Towards causally interpretable meta-analysis:
transporting inferences from multiple studies to a target population

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Thursday 28\textsuperscript{th} March, 2019
Abstract

We take steps towards causally interpretable meta-analysis by describing conditions under which we can transport causal inferences from a collection of randomized trials to a new target population. We discuss the conditions that allow the identification of causal quantities in the target population and provide identification results for potential (counterfactual) outcome means and average treatment effects. Our results highlight the importance of accounting for variation in the treatment assignment mechanisms across the randomized trials when transporting inferences. Last, we propose estimators of the potential outcome means that rely on different working models and provide code for their implementation in statistical software.
1 Introduction

For many comparative effectiveness research questions, evidence is available from multiple randomized trials conducted independently in different underlying populations. When policy-makers have evidence from multiple trials on the same interventions, they typically want to combine information across the trials to draw causal inferences about the effects of the interventions on some specific target population that is different from the populations underlying the trials. In other words, policy-makers want to synthesize the trial evidence and transport inferences to a new target population.

“Meta-analysis” is an umbrella term for various statistical methods that synthesize evidence across multiple trials [1]. The vast majority of meta-analyses rely on summary statistics from the trials to estimate features of the distribution of average treatment effects (or effect sizes) over studies using random effects models, or to summarize the observed study data using common effect models (often referred to as fixed-effect models) [2,3]. Even when individual participant data are available [4], the most common approach is a two-step procedure of obtaining trial-specific estimates and their precision, then combining them using the same methods as for meta-analyses that rely on summary statistics [5]. Standard meta-analysis methods produce results that do not have a clear causal interpretation when each trial samples eligible individuals from a different underlying population (e.g., from centers with different referral patterns or in different geographic locations) and treatment effects vary across the sampled populations. The problem is that meta-analyses combine estimates of trial-specific average treatment effects using weights that reflect the precision of the estimates themselves (and their variability, in the case of random effects meta-analyses), but do
not reflect the “relevance” of each study to the target population.

In this paper, we take steps towards “causally interpretable” meta-analysis using individual participant data. We consider methods for extending inferences about treatment-specific means and average treatment effects from a collection of randomized trials to a target population that is chosen on scientific or policy grounds and may be different from any of the of the populations sampled in the randomized trials. We discuss the conditions that allow the identification of causal quantities in the target population and provide identification results for potential (counterfactual) outcome means and average treatment effects. Our results highlight the importance of accounting for variation in the treatment assignment mechanisms across the randomized trials when transporting inferences. Last, we propose estimators of the potential outcome means that rely on different working models and provide code for their implementation in statistical software.

2 Causal quantities of interest

Suppose we have data from a collection of randomized trials $\mathcal{S}$ indexed by $s = 1, \ldots, m$. From each individual in each trial we have information on treatments $A$, baseline covariates $X$, and outcomes $Y$ measured at a single time-point post-treatment assignment (we do not consider failure-time outcomes in this paper). An individual can participate in at most one trial. To simplify exposition, we assume that the same finite set of assigned treatments, $\mathcal{A}$, has been compared in each trial of the collection. From each trial $s \in \mathcal{S}$, the data consists of independent and identically distributed random tuples $(X_i, S_i = s, A_i, Y_i), i = 1, \ldots, n_s$, where $n_s$ denotes the total number of randomized individuals in trial $s$. Throughout, we
use $I(\cdot)$ to denote the indicator function; for example, $I(S \in \mathcal{S})$ is a random variable that denotes participation in any of the trials in the collection $\mathcal{S}$, such that $I(S \in \mathcal{S}) = 1$ when $S \in \mathcal{S}$; and 0, otherwise.

We also obtain a simple random sample from the target population of scientific or policy interest. The individuals in this sample are not participating in any of the trials (either because they were not invited or were invited but declined to participate). We collect baseline covariate data from them, but need not collect treatment or outcome data. We use the convention that $S = 0$ for target population so that the data from the sample consists of independent and identically distributed tuples $(X_i, S_i = 0), i = 1, \ldots, n_0$, where $n_0$ is the total number of sampled individuals. The total number of observations, including the trials and the sample from the target population, is $n = \sum_{j=0}^{m} n_j$.

