}\right|_{\theta=\theta_0} = \mathrm{E}\{\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)s_{O^{\circ}}(O;\theta_0)\}.
$$

This implies that $\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)$ is an influence function for Δ^*. Because $\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)$ is an element of the tangent space $\mathscr{T}^{\mathrm{tr}}_{\mathrm{CDR}}$, its projection on $\mathscr{T}^{\mathrm{tr}}_{\mathrm{CDR}}$ is itself. Therefore, $\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)$ is the efficient influence function for Δ^* in the nonparametric model.

A.2. Proof of Theorem 1

(i) Derivation of the optimal CIR design. Since $\mathrm{E}\{\psi^{\mathrm{tr}}_{\mathrm{CIR}}(O)\} = 0$, the variance of $\psi^{\mathrm{tr}}_{\mathrm{CIR}}(O)$ is equal to

$$
\begin{aligned}
\mathrm{var}\{\psi^{\mathrm{tr}}_{\mathrm{CIR}}(O)\} &= \mathrm{E}\{\psi^{\mathrm{tr}}_{\mathrm{CIR}}(O)\}^2 \\
&= \mathrm{E}\left[\frac{(1-Z)\{\delta(W^*)-\Delta^*\}}{1-\gamma}\right]^2 + \mathrm{E}\left[\frac{ZAr(W)\{Y-m(1,W)\}}{\gamma\pi}\right]^2 \\
&\quad + \mathrm{E}\left[\frac{Z(1-A)r(W)\{Y-m(0,W)\}}{\gamma\{1-\pi\}}\right]^2 .
\end{aligned}
$$

By conditioning on Z, we have

$$
\mathrm{E}\left[\frac{ZAr(W)\{Y-m(1,W)\}}{\gamma\pi}\right]^2 = \mathrm{E}\left[\frac{A\{r(W)\}^2\{Y-m(1,W)\}^2}{\gamma^2\pi^2}|Z=1\right]\mathrm{pr}(Z=1).
$$

Further conditioning on W and A yields

$$
\begin{aligned}
&\mathrm{E}\left[\frac{Ar(W)^2\{Y-m(1,W)\}^2}{\gamma^2\pi^2}|Z=1\right]\\
&=\mathrm{E}\left(\frac{r(W)^2}{\gamma^2\pi^2}\,\mathrm{E}\left[A\{Y-m(1,W)\}^2|Z=1,W\right]\right)\\
&=\mathrm{E}\left(\frac{r(W)^2}{\gamma^2\pi^2}\,\mathrm{E}\left[A\{Y-m(1,W)\}^2|Z=1,W,A=1\right]\mathrm{pr}(A=1|Z=1,W)\right)\\
&=\mathrm{E}\left\{\frac{r(W)^2v_1(W)}{\gamma^2\pi}\right\},
\end{aligned}
$$

where $v_1(W)=\mathrm{var}\{Y|W,A=1\}$. Analogously, we can obtain that

$$
\mathrm{E}\left[\frac{Z(1-A)r(W)\{Y-m(0,W)\}}{\gamma\{1-\pi\}}\right]^2=\mathrm{E}\left\{\frac{r(W)^2v_0(W)}{\gamma^2(1-\pi)}\right\}\mathrm{pr}(Z=1).
$$

where $v_0(W)=\mathrm{var}\{Y|W,A=0\}$. Note that $\mathrm{E}\left[(1-Z)\{\delta(W^{\circ})-\Delta^*\}\right]^2$ does not depend on π. Then we can write

$$
\mathrm{var}\{\psi^{\mathrm{tr}}_{\mathrm{CIR}}(O)\}=\text{const.}+\frac{\mathrm{pr}(Z=1)}{\pi\gamma^2}\,\mathrm{E}\left\{r(W)^2v_1(W)\right\}+\frac{\mathrm{pr}(Z=1)}{(1-\pi)\gamma^2}\left\{r(W)^2v_0(W)\right\},
$$

where "const." represents a quantity that does not depend on π. It is easy to see that the preceding display is minimized by setting π equal to

$$
\pi^{\mathrm{tr}}_{\mathrm{opt}}=\frac{[\mathrm{E}\{r(W)^2v_1(W)\}]^{1/2}}{[\mathrm{E}\{r(W)^2v_1(W)\}]^{1/2}+[\mathrm{E}\{r(W)^2v_0(W)\}]^{1/2}}.
$$

(ii) Derivation of the optimal CDR design. Recall that

$$
\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)=\frac{(1-Z)\{\delta(W^*)-\Delta^*\}}{1-\gamma}+\frac{ZAr(W)\{Y-m(1,W)\}}{\gamma p(W)}-\frac{Z(1-A)r(W)\{Y-m(0,W)\}}{\gamma\{1-p(W)\}}
$$

The variance of $\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)$ is equal to

$$
\begin{aligned}
\mathrm{var}\{\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)\}=\;&\mathrm{E}\left[\frac{(1-Z)\{\delta(W^*)-\Delta^*\}}{1-\gamma}\right]^2+\mathrm{E}\left[\frac{ZAr(W)\{Y-m(1,W)\}}{\gamma p(W)^2}\right]^2\\
&+\mathrm{E}\left[\frac{Z(1-A)r(W)\{Y-m(0,W)\}}{\gamma\{1-p(W)\}^2}\right]^2.
\end{aligned}
$$

By conditioning on Z, the second term of the preceding display can be written as

$$
\mathrm{E}\left[\frac{ZAr(W)\{Y-m(1,W)\}}{\gamma p(W)}\right]^2=\mathrm{E}\left[\frac{Ar(W)^2\{Y-m(1,W)\}^2}{\gamma^2p(W)^2}|Z=1\right]\mathrm{pr}(Z=1).
$$

Further conditioning on W and A, we have

$$
\begin{aligned}
&\mathrm{E}\left[\frac{Ar(W)^2\{Y-m(1,W)\}^2}{\gamma^2 p(W)^2}|Z=1\right]\mathrm{pr}(Z=1)\\
&=\mathrm{E}\left(\frac{r(W)^2}{\gamma^2 p(W)^2}\mathrm{E}\left[A\{Y-m(1,W)\}^2|Z=1,W\right]\right)\mathrm{pr}(Z=1)\\
&=\mathrm{E}\left(\frac{r(W)^2}{\gamma^2 p(W)^2}\mathrm{E}\left[A\{Y-m(1,W)\}^2|Z=1,W,A=1\right]\mathrm{pr}(A=1|Z=1,W)\right)\mathrm{pr}(Z=1)\\
&=\mathrm{E}\left\{\frac{r(W)^2 v_1(W)}{\gamma^2 p(W)}\right\}\mathrm{pr}(Z=1),
\end{aligned}
$$

