Abstract

A common concern when trying to draw causal inferences from observational data is that the measured covariates are insufficiently rich to account for all sources of confounding. In practice, many of the covariates may only be proxies of the latent confounding mechanism. Recent work has shown that in certain settings where the standard ‘no unmeasured confounding’ assumption fails, proxy variables can be leveraged to identify causal effects. Results currently exist for the total causal effect of an intervention, but little consideration has been given to learning about the direct or indirect pathways of the effect through a mediator variable. In this work, we describe three separate proximal identification results for natural direct and indirect effects in the presence of unmeasured confounding. We then develop a semiparametric framework for inference on natural (in)direct effects, which leads us to locally efficient, multiply robust estimators.

Keywords: Causal inference, mediation, semiparametric inference, unmeasured confounding.

1 Introduction

The last few decades has seen the emergence of a literature on causal mediation analysis (Robins & Greenland, 1992; Pearl, 2001; VanderWeele & Vansteelandt, 2009; Imai et al., 2010; Tchetgen Tchetgen & Shpitser, 2012). This literature provides nonparametric definitions of direct and indirect effects in terms of contrasts of potential outcomes, as well
as conditions necessary to identify and estimate these effects from data. Estimands that have received particular focus are *natural direct and indirect effects*, which are useful for understanding the mechanism underlying the effect of a particular intervention as they combine to produce the total causal effect.

The majority of work on identification of natural direct and indirect effects assumes that the measured covariates are sufficiently rich to account for confounding between the exposure and outcome, the mediator and outcome and the exposure and mediator. In practice, it is likely that many key confounding variables (e.g. disease severity, socio-economic status) cannot be ascertained with certainty from the measured covariates. At best, some of the measured covariates may be confounder *proxies* e.g. mis-measured versions of the underlying confounders. This insight has led to work on leveraging proxy variables to help remove confounding bias in observational studies, with focus on the total effect of intervention. Negative control are examples of such proxies ([Lipsitch et al., 2010; Shi et al., 2020b]; we refer to [Shi et al. (2020b)] and [Tchetgen Tchetgen et al. (2020)] for further examples in observational studies.

If we are able to collect data on a sufficient number of proxies, confounding bias can sometimes be successfully removed in settings where standard analyses under a ‘no unmeasured confounding’ assumption would fail. Building on results in [Kuroki & Pearl (2014); Miao et al. (2018a)] established nonparametric identification of the average treatment effect under a ‘double negative control design’ (where both a negative control exposure and outcome are measured). [Tchetgen Tchetgen et al. (2020)] extend these results to settings with time-varying exposures and (potentially unmeasured) confounders. For estimation, they propose proximal $g$-computation, a generalisation of Robins’ parametric $g$-computation algorithm ([Robins, 1986]). Under a proximal identification strategy, [Cui et al. (2020)] develop semiparametric inference for the average treatment effect.

We consider identification and estimation of natural direct and indirect effects in the presence of unmeasured confounding. As an example, we consider the Job Corps study ([Schochet et al., 2008]). Beyond understanding the total effect of a job training intervention, the investigators were also interested in whether the intervention reduced criminal activity due to increased employment. It was possible that the association between program participation, employment and criminal activity were subject to confounding by latent factor, such as motivation, that was only partially captured by the pre-treatment covariates. In this work, we establish sufficient conditions for nonparametric identification of mediation estimands using a pair of proxy variables, giving three separate identification strategies. These each rely on modelling and estimation of different combinations of ‘confounding bridge’ functions ([Miao et al., 2018a]). To reduce sensitivity to model misspecification, we
obtain the efficient influence function under a semiparametric model for the observed data distribution, which leads us to estimators that are multiply robust. Our identification and estimation results allow for continuous or discrete outcomes and mediators. As far as we are aware, this is the first paper to use proxy variables for identification and inference for direct and indirect effects, with the exception of Cheng et al. (2021). However, their identification strategy is distinct from ours, as they rely on deep latent variable models. They also did not consider semiparametric inference and the issues of efficiency/robustness explored here.

2 Nonparametric proximal identification of the mediation functional

2.1 Preliminaries

We consider a setting where one is interested in the effect of a binary treatment $A$ on an outcome $Y$ that is mediated via a single intermediate variable $M$. We use $U$ to refer to an unmeasured, potentially vector-valued confounding variable, which may be discrete, continuous, or a combination of both types. Let $Y(a, m)$ refer to the potential outcome that would be observed for someone if they were assigned to a given treatment at level $a$ and mediator at $m$; similarly, $M(a)$ denotes the potential outcome for the mediator if treatment had taken value $a$. Then the total average treatment effect of $A$ on $Y$ can be decomposed as

$$E\{Y(1) - Y(0)\} = E[Y\{1, M(1)\} - Y\{1, M(0)\}] + E[Y\{1, M(0)\} - Y\{0, M(0)\}]$$

The first term $E[Y\{1, M(1)\} - Y\{1, M(0)\}]$ on the right hand side of the equality is an example of a natural indirect effect, and captures the expected mean difference in $Y$ if all individuals were assigned treatment $A = 1$, but the mediator was changed to the level it would take with $A = 0$. The second term $E[Y\{1, M(0)\} - Y\{0, M(0)\}]$ is a natural direct effect, and captures the effect of setting $A = 1$ versus $A = 0$ if everyone’s mediator were at the level it would take with $A = 0$. Note that $E[Y\{1, M(1)\}] = E\{Y(1)\}$ and $E[Y\{0, M(0)\}] = E\{Y(0)\}$; results on nonparametric identification and inference for these quantities in a proximal learning setting already exist in Tchetgen Tchetgen et al. (2020) and Cui et al. (2020). We will therefore focus on the mediation functional $\psi = E[Y\{1, M(0)\}]$ in the remainder of the article.
In order to identify $\psi$ when one has access to a measured, potentially vector-valued covariate $L$, and supposing $M$ takes on values in $S$, then one typically invokes the following conditional exchangeability assumptions: $Y(a,m) \perp A|L$ for $a = 0, 1$ and each $m \in S$; $M(a) \perp A|L$ for $a = 0, 1$; and $Y(a,m) \perp M(a)|A = a, L$ for $a = 0, 1$ and each $m \in S$. In addition, the cross-world assumption $Y(a,m) \perp M(a')|A = a, L$ for $a, a' = 0, 1$ and each $m \in S$ is usually invoked (Robins & Richardson, 2010). It is known as such because independence between the counterfactual outcome and mediator values is required to hold across two different worlds (of potentially conflicting values of treatment). If these hold, in addition to standard positivity and consistency conditions (Robins, 1986), then $\psi$ can be identified via the mediation formula

$$\psi = \int \int E(Y|A = 1, m, l)dF(m|A = 0, l)dF(l)$$

(Pearl, 2001). If one were to interpret the causal diagram in Figure 1(a) as a nonparametric structural equation model with independent errors, then the above conditional independences are consistent with that diagram.