Let $Y^a$ denote the outcome under intervention treatment assignment $a \in \mathcal{A}$. We are interested in estimating the potential outcome mean in the population of non-randomized individuals, $E[Y^a | S = 0]$ for each $a \in \mathcal{A}$, as well as the average causal effect among non-randomized individuals, $E[Y^a - Y^{a'} | S = 0]$ for each $a, a' \in \mathcal{A}$.

3 A causal structure for multiple trials

When combining information from multiple studies, a common concern is “confounding by trial.” Intuitively, the concern is that, even though each study is individually randomized, there are important between-study differences in unmeasured baseline characteristics, such that a naive “pooled” analysis of the trials may exhibit confounding of the treatment–outcome association if the treatment assignment mechanism varies across trials (e.g., if not
all trials have a 1:1 allocation ratio). The standard solution is to stratify all analyses by trial.

In Figure 1, panel (A), we consider a causal directed acyclic graph (DAG) \cite{6,7} such that confounding by study is present, yet transportability to a target population is possible (as will be shown in the next section). With only slight abuse of notation, we use the same symbols to denote nodes on the DAG as we do for the random variables defined in the previous section. We depict the causal structure separately in the collection of trials $I(S \in S) = 1$ in panel (B), and among non-randomized individuals $S = 0$ in panel (C). In the latter, there is confounding of the treatment effect $A \rightarrow Y$ by unmeasured variables $U^*$; such confounding is absent among the randomized trials. The $X \rightarrow A$ effect can be present both in trial participants $I(S \in S) = 1$ and non-participants $S = 0$, as depicted in panels (B) and (C); in the former, it represents the use of conditional randomization in some of the randomized trials; in the latter, it represents known and measured drivers of treatment choice in the target population (i.e., known confounding variables). The $S \rightarrow A$ edge signifies that the treatment assignment mechanism may vary across trials. For example, the randomization ratio (in marginally randomized trials) or the conditional treatment assignment probabilities (in conditionally randomized trials) may differ across trials.

We also allow for measured common causes $X$ of participation in any trial $I(S \in S)$ and the outcome; and for measured causes $X$ and unmeasured causes $U$ of participation in a specific trial $S$ and the outcome. The variables depicted by $U$ are the source of “confounding by trial” – because of the unblocked $A \leftarrow S \leftarrow U \rightarrow Y$ path, any analysis not stratified by trial will produce invalid results. Note also that confounding by study cannot arise when there is no $S \rightarrow A$ effect. Intuitively, if the treatment assignment mechanism does not
vary across trials, confounding by trial cannot occur, even if there exist common causes of enrolling in a specific trial \((S)\) and the outcome.

The DAG in panel (A) encodes two additional key assumptions: (1) there is no unmeasured common cause of trial participation \(I(S \in S)\) and the outcome \(Y\), and (2) there is no direct effect of participation in any trial \(I(S \in S)\) or participation in a specific trial \(S\) on the outcome. As we discuss in the next section, the absence of unmeasured common causes of trial participation and the outcome allows us to transport inferences from the collection of trials to the target population using the observed data. The absence of direct trial participation or trial choice effects on the outcome renders the transported inferences context-free, in the sense that inferences do not depend on intervening on the trial participation status of members of the target population, just on intervening to assign treatment.

Last, to focus on issues related to selective trial participation and trial choice, we assume complete adherence to the assigned treatment and no loss-to-followup.

4 Identification

4.1 Treatment assignment mechanism varies across trials

We begin by considering identification in the general case where treatment assignment mechanisms are allowed to vary across trials.

4.1.1 Identifiability conditions

The following are sufficient conditions for identifying the potential outcome mean in the target population \(E[Y^a|S = 0]\) when the treatment assignment mechanism varies across
trials.

I. Consistency of potential outcomes: If $A_i = a$, then $Y_i^a = Y_i$, for every individual $i$. As noted in the previous section, implicit in this notation is the absence of a direct effect of participation in any trial $I(S \in S)$ or participation in a specific trial $S$ on the outcome.