A similar argument can be used to obtain

$$
\mathrm{E}\left[\frac{Z(1-A)r(W)\{Y-m(0,W)\}}{\gamma\{1-p(W)\}^2}\right]^2=\mathrm{E}\left[\frac{r(W)^2 v_0(W)}{\gamma^2\{1-p(W)\}}\right]\mathrm{pr}(Z=1).
$$

Because $\mathrm{E}\left[(1-Z)\{\delta(W^*)-\Delta^*\}\right]^2=\mathrm{E}\left[\{\delta(W^*)-\Delta^*\}^2|Z=0\right]\mathrm{pr}(Z=0)$ is not a function of $p(W)$, we have

$$
\mathrm{var}\{\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)\}=\text{const.}+\mathrm{E}\left[\frac{r(W)^2 v_1(W)}{\gamma^2 p(W)}+\frac{r(W)^2 v_0(W)}{\gamma^2\{1-p(W)\}}\right]\mathrm{pr}(Z=1).
$$

The variance $\mathrm{var}\{\psi^{\mathrm{tr}}_{\mathrm{CDR}}(O)\}$ is minimized by choosing $p(w)$ to minimize

$$
\frac{r(W)^2 v_1(w)}{\gamma^2 p(w)}+\frac{r(W)^2 v_0(w)}{\gamma^2\{1-p(w)\}}
$$

for each possible value w of W. The minimizer is obtained as

$$
p^{\mathrm{tr}}_{\mathrm{opt}}(w)=\frac{v_1(w)^{1/2}}{v_1(w)^{1/2}+v_0(w)^{1/2}}.
$$

B. Proofs of Lemma 2 and Theorem 2

B.1. Proof of Lemma 2

We use a similar strategy as in Section A to derive the efficient influence functions for Δ^* under CIR and CDR in the case of generalization. Let Z be the indicator of trial participation ($Z=1$ if in the trial and $Z=0$ otherwise). Note that $W^*=W$ if $Z=1$. We view the observed data

$\{(W_i, A_i, Y_i), i = 1, \cdots, n\}$ and $\{W_j^* : Z_j = 0\}$ as independent copies of $\{O^* = (Z, W^*, A^*, Y^*)\}$, where $A^* = ZA$ and $Y^* = ZY$.

Under CIR, the treatment assignment is independent of the baseline covariates. Hence the joint density of O^* (with respect to some σ-finite measure) is given by

$$f_{O^*}(o) = f_{O^*}(z, w, a, y) = f^*(w)\{1 - e(w)\}^{1-z}\{e(w)\mathrm{pr}(A = a) f_a(y|w)\}^z,$$

where $f^*(w)$ is the density of $W^* = w$, $e(w) = \mathrm{pr}(Z = 1|W^* = w)$, and $f_a(y|w)$ is the conditional density of $(Y^* = y|Z = 1, W^* = w, A^* = a) = (Y = y|W = w, A = a)$. Consider a regular parametric submodel indexed by θ,

$$f^*(w;\theta)\{1 - e(w;\theta)\}^{1-z}\{e(w;\theta)\mathrm{pr}(A = a) f_a(y|w;\theta)\}^z,$$

which equals the true distribution when $\theta = \theta_0$. The corresponding score for θ at θ_0 is derived as

$$\begin{aligned} s_{O^*}(o;\theta_0) &= s_{O^*}(z, w, a, y;\theta_0) \\ &= s^*(w, \theta_0) + \frac{\dot{e}(w;\theta_0)\{z - e(w, \theta_0)\}}{e(w, \theta_0)\{1 - e(w, \theta_0)\}} + zas_1(y|w;\theta_0) + z(1 - a)s_0(y|w;\theta_0), \end{aligned}$$

where $s^*(w, \theta) = \partial \log f^*(w;\theta)/\partial\theta$, $s_a(y|w;\theta) = \partial \log f_a(y|w;\theta)/\partial\theta$ $(a = 0, 1)$, and $\dot{e}(w;\theta) = \partial e(w;\theta)/\partial\theta$. Based on this, the tangent space for the nonparametric model for O is given by

$$\mathscr{T}_{\mathrm{CIR}}^{\mathrm{gen}} = b_1(w) + b_2(w)\{z - e(w)\} + zah_1(y|w) + z(1 - a)h_0(y|w),$$

where $b_1(w)$ is an arbitrary function such that $\mathrm{E}\{b_1(W^*)\} = 0$ and $\mathrm{var}\{b_1(W^*)\} < \infty$, $b_2(w)$ is an arbitrary function such that $\mathrm{var}\{b_2(W^*)\} < \infty$, $h_a(y|w)(a = 0, 1)$ satisfies the constraint $\mathrm{E}\{h_a(Y|W)|A = a, W = w\} = 0$ for all w.

Under the above parametric submodel, we can write the treatment effect as a functional of f_O:

$$\Delta^*(\theta) = \int\int y\{f_1(y|w;\theta) - f_0(y|w;\theta)\}f^*(w;\theta)dydw.$$

It follows that

$$\begin{aligned} \frac{\partial\Delta^*(\theta)}{\partial\theta}\Big|_{\theta=\theta_0} &= \int\int y\{s_1(y|w;\theta_0)f_1(y|w;\theta_0) - s_0(y|w;\theta_0)f_0(y|w;\theta_0)\}f^*(w;\theta_0)dydw \\ &+ \int\int y\{f_1(y|w;\theta_0) - f_0(y|w;\theta_0)\}s^*(w;\theta_0)f^*(w;\theta_0)dydw. \end{aligned}$$

We define

$$\psi_{\text{CIR}}^{\text{gen}}(O) = \delta(W^*) - \Delta^* + \frac{ZA\{Y - m(1, W^*)\}}{\pi e(W^*)} - \frac{Z(1-A)\{Y - m(0, W^*)\}}{\{1-\pi\}e(W^*)},$$

where $\pi = \text{pr}(A = 1)$, $m(a, w) = \text{E}(Y|A = a, W = w)$, and $\delta(w) = m(1, w) - m(0, w)$. Clearly, $\psi_{\text{CIR}}^{\text{gen}}(O)$ is an element of the tangent space $\mathscr{T}_{\text{CIR}}^{\text{gen}}$. It can be verified that

$$\left.\frac{\partial \Delta^*(\theta)}{\partial \theta}\right|_{\theta=\theta_0} = \text{E}\{\psi_{\text{CIR}}^{\text{gen}}(O) s_{O^*}(O; \theta_0)\}.$$

This implies that $\psi_{\text{CIR}}^{\text{gen}}(O)$ is an influence function for Δ^*. Because the projection of $\psi_{\text{CIR}}^{\text{gen}}(O)$ on $\mathscr{T}_{\text{CIR}}^{\text{gen}}$ is itself, $\psi_{\text{CIR}}^{\text{gen}}(O)$ is the efficient influence function for Δ^* in the nonparametric model.

