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Supporting Information for

"Efficient and robust methods for causally interpretable meta-analysis: transporting inferences from multiple randomized trials to a target population"

by

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Web Appendix A Identification of potential outcome means

A.1 Identification using the collection of trials

THEOREM 1 (Identification of potential outcome means): *Under conditions A1 through A5, the potential outcome mean in the target population under treatment* $a \in \mathcal{A}$, $\mathrm{E}[Y^a|R=0]$, *is identifiable by the observed data functional*

$$\psi(a) \equiv \mathrm{E}\left[\,\mathrm{E}[Y|X, R=1, A=a]\big|R=0\right], \tag{S1}$$

which can be equivalently expressed as

$$\psi(a) = \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\frac{I(R=1,A=a)Y\Pr[R=0|X]}{\Pr[R=1|X]\Pr[A=a|X,R=1]}\right]. \tag{S2}$$

Proof. By conditions *A4* and *A5* from the main text and the definition of R, we have $\mathrm{E}[Y^a|X=x,S=s] = \mathrm{E}[Y^a|X=x,S=0] = \mathrm{E}[Y^a|X=x,R=0]$, for every $s \in \mathcal{S}$ and every x such that $f(x,S=0) \neq 0$. This implies that the conditional counterfactual outcome means in the trials are all equal between them and with the conditional counterfactual outcome mean in the target population, that is, for every $a \in \mathcal{A}$ and every x such that $f(x,S=0) \neq 0$,

$$\begin{aligned}\mathrm{E}[Y^a|X=x,S=1] = \ldots = \mathrm{E}[Y^a|X=x,S=m] \\ = \mathrm{E}[Y^a|X=x,R=1] \\ = \mathrm{E}[Y^a|X=x,R=0],\end{aligned}$$

where we use $\mathrm{E}[Y^a|X=x,R=1]$ to denote the common, across-trials, potential outcome mean under treatment a, conditional on covariates, in the the collection of trials $\mathcal{S}$.

Using conditions *A1* through *A3*, the above result implies that, for every $a \in \mathcal{A}$ and every x such that $f(x,S=0) \neq 0$,

$$\begin{aligned}\mathrm{E}[Y|X=x,S=1,A=a] = \ldots = \mathrm{E}[Y|X=x,S=m,A=a] \\ = \mathrm{E}[Y|X=x,R=1,A=a] \\ = \mathrm{E}[Y^a|X=x,R=0],\end{aligned} \tag{S3}$$

where $\mathrm{E}[Y|X = x, R = 1, A = a]$ is the common, across-trials, outcome mean among individuals receiving treatment a, conditional on covariates, in the the collection $\mathcal{S}$.

Thus, using the law of total expectation and the second-to-last equality in (S3) we obtain

$$\begin{aligned}\mathrm{E}[Y^a|R=0] &= \mathrm{E}\left[\,\mathrm{E}[Y^a|X,R=0]\big|R=0\right] \\ &= \mathrm{E}\left[\,\mathrm{E}[Y|X,R=1,A=a]\big|R=0\right] \\ &\equiv \psi(a),\end{aligned}$$

which completes the derivation of the result in (6). We can re-express (6) to use weighting,

$$\begin{aligned}\psi(a) &\equiv \mathrm{E}\left[\,\mathrm{E}[Y|X,R=1,A=a]\big|R=0\right] \\ &= \mathrm{E}\left[\,\mathrm{E}\left[\frac{I(R=1,A=a)Y}{\Pr[R=1|X]\Pr[A=a|X,R=1]}\Big|X\right]\,\middle|\,R=0\right] \\ &= \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=0)\,\mathrm{E}\left[\frac{I(R=1,A=a)Y}{\Pr[R=1|X]\Pr[A=a|X,R=1]}\Big|X\right]\,\right] \\ &= \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\,\mathrm{E}\left[\frac{I(R=1,A=a)Y\Pr[R=0|X]}{\Pr[R=1|X]\Pr[A=a|X,R=1]}\Big|X\right]\,\right] \\ &= \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\frac{I(R=1,A=a)Y\Pr[R=0|X]}{\Pr[R=1|X]\Pr[A=a|X,R=1]}\right].\end{aligned}$$

Remark 1: The derivation of (7) from (6) relies on the positivity conditions and does not use any causal (counterfactual) conditions. Thus, the result holds whether or not $\psi(a)$ has a causal interpretation.

It is worth noting that we can derive the main identification result of Theorem 1 in an alternative way, using the implications of the identifiability conditions derived in Section 3. We now give this alternative proof.

Proof. [Alternative proof of the first part of Theorem 1] We have shown that identifiability

conditions *A2* and *A4* imply that $Y^a \perp\!\!\!\perp R|X$ and $Y^a \perp\!\!\!\perp (S, A)|(X, R = 1)$. Furthermore, the second of these independence conditions implies that $Y^a \perp\!\!\!\perp A|(X, R = 1)$.

Using the law of total expectation, the independence conditions $Y^a \perp\!\!\!\perp R|X$ and $Y^a \perp\!\!\!\perp A|(X, R = 1)$, and identifiability condition *A1*, we obtain

$$\begin{aligned}
\mathrm{E}[Y^a|R=0] &= \mathrm{E}\left[\mathrm{E}[Y^a|X, R=0]\middle|R=0\right] \\
&= \mathrm{E}\left[\mathrm{E}[Y^a|X, R=1]\middle|R=0\right] \\
&= \mathrm{E}\left[\mathrm{E}[Y^a|X, R=1, A=a]\middle|R=0\right] \\
&= \mathrm{E}\left[\mathrm{E}[Y|X, R=1, A=a]\middle|R=0\right] \\
&\equiv \psi(a).
\end{aligned}$$

Here, all quantities are well-defined because positivity condition *A5* implies that $\Pr[R = 1|X = x] > 0$ for every x such that $f(x, R = 0) \neq 0$; and positivity condition *A3* implies that $\Pr[A = a|X = x, R = 1] > 0$ for every treatment $a \in \mathcal{A}$, and every x such that $f(x, R = 1) \neq 0$.

Web Appendix B Identification under weaker positivity conditions

B.1 Weaker positivity conditions for Theorem 1

The alternative proof of Theorem 1 at the end of the previous section of the Appendix, suggests that identification is possible under weaker positivity conditions.

To show this, suppose that the independence conditions $Y^a \perp\!\!\!\perp R|X$ and $Y^a \perp\!\!\!\perp A|(X, R = 1)$ hold. That can be the case *either* because identifiability conditions *A2* and *A4* hold (as in the main text) *or* because the independence conditions are taken as primitive assumptions (i.e., not derived from others). These independence conditions have intuitive interpretations and their plausibility can be evaluated using background scientific knowledge: $Y^a \perp\!\!\!\perp R|X$ means that participation in the collection of trials is independent of the potential outcome given the baseline covariates; $Y^a \perp\!\!\!\perp A|(X, R = 1)$ means that treatment is "unconfounded" in the collection of trials, conditional on baseline covariates.

Suppose, then, that $Y^a \perp\!\!\!\perp R|X$ and $Y^a \perp\!\!\!\perp A|(X, R = 1)$ hold. The alternative proof of Theorem 1 suggests that $\psi(a)$ is identifiable under the following positivity conditions:

A3. Positivity of the probability of treatment in the collection of trials:* for each treatment $a \in \mathcal{A}$, if $f(x, R = 1) \neq 0$, then $\Pr[A = a|X = x, R = 1] > 0$.

A5. Positivity of the probability of participation in the collection of trials:* if $f(x, R = 0) \neq 0$, then $\Pr[R = 1|X = x] > 0$.

We can now state the following theorem:

THEOREM 2 (Identification under weaker positivity conditions): *If* $Y^a \perp\!\!\!\perp R|X$ *and* $Y^a \perp\!\!\!\perp A|(X, R = 1)$ *and conditions A1, A3*, and A5* hold, then the potential outcome mean in the target population under treatment* $a \in \mathcal{A}$, $\mathrm{E}[Y^a|R = 0]$, *is identifiable by* $\psi(a)$.

Proof. The proof follows from the arguments presented in the *Alternative proof of the first part of Theorem 1* at the end of Web Appendix A.

B.2 Weaker overlap and exchangeability conditions for potential outcome means

Let $\mathcal{X}_s$ for $s \in \{0, 1, \ldots, m\}$ denote the support of the random vector X in trial $S = s$. That is,

$$\mathcal{X}_s \equiv \{x : f(x|S = s) > 0\}.$$

Recall that for each covariate pattern $X = x$ that can occur in collection of trials, that is, for each $x \in \bigcup_{s \in \mathcal{S}} \mathcal{X}_s$, we define $\mathcal{S}_x$ as the subset of trials in $\mathcal{S}$ such that x belongs in their support set. That is,

$$\mathcal{S}_x \equiv \{s : s \in \mathcal{S}, x \in \mathcal{X}_s\}.$$

Note that $\mathcal{S}_x \subseteq \mathcal{S}$; intuitively, $\mathcal{S}_x$ denotes the subset of trials where the covariate pattern $X = x$ can occur.