II. Exchangeability over $A$ in each trial: $E[Y^a | X, S = s, A = a] = E[Y^a | X, S = s]$ for each trial $s \in S$ and each treatment $a \in A$.

III. Positivity of treatment assignment in each trial: $\Pr[A = a | X = x, S = s] > 0$, for each treatment $a \in A$ and each $x$ with positive density in the target population, $f_{X|S}(x|S = 0) > 0$, and each trial $s \in S$ with $\Pr[S = s | X = x, I(S \in S) = 1] > 0$.

IV. Mean transportability: $E[Y^a | X, S = 0] = E[Y^a | X, I(S \in S) = 1]$ for each $a \in A$. As noted in the previous section, this condition follows from the absence of common causes of trial participation and the outcome; the condition can be verified by applying the d-separation criterion \cite{6} in Figure 1, panel (A), because the graph implies the independence $Y^a \perp I(S \in S)|X$, and the event $S = 0$ is equivalent to the event $I(S \in S) = 0$ in our setup.

V. Positivity of trial participation: $\Pr[I(S \in S) = 1 | X = x] > 0$ for every $x$ with positive density in the target population, $f_{X|S}(x|S = 0) > 0$. Informally, this condition means that, for covariates needed to establish mean transportability, each covariate pattern in the target population should have positive probability of occurring in the collection of trials but not necessarily in each trial. For example, consider two randomized trials comparing the same anti-hypertensive treatments, one enrolling patients with mild and the other with severe hypertension. Condition $V$ means that we can transport inferences from the two trials to a
target population that consists of a mixture of patients with mild and severe hypertension. This is a manifestation of the commonly held belief that by combining information across diverse trials, inferences can be drawn about populations broader than those enrolled in each trial.

Last, note that we use $X$ generically to denote baseline covariates. It is possible however, that strict subsets of $X$ are adequate to satisfy the different exchangeability conditions. For example, if all trials are marginally randomized the mean exchangeability over treatment assignment $A$ among trial participants will hold unconditionally.

4.1.2 Identification

As we show in Appendix A, under assumptions $I$ through $V$, the potential outcome mean in the target population under treatment $a$, $E[Y^a|S = 0]$, equals the following functional of the observed data distribution:

$$
\psi(a) \equiv E \left[ \sum_{s \in S} E[Y|X, S = s, A = a] \Pr[S = s|X, I(S \in S) = 1] \bigg| S = 0 \right].
$$

(1)

This result formalizes the intuition that analyses combining information from multiple trials need to be “stratified” by trial.

An algebraically equivalent expression for $\psi(a)$ that uses weighting can be obtained under the positivity conditions (see Appendix A):

$$
\psi(a) = \frac{1}{\Pr[S = 0]} \sum_{s \in S} E \left[ \frac{I(S = s, A = a) Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right]
$$

$$
= \frac{1}{\Pr[S = 0]} E \left[ \frac{I(S \in S, A = a) Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right].
$$

(2)
The average treatment effect comparing treatments \(a, a' \in \mathcal{A}\) can be identified by differencing, because

\[
E[Y^a - Y^{a'}|S = 0] = E[Y^a|S = 0] - E[Y^{a'}|S = 0] = \psi(a) - \psi(a').
\]

### 4.2 Treatment assignment mechanism does not vary across trials

The assignment mechanism does not vary across trials if all trials are marginally randomized with the same randomization ratio or conditionally randomized with the same conditional probability of treatment function. In such cases, the DAG of panel (B) in Figure 1 should be modified by removing the \(S \rightarrow A\) edge. Absence of that edge implies that \(Y^a \perp \perp A|X, I(S \in S) = 1\), even if unmeasured common causes of trial choice and the outcome exist (i.e., even if \(U\) is a common cause of \(S\) and \(Y\)). We now examine the implications of this independence condition for identification and estimation of potential outcome means in the target population.

#### 4.2.1 Identifiability conditions

We retain conditions \(I, IV,\) and \(V\) from the previous sub-section, but modify conditions \(II\) and \(III\).