The cross-world assumption has been the subject of much controversy, given that it can never be empirically verified or guaranteed by any study design. This has therefore led to an alternative way of conceptualising natural direct and indirect effects via ‘treatment-splitting’ without reference to cross-world counterfactuals (Robins & Richardson, 2010; Robins et al., 2020). In what follows, we will adopt the more traditional cross-world framework for mediation analysis, but expect that all of our results for identification of $\psi$ carry over to the split-treatment approach, which is left to future work.
2.2 The proximal mediation formula

Figure 1(b) displays a setting where the previous conditional exchangeability and the cross-world assumptions would not hold due to the presence of the unmeasured variable $U$, which is a common cause of $A$, $M$ and $Y$. We will now assume that the observed covariates $L$ can be divided into three buckets ($X, Z, W$). Here, $Z$ and $W$ are proxy variables that are only associated with $A$, $M$ and $Y$ via an unmeasured common cause. Lastly, $X$ is a common cause of $A$, $M$ and $Y$. The failure of conditional exchangeability means that an analysis which would adjust for $X$, $Z$ and $W$ via conditioning on them in the mediation formula would return biased results due to residual confounding from $U$. In what follows, we will therefore adopt a different approach for identification of $\psi$, based on leveraging the proxy variables $Z$ and $W$ to learn about $U$. Before giving the first identification result, we discuss the assumptions involved.

**Assumption 1. (Consistency):**

1. $M(a) = M$ almost surely for those with $A = a$.
2. $Y(a, m) = Y$ almost surely for those with $A = a$ and $M = m$.

**Assumption 2. (Positivity):**
1. \( f_{M|A,U,X}(m|A,U,X) > 0 \) almost surely for all \( m \in S \).
2. \( \Pr(A = a|U,X) > 0 \) almost surely for \( a = 0,1 \).

**Assumption 3.** (Latent conditional exchangeability):

1. \( Y(a,m) \perp A|U,X \) for \( a = 0,1 \) and each \( m \in S \).
2. \( Y(a,m) \perp M(a)|A = a,U,X \) for \( a = 0,1 \) and each \( m \in S \).
3. \( M(a) \perp A|U,X \) for \( a = 0,1 \) and each \( m \in S \).

**Assumption 4.** (Latent cross-world assumption):
\( Y(a,m) \perp M(a^*)|U,X \) for \( a,a^* = 0,1 \) and each \( m \in S \).

These first assumptions are similar to those made in standard mediation analyses, except that they also allow for the existence of an unmeasured variable \( U \). The following assumptions will directly enable us to leverage information from the proxy variables.

**Assumption 5.** (Exposure- and outcome-inducing proxies):

1. \( Z \perp Y(a,m)|A,M(a),U,X \) for \( a = 0,1 \) and each \( m \in S \).
2. \( Z \perp M(a)|A,U,X \) for \( a = 0,1 \).
3. \( W \perp M(a)|U,X \) for \( a = 0,1 \).
4. \( W \perp (A,Z)|M(a),U,X \) for \( a = 0,1 \).

These assumptions essentially require that \( A \) and \( M \) have no direct causal effect on \( W \), and that \( Z \) has no causal effect on \( M \) or \( Y \). Also, \( Z \) and \( W \) are only associated via the unmeasured common cause \( U \). These assumptions formally encode what it means for \( Z \) and \( W \) to be proxies, in the sense that they become uninformative about confounding conditional on \( U \). They are compatible with the causal diagram in Figure 1b. However, there are many other diagrams that may be compatible with Assumptions 5.3 and 5.4, some of which are given in Figure 2 in the Supplementary Material. For example, \( Z \) can be a direct cause of \( A \), and \( W \) can cause \( Y \). In general, these assumptions are not testable given that they involve the unmeasured \( U \).

Identification of the mediation functional requires existence of multiple ‘confounding bridge’ functions (Miao et al., 2018b). We also need to ensure the confounding bridge functions can be identified from the data, given that we have access to \( Z \). Formalising both
of these types of condition in general settings is subtle, since the confounding bridge function will be defined as the solution to an integral equation. We formalise them using the completeness conditions below:

**Assumption 6. (Completeness):**

1. For any square-integrable function \( g(u) \), if \( E\{g(U)|Z = z, A = 1, M = m, X = x\} = 0 \) for any \( z, m \) and \( x \) almost surely, then \( g(U) = 0 \) almost surely.

2. For any square-integrable function \( g(u) \), if \( E\{g(U)|Z = z, A = 0, X = x\} = 0 \) for any \( z \) and \( x \) almost surely, then \( g(U) = 0 \) almost surely.

Completeness is a technical condition that arises in conjunction with sufficiency in the theory of statistical inference. In causal inference, it has been invoked for identification in the context of nonparametric regression with an instrumental variable [Newey & Powell, 2003], where it is used as an analogue of the rank and order conditions that arise in the classical instrumental variable setup. This assumption essentially means that any variation in \( U \) is associated with a form of variation in \( Z \) given \( A = 1, M \) and \( X \) and given \( A = 0 \) and \( X \). Further discussion of completeness in this context is left to the Supplementary Material.

We are now in a position to give our first identification result.