B.2.1 Identifiability conditions

Using this additional notation, consider the following identifiability conditions:

A4†. Exchangeability in mean over S: For every x such that $f(x|S = 0) > 0$ and every $s \in \mathcal{S}_x$,

$$\mathrm{E}[Y^a|X = x, S = 0] = \mathrm{E}[Y^a|X = x, S = s].$$

A5†. Overlap of the collection $\mathcal{S}$ with the target population: $\bigcup_{s \in \mathcal{S}} (\mathcal{X}_s \cap \mathcal{X}_0) = \mathcal{X}_0$.

Note that $\bigcup_{s \in \mathcal{S}} (\mathcal{X}_s \cap \mathcal{X}_0) = \mathcal{X}_0 \iff \mathcal{X}_0 \cap \big(\bigcup_{s \in \mathcal{S}} \mathcal{X}_s \big) = \mathcal{X}_0 \implies \mathcal{X}_0 \subseteq \bigcup_{s \in \mathcal{S}} \mathcal{X}_s$; where the equivalence follows from claim 3 of Proposition A.4. in Proschan and Shaw (2018).

B.2.2 Identification

THEOREM 3 (Identification under weaker overlap and exchangeability conditions): *Under identifiability conditions A1 through A3, A4† and A5†, for every $a \in \mathcal{A}$,* $\mathrm{E}[Y^a|S = 0]$ *is*

identifiable by

$$\phi(a) \equiv \int \mathrm{E}\left[Y|X=x, I(S \in \mathcal{S}_x)=1, A=a\right] f(x|S=0)dx.$$

Proof. By condition $A5^{\dagger}$, for each x such that $f(x, S=0) \neq 0$, there exists a non-empty set $\mathcal{S}_x$ of trials where $X=x$ has positive density.

By condition $A4^{\dagger}$, for each x such that $f(x, S=0) \neq 0$ and for each trial $s \in \mathcal{S}_x$,

$$\mathrm{E}[Y^a|X=x, S=s] = \mathrm{E}[Y^a|X=x, S=0].$$

For each x such that $f(x, S=0) \neq 0$ and for each trial $s \in \mathcal{S}_x$, by definition,

$$\mathrm{E}[Y^a|X=x, S=s] = \mathrm{E}[Y^a|X=x, S=s, I(S \in \mathcal{S}_x)=1].$$

Thus, for each x such that $f(x, S=0) \neq 0$ and for each trial in $s \in \mathcal{S}_x$,

$$\mathrm{E}[Y^a|X=x, S=0] = \mathrm{E}[Y^a|X=x, S=s, I(S \in \mathcal{S}_x)=1]. \tag{S4}$$

By conditions *A2* and *A3*, for each x such that $f(x, S=0) \neq 0$ and for each trial $s \in \mathcal{S}_x$,

$$\mathrm{E}[Y^a|X=x, S=s, I(S \in \mathcal{S}_x)=1] = \mathrm{E}[Y^a|X=x, S=s, I(S \in \mathcal{S}_x)=1, A=a].$$

By condition *A1*, and the above result, for each x such that $f(x, S=0) \neq 0$ and for each trial $s \in \mathcal{S}_x$,

$$\mathrm{E}[Y^a|X=x, S=s, I(S \in \mathcal{S}_x)=1] = \mathrm{E}[Y|X=x, S=s, I(S \in \mathcal{S}_x)=1, A=a].$$

Combining the above result and the result in (S4), for each x such that $f(x, S=0) \neq 0$ and for each trial $s \in \mathcal{S}_x$, we obtain

$$\mathrm{E}[Y^a|X=x, S=0] = \mathrm{E}[Y|X=x, S=s, I(S \in \mathcal{S}_x)=1, A=a].$$

The left hand side above does not depend on s, so it has to be that, for each x such that $f(x, S=0) \neq 0$ and for each trial $s \in \mathcal{S}_x$,

$$\mathrm{E}[Y|X=x, S=s, I(S \in \mathcal{S}_x)=1, A=a] = \mathrm{E}[Y|X=x, I(S \in \mathcal{S}_x)=1, A=a].$$

Thus, we can conclude that that for every x such that $f(x, S = 0) \neq 0$,

$$\mathrm{E}[Y^a|X = x, S = 0] = \mathrm{E}[Y|X = x, I(S \in \mathcal{S}_x) = 1, A = a]. \tag{S5}$$

From the law of total expectation,

$$\mathrm{E}[Y^a|S = 0] = \int\limits_{x:f(x,S=0)\neq 0} \mathrm{E}\left[Y^a|X = x, S = 0\right] f(x|S = 0)dx$$

Using the result in (S5), completes the proof, because

$$\mathrm{E}[Y^a|S = 0] = \int\limits_{x:f(x,S=0)\neq 0} \mathrm{E}[Y|X = x, I(S \in \mathcal{S}_x) = 1, A = a] f(x|S = 0)dx \equiv \phi(a).$$

Web Appendix C Identification of average treatment effects under exchangeability in effect measure

In this Appendix, we discuss identification of average treatment effects under the weaker condition of exchangeability in effect measure. Consider the following condition:

A4‡. *Exchangeability in effect measure over S:* for every pair of treatments a and a', with $a \in \mathcal{A}$ and $a' \in \mathcal{A}$, for every $s \in \mathcal{S}$, and for every x such that $f(x, S = s) > 0$, we have $\mathrm{E}[Y^a - Y^{a'}|X = x, S = s] = \mathrm{E}[Y^a - Y^{a'}|X = x, R = 0]$.

Remark 2: Condition A4‡ is weaker than condition A4, in the sense that A4 $\implies$ A4‡, but A4‡ $\not\Longrightarrow$ A4.

We now use condition *A4*‡ to derive more general identification results for average treatment effects. Note that, under this condition, the potential outcome means are no longer identifiable.

Theorem 4 (Identification under exchangeability in effect measure): *Under conditions A1 through A3, A4*‡*, and A5, the average treatment effect in the target population comparing treatments* $a \in \mathcal{A}$ *and* $a' \in \mathcal{A}$, $\mathrm{E}[Y^a - Y^{a'}|R = 0]$, *is identifiable by the observed data functional*

$$\rho(a, a') \equiv \mathrm{E}\left[\tau(a, a'; X)\middle|R = 0\right] \tag{S6}$$

where,

$$\tau(a, a'; X) \equiv \mathrm{E}[Y|X, S = s, A = a] - \mathrm{E}[Y|X, S = s, A = a'],$$

does not vary over $s \in \mathcal{S}$. *Furthermore,* $\rho(a, a')$ *can be re-expressed as*

$$\rho(a, a') = \frac{1}{\Pr[R = 0]} \mathrm{E}\left[w(a, a'; R, X, S, A)Y\right], \tag{S7}$$

where

$$w(a, a'; R, X, S, A) \equiv \left(\frac{I(R = 1, A = a)}{\Pr[A = a|X, S, R = 1]} - \frac{I(R = 1, A = a')}{\Pr[A = a'|X, S, R = 1]} \right) \frac{\Pr[R = 0|X]}{\Pr[R = 1|X]}.$$

Proof. For each specific $s^* \in \mathcal{S}$ and for X values in the the support of the target population, we have

$$\begin{aligned} &\mathrm{E}[Y^a - Y^{a'}|X, R = 0] \\ &\quad = \mathrm{E}[Y^a - Y^{a'}|X, S = s^*] \\ &\quad = \mathrm{E}[Y^a|X, S = s^*] - \mathrm{E}[Y^{a'}|X, S = s^*] \\ &\quad = \mathrm{E}[Y^a|X, S = s^*, A = a] - \mathrm{E}[Y^{a'}|X, S = s^*, A = a'] \\ &\quad = \mathrm{E}[Y|X, S = s^*, A = a] - \mathrm{E}[Y|X, S = s^*, A = a']. \end{aligned} \tag{S8}$$

Because the above result, by assumption, holds for every trial $s^* \in \mathcal{S}$, we conclude that

$$\mathrm{E}[Y^a - Y^{a'}|X, R = 0] = \mathrm{E}[Y|X, S = s, A = a] - \mathrm{E}[Y|X, S = s, A = a'], \text{ for every } s \in \mathcal{S}.$$

Using $\tau(a, a'; X)$ to denote the common conditional mean difference function,

$$\tau(a, a'; X) \equiv \mathrm{E}[Y|X, S = s, A = a] - \mathrm{E}[Y|X, S = s, A = a'], \text{ for every } s \in \mathcal{S},$$

we have, by assumption $A4^{\ddagger}$,

$$\tau(a, a'; X) = \mathrm{E}[Y^a - Y^{a'}|X, R = 0].$$

Taking expectations we obtain

$$\begin{aligned} \mathrm{E}[Y^a - Y^{a'}|R = 0] &= \mathrm{E}\left[\mathrm{E}[Y^a - Y^{a'}|X, R = 0] \middle| R = 0 \right] \\ &= \mathrm{E}\left[\tau(a, a'; X) \middle| R = 0 \right] \\ &\equiv \rho(a, a'), \end{aligned} \tag{S9}$$

which establishes that the average treatment effect in the target population is identified by $\rho(a, a')$.