\(II^*. \textit{Exchangeability over } A \textit{ in the aggregate}: E[Y^a|X, I(S \in S) = 1] = E[Y^a|X, I(S \in S) = 1, A = a], \text{ for each } a \in \mathcal{A}.\) Note that this condition does not hold in the DAG of panel (B) in Figure 1, but it holds if the graph is modified by removing the \(S \rightarrow A\) edge (or by eliminating the unmeasured variable \(U\)).
III*. Positivity of treatment assignment in the aggregate: \( \Pr[A = a | X = x, I(S \in \mathcal{S}) = 1] > 0 \) for each treatment \( a \in \mathcal{A} \), and each \( x \) that has positive density in the target population, \( f_{X|S}(x | S = 0) > 0 \).

We refer to the modified conditions II* and III* as “in the aggregate” because they pertain to the entire collection of trials, not each trial individually. Intuitively, when the treatment assignment mechanism does not vary over the trials, we can treat the collection of trial data as a single aggregated trial.

4.2.2 Identification

Under conditions I, II*, III*, IV, and V, the potential outcome mean under treatment \( a \in \mathcal{A} \) in the target population equals the following functional of the observed data distribution:

\[
\phi(a) \equiv \mathbb{E}[\mathbb{E}[Y | X, I(S \in \mathcal{S}) = 1, A = a | S = 0] | S = 0].
\]  

(3)

As we show in Appendix A, an algebraically equivalent expression for \( \phi(a) \) that uses weighting can be obtained under the positivity conditions:

\[
\phi(a) = \frac{1}{\Pr[S = 0]} \mathbb{E}\left[ \frac{I(S \in \mathcal{S}, A = a) Y \Pr[S = 0 | X]}{\Pr[I(S \in \mathcal{S}) = 1 | X] \Pr[A = a | X, I(S \in \mathcal{S}) = 1]} \right].
\]  

(4)

As before, the average treatment effect comparing treatments \( a, a' \in \mathcal{A} \) can be identified by differencing,

\[
\mathbb{E}[Y^a - Y^{a'} | S = 0] = \phi(a) - \phi(a').
\]
4.3 Identification under transportability in measure

As we note in Appendix B, if the focus of the investigation is the identification of average treatment effects (not potential outcome means), identification is possible under a weaker condition of “transportability in measure” [8] – essentially, an assumption that conditional average treatment effects (but not necessarily their component potential outcome means) are transportable. Because the potential outcome means are of inherent scientific interest, in the remainder of the paper we focus on their estimation.

5 Estimation

5.1 Treatment assignment mechanism varies across trials

The identification results in the previous section suggest several reasonable estimators when the treatment assignment varies by study (i.e., when confounding by study might be present):

Estimation by modeling the expectation of the outcome and the probability of trial choice (g-formula): The identification result in (1) suggests the following outcome model-based estimator,

$$
\hat{\psi}(a) = \left\{ \sum_{i=1}^{n} I(S_i = 0) \right\}^{-1} \sum_{i=1}^{n} I(S_i = 0) \sum_{s \in \mathcal{S}} \hat{g}_{s,a}(X_i) \hat{p}_s(X_i),
$$

where $\hat{g}_{s,a}(X)$ is an estimator for $E[Y|X, S = s, A = a]$ and $\hat{p}_s(X)$ is an estimator for $Pr[S = s|X, I(S \in \mathcal{S}) = 1]$.

Estimation by modeling the probability of trial participation and treatment: Similarly, the
identification result in (2) suggests the following weighting estimator

\[
\hat{\psi}_w(a) = \left\{ \sum_{i=1}^{n} I(S_i = 0) \right\}^{-1} \sum_{s \in \mathcal{S}} \sum_{i=1}^{n} I(S_i = s, A_i = a) \frac{1 - \hat{p}(X_i)}{\hat{p}(X_i) \hat{e}_a(X_i, S_i)} Y_i
\]