**Theorem 2.1.** Suppose that there exist the following confounding bridge functions \( h_1(w, M, X) \) and \( h_0(w, X) \) that satisfy

\[
E(Y|Z, A = 1, M, X) = \int h_1(w, M, X)dF(w|Z, A = 1, M, X) \quad (2)
\]

\[
E\{h_1(W, M, X)|Z, A = 0, X\} = \int h_0(w, X)dF(w|Z, A = 0, X) \quad (3)
\]

Then under Assumptions 1-6, it follows that

\[
E(Y|U, A = 1, M, X) = \int h_1(w, M, X)dF(w|U, A = 1, M, X) \quad (4)
\]

\[
E\{h_1(W, M, X)|U, A = 0, X\} = \int h_0(w, X)dF(w|U, A = 0, X)
\]

and furthermore that \( E[Y\{1, M(0)\}] \) is identified as

\[
\psi = \int \int h_0(w, x)dF(w|x)dF(x)
\]

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The proof of this result, as well as all others in this paper, is given in the Supplementary Material. We name expression (5) the proximal mediation formula, since it generalises Pearl’s fundamental mediation formula (1) to settings where key confounders are unmeasured. Similar to the proximal g-formula in Tchetgen Tchetgen et al. (2020), (5) is expressed in terms of nested bridge functions. Interestingly, although inferring natural (in)direct effects involves understanding the effect that the exposure has on the mediator, as well as interventions on the mediator, $\psi$ can be identified without a need for additional proxy variables. Nevertheless, compared with proximal identification of the average causal effect, additional restrictions are placed on the exposure- and outcome-inducing proxies, in terms of their relationship to $M$. For example, neither $Z$ nor $W$ are allowed to cause $M$. Such assumptions could be relaxed by collecting data on separate proxies for each bridge function; we will investigate this in future work.

Equations (2) and (3) refer to inverse problems that are known as Fredholm integral equations of the first kind. We refer to Miao et al. (2018a) and Cui et al. (2020) for mathematical conditions that ensure these equations admit solutions. We note that the solutions to these equations are not required to be unique, as all solutions yield a unique value of $\psi$. The identification assumptions may nevertheless be adjusted in order to guarantee a unique solution. Unlike Assumptions 1 and 3-6, the condition that (2) and (3) admit solutions is potentially empirically verifiable.

2.3 Alternative identification strategies

In this section, we establish two alternative proximal identification results to the proximal mediation formula, which rely on alternative assumptions regarding completeness and the existence of relevant confounding bridge functions, which are given in the Supplementary Material.

**Theorem 2.2.** (Part 1) Suppose that there exists the following confounding bridge functions $h_1(w, M, X)$ that satisfies (2) and $q_0(z, X)$ that satisfies

$$\frac{1}{f(A = 0|W, X)} = E\{q_0(Z, X)|W, A = 0, X\} \quad (6)$$

Under Assumptions 1-3 and 6.1 above and Assumption 8.2 in the Supplementary Material, we have that

$$\frac{1}{f(A = 0|U, X)} = E\{q_0(Z, X)|U, A = 0, X\} \quad (7)$$
as well as (4), and furthermore that \( E \{ Y \{ 1, M(0) \} \} \) is identified as

\[
\psi = \int \int I(a = 0) q_0(z, x) h_1(w, m, x) dF(w, z, a, m|x)dF(x)
\]

(Part 2) Alternatively, suppose that there exists confounding bridge functions \( q_0(z, X) \) that satisfies (6) and \( q_1(z, M, X) \) that satisfies

\[
E\{q_0(Z, X)|W, A = 0, M, X\} \frac{f(A = 0|W, M, X)}{f(A = 1|W, M, X)} = E\{q_1(Z, M, X)|W, A = 1, M, X\} \quad (8)
\]

Under Assumptions 7.5 and 8.1-8.2 in the Supplementary Material we have that

\[
E\{q_0(Z, X)|U, A = 0, M, X\} \frac{f(A = 0|U, M, X)}{f(A = 1|U, M, X)} = E\{q_1(Z, M, X)|U, A = 1, M, X\}
\]

and (7), and \( E[Y\{1, M(0)\}] \) is identified as

\[
\psi = \int \int I(a = 1) q_1(z, m, x) ydF(y, z, a, m|x)dF(x) \quad (9)
\]

We therefore have three results for proximal identification, each of which relies on two confounding bridge assumptions. The strategy given in the first part of the above theorem relies on a combination of outcome- and treatment-inducing confounding bridge functions, whereas the final strategy relies on two nested treatment-inducing confounding bridge functions. The result (7) follows from \( \text{Cui et al. (2020)} \), and formal conditions for existence of solutions to (6) and (8) are given in that paper.

3 Semiparametric inference

3.1 The semiparametric efficiency bound

In this section, we will consider inference for \( \psi \) under the semiparametric model \( M_{sp} \) which places no restrictions on the observed data distribution besides existence (but not necessarily uniqueness) of bridge functions \( h_1 \) and \( h_0 \) that solve (2) and (3). Note that assumed existence of the outcome bridge functions places restrictions on the tangent space. Under additional regularity conditions (described below), we can also obtain the semiparametric efficiency bound under \( M_{sp} \).
Assumption 7. (Regularity conditions):

1. Let $T_1 : L_2(W, M, X) \to L_2(Z, A = 1, M, X)$ denote the operator given by $T_1(g) \equiv E\{g(W, M, X)|Z, A = 1, M, X\}$. At the true data generating mechanism, $T_1$ is surjective.

2. Let $T_0 : L_2(W, M, X) \to L_2(Z, A = 0, X)$ denote the operator given by $T_0(g) \equiv E\{g(W, M, X)|Z, A = 0, X\}$. Then at the true data generating mechanism, $T_0$ is surjective.

As noted in Ying et al. (2021), this condition relies on the functions $L_2(W, M, X)$ being rich enough such that any element in $L_2(Z, A = 1, M, X)$ and $L_2(Z, A = 0, X)$ can be generated via the conditional expectation map. Then we arrive at the following result.

Theorem 3.1. Assume that there exist bridge functions $h_1$ and $h_0$ at all data laws that belong to the semiparametric model $\mathcal{M}_{sp}$. Furthermore, suppose that at the true data law there exists $q_0$ and $q_1$ which solve (7) and (8), and that Assumption 6 holds, such that $\psi$ is unique. Then

$$IF_\psi = I(A = 1)q_1(Z, M, X)\{Y - h_1(W, M, X)\}$$
$$+ I(A = 0)q_0(Z, X)\{h_1(W, M, X) - h_0(W, X)\} + h_0(W, X) - \psi$$

is a valid influence function for $\psi$ under $\mathcal{M}_{sp}$. Furthermore, the efficiency bound at the submodel where Assumption 7 holds and all bridge functions are unique is $E(IF_\psi^2)$.