Furthermore, for each specific $s^* \in \mathcal{S}$, using the result in (S8), we have

$$
\begin{aligned}
&\mathrm{E}[Y^a - Y^{a'}|X, R=0] \\
&\quad = \mathrm{E}[Y|X, S=s^*, A=a] - \mathrm{E}[Y|X, S=s^*, A=a'] \\
&\quad = \mathrm{E}\left[\frac{I(A=a)Y}{\Pr[A=a|X,S=s^*,R=1]}\Big|X, S=s^*\right] - \mathrm{E}\left[\frac{I(A=a')Y}{\Pr[A=a'|X,S=s^*,R=1]}|X, S=s^*\right] \\
&\quad = \mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S=s^*,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S=s^*,R=1]}\right) Y\Big|X, S=s^*\right] \\
&\quad = \mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]}\right) Y\Big|X, S=s^*\right].
\end{aligned}
$$

Because the above result, by assumption, holds for every trial $s^* \in \mathcal{S}$, we conclude that

$$
\begin{aligned}
&\mathrm{E}[Y^a - Y^{a'}|X, R=0] = \\
&\qquad \mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]}\right) Y\Big|X, R=1\right].
\end{aligned} \tag{S10}
$$

Taking expectations, then, we obtain

$$
\begin{aligned}
&\mathrm{E}[Y^a - Y^{a'}|R=0] \\
&\quad = \mathrm{E}\left[\,\mathrm{E}[Y^a - Y^{a'}|X, R=0]\big|R=0\right] \\
&\quad = \mathrm{E}\left[\mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]}\right) Y\Big|X, R=1\right]\Big|R=0\right].
\end{aligned} \tag{S11}
$$

Combining the above result with (S9) we obtain the expression for $\rho(a, a')$ in (S7):

$$
\begin{aligned}
&\rho(a, a') \\
&\quad = \mathrm{E}\left[\mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]}\right) Y\Big|X, R=1\right]\Big|R=0\right] \\
&\quad = \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=0)\,\mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]}\right) Y\Big|X, R=1\right]\right] \\
&\quad = \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\Pr[R=0|X]\,\mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]}\right) Y\Big|X, R=1\right]\right] \\
&\quad = \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]}\right) \frac{I(R=1)Y\Pr[R=0|X]}{\Pr[R=1|X]}\Big|X\right]\right] \\
&\quad = \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]}\right) \frac{I(R=1)Y\Pr[R=0|X]}{\Pr[R=1|X]}\right].
\end{aligned}
$$

REMARK 3: Yet another expression for $\rho(a, a')$ can be obtained,

$$
\begin{aligned}
&\rho(a, a') \\
&= \mathrm{E}\left[\mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]} \right) Y \middle| X, R=1 \right] \middle| R=0 \right] \\
&= \mathrm{E}\left[\mathrm{E}\left[\mathrm{E}\left[\left(\frac{I(A=a)}{\Pr[A=a|X,S,R=1]} - \frac{I(A=a')}{\Pr[A=a'|X,S,R=1]} \right) Y \middle| X, R=1, S \right] \middle| X, R=1 \right] \middle| R=0 \right] \\
&= \mathrm{E}\left[\mathrm{E}\left[\frac{\mathrm{E}\left[I(A=a) Y | X, R=1, S \right]}{\Pr[A=a|X,S,R=1]} \middle| X, R=1 \right] \middle| R=0 \right] \\
&\qquad - \mathrm{E}\left[\mathrm{E}\left[\frac{\mathrm{E}\left[I(A=a') Y | X, R=1, S \right]}{\Pr[A=a'|X,S,R=1]} \middle| X, R=1 \right] \middle| R=0 \right] \\
&= \mathrm{E}\Big[\mathrm{E}\big[\mathrm{E}[Y|X,R=1,S,A=a] - \mathrm{E}[Y|X,R=1,S,A=a'] \big| X, R=1 \big] \Big| R=0 \Big],
\end{aligned}
$$

where, it is worth noting that under the identifiability conditions the difference $\mathrm{E}[Y|X, R = 1, S, A = a] - \mathrm{E}[Y|X, R = 1, S, A = a']$ does not depend on S (even if each of its two component conditional expectations does depend on S).

Web Appendix D Influence function for $\psi(a)$

D.1 Influence function under the nonparametric model

Recall that under the nonparametric model, $\mathcal{M}_{\text{np}}$, for the observable data, $O = (X, S, R, A, Y)$, the density of the law of the observable data can be written as

$$p(r, x, s, a, y) = p(r)p(x|r)p(s|x, r)p(a|r, x, s)p(y|r, x, s, a).$$

Under this model, the tangent space is the Hilbert space of mean zero random variables with finite variance and can be decomposed as $L_2^0 = \Lambda_R \oplus \Lambda_{X|R} \oplus \Lambda_{S|R,X} \oplus \Lambda_{A|R,X,S} \oplus \Lambda_{Y|R,X,S,A}$. We now derive the influence function for $\psi(a)$ under this nonparametric model.

Recall that

$$\psi(a) \equiv \mathrm{E}\left[\mathrm{E}[Y|X, R = 1, A = a]\middle|R = 0\right].$$

We will use the path differentiability of $\psi(a)$ to obtain the efficient influence function under the non-parametric model for the observed data (Bickel et al., 1993). To do so, we examine the derivative of $\psi_{p_t}(a)$ with respect to t; where the subscript p_t denotes the dependence of $\psi(a)$ on a one-dimensional parametric sub-model p_t, indexed by $t \in [0, 1)$, with $t = 0$ denoting the "true" data law.

$$\begin{aligned}
\left.\frac{\partial \psi_{p_t}(a)}{\partial t}\right|_{t=0} &= \left.\frac{\partial}{\partial t}\,\mathrm{E}_{p_t}\left[\mathrm{E}_{p_t}[Y|X, R = 1, A = a]\middle|R = 0\right]\right|_{t=0} \\
&= \left.\frac{\partial}{\partial t}\,\mathrm{E}_{p_t}\left[\mathrm{E}_{p_0}[Y|X, R = 1, A = a]\middle|R = 0\right]\right|_{t=0} \\
&\qquad + \mathrm{E}_{p_0}\left[\left.\frac{\partial}{\partial t}\,\mathrm{E}_{p_t}[Y|X, R = 1, A = a]\right|_{t=0}\middle|R = 0\right].
\end{aligned}$$

Working on each of the two terms in the last expression above,

$$\frac{\partial}{\partial t}\,\mathrm{E}_{p_t}\left[\,\mathrm{E}_{p_0}[Y|X,R=1,A=a]\big|R=0\right]\Big|_{t=0}$$
$$=\frac{1}{\Pr_{p_0}[R=0]}\,\mathrm{E}_{p_0}\left[I(R=0)\Big\{\,\mathrm{E}_{p_0}[Y|X,R=1,A=a]-\psi_{p_0}(a)\Big\}u(O)\right],\ \text{and}$$
$$\mathrm{E}_{p_0}\left[\frac{\partial}{\partial t}\,\mathrm{E}_{p_t}[Y|X,R=1,A=a]\Big|_{t=0}\Big|R=0\right]$$
$$=\frac{1}{\Pr_{p_0}[R=0]}\,\mathrm{E}_{p_0}\left[\frac{I(R=1,A=a)\Pr_{p_0}[R=0|X]}{\Pr_{p_0}[R=1|X]\Pr_{p_0}[A=a|X,R=1]}\big\{Y-\mathrm{E}_{p_0}[Y|X,R=1,A=a]\big\}u(O)\right],$$

where $u(O)$ denotes the score of the observable data, $O=(R,X,S,A,Y)$.