Under CDR, the treatment depends on the covariates, i.e., $\text{pr}(A = 1 \mid W = w) = p(w)$. By applying arguments analogous to those used for CIR, we derive the efficient influence function for Δ^* as

$$\psi_{\text{CDR}}^{\text{gen}}(O) = \delta(W^*) - \Delta^* + \frac{ZA\{Y - m(1, W^*)\}}{e(W^*)p(W^*)} - \frac{Z(1-A)\{Y - m(0, W^*)\}}{e(W^*)\{1-p(W^*)\}}.$$

B.2. Proof of Theorem 2

(i) Derivation of the optimal CIR design. The variance of $\psi_{\text{CIR}}^{\text{gen}}(O)$ is equal to

$$\begin{aligned}
\text{var}\{\psi_{\text{CIR}}^{\text{gen}}(O)\} = {} & \text{var}\{\delta(W^*) - \Delta^*\} + \text{var}\left[\frac{ZA\{Y - m(1, W^*)\}}{\pi e(W^*)}\right] + \text{var}\left[\frac{Z(1-A)\{Y - m(0, W^*)\}}{\{1-\pi\}e(W^*)}\right] \\
& + 2\text{cov}\left[\delta(W^*) - \Delta^*,\ \frac{ZA\{Y - m(1, W^*)\}}{\pi e(W^*)}\right] \\
& - 2\text{cov}\left[\delta(W^*) - \Delta^*,\ \frac{Z(1-A)\{Y - m(0, W)\}}{\{1-\pi\}e(W^*)}\right].
\end{aligned}$$

By conditioning on Z, we have

$$\text{var}\left[\frac{ZA\{Y - m(1, W^*)\}}{\pi e(W)}\right] = \text{E}\left[\frac{ZA\{Y - m(1, W)\}}{\pi e(W)}\right]^2 = \text{E}\left[\frac{A\{Y - m(1, W)\}^2}{\pi^2 e^2(W)} | Z = 1\right] \text{pr}(Z = 1)$$

Further conditioning on W and A yields

$$
\begin{aligned}
&\mathrm{E}\left[\frac{A\{Y-m(1,W)\}^2}{\pi^2 e^2(W)}|Z=1\right]\\
&=\mathrm{E}\left(\frac{\mathrm{E}\left[A\{Y-m(1,W)\}^2|Z=1,W\right]}{\pi^2 e^2(W)}\right)\\
&=\mathrm{E}\left(\frac{1}{\pi^2 e^2(W)}\,\mathrm{E}\left[A\{Y-m(1,W)\}^2|Z=1,W,A=1\right]\mathrm{pr}(A=1|Z=1,W)\right)\\
&=\mathrm{E}\left\{\frac{v_1(W)}{\pi e^2(W)}\right\},
\end{aligned}
$$

where $v_1(W)=\mathrm{var}\{Y|W,A=1\}$. It can be similarly obtained that

$$
\mathrm{var}\left[\frac{Z(1-A)\{Y-m(0,W)\}}{(1-\pi)e(W)}\right]=\mathrm{E}\left[\frac{v_0(W)}{(1-\pi)e^2(W)}\right]\mathrm{pr}(Z=1),
$$

where $v_0(W)=\mathrm{var}\{Y|W,A=0\}$. It is easy to show that

$$
\mathrm{cov}\left[\delta(W^*)-\Delta^*,\ \frac{ZA\{Y-m(1,W^*)\}}{\pi e(W^*)}\right]=0
$$

and

$$
\mathrm{cov}\left[\delta(W^*)-\Delta^*,\ \frac{Z(1-A)\{Y-m(0,W^*)\}}{\{1-\pi\}e(W^*)}\right]=0.
$$

Note that $\mathrm{var}\{\delta(W^*)-\Delta^*\}$ does not depend on π. Then we can write

$$
\mathrm{var}\{\psi_{\text{CIR}}^{\text{gen}}(O)\}=\text{const.}+\frac{\mathrm{pr}(Z=1)}{\pi}\,\mathrm{E}\left[\frac{v_1(W)}{e^2(W)}\right]+\frac{\mathrm{pr}(Z=1)}{1-\pi}\,\mathrm{E}\left[\frac{v_0(W)}{e^2(W)}\right],
$$

where "const." represents a quantity that does not depend on π. It is easy to see that the preceding display is minimized by setting π equal to

$$
\begin{aligned}
\pi_{\text{opt}}^{\text{gen}}&=\frac{[\mathrm{E}\{e(W)^{-2}v_1(W)\}]^{1/2}}{[\mathrm{E}\{e(W)^{-2}v_1(W)\}]^{1/2}+[\mathrm{E}\{e(W)^{-2}v_0(W)\}]^{1/2}}\\
&=\frac{(\mathrm{E}[\{\mathrm{pr}(Z=1)/e(W)\}^2 v_1(W)])^{1/2}}{(\mathrm{E}[\{\mathrm{pr}(Z=1)/e(W)\}^2 v_1(W)])^{1/2}+(\mathrm{E}[\{\mathrm{pr}(Z=1)/e(W)\}^2 v_0(W)])^{1/2}}\\
&=\frac{[\mathrm{E}\{r(W)^2 v_1(W)\}]^{1/2}}{[\mathrm{E}\{r(W)^2 v_1(W)\}]^{1/2}+[\mathrm{E}\{r(W)^2 v_0(W)\}]^{1/2}},
\end{aligned}
$$

where the third equality follows from $r(w)=\mathrm{pr}(Z=1)/e(w)$.