3.2 Multiply robust estimation

We will consider the setting where $L$ is high-dimensional, and parametric working models for $h_1$, $h_0$, $q_0$ and $q_1$ may be useful as a form of dimension-reduction. In that case, we show that an estimator of $\psi$ based on the efficient influence function is multiply robust, in the sense that only certain combinations of these working models need to be correctly specified in order to yield an unbiased estimator. To make this more concrete, consider the following semiparametric models that impose certain restrictions on the observed data distribution:

- $\mathcal{M}_1 : h_1(W, M, X)$ and $h_0(W, X)$ are assumed to be correctly specified;
- $\mathcal{M}_2 : h_1(W, M, X)$ and $q_0(Z, X)$ are assumed to be correctly specified;
- $\mathcal{M}_3 : q_1(Z, M, X)$ and $q_0(Z, X)$ are assumed to be correctly specified.
Here, \( M_1, M_2 \) and \( M_3 \) are all submodels of \( M_{sp} \). The proposed approach will rely on models for the confounding bridge functions, but we will show that only one of \( M_1, M_2 \) and \( M_3 \) needs to hold to ensure unbiased estimation of the target parameter.

We shall first consider how to obtain inference in the submodels \( M_1, M_2 \) and \( M_3 \). Let \( h_1(W, M, X; \beta_1) \) and \( h_0(W, X; \beta_0) \) denote models for the respective bridge functions \( h_1(W, M, X) \) and \( h_0(W, X) \), indexed by finite-dimensional parameters \( \beta_1 \) and \( \beta_0 \). Likewise, \( q_1(Z, M, X; \gamma_1) \) and \( q_0(Z, X; \gamma_0) \) are models for the bridge functions \( q_1(Z, M, X) \) and \( q_0(Z, X) \) indexed by the finite-dimensional parameters \( \gamma_1 \) and \( \gamma_0 \) respectively. It follows from \( \text{Cui et al. (2020)} \) that one can obtain estimates \( \hat{\beta}_1, \hat{\beta}_0 \) and \( \hat{\gamma}_0 \) of \( \beta_1, \beta_0 \) and \( \gamma_0 \) as the solutions to the (respective) estimating equations:

\[
\begin{align*}
\sum_{i=1}^{n} A_i \{ Y_i - h_1(W_i, M_i, X_i; \beta_1) \} c_1(Z_i, M_i, X_i) &= 0 \\
\sum_{i=1}^{n} (1 - A_i) \{ h_1(W_i, M_i, X_i; \beta_1) - h_0(W_i, X_i; \beta_0) \} c_0(Z_i, X_i) &= 0 \\
\sum_{i=1}^{n} \{(1 - A_i) q_0(Z_i, X_i; \gamma_0) - 1\} d_0(W_i, X_i) &= 0
\end{align*}
\]

where the first two sets of equations can be solved sequentially; here \( c_1(Z_i, M_i, X_i) \) is a function of the same dimension as \( \beta_1 \), and \( c_0(Z_i, X_i) \) and \( d_0(W_i, X_i) \) are similarly defined. Although \( \hat{\beta}_0 \) and hence \( h_0(W, X; \hat{\beta}_0) \) depends on \( \hat{\beta}_1 \), this dependence is suppressed to simplify notation. The above estimating equations can be implemented using software for generalised method of moments or (when models are linear) two-stage least squares. Interestingly, despite the fact that \( (8) \) suggests that estimation of \( \gamma_0 \) would require postulation of a model for \( 1/f(A = 0|W, X) \), \( \text{Cui et al. (2020)} \) show that this is not the case. The efficient choices of \( c_1(Z_i, M_i, X_i) \), \( c_0(Z_i, X_i) \) and \( d_0(W_i, X_i) \) are all implied by results in the Appendix of \( \text{Cui et al. (2020)} \). Since the resulting efficiency gain compared to using the choices \( c_1(Z_i, M_i, X_i) = (1, Z_i^T, M_i, X_i^T)^T \), \( c_0(Z_i, X_i) = (1, Z_i^T, X_i^T)^T \) and \( d_0(W_i, X_i) = (1, W_i^T, X_i^T)^T \) is likely to be modest in most situations \( \text{Stephens et al. (2014)} \), we do not consider locally efficient estimation of the nuisance parameters any further.

Since \( q_1 \) involves solving an integral equation \( (8) \) involving the ratio of propensity score functions, the results from previous work do not extend to inference for \( \gamma_1 \). The following theorem then suggests how to obtain semiparametric inference under model \( M_3 \), and is more generally relevant for estimation of the average treatment effect in the (un)treated:
**Theorem 3.2.** All influence functions of regular and asymptotically linear estimators of $\gamma_1$ under the semiparametric model $M_3$ are of the form

$$-V^{-1}\left[\left\{Aq_1(Z, M, X; \gamma_1) - (1 - A)q_0(Z, X; \gamma_0)\right\}d_1(W, M, X)$$

$$- E\left\{\frac{\partial q_0(Z, X; \gamma_0)}{\partial \gamma_0}(1 - A)d_1(W, M, X)\right\}\varphi(W, Z, A, X; \gamma_0)\right]$$

for some function $d_1(W, M, X)$ that is the same dimension as $\gamma_1$, where

$$V = E\left\{\frac{\partial q_1(Z, M, X; \gamma_1)}{\partial \gamma_1}Ad_1(W, M, X)\right\}$$

and $\varphi(W, Z, A, X; \gamma_0)$ is the influence function for an estimator of $\gamma_0$.