Combining these results,

$$\frac{\partial\psi_{p_t}(a)}{\partial t}\Big|_{t=0}=\mathrm{E}_{p_0}\left[\frac{1}{\Pr_{p_0}[R=0]}\left\{I(R=0)\Big\{\,\mathrm{E}_{p_0}[Y|X,R=1,A=a]-\psi_{p_0}(a)\Big\}\right.\right.$$
$$\left.\left.+\frac{I(R=1,A=a)\Pr_{p_0}[R=0|X]}{\Pr_{p_0}[R=1|X]\Pr_{p_0}[A=a|X,R=1]}\Big\{Y-\mathrm{E}_{p_0}[Y|X,R=1,A=a]\Big\}\right\}u(O)\right].$$

It follows that the influence function of $\psi(a)$, under the nonparametric model is

$$\Psi^1_{p_0}(a)=\frac{1}{\Pr_{p_0}[R=0]}\left\{I(R=0)\Big\{\,\mathrm{E}_{p_0}[Y|X,R=1,A=a]-\psi_{p_0}(a)\Big\}\right.$$
$$\left.+\frac{I(R=1,A=a)\Pr_{p_0}[R=0|X]}{\Pr_{p_0}[R=1|X]\Pr_{p_0}[A=a|X,R=1]}\Big\{Y-\mathrm{E}_{p_0}[Y|X,R=1,A=a]\Big\}\right\}.$$

D.2 Influence function under semiparametric models

We need to examine the implications for the influence function of $\psi(a)$ of two kinds of restrictions on the law of the observed data. First, we need to examine the impact of the independence condition $Y \perp\!\!\!\perp S|(X,R,A=a)$, derived in Section 3 of the main text. Second, we need to examine the impact of knowing the probability of treatment, that is, of knowing the conditional density $p(a|x,s)$; this might be the case, for example, because treatment assignment in the collection of trial $\mathcal{S}$ is under the control of the investigators and only a single (non-experimental) treatment is available in the target population.

D.2.1 Incorporating the restriction $Y \perp\!\!\!\perp S|(X, R, A = a)$

Consider the semiparamatric model $\mathcal{M}_{\text{semi}}$ that incorporates the restriction $Y \perp\!\!\!\perp S|(X, R, A = a)$. Under this model, the density of the law of the observable data is

$$p(r, x, s, a, y) = p(r)p(x|r)p(s|x, r)p(a|r, x, s)p(y|r, x, a),$$

and we obtain the decomposition $\Lambda_{\text{semi}} = \Lambda_R \oplus \Lambda_{X|R} \oplus \Lambda_{S|R,X} \oplus \Lambda_{A|R,X,S} \oplus \Lambda_{Y|R,X,A}$. Rewriting the influence function under the nonparametric model as the sum of two terms, we obtain

$$\begin{aligned}\Psi^1_{p_0}(a) = &\frac{I(R = 1, A = a)\Pr_{p_0}[R = 0|X]}{\Pr_{p_0}[R = 0]\Pr_{p_0}[R = 1|X]\Pr_{p_0}[A = a|X, R = 1]}\Big\{Y - \mathrm{E}_{p_0}[Y|X, R = 1, A = a]\Big\} \\ &+ \frac{I(R = 0)}{\Pr_{p_0}[R = 0]}\Big\{\mathrm{E}_{p_0}[Y|X, R = 1, A = a] - \psi_{p_0}(a)\Big\}.\end{aligned} \tag{S12}$$

It is easy to see that the first term is a function of (R, X, A, Y) that has mean zero conditional on (R, X, A), and thus belongs to $\Lambda_{Y|R,X,A}$. Furthermore, the second term in the above expression is a function of (R, X) that has mean zero conditional on R, and thus belongs to $\Lambda_{X|R}$. From these observations we conclude that he influence function under the semiparametric model, $\Psi^1_{p_0}(a)$, belongs to Λ_{semi} and its projection onto that space is equal to itself. We can conclude that the unique influence function under the nonparametric model, $\Psi^1_{p_0}(a)$, is also the efficient influence function under the semiparametric model $\mathcal{M}_{\text{semi}}$.

D.2.2 Knowing the probability of treatment

Consider now the semiparametric model $\mathcal{M}^*_{\text{semi}}$ for the law of the observed data where the restriction $Y \perp\!\!\!\perp S|(X, R, A = a)$ holds and $p(a|x, s)$ is known. Then, we obtain the decomposition $\Lambda^*_{\text{semi}} = \Lambda_R \oplus \Lambda_{X|R} \oplus \Lambda_{S|R,X} \oplus \Lambda_{Y|R,X,A}$. Considering the expression for the influence function in (S12), it is again easy to see that the first term is a function of (R, X, A, Y) that has mean zero conditional on (R, X, A) thus it belongs to $\Lambda_{Y|R,X,A}$. Furthermore, the second term in the above expression is a function of (R, X) that has mean zero conditional on R thus it belongs to $\Lambda_{X|R}$. Thus, the influence function under the nonparametric model, $\Psi^1_{p_0}(a)$,

belongs to Λ^*_{semi} and its projection onto that space is equal to itself. We can conclude that the unique influence function under the nonparametric model, $\Psi^1_{p_0}(a)$, is also the efficient influence function under the semiparametric model $\mathcal{M}^*_{\text{semi}}$.

D.3 Influence function under the biased sampling model

Following the arguments in Breslow et al. (2000), the identifiability of $\psi(a)$ under the biased sampling model implies that influence functions for $\psi(a)$ under sampling from $q(x, s, a, y)$ are equivalent to those under sampling from $p(x, s, a, y)$, with densities from $q(x, s, a, y)$ replacing those under $p(x, s, a, y)$ (see Kennedy et al. (2015) for a similar argument in the context of matched cohort studies and Dahabreh et al. (2020) in the context of transporting inferences from a single randomized trial). Specifically, under the biased sampling model, the influence function of $\psi(a)$ is

$$\Psi^1_{q_0}(a) = \frac{1}{\Pr_{q_0}[R=0]}\Bigg\{ I(R=0)\Big\{ \mathrm{E}_{q_0}[Y|X, R=1, A=a] - \psi_{q_0}(a)\Big\} \\ + \frac{I(R=1, A=a)\Pr_{q_0}[R=0|X]}{\Pr_{q_0}[R=1|X]\Pr_{q_0}[A=a|X, R=1]}\Big\{Y - \mathrm{E}_{q_0}[Y|X, R=1, A=a]\Big\}\Bigg\},$$

which we have used to obtain the estimator $\widehat{\psi}(a)$, given in the main text.

Web Appendix E Asymptotic properties of the estimator

THEOREM 5: *If assumptions* (i) *through* (iv) *hold, then*

(1) $\widehat{\psi}_{aug}(a) \xrightarrow{a.s.} \psi(a)$*; and*

(2) $\widehat{\psi}_{aug}(a)$ *has the asymptotic representation*

$$\sqrt{n}\big(\widehat{\psi}_{aug}(a) - \psi(a)\big) = \mathbb{G}_n\big(H(\gamma^*, g_a^*(X), e_a^*(X), p^*(X))\big) + Rem + o_P(1), \tag{S13}$$

where $\mathbb{G}_n\big(H(\gamma^*, g_a^*(X), e_a^*(X), p^*(X))\big)$ *is asymptotically normal and*

$$Rem \leqslant \sqrt{n} O_P\Bigg(\Big(\big|\big|\Pr[R=1|X] - \widehat{p}(X)\big|\big|_2 + \big|\big|\Pr[A=a|X,R=1] - \widehat{e}_a(X)\big|\big|_2\Big) \times \big|\big|\widehat{g}_a(X) - \mathrm{E}[Y|X,R=1,A=a]\big|\big|_2\Bigg). \tag{S14}$$

Proof. Unless otherwise stated, in this proof, all convergence results refer to convergence almost surely.

As $n \longrightarrow \infty$,

$$\widehat{\psi}_{\text{aug}}(a) \longrightarrow \frac{1}{\Pr[R=0]}\Bigg\{ \mathrm{E}\left[I(R=1,A=a)\frac{1-p^*(X)}{p^*(X)e_a^*(X)}\Big\{Y - g_a^*(X)\Big\}\right] + \mathrm{E}\left[I(R=0)g_a^*(X)\right]\Bigg\}. \tag{S15}$$

We now study the asymptotic limit of the right-hand-side of (S15) by considering the two different cases presented in Assumption (iv).