(ii) Derivation of the optimal CDR design. The variance of $\psi_{\mathrm{CDR}}^{\mathrm{gen}}(O)$ is equal to

$$
\begin{aligned}
\mathrm{var}\{\psi_{\mathrm{CDR}}^{\mathrm{gen}}(O)\} = \mathrm{var}\{\delta(W^*) - \Delta^*\} &+ \mathrm{var}\left[\frac{ZA\{Y - m(1, W^*)\}}{p(W)e(W^*)}\right] + \mathrm{var}\left[\frac{Z(1-A)\{Y - m(0, W^*)\}}{\{1-p(W^*)\}e(W^*)}\right] \\
&+ 2\mathrm{cov}\left[\delta(W^*) - \Delta^*,\ \frac{ZA\{Y - m(1, W^*)\}}{p(W^*)e(W^*)}\right] \\
&- 2\mathrm{cov}\left[\delta(W^*) - \Delta^*,\ \frac{Z(1-A)\{Y - m(0, W^*)\}}{\{1-p(W^*)\}e(W^*)}\right].
\end{aligned}
$$

By conditioning on Z, W, and A successively, we obtain

$$
\begin{aligned}
\mathrm{var}\left[\frac{ZA\{Y - m(1, W^*)\}}{p(W^*)e(W^*)}\right] &= \mathrm{E}\left[\frac{A\{Y - m(1, W)\}^2}{\{p(W)\}^2 e^2(W)} | Z = 1\right] \mathrm{pr}(Z = 1) \\
&= \mathrm{E}\left(\frac{\mathrm{E}\left[A\{Y - m(1, W)\}^2 | Z = 1, W\right]}{\{p(W)\}^2 e^2(W)}\right) \mathrm{pr}(Z = 1) \\
&= \mathrm{E}\left(\frac{\mathrm{E}\left[A\{Y - m(1, W)\}^2 | Z = 1, W, A = 1\right]}{p(W) e^2(W)}\right) \mathrm{pr}(Z = 1) \\
&= \mathrm{E}\left\{\frac{v_1(W)}{p(W)e^2(W)}\right\} \mathrm{pr}(Z = 1)
\end{aligned}
$$

and

$$
\mathrm{var}\left[\frac{Z(1-A)\{Y - m(0, W^*)\}}{\{1-p(W^*)\}e(W^*)}\right] = \mathrm{E}\left[\frac{v_0(W)}{\{1-p(W)\}e^2(W)}\right] \mathrm{pr}(Z = 1),
$$

where $v_0(W) = \mathrm{var}\{Y | W, A = 0\}$. It is easy to see that

$$
\mathrm{cov}\left[\delta(W^*) - \Delta^*,\ \frac{ZA\{Y - m(1, W^*)\}}{p(W^*)e(W^*)}\right] = 0
$$

and

$$
\mathrm{cov}\left[\delta(W^*) - \Delta^*,\ \frac{Z(1-A)\{Y - m(0, W^*)\}}{\{1-p(W^*)\}e(W^*)}\right] = 0.
$$

Because $\mathrm{var}\{\delta(W^*) - \Delta^*\}$ does not depend on p, we have

$$
\mathrm{var}\{\psi_{\mathrm{CDR}}^{\mathrm{gen}}(O)\} = \mathrm{const.} + \mathrm{pr}(Z = 1)\,\mathrm{E}\left[\frac{v_1(W)}{p(W)e^2(W)} + \frac{v_0(W)}{\{1-p(W)\}e^2(W)}\right].
$$

where "const." represents a quantity that does not depend on p. For each possible value w of W, the minimizer of $\mathrm{var}\{\psi_{\mathrm{CDR}}^{\mathrm{gen}}(O)\}$ with respect to p is equal to

$$
p_{\mathrm{opt}}^{\mathrm{gen}}(w) = \frac{v_1(w)^{1/2}}{v_1(w)^{1/2} + v_0(w)^{1/2}}.
$$

C. Proofs of Lemma 3 and Theorem 3

C.1. Proof of Lemma 3

To derive the efficient influence functions of Δ^*, we first obtain those corresponding to the subgroup-specific treatment effects, Δ_k $(k = 1, \ldots, K)$. The observed data consist of $\{(W_i, A_i, Y_i), i = 1, \cdots, n\}$, which are independent copies of $O = (W, A, Y)$. Under CIR, the joint density of O is expressed as

$$f_O(o) = f_O(w, a, y) = f(w)\mathrm{pr}(A = a) f_a(y|w),$$

where $f(w)$ is the density of $W = w$ and $f_a(y|w)$ is the conditional density of $(Y = y|W = w, A = a)$. We consider a parametric submodel indexed by θ:

$$f(w; \theta)\mathrm{pr}(A = a) f_a(y|w; \theta),$$

which is the true distribution at $\theta = \theta_0$. By taking the derivative with respect to θ, the score function at θ_0 is equal to

$$s(o; \theta_0) = s(w, \theta_0) + a s_1(y|w; \theta_0) + (1 - a) s_0(y|w; \theta_0),$$

where $s(w, \theta) = \partial \log f(w; \theta)/\partial\theta$ and $s_a(y|w; \theta) = \partial \log f_a(y|w; \theta)/\partial\theta$ $(a = 0, 1)$. The tangent space for the nonparametric model for O is thus defined as

$$\mathcal{T}_{\mathrm{CIR}}^{\mathrm{ps}} = \{b_1(w) + a h_1(y|w) + (1 - a) h_0(y|w)\},$$

where $b_1(w)$ is an arbitrary function such that $\mathrm{E}\{b_1(W)\} = 0$ and $h_a(y|w)(a = 0, 1)$ satisfies the constraint $\mathrm{E}\{h_a(Y|W)|A = a, W = w\} = 0$ for all w.