This theorem indicates that inference for $\gamma_1$ can be obtained without the need to model either $f(A = 0|W, M, X)$ or $f(A = 1|W, M, X)$ (or their ratio). Indeed, it suggests an estimation strategy for $\gamma_1$; namely, after obtaining $\hat{\gamma}_0$ as previously described, one can obtain $\hat{\gamma}_1$ as the solution to the equations:

$$\sum_{i=1}^{n}\{A_iq_1(Z_i, M_i, X_i; \gamma_1) - (1 - A_i)q_0(Z_i, X_i; \hat{\gamma}_0)\}(1, W_i^T, M_i, X_i^T)^T = 0$$

Consistent estimation of $\gamma_1$ nevertheless relies on consistent estimation of $\gamma_0$. Given that $q_1(Z, M, X; \gamma_1)$ and $q_0(Z, X; \gamma_0)$ are both confounding bridges for the treatment assignment mechanism, this raises the question of how to postulate models for the two bridge functions that are compatible. A brief discussion on model compatibility comes in the Section 4, with more detailed results in the Supplementary Material.

Once we have strategies for estimating nuisance parameters indexing the bridge functions, one can construct proximal outcome regression (P-OR), hybrid (P-hybrid) and IPW (P-IPW) estimators of $\psi$:

$$\hat{\psi}_{P-OR} = \frac{1}{n}\sum_{i=1}^{n}h_0(W_i, X_i; \hat{\gamma}_0)$$

$$\hat{\psi}_{P-hybrid} = \frac{1}{n}\sum_{i=1}^{n}(1 - A_i)q_0(Z_i, X_i; \hat{\gamma}_0)h_1(W_i, M_i, X_i; \hat{\beta}_1)$$

$$\hat{\psi}_{P-IPW} = \frac{1}{n}\sum_{i=1}^{n}A_iq_1(Z_i, M_i, X_i; \hat{\gamma}_1)Y_i$$
Then \( \hat{\psi}_{P-OR} \) is a consistent and asymptotically normal (CAN) estimator under model \( M_1 \), \( \hat{\psi}_{P-hybrid} \) is CAN under model \( M_2 \) and \( \hat{\psi}_{P-IPW} \) is CAN under model \( M_3 \). Correctly specifying models for the different bridge functions may be challenging, since they are defined as solutions to integral equations, rather than the conditional expectations or probabilities more common in causal inference e.g. \( E(Y|A = 1, L) \) or \( f(A = 1|L) \). The development of a proximal multiply robust estimator (P-MR), which enables the relaxation of parametric modelling assumptions, is therefore of interest.

**Theorem 3.3.** Under typical regularity conditions,

\[
\hat{\psi}_{P-MR} = \frac{1}{n} \sum_{i=1}^{n} A_i g_1(Z_i, M_i, X_i; \hat{\gamma}_1) \{Y_i - h_1(W_i, M_i, X_i; \hat{\beta}_1)\} \\
+ (1 - A_i) q_0(Z_i, X_i; \hat{\gamma}_0) \{h_1(W_i, M_i, X_i; \hat{\beta}_1) - h_0(W_i, X_i; \hat{\gamma}_0)\} + h_0(W_i, X_i; \hat{\gamma}_0)
\]

is a CAN estimator of \( \psi \) under the union model \( M_{union} = M_1 \cup M_2 \cup M_3 \). Furthermore, under model \( M_{union} \), \( \hat{\psi}_{P-MR} \) attains the semiparametric efficiency bound at the intersection submodel \( M_1 \cap M_2 \cap M_3 \) where Assumption also holds.

Using standard M-estimation arguments, and the influence functions for the nuisance parameter estimators, one can construct a nonparametric ‘sandwich’ estimator of the standard error for \( \hat{\psi}_{P-MR} \) which is robust to potential model misspecification; an alternative option is the nonparametric bootstrap. A weakness of our estimator is that when \( Y \) is binary, \( \hat{\psi}_{P-MR} \) is not guaranteed to fall within the (0,1) interval. This is an important topic for future work and could be remedied e.g. by adapting in the proposal in Section 5 of Tchetgen Tchetgen & Shpitser (2012).

## 4 Simulation studies

In order to evaluate the finite sample performance of the proposed estimators, we conducted a simulation study. Specifically, we generated data \((Y, A, M, X, W, Z)\) by \( X, U \sim MVN((0.25, 0.25, 0)^T, \Sigma) ; f(A = 1|X, U) = expit(-(0.5, 0.5)^T X - 0.4U) ; Z|A, X, U \sim N(0.2 - 0.52A + (0.2, 0.2)^T X - U, 1) ; W|X, U \sim N(0.3 + (0.2, 0.2)^T X - 0.6U, 1) \) and \( M|A, X, U \sim N(-0.3A - (0.5, 0.5)^T X + 0.4U, 1) \), where \( X = (X_1, X_2) \) and

\[
\Sigma = \begin{pmatrix}
\sigma_{x_1}^2 & \sigma_{x_1 x_2} & \sigma_{x_1 u} \\
\sigma_{x_1 x_2} & \sigma_{x_2}^2 & \sigma_{x_2 u} \\
\sigma_{x_1 u} & \sigma_{x_2 u} & \sigma_u^2
\end{pmatrix} = \begin{pmatrix}
0.25 & 0 & 0.05 \\
0 & 0.25 & 0.05 \\
0.05 & 0.05 & 1
\end{pmatrix}.
\]
Finally, \( Y = 2 + 2A + M + 2W - (1, 1)^T X - U + 2\epsilon^* \) where \( \epsilon^* \sim \mathcal{N}(0, 1) \). Since \( W \) and \( M \) are linear in \( X \), \( U \) and the exposure, it follows that this data generating mechanism is compatible with the following models for \( h \) and \( \gamma \) enforced here), it follows that the expression for \( q \) proximal estimator \( \hat{\theta} \) satisfies (6) and (8). Under the additional constraint that \( \epsilon = -\gamma_{1, z}\sigma^2_{z|u,a,x} \) (which is enforced here), it follows that the expression for \( q \) simplifies to

\[
q_1(Z, M, X) = q_0(Z, X) \exp(\gamma_{1,0} + \gamma_{1,z}Z + \gamma_{1,m}M + \gamma_{1,x}X) - q_0(Z, X) \exp(\gamma_{1,0} + \gamma_{1,z}\epsilon_a + \gamma_{1,z}(Z + \gamma_{1,m}M + \gamma_{1,x}X))
\]

satisfies (6) and (8). Under the additional constraint that \( \epsilon_a = -\gamma_{1,z}\sigma^2_{z|u,a,x} \) (which is enforced here), it follows that the expression for \( q \) simplifies to

\[
q_1(Z, M, X) = q_0(Z, X) \exp(\gamma_{1,0} + \gamma_{1,z}Z + \gamma_{1,m}M + \gamma_{1,x}X).
\]