\[
= \left\{ \sum_{i=1}^{n} I(S_i = 0) \right\}^{-1} \sum_{i=1}^{n} I(S_i \in \mathcal{S}, A_i = a) \frac{1 - \hat{p}(X_i)}{\hat{p}(X_i) \hat{e}_a(X_i, S_i)} Y_i,
\]

where \( \hat{p}(X) \) is an estimator for \( \Pr[I(S \in \mathcal{S}) = 1|X] \) and \( \hat{e}_a(X, S) \) is an estimator for \( \Pr[A = a|X, I(S \in \mathcal{S}) = 1, S] \). Note that the assignment mechanism in each trial is known and thus it should always be possible to choose a consistent estimator \( \hat{e}_a(X, S) \) for \( \Pr[A = a|X, I(S \in \mathcal{S}) = 1, S] \) (or use the “true” conditional randomization probability).

### 5.2 Treatment assignment mechanism does not vary across trials

When the treatment assignment mechanism does not vary across trials, it is again possible to obtain estimators for the potential outcome mean that rely on working models for the conditional outcome mean among all randomized individuals receiving treatment \( a \) and the conditional probability of participation in any trial (vs. not participating in a trial). The expressions for the various estimators simplify because, when the treatment assignment mechanism does not vary across trials, we are essentially treating the collection of randomized trials as a single aggregate trial (compare, for example, with the results in [9]).

**Estimation by modeling the expectation of the outcome (g-formula):** The first option is to use the sample analog of (3),

\[
\hat{\phi}_g(a) = \left\{ \sum_{i=1}^{n} I(S_i = 0) \right\}^{-1} \sum_{i=1}^{n} I(S_i = 0) \hat{h}_a(X_i),
\]

\( 7 \)
where \( \hat{h}_a(X) \) is an estimator for \( \text{E}[Y|X, I(S \in S) = 1, A = a] \), the conditional expectation of the outcome in the collection randomized trials. The outcome model-based estimator converges in probability to \( \phi(a) \) when \( \hat{h}_a(X) \) is a consistent estimator of \( \text{E}[Y|X, I(S \in S) = 1, A = a] \). Note that, in contrast to the estimator in (5), the estimator in (7) does not involve modeling the trial choice.

Estimation by modeling the probability of trial participation and treatment: A second option, similar to estimators for transporting inferences from a single trial [9, 10], is to use the sample-analog of (4),

\[
\hat{\phi}_w(a) = \left\{ \sum_{i=1}^{n} I(S_i = 0) \right\}^{-1} \sum_{i=1}^{n} I(S_i \in S, A_i = a) \frac{1 - \hat{p}(X_i)}{\hat{p}(X_i)\hat{\ell}_a(X_i)} Y_i, \tag{8}
\]

where \( \hat{p}(X) \) is an estimator for \( \text{Pr}[I(S \in S) = 1|X] \) and \( \hat{\ell}_a(X) \) is an estimator for \( \text{Pr}[A = a|X, I(S \in S) = 1] \). The inverse odds weighted estimator converges in probability to \( \phi(a) \) when \( \hat{p}(X) \) is a consistent estimator of the probability of trial participation (it is always possible to choose a consistent estimator of the probability of treatment).

### 5.3 Inference

To construct Wald-style confidence intervals for \( \psi(a) \) or \( \phi(a) \), when using parametric models, we can easily obtain the sandwich estimator [11] of the sampling variance for each estimator in Subsections 5.1 and 5.2. Alternatively, we can use the non-parametric bootstrap [12].
5.4 Implementation in software

In Appendix C we provide R code implementing the estimators described above using the geex package. Our implementation uses parametric specifications for all working models: we use estimating equations for binary or multinomial logistic regression models for \( p_s(X), p(X), e_a(X, S), \) and \( \ell_a(X) \); and estimating equations for linear regression models, separate for each treatment group, for \( g_{s,a}(X, S) \) and \( h_a(X) \). All estimating equations can be easily replaced by those appropriate for other generalized linear models [13], as needed. Because we estimate the working model parameters jointly with the target parameters of the estimators in equations (5) through (8), the sampling variances appropriately account for uncertainty [11,14].