Under the above parametric submodel, we have

$$\Delta_k(\theta) = \frac{\iint y\{f_1(y|w; \theta) - f_0(y|w; \theta)\} f(w; \theta) I(w \in \mathcal{W}_k) dy dw}{\int f(w; \theta) I(w \in \mathcal{W}_k) dw}.$$

and

$$
\begin{aligned}
\frac{\partial \Delta_k(\theta)}{\partial \theta}|_{\theta=\theta_0} = & \frac{\iint y\{s_1(y|w;\theta_0) f_1(y|w;\theta_0) - s_0(y|w;\theta_0) f_0(y|w;\theta_0)\} f(w;\theta_0) I(w \in \mathcal{W}_k) dy dw}{\int f(w;\theta_0) I(w \in \mathcal{W}_k) dw} \\
& + \frac{\iint y\{f_1(y|w;\theta_0) - f_0(y|w;\theta_0)\} s(w;\theta_0) f(w;\theta_0) I(w \in \mathcal{W}_k) dy dw}{\int f(w;\theta_0) I(w \in \mathcal{W}_k) dw} \\
& - \Delta_k(\theta_0) \frac{\int s(w;\theta_0) f(w;\theta_0) I(w \in \mathcal{W}_k) dw}{\int f(w;\theta_0) I(w \in \mathcal{W}_k) dw}.
\end{aligned}
$$

Let

$$
\begin{aligned}
\psi^{\mathrm{ps}}_{\mathrm{CIR},k}(O) = & \frac{I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}}{\tau_k} + \frac{I(W \in \mathcal{W}_k) A\{Y - m(1,W)\}}{\pi \tau_k} \\
& - \frac{I(W \in \mathcal{W}_k)(1-A)\{Y - m(0,W)\}}{\{1-\pi\}\tau_k},
\end{aligned}
$$

where $\tau_k = \int f(w) I(w \in \mathcal{W}_k) dw = \mathrm{pr}(W \in \mathcal{W}_k)$. It is evident that $\psi^{\mathrm{ps}}_{\mathrm{CIR},k}(O)$ belongs to the tangent space $\mathscr{T}^{\mathrm{ps}}_{\mathrm{CIR}}$. Moreover, we find that

$$
\frac{\partial \Delta_k(\theta)}{\partial \theta}|_{\theta=\theta_0} = \mathrm{E}\{\psi^{\mathrm{ps}}_{\mathrm{CIR},k}(O) s(O;\theta_0)\}.
$$

These two observations together suggest that $\psi^{\mathrm{ps}}_{\mathrm{CIR},k}(O)$ is the efficient influence function for Δ_k in the nonparametric model. The efficient influence function for Δ^* is therefore obtained as

$$
\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O) = \sum_{k=1}^{K} \frac{I(W \in \mathcal{W}_k)\tau_k^*}{\tau_k} \left[\{\delta(W) - \Delta_k\} + \frac{A\{Y - m(1,W)\}}{\pi} - \frac{(1-A)\{Y - m(0,W)\}}{1-\pi} \right],
$$

where τ_k^* $(k = 1, \ldots, K)$ are known weights for the subgroups $\mathcal{W}_k$ in the target population.

Under CDR, the efficient influence function for Δ^* can be derived by replacing π with $p(w) = \mathrm{pr}(A = 1 \mid W = w)$ for π in $\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O)$, that is,

$$
\psi^{\mathrm{ps}}_{\mathrm{CDR}}(O) = \sum_{k=1}^{K} \frac{I(W \in \mathcal{W}_k)\tau_k^*}{\tau_k} \left[\{\delta(W) - \Delta_k\} + \frac{A\{Y - m(1,W)\}}{p(W)} - \frac{(1-A)\{Y - m(0,W)\}}{1-p(W)} \right].
$$

C.2. Proof of Theorem 3

(i) Derivation of the optimal CIR design. The variance of $\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O)$ is equal to

$$
\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O)\right\} = \sum_{k=1}^{K} (\tau_k^*)^2 \mathrm{var}\{\psi^{\mathrm{ps}}_{\mathrm{CIR},k}(O)\}.
$$

Note that

$$
\begin{aligned}
&\mathrm{E}\left([I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}]\left[\frac{I(W \in \mathcal{W}_k)A\{Y - m(1,W)\}}{\pi}\right]\right) \\
&= \mathrm{E}\left(\frac{I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}}{\pi}\mathrm{E}\left[\{Y - m(1,W)\} \mid A = 1, W\right]\right)\mathrm{pr}(A = 1) \\
&= 0,
\end{aligned}
$$

and

$$
\begin{aligned}
&\mathrm{E}\left([I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}]\left[\frac{I(W \in \mathcal{W}_k)(1-A)\{Y - m(0,W)\}}{1-\pi}\right]\right) \\
&= \mathrm{E}\left(\frac{I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}}{1-\pi}\mathrm{E}\left[\{Y - m(0,W)\} \mid A = 0, W\right]\right)\mathrm{pr}(A = 0) \\
&= 0.
\end{aligned}
$$

Then we have

$$
\begin{aligned}
\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O)\right\} = &\sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}\right]^2 \\
&+ \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[\frac{I(W \in \mathcal{W}_k)A\{Y - m(1,W)\}}{\pi}\right]^2 \\
&+ \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[\frac{I(W \in \mathcal{W}_k)(1-A)\{Y - m(0,W)\}}{1-\pi}\right]^2,
\end{aligned}
$$

Because the first term of $\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O)\right\}$ does not depend on π, we obtain

$$
\begin{aligned}
\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O)\right\} = \text{const.} &+ \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[\frac{I(W \in \mathcal{W}_k)A\{Y - m(1,W)\}}{\pi}\right]^2 \\
&+ \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[\frac{I(W \in \mathcal{W}_k)(1-A)\{Y - m(0,W)\}}{1-\pi}\right]^2.
\end{aligned}
$$

By sequentially conditioning on A and W, it can be obtained that

$$
\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O)\right\} = \text{const.} + \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2\left[\frac{\mathrm{E}\{v_1(W)I(W \in \mathcal{W}_k)\}}{\pi}\right] + \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2\left[\frac{\mathrm{E}\{v_0(W)I(W \in \mathcal{W}_k)\}}{1-\pi}\right],
$$

where $v_a(W) = \mathrm{var}(Y \mid W, A = a)$ $(a = 0, 1)$. The minimizer of $\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CIR}}(O)\right\}$ with respect to π is thus equal to