Let \( \hat{\delta}_{P-DR} \) be the proximal doubly robust (P-DR) estimator of \( E\{Y(0)\} \) considered in Cui et al. (2020). We considered four proximal mediation estimators of the natural direct effect \( E\{Y (1, M(0))\} - E\{Y (0)\} \): \( \hat{\theta}_{P-OR} = \hat{\psi}_{P-OR} - \hat{\delta}_{P-DR}, \hat{\theta}_{P-hybrid} = \hat{\psi}_{P-hybrid} - \hat{\delta}_{P-DR}, \hat{\theta}_{P-IPW} = \hat{\psi}_{P-IPW} - \hat{\delta}_{P-DR} \) and \( \hat{\theta}_{P-MR} = \hat{\psi}_{P-MR} - \hat{\delta}_{P-DR} \). We evaluated the performance of the proposed settings in settings where either all bridge functions were correctly modelled (Experiment 1), \( q_1 \) and \( q_0 \) were misspecified (Experiment 2), \( q_1 \) and \( h_0 \) were misspecified (Experiment 3), or \( h_1 \) and \( h_0 \) were misspecified (Experiment 4). We misspecified the models by including \(|X_1|^{1/2} \) and \(|X_2|^{1/2} \) in the bridge function rather than \( X = (X_1, X_2)^T \). We conducted simulations at \( n = 2,000 \) and repeated each experiment 1,000 times.

The results are given in Table 1. As a benchmark, we also considered a naïve non-proximal estimator \( \hat{\theta}_{OLS} \) of the direct effect, based on linearly regressing \( Y \) on \( A, M \) and \( L \); its Monte Carlo bias was 0.5, with 95% confidence intervals that included the true value only 29% of the time. When all bridge functions were correctly specified, the different proximal estimators had comparable performance, with \( \hat{\theta}_{P-OR} \) and \( \hat{\theta}_{P-MR} \) exhibiting slightly greater efficiency compared with the other methods. Across the different mechanisms of misspecification considered, we see that only the multiply robust estimator continues to have low bias, with confidence intervals that possess (approximately) their advertised coverage.
Table 1: Simulation results from Experiments 1-4. Exp: Experiment; Est: estimator; MSE: mean squared error; Bias: Monte Carlo bias; Coverage: 95% confidence interval (CI) coverage; Mean Length: average 95% CI length; Med. Length: median 95% CI length.

| Exp | Est     | Bias | MSE | Coverage | Mean Length | Med. Length |
|-----|---------|------|-----|----------|-------------|-------------|
| 1   | $\hat{\theta}_{P-IPW}$ | 0.00 | 0.02 | 0.95     | 0.51        | 0.50        |
|     | $\hat{\theta}_{P-hybrid}$ | 0.00 | 0.02 | 0.96     | 0.50        | 0.50        |
|     | $\hat{\theta}_{P-OR}$     | 0.00 | 0.02 | 0.96     | 0.50        | 0.50        |
|     | $\hat{\theta}_{P-MR}$     | 0.00 | 0.02 | 0.95     | 0.50        | 0.50        |
| 2   | $\hat{\theta}_{P-IPW}$ | 0.19 | 0.05 | 0.71     | 0.52        | 0.51        |
|     | $\hat{\theta}_{P-hybrid}$ | -0.15 | 0.04 | 0.82     | 0.52        | 0.52        |
|     | $\hat{\theta}_{P-OR}$     | 0.00 | 0.02 | 0.95     | 0.50        | 0.50        |
|     | $\hat{\theta}_{P-MR}$     | 0.00 | 0.02 | 0.95     | 0.50        | 0.50        |
| 3   | $\hat{\theta}_{P-IPW}$ | 0.38 | 0.16 | 0.30     | 0.60        | 0.59        |
|     | $\hat{\theta}_{P-hybrid}$ | 0.00 | 0.02 | 0.95     | 0.50        | 0.50        |
|     | $\hat{\theta}_{P-OR}$     | -0.14 | 0.04 | 0.81     | 0.52        | 0.51        |
|     | $\hat{\theta}_{P-MR}$     | 0.00 | 0.02 | 0.95     | 0.51        | 0.50        |
| 4   | $\hat{\theta}_{P-IPW}$ | -0.01 | 0.02 | 0.94     | 0.51        | 0.51        |
|     | $\hat{\theta}_{P-hybrid}$ | 0.21 | 0.06 | 0.66     | 0.53        | 0.53        |
|     | $\hat{\theta}_{P-OR}$     | 0.17 | 0.05 | 0.72     | 0.52        | 0.51        |
|     | $\hat{\theta}_{P-MR}$     | -0.01 | 0.02 | 0.95     | 0.51        | 0.51        |
In a further set of simulation studies, we considered sensitivity of the different proposals to changes in the confounding mechanism as well as violations of the structural assumptions that underpin the methods. First, in Experiment 5 we changed the above data-generating mechanism such that \( f(A = 1|X, U) \), \( f(M|A, X, U) \) and \( f(Y|A, M, W, X, U) \) no longer depended on \( U \), to check how the methods performed when there was no unmeasured confounding. In this specific setting, to construct the benchmark estimator \( \hat{\theta}_{OLS} \) we adjusted for \( A, M, X \) and \( W \) but not \( Z \), to avoid collider bias induced via an association between \( A \) and \( U \). In Experiment 6, we considered violations of the exclusion restriction Assumption 5.2, by generating \( Y = 2 + 2A + M + 2W - (1,1)^T X - U - 0.5Z + 2\epsilon^* \). In Experiment 7, we considered violations of the exclusion restriction Assumption 5.4, by generating \( W \) from \( W|X, U, A \sim N(0.3 + (0.2, 0.2)^T X - 0.6U + 0.2A, 1) \). In Experiment 8, we looked at a near-violation of the completeness conditions, where the coefficient for \( U \) in the model for \( E(W|X, U) \) was reduced in strength to 0.05, such that \( W \) was only weakly \( U \)-relevant and the conditional associations between \( W \) and \( Z \) were also weak. In 9), we reversed this such that \( Z \) was now only weakly \( U \)-relevant. Each of the models used to construct the bridge functions included \( X \), rather than the transformations considered in Experiments 2-4. Values of the parameters in the data-generating mechanism were adjusted where necessary, to ensure that all bridge functions were correctly specified. The results of Experiments 5-9 are shown in Table 3 in the Supplementary Material. We see that in settings where conditional exchangeability holds, the proximal estimators perform similarly in terms of bias compared with \( \hat{\theta}_{OLS} \), but displayed a decrease in efficiency. When the exclusion restrictions are violated, in this case the proximal estimators performed similarly or slightly worse than the naïve, biased OLS estimator. When \( Z \) or \( W \) are not \( U \)-relevant, we see that the standard errors for the proximal estimators can dramatically inflate; this is unsurprising, given how common instrumental variable estimators perform when instruments are weak/irrelevant. The proximal estimators also typically displayed considerably larger bias than \( \hat{\theta}_{OLS} \), but smaller median bias. The multiply robust estimator \( \hat{\theta}_{P-MR} \) generally displayed smaller mean and median bias compared with the other methods in Experiments 8 and 9.