6 Discussion

When multiple randomized trials investigate the same research question it is natural to want to understand what causal inferences can be drawn by considering the totality of available evidence. Traditional approaches to evidence synthesis, the leading example being meta-analysis, focus on modeling aspects of the distribution of study effects (such as the first or second moment in standard random effects meta-analysis models) or producing statistically optimal summaries of available data [2,3]. In general, such analyses do not produce causally interpretable estimates of the effect of well-defined interventions on a well-defined target population, except under the highly implausible assumption that the “true” marginal treatment effects does not vary (this assumption is testable in the collection of trials using tests of heterogeneity).

We provided identification and estimation results that can be used to transport potential
outcome means and average treatment effects from a collection of clinical trials to a target population from which only baseline covariate data need be available. We focused on the practical implications of variation in the treatment assignment mechanism across studies and proposed estimators for potential outcome means and average treatment effects. Our approach explicitly targets a well-defined population that is chosen on scientific or policy grounds and may be different from any of the of the populations sampled in the randomized trials. In our experience, policy-makers who use evidence syntheses to inform their decisions are not interested in the populations underlying the completed randomized trials and typically have a new target population in mind. Nevertheless, in the rare case where one of the randomized trials in $S$ is representative of the target population, the methods described in this paper can be easily modified to treat the trial data as a sample from the target population.

Previous work on the causal interpretation of meta-analyses has focused on identifiability conditions and their use to examine the presence of heterogeneity across studies [15] or the causal interpretation of meta-analyses using published aggregate (summary) data [16]. Of note, our estimators are different from those used in the applied illustration of a recently proposed framework for causally interpretable meta-analysis; estimation in that work relied on conventional multivariable regression models for conditional average treatment effects [15].

A strength of our approach is that the (non-parametric) identifiability conditions are delineated from any additional modeling assumptions that may be needed for estimation, especially when the vector of baseline covariates is high dimensional [17]. In this paper, we focused on simple g-formula and weighting estimators that can be easily implemented in standard statistical packages. A downside of these estimators is that in order to produce valid
results, all working models each estimator relies on need to be correctly specified. It has not escaped our attention, however, that it is possible to obtain doubly robust [18] estimators of \( \psi(a) \) and \( \phi(a) \). We have derived such estimators in a companion technical report (available upon request) and we are comparing their performance against the estimators described herein.

In summary, we have taken steps towards causally interpretable meta-analysis by considering the identification and estimation of potential outcome means and average treatment effects when transporting inferences from a collection of randomized trials to a well-defined target population. To deploy the methods for applied evidence synthesis, several extensions will be needed to address complications, such as systematically missing data and measurement error in covariates, which we expect will occur quite often.

**Acknowledgement**

This work was supported in part by Patient-Centered Outcomes Research Institute (PCORI) awards ME-1306-03758 and ME-1502-27794 (Dahabreh); National Institutes of Health (NIH) grant R37 AI102634 (Hernán); and Agency for Healthcare Research and Quality (AHRQ) National Research Service Award T32AGHS00001 (Robertson). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or AHRQ. Statements in this paper do not necessarily represent the views of the PCORI, its Board of Governors, the Methodology Committee, the NIH, or AHRQ.
Figure

Figure 1: DAG depicting baseline covariates $X$, participation in any trial $I(S \in \mathcal{S})$, participation in a specific trial $S$, treatment $A$, and outcome $Y$ in (A) trial participants and non-participants combined; (B) trial participants $I(S \in \mathcal{S})=1$; and (C) non-participants $I(S \in \mathcal{S})=0$, so that $S=0$. 

(A)

(B)

(C)
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Appendix A  Identification results

In this Appendix, we collect results about the identification of potential outcome means. Results about the identification of average treatment effects follow immediately from the results on potential outcome means. In Appendix B, we discuss identification of average treatment effects under the weaker condition of transportability in measure.