$$\begin{aligned}
\pi^{\mathrm{ps}}_{\mathrm{opt}} &= \frac{[\sum_{k=1}^{K}(\tau_k^*/\tau_k)^2 \,\mathrm{E}\{v_1(W)I(W \in \mathcal{W}_k)\}]^{1/2}}{[\sum_{k=1}^{K}(\tau_k^*/\tau_k)^2 \,\mathrm{E}\{v_1(W)I(W \in \mathcal{W}_k)\}]^{1/2} + [\sum_{k=1}^{K}(\tau_k^*/\tau_k)^2 \,\mathrm{E}\{v_0(W)I(W \in \mathcal{W}_k)\}]^{1/2}} \\
&= \frac{(\mathrm{E}[\{\sum_{k=1}^{K} I(W \in \mathcal{W}_k)\tau_k^*/\tau_k\}^2 v_1(W)])^{1/2}}{(\mathrm{E}[\{\sum_{k=1}^{K} I(W \in \mathcal{W}_k)\tau_k^*/\tau_k\}^2 v_1(W)])^{1/2} + (\mathrm{E}[\{\sum_{k=1}^{K} I(W \in \mathcal{W}_k)\tau_k^*/\tau_k\}^2 v_0(W)])^{1/2}} \\
&= \frac{[\mathrm{E}\{r(W)^2 v_1(W)\}]^{1/2}}{[\mathrm{E}\{r(W)^2 v_1(W)\}]^{1/2} + [\mathrm{E}\{r(W)^2 v_0(W)\}]^{1/2}},
\end{aligned}$$

where $r(W) = \sum_{k=1}^{K} I(W \in \mathcal{W}_k)\tau_k^*/\tau_k$.

(ii) Derivation of the optimal CDR design. We observe that

$$\begin{aligned}
\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CDR}}(O)\right\} &= \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}\right]^2 \\
&\quad + \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[\frac{I(W \in \mathcal{W}_k)A\{Y - m(1, W)\}}{p(W)}\right]^2 \\
&\quad + \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[\frac{I(W \in \mathcal{W}_k)(1 - A)\{Y - m(0, W)\}}{1 - p(W)}\right]^2 \\
&\quad - 2\sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left([I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}]\left[\frac{I(W \in \mathcal{W}_k)A\{Y - m(1, W)\}}{p(W)}\right]\right) \\
&\quad - 2\sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left([I(W \in \mathcal{W}_k)\{\delta(W) - \Delta_k\}]\left[\frac{I(W \in \mathcal{W}_k)(1 - A)\{Y - m(0, W)\}}{1 - p(W)}\right]\right).
\end{aligned}$$

Following the same reasoning as for CIR, we obtain

$$\begin{aligned}
\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CDR}}(O)\right\} = \text{const.} &+ \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[\frac{I(W \in \mathcal{W}_k)A\{Y - m(1, W)\}}{p(W)}\right]^2 \\
&+ \sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 \mathrm{E}\left[\frac{I(W \in \mathcal{W}_k)(1 - A)\{Y - m(0, W)\}}{1 - p(W)}\right]^2.
\end{aligned}$$

Minimizing $\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CDR}}(O)\right\}$ with respect to p is equivalent to minimizing

$$\left\{\sum_{k=1}^{K}\left(\frac{\tau_k^*}{\tau_k}\right)^2 I(w \in \mathcal{W}_k)\right\}\left\{\frac{v_1(w)}{p(w)} + \frac{v_0(w)}{1 - p(w)}\right\},$$

for each possible value w of W. Therefore, for each value w of W, the minimizer of $\mathrm{var}\left\{\psi^{\mathrm{ps}}_{\mathrm{CDR}}(O)\right\}$

is equal to

$$p_{\text{opt}}^{\text{ps}}(w) = \frac{v_1(w)^{1/2}}{v_1(w)^{1/2} + v_0(w)^{1/2}}.$$

D. Estimators

D.1. The case of transportation

(i) Under the CIR design. If the conditional outcome mean function $m(a, w)$ and the density ratio $r(w)$ were known, a locally efficient estimator of Δ^* could be obtained by solving $\sum_{i=1}^{n+n^*} \psi_{\text{CIR}}^{\text{tr}}(O_i) = 0$. The resulting "estimator" is

$$(n^*)^{-1} \sum_{i=1}^{n+n^*} (1 - Z_i)\delta(W_i^*) + (n^*)^{-1} \sum_{i=1}^{n+n^*} \frac{Z_i(1-\gamma)A_i r(W_i)\{Y_i - m(1, W_i)\}}{\gamma\pi}$$
$$- (n^*)^{-1} \sum_{i=1}^{n+n^*} \frac{Z_i(1-\gamma)(1-A_i)r(W_i)\{Y_i - m(0, W_i)\}}{\gamma(1-\pi)}.$$

Recall that $e^\circ(w) = \text{pr}(Z = 1 \mid W^\circ = w)$ and $r(w) = \{\text{pr}(Z = 1)(1 - e^\circ(w))\}/\{\text{pr}(Z = 0)e^\circ(w)\}$. In practice, both $e^\circ(w)$ and $m(a, w)$ are unknown and must be estimated. Suppose that parametric models are specified for the propensity score $e^\circ(w)$ and the outcome regression $m(a, w)$. Substituting the resulting estimators into the above expression yields a plug-in estimator of Δ^*. The final estimator of Δ^* is doubly robust in the sense that it is consistent if either the propensity score model or the outcome regression model is correctly specified.

An alternative strategy estimates Δ^* using a debiased machine learning (DML) approach (Chernozhukov et al., 2018). Instead of imposing parametric model specification, the DML approach estimates the nuisance functions $m(a, w)$ and $e^\circ(w)$ using a machine learning algorithm or an ensemble of algorithms. Let $\hat{m}(a, w)$ and $\hat{e}^\circ(w)$ denote the resulting estimators. A cross-fitting procedure is then used to construct the estimator of Δ^*. To implement cross-fitting, we partition the combined sample from the trial and target populations into L subsamples of approximately equal size and define $[n + n^*] = \{1, \cdots, n + n^*\}$. Without loss of generality, assume that the first

n observations correspond to the trial population. Let $S_i, i = 1, \cdots, n + n^*$, be a random sample from the discrete uniform distribution on $[L] = \{1, \cdots, L\}$, and define the ℓth subsample as $\mathcal{I}_\ell = \{i \in [n + n^*] : S_i = \ell\}$. For each fold $\ell \in [L]$, estimate $e^\circ(w)$ using observations in the complement set $[1 : (n + n^*)]\backslash\mathcal{I}_\ell$, yielding the estimator $\hat{e}^{\circ(-\ell)}(w)$. Similarly, estimate $m(a, w)$ using the trial observations in the complement set $[1 : n]\backslash\mathcal{I}_\ell$, which produces the estimator $\hat{m}^{-(\ell)}(a, w)$. Combining the fold-specific nuisance estimators yields the cross-fitted DML estimator of Δ^*:

$$
\begin{aligned}
\hat{\Delta}^{*\text{tr}}_{\text{CIR}} = (n^*)^{-1} \sum_{i=1}^{n+n^*} (1 - Z_i)\{\hat{m}^{-(S_i)}(1, W_i^*) - \hat{m}^{-(S_i)}(0, W_i^*)\} \\
+ (n^*)^{-1} \sum_{i=1}^{n+n^*} \frac{Z_i A_i \{1 - \hat{e}^{\circ(-S_i)}(W_i)\}\{Y_i - \hat{m}^{-(S_i)}(1, W_i)\}}{\pi \hat{e}^{\circ(-S_i)}(W_i)} \\
- (n^*)^{-1} \sum_{i=1}^{n+n^*} \frac{Z_i (1 - A_i)\{1 - \hat{e}^{\circ(-S_i)}(W_i)\}\{Y_i - \hat{m}^{-(S_i)}(0, W_i)\}}{(1 - \pi)\hat{e}^{\circ(-S_i)}(W_i)}.
\end{aligned}
\tag{S1}
$$