5 Data analysis

In the Job Corps study, participants were randomised from November 1994 to February 1996 either to treatment (access to the Job Corps program) or to control (no access). However, since individuals could choose whether to participate in the program or not, we will treat the exposure of interest \((did \ the \ individual \ attend \ class \ in \ the \ year \ following \ assign-\)
The outcome of interest was the number of arrests in the fourth year after assignment, and the mediator of interest was the percentage of weeks employed in the second year. Although data on a rich set of covariates was measured at baseline, it was nevertheless possible that unmeasured confounding could lead to biased estimates of both direct and indirect effects. Investigators collected information on factors that were known to be associated with duration in the program e.g. expectations of the program, interactions with recruiters. Huber et al. (2020) note that such variables may be strongly correlated with motivation, considered as an important latent source of confounding. They therefore adjusted for these variables in the analysis in the same way as standard measured confounders. In contrast, we treated these variables as proxies of a unmeasured confounder, and changed the analysis accordingly. Similar to Tchetgen Tchetgen et al. (2020), we restricted consideration to four potential proxies strongly correlated with the exposure and/or the outcome: time being spent spoken to by recruiter, worried about the Job Corps program, expected improvement in social skills and whether the first contact by the recruiter was in the office or not. Since there was no a priori understanding as to whether these were candidates for $Z$ or $W$, we used the algorithm described in Tchetgen Tchetgen et al. (2020) to assign them. This led to the first two being used for $Z$, and the second two used for $W$.

Our sample consisted of 10,775 participants; further information on the sample is given in Huber et al. (2020). 257 participants had missing data on $Z$, who were removed from the analysis. Linear and logistic models were postulated for the outcome and exposure bridge functions respectively. We considered both proximal IPW, hybrid, outcome regression and multiply robust estimators of $E[Y\{1, M(0)\}]$ and $E[Y\{0, M(1)\}]$. We contrasted our estimator with a standard multiply robust (S-MR) approach $\hat{\theta}_{S-MR}$ based on the efficient influence function derived in Tchetgen Tchetgen & Shpitser (2012) that is valid under conditional exchangeability-type assumptions; we again postulated linear models for $E(Y|A = a, M, X, Z, W)$ and $E\{E(Y|A = a, M, X, Z, W)|A = a^*, X, Z, W\}$ and a logistic model for the odds $P(A = 1|M, X, Z, W)/P(A = 0|M, X, Z, W)$ and for $P(A = 1|X, Z, W)$. All outcome regression models for the confounding bridge functions and otherwise were fit separately in control and treatment groups, to allow for treatment-mediator and treatment-covariate interactions. Since the set of covariates measured at baseline was relatively high in dimension, we excluded variables with amounts of missingness $>50\%$, or which had some missing values and were highly correlated with variables that were fully observed. For all other variables with missingness, we used the missing indicator method as in Huber et al. (2020). Standard errors for all estimators were calculated using sandwich estimators. In the Supplementary Material, following the AGReMA statement on good practice for con-
ducting and reporting mediation analysis (Lee et al., 2021), we provide further information on the study and data analysis.

Table 2: Results from the analysis of the Job Corps study. CI: confidence interval.

| Estimand | S-MR       | 95% CI          | P-MR       | 95% CI          |
|----------|------------|-----------------|------------|-----------------|
| $E[Y \{1, M(0)\} - Y \{0, M(0)\}]$ | -0.0107    | -0.0341, 0.0128 | 0.0057     | -0.0699, 0.0813 |
| $E[Y \{1, M(1)\} - Y \{0, M(1)\}]$ | -0.0110    | -0.0345, 0.0124 | -0.0016    | -0.0781, 0.0749 |
| $E[Y \{1, M(1)\} - Y \{1, M(0)\}]$ | 0.0006     | -0.0229, 0.0241 | -0.0088    | -0.0314, 0.0138 |
| $E[Y \{0, M(1)\} - Y \{0, M(0)\}]$ | 0.0009     | -0.0001, 0.0019 | -0.0016    | -0.0110, 0.0078 |

Results for the standard and proximal multiply robust approaches can be seen in Table 2. The total effect estimate given by the standard approach was -0.01 (95% confidence interval (CI): -0.022, 0.002) and for the proximal approach, it was -0.003 (95% CI: -0.040, 0.033). The estimates of the direct and indirect effects yielded by both approaches are also close to the null, and all 95% confidence intervals contain the null. The direct effects estimates under the proximal approach tended to be closer to the null; and the indirect effects were slightly larger in magnitude (although still very small). The results of the other estimators can be found in the Supplementary Material; the multiply robust estimator $\hat{\theta}_{P-MR}$ tended to agree more closely with $\hat{\theta}_{P-hybrid}$, although there was not a large disparity between the point estimates.