When the treatment assignment mechanism varies across studies

Proposition 1. Under assumptions I through V in the main text, the potential outcome mean under treatment \( a \in \mathcal{A} \) in the target population, \( E[Y^a|S = 0] \), is identified by the following functional of the observed data distribution:

\[
\psi(a) \equiv \mathbb{E}\left[ \sum_{s \in S} \mathbb{E}[Y|X, S = s, A = a] \Pr[S = s|X, I(S \in \mathcal{S}) = 1] | S = 0 \right].
\]

Proof:

\[
E[Y^a|S = 0] = E\left[ E[Y^a|X, S = 0]|S = 0 \right]
= E\left[ E[Y^a|X, I(S \in \mathcal{S}) = 1]|S = 0 \right]
= E\left[ \sum_{s \in S} E[Y^a|X, S = s] \Pr[S = s|X, I(S \in \mathcal{S}) = 1]|S = 0 \right]
= E\left[ \sum_{s \in S} E[Y|X, S = s, A = a] \Pr[S = s|X, I(S \in \mathcal{S}) = 1]|S = 0 \right]
= \psi(a).
\]

\[\square\]
Proposition 2. Under positivity conditions III and V,

\[ \psi(a) = \frac{1}{\Pr[S = 0]} \sum_{s \in S} E \left[ \frac{I(S = s, A = a) Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right] \]

\[ = \frac{1}{\Pr[S = 0]} E \left[ \frac{I(S \in S, A = a) Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right]. \]  

(A.1)

Proof: We first derive the first expression on the right-hand-side of (A.1).

\[ \psi(a) = E \left[ \sum_{s \in S} E[Y|X, S = s, A = a] \Pr[S = s|X, I(S \in S) = 1]\bigg|S = 0 \right] \]

\[ = E \left[ \sum_{s \in S} E\left[ \frac{I(A = a) Y}{\Pr[A = a|X, S = s]} \bigg|X, S = s \right] \Pr[S = s|X, I(S \in S) = 1]\bigg|S = 0 \right] \]

\[ = E \left[ \sum_{s \in S} E\left[ \frac{I(S = s, A = a) Y}{\Pr[A = a|X, I(S \in S) = 1, S]} \bigg|X, I(S \in S) = 1 \right]\bigg|S = 0 \right] \]

\[ = E \left[ \sum_{s \in S} E\left[ \frac{I(S \in S, S = s, A = a) Y}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \bigg|X \right]\bigg|S = 0 \right] \]

\[ = \frac{1}{\Pr[S = 0]} E \left[ I(S = 0) \sum_{s \in S} E\left[ \frac{I(S = s, A = a) Y}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \bigg|X \right]\right] \]

\[ = \frac{1}{\Pr[S = 0]} E \left[ \sum_{s \in S} E\left[ \frac{I(S = s, A = a) Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \bigg|X \right]\right] \]

\[ = \frac{1}{\Pr[S = 0]} \sum_{s \in S} E\left[ \frac{I(S = s, A = a) Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right]. \]
We now use the above result to derive the second expression on the right-hand-side of (A.1).

\[
\psi(a) = \frac{1}{\Pr[S = 0]} \sum_{s \in S} \mathbb{E} \left[ \frac{I(S = s, A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right]
\]

\[
= \frac{1}{\Pr[S = 0]} \sum_{s \in S} \mathbb{E} \left[ \frac{I(S \in S, S = s, A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right] \Pr[I(S \in S) = 1, S = s]
\]

\[
= \frac{1}{\Pr[S = 0]} \sum_{s \in S} \mathbb{E} \left[ \frac{I(A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right] \Pr[I(S \in S) = 1, S = s] \times \Pr[S = s|I(S \in S) = 1] \Pr[I(S \in S) = 1]
\]

\[
= \frac{\Pr[I(S \in S) = 1]}{\Pr[S = 0]} \sum_{s \in S} \mathbb{E} \left[ \frac{I(A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right] \Pr[I(S \in S) = 1] \times \Pr[S = s|I(S \in S) = 1]
\]

\[
= \frac{\Pr[I(S \in S) = 1]}{\Pr[S = 0]} \mathbb{E} \left[ \frac{I(A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right] \Pr[I(S \in S) = 1]
\]

\[
= \frac{1}{\Pr[S = 0]} \mathbb{E} \left[ \frac{I(S \in S, A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1, S]} \right].
\]

\[\square\]