Case 1: correct specification of the model for the probability of participation in any trial and the treatment assignment model. Assume that the models for $\Pr[R=1|X]$ and $\Pr[A=a|X,R=1]$ are correctly specified, such that

$$\widehat{p}(X) \longrightarrow p^*(X) = \Pr[R=1|X]$$

$$\widehat{e}_a(X) \longrightarrow e_a^*(X) = \Pr[A=a|X,R=1].$$

We do not, however, assume that the asymptotic limit $g_a^*(X)$ is equal the corresponding target parameter. Using iterated expectation arguments for the right-hand-side of (S15) we

obtain

$$\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=1,A=a)\frac{\Pr[R=0|X]}{\Pr[R=1|X]Pr[A=a|X,R=1]}g_a^*(X)\right]$$
$$=\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\Pr[R=0|X]g_a^*(X)\right]$$

and

$$\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=0)g_a^*(X)\right]=\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\Pr[R=0|X]g_a^*(X)\right].$$

Hence,

$$\begin{aligned}
\widehat{\psi}_{\text{aug}}(a) &\longrightarrow \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=1,A=a)\frac{1-p^*(X)}{p^*(X)e_a^*(X)}Y\right]\\
&=\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=1,A=a)\frac{1-\Pr[R=1|X]}{\Pr[R=1|X]\Pr[A=a|X,R=1]}Y\right]\\
&=\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\Pr[R=0|X]\,\mathrm{E}\left[\frac{I(A=a)}{\Pr[A=a|X,R=1]}Y\middle|X,R=1\right]\right]\\
&=\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=0)\,\mathrm{E}\left[\frac{I(A=a)}{\Pr[A=a|X,R=1]}Y\middle|X,R=1\right]\right]\\
&=\mathrm{E}\left[\mathrm{E}\left[\frac{I(A=a)}{\Pr[A=a|X,R=1]}Y\middle|X,R=1\right]\middle|R=0\right]\\
&=\mathrm{E}\left[\,\mathrm{E}[Y|X,R=1,A=a]\middle|R=0\right]\\
&\equiv\psi(a).
\end{aligned}$$

Thus, if the models for $\Pr[R=1|X]$ and $\Pr[A=a|X,R=1]$ are correctly specified, then $\widehat{\psi}_{\text{aug}}(a)\longrightarrow\psi(a)$.

Case 2: correct specification of the model for the outcome mean. Assume that the model for $\mathrm{E}[Y|X,R=1,A=a]$ is correctly specified, such that

$$\widehat{g}_a(X)\longrightarrow g_a^*(X)=\mathrm{E}[Y|X,R=1,A=a].$$

We do not, however, assume that the asymptotic limit $p^*(X)$ equals $\Pr[R=1|X]$ or that the asymptotic limit $e_a^*(X)$ equals $\Pr[A=a|X,R=1]$. Using iterated expectation arguments

for the right-hand-side of (S15) we obtain

$$\begin{aligned}
&\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=1,A=a)\frac{1-p^*(X)}{p^*(X)e_a^*(X)}\Big\{Y-g_a^*(X)\Big\}\right]\\
&=\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\mathrm{E}\left[I(R=1,A=a)\frac{1-p^*(X)}{p^*(X)e_a^*(X)}\Big\{Y-\mathrm{E}[Y|X,A=a,R=1]\Big\}\right]\,\middle|\,X\right]\\
&=\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\Pr[R=1,A=a|X]\frac{1-p^*(X)}{p^*(X)e_a^*(X)}\Big\{\,\mathrm{E}[Y|X,A=a,R=1]-\mathrm{E}[Y|X,A=a,R=1]\Big\}\right]\\
&=0.
\end{aligned}$$

Hence,

$$\begin{aligned}
\widehat{\psi}_{\text{aug}}(a)\longrightarrow\;&\frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=0)g_a^*(X)\right]\\
&=\mathrm{E}\Big[\,\mathrm{E}[Y|X,R=1,A=a]\big|R=0\Big]\\
&\equiv\psi(a).
\end{aligned}$$

Thus, if the model for $\mathrm{E}[Y|X,R=1,A=a]$ is correctly specified, then $\widehat{\psi}_{\text{aug}}(a)\longrightarrow\psi(a)$.

This completes the proof of part (a) of Theorem 5.

Part (b): Decompose

$$\begin{aligned}
\sqrt{n}\big(\widehat{\psi}_{\text{aug}}(a)-\psi(a)\big)=\;&\Big\{\mathbb{G}_n\big(H(\widehat{\gamma},\widehat{g}_a(X),\widehat{e}_a(X),\widehat{p}(X))\big)\\
&-\mathbb{G}_n\big(H(\gamma^*,g_a^*(X),e_a^*(X),p^*(X))\big)\Big\}\\
&+\mathbb{G}_n\big(H(\gamma^*,g_a^*(X),e_a^*(X),p^*(X))\big)\\
&+\underbrace{\sqrt{n}\Big\{\,\mathrm{E}\left[H(\widehat{\gamma},\widehat{g}_a(X),\widehat{e}_a(X),\widehat{p}(X))\right]-\psi(a)\Big\}}_{T}.
\end{aligned}$$

By assumption (i),

$$\mathbb{G}_n\big(H(\widehat{\gamma},\widehat{g}_a(X),\widehat{e}_a(X),\widehat{p}(X))\big)-\mathbb{G}_n\big(H(\gamma^*,g_a^*(X),e_a^*(X),p^*(X))\big)=o_P(1).$$

By the central limit theorem, $\mathbb{G}_n\big(H(\gamma^*,g_a^*(X),e_a^*(X),p^*(X))\big)$ is asymptotically normal. Hence, the asymptotic distribution of $\widehat{\psi}_{\text{aug}}(a)$ depends on the behavior of the term T.

Using assumption (iv), the double robustness of $\widehat{\psi}_{\text{aug}}(a)$, and that $\sqrt{n}\big(\widehat{\gamma}-\Pr[R=0]^{-1}\big)=$

$O_P(1)$, we have

$$T = \sqrt{n}\Bigg\{ \frac{1}{\Pr[R=0]} \Bigg\{ \underbrace{\mathrm{E}\left[I(R=0)\widehat{g}_a(X)\right]}_{T_1} + \underbrace{\mathrm{E}\left[I(R=1,A=a)\frac{1-\widehat{p}(X)}{\widehat{e}_a(X)\widehat{p}(X)}\big\{Y-\widehat{g}_a(X)\big\}\right]}_{T_2} \Bigg\} - \psi(a) \Bigg\} + o_P(1).$$

By iterated expectation,

$$\begin{aligned} T_1 &= \mathrm{E}\left[\mathrm{E}\left[I(R=0)\widehat{g}_a(X)\middle|X\right]\right] \\ &= \mathrm{E}\left[\Pr[R=0|X]\widehat{g}_a(X)\right]. \end{aligned}$$

By iterated expectation,

$$\begin{aligned} \sqrt{n}T_2 &= \sqrt{n}\,\mathrm{E}\left[I(R=1,A=a)\frac{1-\widehat{p}(X)}{\widehat{e}_a(X)\widehat{p}(X)}\big\{Y-\widehat{g}_a(X)\big\}\right] \\ &= \sqrt{n}\,\mathrm{E}\left[\mathrm{E}\left[I(R=1,A=a)\frac{1-\widehat{p}(X)}{\widehat{e}_a(X)\widehat{p}(X)}\big\{Y-\widehat{g}_a(X)\big\}\middle|X\right]\right] \\ &= \sqrt{n}\,\mathrm{E}\left[\mathrm{E}\left[\frac{1-\widehat{p}(X)}{\widehat{p}(X)}\frac{I(A=a)}{\widehat{e}_a(X)}\Pr[R=1|X]\big\{Y-\widehat{g}_a(X)\big\}\middle|X,R=1\right]\right] \\ &= \sqrt{n}\,\mathrm{E}\left[\mathrm{E}\left[\frac{1-\widehat{p}(X)}{\widehat{p}(X)\widehat{e}_a(X)}\Pr[R=1,A=a|X]\big\{Y-\widehat{g}_a(X)\big\}\middle|X,R=1,A=a\right]\right] \\ &= \sqrt{n}\,\mathrm{E}\left[\mathrm{E}\left[\frac{1-\widehat{p}(X)}{\widehat{p}(X)\widehat{e}_a(X)}\Pr[R=1,A=a|X]\left\{\mathrm{E}\left[Y|X,R=1,A=a\right]-\widehat{g}_a(X)\right\}\right]\right] \\ &= \sqrt{n}\,\mathrm{E}\left[\frac{1-\widehat{p}(X)}{\widehat{p}(X)\widehat{e}_a(X)}\Pr[R=1,A=a|X]\left\{\mathrm{E}\left[Y|X,R=1,A=a\right]-\widehat{g}_a(X)\right\}\right] \end{aligned}$$

Rewriting $\psi(a)$ gives

$$\begin{aligned} \psi(a) &= \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[I(R=0)\,\mathrm{E}\left[Y|X,R=1,A=a\right]\right] \\ &= \frac{1}{\Pr[R=0]}\,\mathrm{E}\left[\Pr[R=0|X]\,\mathrm{E}\left[Y|X,R=1,A=a\right]\right]. \end{aligned}$$

Combining the above results,

$$
\begin{aligned}
T = \sqrt{n}\frac{1}{\Pr[R=0]}\Bigg\{ \mathrm{E}\Bigg[\Bigg(\Pr[R=0|X] - \Pr[R=1|X]\frac{1-\widehat{p}(X)}{\widehat{p}(X)}\frac{\Pr[A=a|X,R=1]}{\widehat{e}_a(X)} \Bigg) \\
\times \big(\widehat{g}_a(X) - \mathrm{E}\big[Y|X,R=1,A=a\big]\big) \Bigg] \Bigg\} + o_P(1) \\
= \sqrt{n}\frac{1}{\Pr[R=0]}\Bigg\{ \mathrm{E}\Bigg[\Bigg(\frac{\Pr[R=0|X]\widehat{p}(X) - \Pr[R=1|X](1-\widehat{p}(X))}{\widehat{p}(X)} \\
- \frac{\Pr[R=1|X](1-\widehat{p}(X))}{\widehat{p}(X)\widehat{e}_a(X)}\big(\Pr[A=a|X,R=1] - \widehat{e}_a(X)\big) \Bigg) \\
\times \big(\widehat{g}_a(X) - \mathrm{E}\big[Y|X,R=1,A=a\big]\big) \Bigg] \Bigg\} + o_P(1) \\
\leqslant \sqrt{n} O_P\Bigg(\Big(\big|\big| \Pr[R=1|X] - \widehat{p}(X) \big|\big|_2 + \big|\big| \Pr[A=a|X,R=1] - \widehat{e}_a(X) \big|\big|_2 \Big) \\
\times \big|\big| \widehat{g}_a(X) - \mathrm{E}\big[Y|X,R=1,A=a\big] \big|\big|_2 \Bigg) + o_P(1),
\end{aligned}
$$

where the last step follows from the Cauchy-Schwartz inequality.