Under mild regularity conditions, $\hat{\Delta}^{*\text{tr}}_{\text{CIR}}$ is consistent and asymptotic normal. Furthermore, if the nuisance function estimators satisfy suitable convergence rate conditions, the estimator attains the semiparametric efficiency bound (Chernozhukov et al., 2018).

(ii) Under the CDR design. Under the CDR design, analogous plug-in and cross-fitted DML estimators for Δ^* can be obtained by replacing the constant treatment assignment probability π with the propensity score $p(w)$. The corresponding DML estimator becomes

$$
\begin{aligned}
\hat{\Delta}^{*\text{tr}}_{\text{CDR}} = (n^*)^{-1} \sum_{i=1}^{n+n^*} (1 - Z_i)\{\hat{m}^{-(S_i)}(1, W_i^*) - \hat{m}^{-(S_i)}(0, W_i^*)\} \\
+ (n^*)^{-1} \sum_{i=1}^{n+n^*} \frac{Z_i A_i \{1 - \hat{e}^{\circ(-S_i)}(W_i)\}\{Y_i - \hat{m}^{-(S_i)}(1, W_i)\}}{p(W_i) \hat{e}^{\circ(-S_i)}(W_i)} \\
- (n^*)^{-1} \sum_{i=1}^{n+n^*} \frac{Z_i (1 - A_i)\{1 - \hat{e}^{\circ(-S_i)}(W_i)\}\{Y_i - \hat{m}^{-(S_i)}(0, W_i)\}}{\{1 - p(W_i)\}\hat{e}^{\circ(-S_i)}(W_i)}.
\end{aligned}
$$

D.2. The case of generalization

(i) Under the CIR design. A similar strategy applies to the generalization setting. If the propensity score for trial participation $e(w)$ and the conditional outcome mean model $m(a, w)$ were known, a

locally efficient estimator can be obtained by solving $\sum_{i=1}^{N} \psi_{\text{CIR}}^{\text{gen}}(O_i) = 0$. The resulting "estimator" is

$$N^{-1}\sum_{i=1}^{N}\{m(1,W_i^*) - m(0,W_i^*)\} + N^{-1}\sum_{i=1}^{N}\frac{Z_iA_i\{Y_i - m(1,W_i)\}}{\pi e(W_i)} - N^{-1}\sum_{i=1}^{N}\frac{Z_i(1-A_i)\{Y_i - m(0,W_i)\}}{(1-\pi)e(W_i)}.$$

In practice, the nuisance functions $e(w)$ and $m(a,w)$ must be estimated. One possible approach is to specify parametric models for both functions and substitutes the resulting estimators into the above expression to obtain a plug-in estimator of Δ^*. Alternatively, the DML framework can again be used.

We first partition the sample from the target population into L subsamples of approximately equal size. Define $[N] = \{1,\cdots,N\}$ and generate fold indicators $S_i, i = 1,\cdots,N$ randomly from the uniform distribution on $[L] = \{1,\cdots,L\}$. The ℓth fold is $\mathcal{I}_\ell = \{i \in [N] : S_i = \ell\}$. For each $\ell \in [L]$, estimate the trial participation propensity score $e(w)$ using the observations in the complement set $[1:N]\backslash\mathcal{I}_\ell$, yielding $\hat{e}^{(-\ell)}(w)$. Estimate outcome model $m(a,w)$ using the trial observations in the complement set $[1:n]\backslash\mathcal{I}_\ell$, which produces $\hat{m}^{-(\ell)}(a,w)$. The cross-fitted DML estimator of Δ^* is then obtained as

$$\begin{aligned}\hat{\Delta}_{\text{CIR}}^{*\text{gen}} = N^{-1}&\sum_{i=1}^{N}\{\hat{m}^{-(S_i)}(1,W_i^*) - \hat{m}^{-(S_i)}(0,W_i^*)\}\\ &+ N^{-1}\sum_{i=1}^{N}\frac{Z_iA_i\{Y_i - \hat{m}^{-(S_i)}(1,W_i)\}}{\pi\hat{e}^{-(S_i)}(W_i)} - N^{-1}\sum_{i=1}^{N}\frac{Z_i(1-A_i)\{Y_i - \hat{m}^{-(S_i)}(0,W_i)\}}{(1-\pi)\hat{e}^{-(S_i)}(W_i)}.\end{aligned}$$

(ii) Under the CDR design. Under the CDR design, the construction of plug-in and cross-fitted DML estimators are similar. Replacing the constant treatment assignment probability π with the propensity score $p(w)$ yields the cross-fitted DML estimator

$$\begin{aligned}\hat{\Delta}_{\text{CDR}}^{*\text{gen}} = N^{-1}&\sum_{i=1}^{N}\{\hat{m}^{-(S_i)}(1,W_i^*) - \hat{m}^{-(S_i)}(0,W_i^*)\}\\ &+ N^{-1}\sum_{i=1}^{N}\frac{Z_iA_i\{Y_i - \hat{m}^{-(S_i)}(1,W_i)\}}{p(W_i)\hat{e}^{-(S_i)}(W_i)} - N^{-1}\sum_{i=1}^{N}\frac{Z_i(1-A_i)\{Y_i - \hat{m}^{-(S_i)}(0,W_i)\}}{\{1-p(W_i)\}\hat{e}^{-(S_i)}(W_i)}.\end{aligned}$$