**Remark.** The derivations for Proposition 2 rely on the positivity conditions and do not use any causal (counterfactual) assumptions. Thus, the results hold whether or not \(\psi(a)\) has a causal interpretation.
When the treatment assignment mechanism does not vary across studies

**Proposition 3.** Under conditions I, II\(^*\), III\(^*\), IV, and V, the potential outcome mean under treatment \(a \in A\) in the target population, \(E[Y^a | S = 0]\), equals the following functional of the observed data distribution:

\[
\phi(a) \equiv E \left[ E[Y | X, I(S \in S) = 1, A = a] \mid S = 0 \right].
\]

**Proof:**

\[
E[Y^a | S = 0] = E \left[ E[Y^a | X, S = 0] \mid S = 0 \right]
= E \left[ E[Y^a | X, I(S \in S) = 1] \mid S = 0 \right]
= E \left[ E[Y^a | X, I(S \in S) = 1, A = a] \mid S = 0 \right]
= E \left[ E[Y | X, I(S \in S) = 1, A = a] \mid S = 0 \right]
= \phi(a).
\]

\[\square\]
Proposition 4. Under positivity conditions III$^*$ and V,

$$\phi(a) = \frac{1}{\Pr[S = 0]} \mathbb{E} \left[ \frac{I(S \in S, A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1]} \right].$$

Proof:

$$\phi(a) = \mathbb{E} \left[ \mathbb{E}[Y|X, I(S \in S) = 1, A = a]|S = 0] \right]$$

$$= \mathbb{E} \left[ \frac{I(S \in S, A = a)Y}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1]} |X| \right] \Pr[S = 0]$$

$$= \frac{1}{\Pr[S = 0]} \mathbb{E} \left[ I(S = 0) \mathbb{E} \left[ \frac{I(S \in S, A = a)Y}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1]} |X| \right] \right]$$

$$= \frac{1}{\Pr[S = 0]} \mathbb{E} \left[ \frac{I(S \in S, A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1]} |X| \right]$$

$$= \frac{1}{\Pr[S = 0]} \mathbb{E} \left[ \frac{I(S \in S, A = a)Y \Pr[S = 0|X]}{\Pr[I(S \in S) = 1|X] \Pr[A = a|X, I(S \in S) = 1]} \right].$$

Remark. The derivation for Proposition 4 relies on the positivity conditions and does not use any causal (counterfactual) assumptions. Thus, the result holds whether or not $\phi(a)$ has a causal interpretation.
Appendix B  Identification of average treatment effects under transportability in measure

Consider the following identifiability condition:

$IV^*$. Transportability in measure: For $a, a' \in A$,

$$E[Y^a - Y^{a'}|X, I(S \in \mathcal{S}) = 1] = E[Y^a - Y^{a'}|X, S = 0].$$

Condition $IV^*$ is weaker than condition $IV$, in the sense that condition $IV$ implies condition $IV^*$, but condition $IV^*$ does not imply condition $IV$. Note that, under condition $IV^*$, potential outcome means are not identifiable.

When the treatment assignment mechanism varies across studies

Proposition 5. Under conditions I through III, $IV^*$, and $V$,

$$E[Y^a - Y^{a'}|S = 0] = E \left[ \sum_{s \in \mathcal{S}} \left\{ E[Y|X, S = s, A = a] - E[Y|X, S = s, A = a'] \right\} \Pr[S = s|X, I(S \in \mathcal{S}) = 1]\bigg| S = 0 \right].$$

When the treatment assignment mechanism does not vary across studies

Proposition 6. Under conditions I, $II^*$ through $IV^*$, and $V$,

$$E[Y^a - Y^{a'}|S = 0] = E \left[ E[Y|X, I(S \in \mathcal{S}) = 1, A = a] - E[Y|X, I(S \in \mathcal{S}) = 1, A = a']\bigg| S = 0 \right].$$
Appendix C  Code to implement the estimators

We have provided a simulated dataset (sampledata.csv) and three R scripts that implement
the methods described in this paper.