Web Appendix F Complete simulation results

Table S1: Bias estimates based on 10,000 simulation runs; all sample size scenarios; the probability of treatment in the collection of trials was estimated by averaging the trial-specific treatment probabilities.

a	n	$\sum_{s=1}^{3} n_s$	Balanced	TxAM varies	$\widehat{\psi}_{\text{aug}}(a)$	$\widehat{\psi}_{\text{g}}(a)$	$\widehat{\psi}_{\text{w}}(a)$
1	10000	1000	Yes	No	-0.0006	0.0002	-0.0106
1	10000	1000	Yes	Yes	-0.0029	-0.0013	0.0107
1	10000	1000	No	No	-0.0011	-0.0000	-0.0174
1	10000	1000	No	Yes	0.0015	-0.0002	0.0129
1	10000	2000	Yes	No	0.0022	0.0003	-0.0011
1	10000	2000	Yes	Yes	0.0004	-0.0003	-0.0026
1	10000	2000	No	No	-0.0006	-0.0001	-0.0082
1	10000	2000	No	Yes	0.0011	0.0002	-0.0067
1	10000	5000	Yes	No	-0.0003	0.0002	-0.0030
1	10000	5000	Yes	Yes	-0.0002	-0.0001	0.0035
1	10000	5000	No	No	-0.0003	0.0004	-0.0013
1	10000	5000	No	Yes	-0.0004	0.0002	-0.0012
1	100000	1000	Yes	No	-0.0032	-0.0005	0.0046
1	100000	1000	Yes	Yes	0.0028	0.0007	-0.0074
1	100000	1000	No	No	-0.0020	-0.0010	-0.0272
1	100000	1000	No	Yes	-0.0006	-0.0022	-0.0064
1	100000	2000	Yes	No	-0.0003	0.0002	-0.0104
1	100000	2000	Yes	Yes	-0.0002	0.0008	0.0102
1	100000	2000	No	No	-0.0012	-0.0002	-0.0074
1	100000	2000	No	Yes	0.0009	0.0013	0.0039
1	100000	5000	Yes	No	0.0013	0.0000	0.0041
1	100000	5000	Yes	Yes	-0.0001	-0.0001	-0.0020
1	100000	5000	No	No	0.0002	0.0001	0.0035
1	100000	5000	No	Yes	0.0007	0.0003	0.0026
0	10000	1000	Yes	No	-0.0003	-0.0003	0.0008
0	10000	1000	Yes	Yes	-0.0003	0.0016	0.0075
0	10000	1000	No	No	0.0006	0.0005	0.0183
0	10000	1000	No	Yes	-0.0016	-0.0006	0.0087
0	10000	2000	Yes	No	0.0001	0.0008	0.0083
0	10000	2000	Yes	Yes	0.0006	0.0004	0.0060
0	10000	2000	No	No	0.0010	-0.0003	0.0002
0	10000	2000	No	Yes	0.0002	0.0005	0.0106
0	10000	5000	Yes	No	-0.0000	0.0003	-0.0001
0	10000	5000	Yes	Yes	-0.0000	0.0004	0.0050
0	10000	5000	No	No	0.0001	0.0005	0.0011
0	10000	5000	No	Yes	-0.0007	-0.0005	0.0059
0	100000	1000	Yes	No	-0.0048	-0.0017	-0.0048
0	100000	1000	Yes	Yes	0.0019	-0.0005	-0.0001
0	100000	1000	No	No	-0.0027	-0.0014	-0.0114
0	100000	1000	No	Yes	-0.0014	-0.0019	0.0093
0	100000	2000	Yes	No	0.0013	0.0005	0.0016
0	100000	2000	Yes	Yes	-0.0009	-0.0000	0.0034
0	100000	2000	No	No	-0.0009	-0.0003	0.0064
0	100000	2000	No	Yes	0.0012	0.0006	0.0109
0	100000	5000	Yes	No	0.0005	0.0004	-0.0027
0	100000	5000	Yes	Yes	-0.0001	0.0005	-0.0016
0	100000	5000	No	No	0.0021	0.0004	0.0031
0	100000	5000	No	Yes	-0.0012	-0.0002	-0.0029

In the column titled *Balanced*, *Yes* denotes scenarios in which the trials had on average equal sample sizes; *No* denotes scenarios with unequal trial sample sizes. In the column titled *TxAM varies*, *Yes* denotes scenarios in which the treatment assignment mechanism varied across trials; *No* denotes scenarios in which the mechanism did not vary.

Table S2: Variance estimates based on 10,000 simulation runs; all sample size scenarios; the probability of treatment in the collection of trials was estimated by averaging the trial-specific treatment probabilities.

a	n	$\sum_{s=1}^{3} n_s$	Balanced	TxAM varies	$\widehat{\psi}_{\text{aug}}(a)$	$\widehat{\psi}_{\text{g}}(a)$	$\widehat{\psi}_{\text{w}}(a)$
1	10000	1000	Yes	No	0.0245	0.0075	0.6253
1	10000	1000	Yes	Yes	0.0213	0.0068	0.7541
1	10000	1000	No	No	0.0238	0.0076	0.6189
1	10000	1000	No	Yes	0.0222	0.0075	0.5392
1	10000	2000	Yes	No	0.0105	0.0038	0.2893
1	10000	2000	Yes	Yes	0.0084	0.0035	0.1945
1	10000	2000	No	No	0.0101	0.0038	0.2167
1	10000	2000	No	Yes	0.0088	0.0038	0.1925
1	10000	5000	Yes	No	0.0038	0.0019	0.0727
1	10000	5000	Yes	Yes	0.0033	0.0019	0.0616
1	10000	5000	No	No	0.0038	0.0020	0.0742
1	10000	5000	No	Yes	0.0035	0.0019	0.0613
1	100000	1000	Yes	No	0.0308	0.0080	0.8841
1	100000	1000	Yes	Yes	0.0258	0.0072	0.5534
1	100000	1000	No	No	0.0299	0.0080	0.6868
1	100000	1000	No	Yes	0.0276	0.0077	0.7559
1	100000	2000	Yes	No	0.0144	0.0039	0.3316
1	100000	2000	Yes	Yes	0.0120	0.0035	0.3610
1	100000	2000	No	No	0.0143	0.0039	0.4028
1	100000	2000	No	Yes	0.0128	0.0037	0.2925
1	100000	5000	Yes	No	0.0052	0.0015	0.1469
1	100000	5000	Yes	Yes	0.0043	0.0014	0.1042
1	100000	5000	No	No	0.0057	0.0015	0.1449
1	100000	5000	No	Yes	0.0048	0.0015	0.1203
0	10000	1000	Yes	No	0.0274	0.0073	0.2967
0	10000	1000	Yes	Yes	0.0336	0.0083	0.6326
0	10000	1000	No	No	0.0214	0.0074	0.2273
0	10000	1000	No	Yes	0.0259	0.0077	0.3620
0	10000	2000	Yes	No	0.0103	0.0039	0.1165
0	10000	2000	Yes	Yes	0.0131	0.0042	0.1509
0	10000	2000	No	No	0.0101	0.0039	0.1136
0	10000	2000	No	Yes	0.0118	0.0040	0.1551
0	10000	5000	Yes	No	0.0039	0.0019	0.0433
0	10000	5000	Yes	Yes	0.0048	0.0021	0.0540
0	10000	5000	No	No	0.0038	0.0020	0.0400
0	10000	5000	No	Yes	0.0044	0.0020	0.0480
0	100000	1000	Yes	No	0.0306	0.0080	0.4502
0	100000	1000	Yes	Yes	0.0493	0.0091	1.2177
0	100000	1000	No	No	0.0346	0.0078	0.5608
0	100000	1000	No	Yes	0.0389	0.0082	0.5444
0	100000	2000	Yes	No	0.0151	0.0039	0.1873
0	100000	2000	Yes	Yes	0.0198	0.0043	0.2699
0	100000	2000	No	No	0.0146	0.0038	0.1663
0	100000	2000	No	Yes	0.0218	0.0040	0.3243
0	100000	5000	Yes	No	0.0055	0.0015	0.0703
0	100000	5000	Yes	Yes	0.0080	0.0018	0.1796
0	100000	5000	No	No	0.0052	0.0016	0.0643
0	100000	5000	No	Yes	0.0072	0.0016	0.1091

In the column titled *Balanced*, *Yes* denotes scenarios in which the trials had on average equal sample sizes; *No* denotes scenarios with unequal trial sample sizes. In the column titled *TxAM varies*, *Yes* denotes scenarios in which the treatment assignment mechanism varied across trials; *No* denotes scenarios in which the mechanism did not vary.