D.3. The case of post-stratification

(i) Under the CIR design. In the case of post-stratification, estimation of Δ^* proceeds by first estimating the subgroup-specific treatment effects Δ_k. Efficient estimation of Δ_k can be achieved by applying an efficient estimator to the subgroup of trial participants with $W_i \in \mathcal{W}_k$. Solving the estimating equation $\sum_{i=1}^n \psi_{\text{CIR},k}^{\text{ps}}(O) = 0$ and substituting a model-based estimator of $m(a,w)$, $m(a,w;\hat{\beta})$, yields the estimator

$$\frac{1}{\sum_{i=1}^n I(W_i \in \mathcal{W}_k)} \sum_{i=1}^n I(W_i \in \mathcal{W}_k)\Big[\{m(1,W_i;\hat{\beta}) - m(0,W_i;\hat{\beta})\} + \frac{A_i\{Y_i - m(1,W_i;\hat{\beta})\}}{\pi} - \frac{(1-A_i)\{Y_i - m(0,W_i;\hat{\beta})\}}{1-\pi}\Big].$$

The estimator of Δ^* is obtained by combining the subgroup-specific estimators using the weights $\{\tau_k^*, k = 1, \cdots, K\}$. Correct specification of the outcome regression model ensures that the plug-in estimator of Δ^* is locally efficient. A DML estimator of Δ^* can also be constructed by applying a cross-fitting procedure similar to the procedures described in Sections D.1 and D.2 separately within each subgroup $\mathcal{W}_k$.

(ii) Under the CDR design. For the CDR design, the plug-in and DML estimators follow the same structure as the corresponding estimators under the CIR design. The only modification involves replacing the constant treatment assignment probability π with the propensity score $p(w)$.

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Table S1: Additional simulation results for ATE estimation: empirical bias, standard deviation (SD), median standard error (SE), and coverage proportion (CP).

	Δ				Δ^*_{tr}				Δ^*_{gen}				Δ^*_{ps}			
Allocation	Bias	SD	SE	CP	Bias	SD	SE	CP	Bias	SD	SE	CP	Bias	SD	SE	CP
$\pi = 0.5$	0.004	0.118	0.118	0.947	-0.006	0.178	0.159	0.931	-0.006	0.131	0.120	0.939	0.004	0.122	0.123	0.948
$\pi_{\text{opt}} \approx 0.693$	-0.001	0.111	0.111	0.949	-0.008	0.220	0.184	0.920	0.001	0.148	0.128	0.926	0.002	0.146	0.141	0.937
$\pi^{\text{tr}}_{\text{opt}} \approx 0.275$	-0.002	0.149	0.148	0.945	-0.003	0.166	0.158	0.940	-0.001	0.143	0.135	0.942	0.002	0.128	0.126	0.948
$\pi^{\text{gen}}_{\text{opt}} \approx 0.440$	-0.002	0.121	0.123	0.954	0.004	0.174	0.159	0.937	-0.002	0.131	0.123	0.949	0.001	0.119	0.120	0.952
$\pi^{\text{ps}}_{\text{opt}} \approx 0.389$	-0.001	0.130	0.128	0.945	-0.004	0.170	0.155	0.935	-0.002	0.134	0.123	0.945	0.004	0.118	0.120	0.957
$p_{\text{opt}}(W)$	0.002	0.103	0.102	0.945	-0.004	0.157	0.146	0.936	-0.003	0.117	0.108	0.946	0.004	0.114	0.113	0.947

Δ: ATE in the trial population; Δ^*_{tr}: estimand for transportation; Δ^*_{gen}: estimand for generalization; Δ^*_{ps}: estimand for post-stratification.

Table S2: Additional simulation results for LMR estimation: empirical bias, standard deviation (SD), median standard error (SE), and coverage proportion (CP).

	$\Delta(\log)$				$\Delta^*_{\mathrm{tr}}(\log)$				$\Delta^*_{\mathrm{gen}}(\log)$				$\Delta^*_{\mathrm{ps}}(\log)$			
Allocation	Bias	SD	SE	CP	Bias	SD	SE	CP	Bias	SD	SE	CP	Bias	SD	SE	CP
$\pi = 0.5$	0.001	0.217	0.216	0.950	-0.009	0.345	0.310	0.924	-0.029	0.255	0.229	0.922	-0.002	0.253	0.244	0.939
$\pi_{\mathrm{opt}} \approx 0.684$	0.005	0.210	0.209	0.948	0.012	0.344	0.317	0.934	-0.009	0.231	0.216	0.932	0.002	0.244	0.240	0.944
$\pi^{\mathrm{tr}}_{\mathrm{opt}} \approx 0.584$	-0.002	0.218	0.211	0.947	0.001	0.334	0.310	0.932	-0.019	0.243	0.217	0.932	-0.005	0.251	0.239	0.936
$\pi^{\mathrm{gen}}_{\mathrm{opt}} \approx 0.725$	0.002	0.211	0.210	0.953	0.017	0.343	0.323	0.938	-0.011	0.230	0.214	0.935	0.007	0.253	0.243	0.941
$\pi^{\mathrm{ps}}_{\mathrm{opt}} \approx 0.633$	0.001	0.212	0.210	0.953	-0.005	0.339	0.310	0.934	-0.012	0.237	0.215	0.926	0.005	0.242	0.240	0.945
$p_{\mathrm{opt}}(W)$	0.003	0.191	0.189	0.948	0.023	0.357	0.307	0.935	-0.005	0.201	0.188	0.940	0.002	0.215	0.211	0.944
$p^{\mathrm{tr}}_{\mathrm{opt}}(W)$	-0.010	0.232	0.235	0.943	-0.007	0.298	0.276	0.938	-0.015	0.214	0.205	0.944	-0.010	0.260	0.240	0.935
$p^{\mathrm{gen}}_{\mathrm{opt}}(W)$	-0.004	0.200	0.197	0.947	0.005	0.315	0.279	0.935	-0.008	0.197	0.186	0.939	0.003	0.217	0.214	0.948
$p^{\mathrm{ps}}_{\mathrm{opt}}(W)$	0.002	0.201	0.192	0.946	0.019	0.330	0.286	0.935	-0.007	0.201	0.186	0.935	0.000	0.213	0.212	0.944

$\Delta(\log)$: LMR in the trial population; $\Delta^*_{\mathrm{tr}}(\log)$: estimand for transportation; $\Delta^*_{\mathrm{gen}}(\log)$: estimand for generalization; $\Delta^*_{\mathrm{ps}}(\log)$: estimand for post-stratification.