Table S3: Bias estimates based on 10,000 simulation runs; all sample size scenarios; the probability of treatment in the collection of trials was estimated by (misspecified) logistic regression with main covariate effects, fit over all trials.

a	n	$\sum_{s=1}^{3} n_s$	Balanced	TxAM varies	$\widehat{\psi}_{\text{aug}}(a)$	$\widehat{\psi}_{\text{g}}(a)$	$\widehat{\psi}_{\text{w}}(a)$
1	10000	1000	Yes	No	-0.0006	0.0002	-0.0105
1	10000	1000	Yes	Yes	-0.0027	-0.0013	-0.0746
1	10000	1000	No	No	-0.0011	-0.0000	-0.0212
1	10000	1000	No	Yes	0.0013	-0.0002	-0.0219
1	10000	2000	Yes	No	0.0021	0.0003	-0.0002
1	10000	2000	Yes	Yes	0.0003	-0.0003	-0.0761
1	10000	2000	No	No	-0.0006	-0.0001	-0.0082
1	10000	2000	No	Yes	0.0010	0.0002	-0.0378
1	10000	5000	Yes	No	-0.0003	0.0002	-0.0032
1	10000	5000	Yes	Yes	-0.0002	-0.0001	-0.0622
1	10000	5000	No	No	-0.0002	0.0004	-0.0001
1	10000	5000	No	Yes	-0.0003	0.0002	-0.0305
1	100000	1000	Yes	No	-0.0031	-0.0005	0.0044
1	100000	1000	Yes	Yes	0.0023	0.0007	-0.1003
1	100000	1000	No	No	-0.0019	-0.0010	-0.0287
1	100000	1000	No	Yes	-0.0007	-0.0022	-0.0475
1	100000	2000	Yes	No	-0.0002	0.0002	-0.0105
1	100000	2000	Yes	Yes	-0.0001	0.0008	-0.0820
1	100000	2000	No	No	-0.0011	-0.0002	-0.0075
1	100000	2000	No	Yes	0.0011	0.0013	-0.0355
1	100000	5000	Yes	No	0.0013	0.0000	0.0035
1	100000	5000	Yes	Yes	-0.0001	-0.0001	-0.0866
1	100000	5000	No	No	0.0001	0.0001	0.0036
1	100000	5000	No	Yes	0.0007	0.0003	-0.0337
0	10000	1000	Yes	No	-0.0005	-0.0003	0.0014
0	10000	1000	Yes	Yes	-0.0004	0.0016	-0.0989
0	10000	1000	No	No	0.0007	0.0005	0.0169
0	10000	1000	No	Yes	-0.0015	-0.0006	-0.0198
0	10000	2000	Yes	No	0.0000	0.0008	0.0084
0	10000	2000	Yes	Yes	0.0003	0.0004	-0.0893
0	10000	2000	No	No	0.0009	-0.0003	-0.0000
0	10000	2000	No	Yes	0.0002	0.0005	-0.0171
0	10000	5000	Yes	No	-0.0001	0.0003	-0.0005
0	10000	5000	Yes	Yes	-0.0002	0.0004	-0.0847
0	10000	5000	No	No	0.0001	0.0005	0.0017
0	10000	5000	No	Yes	-0.0006	-0.0005	-0.0207
0	100000	1000	Yes	No	-0.0045	-0.0017	-0.0052
0	100000	1000	Yes	Yes	0.0020	-0.0005	-0.1137
0	100000	1000	No	No	-0.0025	-0.0014	-0.0109
0	100000	1000	No	Yes	-0.0016	-0.0019	-0.0262
0	100000	2000	Yes	No	0.0015	0.0005	0.0010
0	100000	2000	Yes	Yes	-0.0010	-0.0000	-0.1093
0	100000	2000	No	No	-0.0010	-0.0003	0.0055
0	100000	2000	No	Yes	0.0011	0.0006	-0.0205
0	100000	5000	Yes	No	0.0004	0.0004	-0.0032
0	100000	5000	Yes	Yes	-0.0003	0.0005	-0.1133
0	100000	5000	No	No	0.0022	0.0004	0.0028
0	100000	5000	No	Yes	-0.0014	-0.0002	-0.0335

In the column titled *Balanced*, *Yes* denotes scenarios in which the trials had on average equal sample sizes; *No* denotes scenarios with unequal trial sample sizes. In the column titled *TxAM varies*, *Yes* denotes scenarios in which the treatment assignment mechanism varied across trials; *No* denotes scenarios in which the mechanism did not vary.

Table S4: Variance estimates based on 10,000 simulation runs; all sample size scenarios; the probability of treatment in the collection of trials was estimated by (misspecified) logistic regression with main covariate effects, fit over all trials.

a	n	$\sum_{s=1}^{3} n_s$	Balanced	TxAM varies	$\widehat{\psi}_{\text{aug}}(a)$	$\widehat{\psi}_{\text{g}}(a)$	$\widehat{\psi}_{\text{w}}(a)$
1	10000	1000	Yes	No	0.0242	0.0075	0.6533
1	10000	1000	Yes	Yes	0.0169	0.0068	0.4393
1	10000	1000	No	No	0.0236	0.0076	0.5509
1	10000	1000	No	Yes	0.0207	0.0075	0.4837
1	10000	2000	Yes	No	0.0105	0.0038	0.3004
1	10000	2000	Yes	Yes	0.0074	0.0035	0.1517
1	10000	2000	No	No	0.0099	0.0038	0.2179
1	10000	2000	No	Yes	0.0084	0.0038	0.1759
1	10000	5000	Yes	No	0.0038	0.0019	0.0747
1	10000	5000	Yes	Yes	0.0031	0.0019	0.0502
1	10000	5000	No	No	0.0038	0.0020	0.0775
1	10000	5000	No	Yes	0.0033	0.0019	0.0570
1	100000	1000	Yes	No	0.0304	0.0080	0.8595
1	100000	1000	Yes	Yes	0.0219	0.0072	0.4252
1	100000	1000	No	No	0.0289	0.0080	0.6763
1	100000	1000	No	Yes	0.0246	0.0077	0.6526
1	100000	2000	Yes	No	0.0144	0.0039	0.3403
1	100000	2000	Yes	Yes	0.0101	0.0035	0.2738
1	100000	2000	No	No	0.0140	0.0039	0.4126
1	100000	2000	No	Yes	0.0118	0.0037	0.2674
1	100000	5000	Yes	No	0.0052	0.0015	0.1492
1	100000	5000	Yes	Yes	0.0037	0.0014	0.0800
1	100000	5000	No	No	0.0057	0.0015	0.1481
1	100000	5000	No	Yes	0.0045	0.0015	0.1092
0	10000	1000	Yes	No	0.0257	0.0073	0.2766
0	10000	1000	Yes	Yes	0.0559	0.0083	1.8462
0	10000	1000	No	No	0.0213	0.0074	0.2304
0	10000	1000	No	Yes	0.0280	0.0077	0.4209
0	10000	2000	Yes	No	0.0103	0.0039	0.1136
0	10000	2000	Yes	Yes	0.0179	0.0042	0.2624
0	10000	2000	No	No	0.0100	0.0039	0.1151
0	10000	2000	No	Yes	0.0129	0.0040	0.1892
0	10000	5000	Yes	No	0.0039	0.0019	0.0449
0	10000	5000	Yes	Yes	0.0061	0.0021	0.0921
0	10000	5000	No	No	0.0038	0.0020	0.0407
0	10000	5000	No	Yes	0.0047	0.0020	0.0570
0	100000	1000	Yes	No	0.0308	0.0080	0.4596
0	100000	1000	Yes	Yes	0.0808	0.0091	1.5679
0	100000	1000	No	No	0.0336	0.0078	0.5078
0	100000	1000	No	Yes	0.0442	0.0082	0.7170
0	100000	2000	Yes	No	0.0152	0.0039	0.1992
0	100000	2000	Yes	Yes	0.0308	0.0043	0.5804
0	100000	2000	No	No	0.0143	0.0038	0.1700
0	100000	2000	No	Yes	0.0258	0.0040	0.4181
0	100000	5000	Yes	No	0.0055	0.0015	0.0732
0	100000	5000	Yes	Yes	0.0144	0.0018	0.5480
0	100000	5000	No	No	0.0052	0.0016	0.0640
0	100000	5000	No	Yes	0.0084	0.0016	0.1516

In the column titled *Balanced*, *Yes* denotes scenarios in which the trials had on average equal sample sizes; *No* denotes scenarios with unequal trial sample sizes. In the column titled *TxAM varies*, *Yes* denotes scenarios in which the treatment assignment mechanism varied across trials; *No* denotes scenarios in which the mechanism did not vary.

Web Appendix G Additional HALT-C results

Table S5: Baseline characteristics in the HALT-C trial, stratified by R.

	$R = 0$	$R = 1$
Number of individuals	199	749
Baseline platelets	171.30 (66.10)	163.44 (65.09)
Age in years	50.06 (7.53)	50.77 (7.20)
Female	60 (30.2)	211 (28.2)
Received pegylated interferon	66 (33.2)	206 (27.5)
White	115 (57.8)	560 (74.8)
Baseline white blood cell count	5.81 (1.92)	5.72 (1.84)
Used recreational drugs	91 (45.7)	338 (45.1)
Received a transfusion	77 (38.7)	298 (39.8)
Body mass index, weight (kg)/height(m)^2	29.93 (5.34)	29.92 (5.54)
Creatinine, mg/dl	0.84 (0.17)	0.85 (0.17)
Ever smoked	155 (77.9)	558 (74.5)
Received interferon and ribavirin	151 (75.9)	627 (83.7)
Reported diabetes	50 (25.1)	116 (15.5)
Serum ferritin, ng/ml	360.18 (378.14)	379.43 (442.94)
Ultrasound evidence of splenomegaly (%)	77 (38.7)	242 (32.3)
Ever drank alcohol	173 (86.9)	611 (81.6)
Hemoglobin, g/dl	14.97 (1.42)	14.98 (1.43)
Aspartate aminotransferase, U/L	92.72 (48.81)	86.88 (61.67)

Results reported as mean (standard deviation) for continuous variables and count (percentage) for binary variables.
kg, kilogram; m, meter; mg, milligram; dl, deciliter; ml, milliliter; g, gram; U/L, units per liter.

Table S6: Baseline characteristics in the HALT-C trial, stratified by S.

Source of data, S	1	2	3	4	5
Number of individuals	48	97	130	66	76
Baseline platelets, $\times$ 1000/mm^3	175.17 (77.85)	162.65 (67.50)	168.19 (68.58)	167.64 (58.12)	178.58 (64.82)
Age in years	51.33 (7.04)	50.23 (6.56)	51.34 (6.40)	50.83 (8.35)	49.86 (6.57)
Female	11 (22.9)	29 (29.9)	32 (24.6)	21 (31.8)	23 (30.3)
Received pegylated interferon	5 (10.4)	25 (25.8)	33 (25.4)	15 (22.7)	19 (25.0)
White	28 (58.3)	75 (77.3)	97 (74.6)	47 (71.2)	67 (88.2)
Baseline white blood cell count, $\times$ 1000/mm^3	5.47 (1.78)	5.80 (1.92)	5.61 (1.81)	5.98 (2.08)	6.02 (1.57)
Used recreational drugs	25 (52.1)	46 (47.4)	66 (50.8)	31 (47.0)	33 (43.4)
Received a transfusion	16 (33.3)	41 (42.3)	52 (40.0)	24 (36.4)	22 (28.9)
Body mass index, weight (kg)/height(m)^2	30.13 (6.20)	29.89 (6.19)	29.25 (4.66)	29.98 (6.09)	30.18 (5.38)
Creatinine, mg/dl	0.80 (0.19)	0.81 (0.13)	0.81 (0.15)	0.81 (0.16)	0.84 (0.17)
Ever smoked	37 (77.1)	73 (75.3)	100 (76.9)	48 (72.7)	60 (78.9)
Received interferon and ribavirin	44 (91.7)	81 (83.5)	111 (85.4)	45 (68.2)	64 (84.2)
Reported diabetes	10 (20.8)	25 (25.8)	13 (10.0)	8 (12.1)	11 (14.5)
Serum ferritin, ng/ml	429.42 (432.51)	303.35 (317.08)	436.21 (518.96)	294.06 (307.87)	289.01 (251.52)
Ultrasound evidence of splenomegaly	12 (25.0)	30 (30.9)	42 (32.3)	27 (40.9)	28 (36.8)
Ever drank alcohol	32 (66.7)	85 (87.6)	121 (93.1)	51 (77.3)	66 (86.8)
Hemoglobin, g/dl	14.91 (1.31)	14.80 (1.18)	15.64 (1.46)	14.93 (1.43)	14.88 (1.38)
Aspartate aminotransferase, U/L	92.94 (58.34)	96.32 (74.43)	85.11 (70.92)	97.33 (66.24)	81.11 (72.95)

Results reported as mean (standard deviation) for continuous variables and count (percentage) for binary variables.
A, indicates randomization to treatment with peginterferon alfa-2a ($A = 1$) versus no treatment ($A = 0$); kg, kilogram; m, meter; mg, milligram; dl, deciliter; ml, milliliter; g, gram; U/L, units per liter.

Table S7: Baseline characteristics in the HALT-C trial, stratified by S.

Source of data, S	6	7	8	9	0
Number of individuals	101	89	100	42	199
Baseline platelets, $\times$ 1000/mm^3	154.53 (60.46)	160.08 (68.25)	152.68 (52.83)	157.31 (70.46)	171.30 (66.10)
Age in years	52.42 (8.35)	49.54 (6.73)	50.44 (7.38)	50.64 (7.54)	50.06 (7.53)
Female	30 (29.7)	24 (27.0)	32 (32.0)	9 (21.4)	60 (30.2)
Received pegylated interferon	35 (34.7)	19 (21.3)	40 (40.0)	15 (35.7)	66 (33.2)
White	64 (63.4)	75 (84.3)	72 (72.0)	35 (83.3)	115 (57.8)
Baseline white blood cell count, $\times$ 1000/mm^3	5.61 (1.79)	5.79 (1.98)	5.63 (1.81)	5.58 (1.77)	5.81 (1.92)
Used recreational drugs	41 (40.6)	38 (42.7)	41 (41.0)	17 (40.5)	91 (45.7)
Received a transfusion	41 (40.6)	42 (47.2)	44 (44.0)	16 (38.1)	77 (38.7)
Body mass index, weight (kg)/height(m)^2	29.65 (5.85)	30.67 (5.12)	29.88 (5.55)	30.44 (5.29)	29.93 (5.34)
Creatinine, mg/dl	0.91 (0.18)	0.92 (0.16)	0.83 (0.15)	0.90 (0.17)	0.84 (0.17)
Ever smoked	74 (73.3)	68 (76.4)	69 (69.0)	29 (69.0)	155 (77.9)
Received interferon and ribavirin	83 (82.2)	80 (89.9)	85 (85.0)	34 (81.0)	151 (75.9)
Reported diabetes	15 (14.9)	13 (14.6)	16 (16.0)	5 (11.9)	50 (25.1)
Serum ferritin, ng/ml	440.21 (671.90)	352.33 (307.69)	398.18 (399.88)	486.74 (498.72)	360.18 (378.14)
Ultrasound evidence of splenomegaly	31 (30.7)	26 (29.2)	33 (33.0)	13 (31.0)	77 (38.7)
Ever drank alcohol	80 (79.2)	62 (69.7)	78 (78.0)	36 (85.7)	173 (86.9)
Hemoglobin, g/dl	14.63 (1.54)	14.97 (1.51)	14.85 (1.28)	14.93 (1.44)	14.97 (1.42)
Aspartate aminotransferase, U/L	85.70 (46.81)	80.64 (51.68)	76.92 (44.07)	97.38 (57.20)	92.72 (48.81)

Results reported as mean (standard deviation) for continuous variables and count (percentage) for binary variables.
A, indicates randomization to treatment with peginterferon alfa-2a ($A = 1$) versus no treatment ($A = 0$); kg, kilogram; m, meter; mg, milligram; dl, deciliter; ml, milliliter; g, gram; U/L, units per liter.

Web Appendix H Code to reproduce the simulation

`Stata` code to reproduce the simulation is available on GitHub:

https://github.com/serobertson/EfficientCausalMetaAnalysis.

`R` code to reproduce the applied analyses is also provided on GitHub, along with a simulated dataset on which the code can be run.

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