6 Discussion

An advantage of doubly/multiply robust methods, used in combination with cross-fitting, is that data-adaptive methods can be used to estimate nuisance parameters, yet their potentially slow rates of convergence are not necessarily inherited by the estimator of the target parameter (Chernozhukov et al., 2018). A complication in proximal learning is that the nuisances are defined as the solutions to integral equations. Progress in this direction is described in Ghassami et al. (2022) and Kallus et al. (2021); it would thus be useful to extend these ideas to mediation analysis. Another avenue for future work would be to extend the results of identification and estimation to more general path-specific effects (Avin et al., 2005; Shpitser, 2013), which are relevant in particular in settings when confounders of the mediator-outcome relationship are affected by the exposure. In such cases the cross-world assumption fails to hold, and standard natural effects are no longer identified. Finally, an important topic more generally in proximal learning is the development of sensitivity
analysis methods. A simple way to check how sensitive results are to categorisation of the $Z$ and $W$ proxies is to permute the labels. The development of more advanced tools to assess deviations from specific key assumptions (e.g. the exclusion restrictions involving the proxies) is left to future work. Under the failure of certain assumptions, methods for partial identification such as nonparametric bounds may also be useful (Robins, 1989; Manski, 1990).

Acknowledgements

The first author gratefully acknowledges support from the Ghent University Special Research Fund and the Research Foundation Flanders. The second and third authors gratefully acknowledge support from the National Institutes of Health.

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Appendix

Additional figures

Figure 2: Other causal diagrams compatible with Assumptions 3 and 5
Completeness

In the present context, the two components of Assumption 6 demand sufficient variability in $Z$ relative to the variability in $U$, and that $Z$ is associated with $U$ (both conditional on $A = 1$, $M$, and $X$, and conditional on $A = 0$ and $X$, at any given values of the mediators, covariates and proxy $Z$). They enable one to use the measured proxies to learn about the unmeasured $U$. Some specific examples regarding completeness are given below:

Example 1. (Binary confounder) Suppose that $W$, $Z$ and $U$ are all binary. Then Assumption 6 reduces to the conditions that $W \not\perp Z | A = 1, M = m, X = x$ for all $m$ and $x$, and that $W \not\perp Z | A = 0, X = x$ for all $x$.

Example 2. (Categorical confounder) Suppose now that $W$, $Z$ and $U$ are categorical, (with number of categories $d_u$, $d_z$ and $d_w$ respectively), then Assumption 6 requires that $\min(d_z,d_w) \geq d_u$ or in other words, that $Z$ and $W$ should each have at least as many categories as $U$. Furthermore, it also implies a rank conditions on relevant matrices based on the conditional distribution of $W$ given $Z$, $A = 1$, $M$ and $X$, as well as $W$ given $Z$, $A = 0$ and $X$ (see Shi et al. (2020a) for details).

Example 3. (Exponential families) Suppose that the distribution of $U$ given $Z$, $A = 1$, $M$ and $X$ is absolutely continuous with probability approaching one, with density $f(U = u | Z = z, A = 1, M = m, X = x) = s(u)t(z, m, x)\exp\{\mu(z, m, x)^T \tau(u)\}$ where $s(u) > 0$, $\tau(u)$ is one-to-one in $u$ and the support of $\mu(z, m, x)$ is an open set. Then Assumption 6(i) holds (Newey & Powell, 2003), and the remaining condition in Assumption 6 can be shown similarly.

Sufficient conditions for completeness have also been given for location-scale families (Hu & Shiu, 2018), as well as in nonparametric models (D’Haultfoeuille, 2011; Darolles et al., 2011). One can see (in particular from the order condition in Example 2) that accumulating data on a rich collection of proxy variables provides a better opportunity to control for an unmeasured $U$. For example, if $Z$ and $W$ are categorical but $U$ has infinite support, the completeness conditions would generally fail to hold.

Derivation of conditional independencies

In the proofs that follow, we will make repeated use of conditional independencies that are implied by Assumptions 1, 3 and 5. We will make use of the graphoid axioms of conditional independence for random variables $R_1$, $R_2$, $R_3$, $R_4$ (Dawid, 1979):
1. $R_1 \parallel R_2 \mid R_3 \rightarrow R_2 \parallel R_1 \mid R_3$.

2. $R_1 \parallel (R_2, R_4) \mid R_3 \rightarrow R_1 \parallel R_2 \mid R_3$ and $R_1 \parallel R_4 \mid R_3$.

3. $R_1 \parallel (R_2, R_4) \mid R_3 \rightarrow R_1 \parallel R_2 \mid R_3, R_4$.

4. $R_1 \parallel R_2 \mid R_3$ and $R_1 \parallel R_4 \mid R_3, R_2 \rightarrow R_1 \parallel (R_2, R_4) \mid R_3$.

in order to show to show that

$$Z \parallel Y \mid M, A, U, X$$
$$Z \parallel M \mid A, U, X$$
$$Z \parallel W \mid M, A, U, X$$
$$Z \parallel (W, M) \mid A, U, X$$
$$Z \parallel W \mid A, U, X$$
$$W \parallel A \mid U, X$$
$$W \parallel A \mid M, U, X$$

Then

$$Y(a, m) \parallel (Z, M(a)) \mid A, U, X \quad \text{(Assumptions \texttt{5} 5.1, and 4th axiom)}$$

$$\rightarrow Y(m) \parallel (Z, M) \mid A, U, X \quad \text{(Assumption \texttt{1})}$$

$$\rightarrow Y(m) \parallel Z \mid M, A, U, X \quad \text{(3rd axiom)}$$

$$\rightarrow Y \parallel Z \mid M, A, U, X \quad \text{(Assumption \texttt{1})}$$

$$\rightarrow Z \parallel Y \mid M, A, U, X \quad \text{(1st axiom)}$$

and

$$Z \parallel M(a), A \mid U, X \quad \text{(Assumptions \texttt{3} 3, \texttt{2} 2 and 4th axiom)}$$

$$\rightarrow Z \parallel M(a) \mid A, U, X \quad \text{(3rd axiom)}$$

$$\rightarrow Z \parallel M \mid A, U, X \quad \text{(Assumption \texttt{1})}$$

and

$$W \parallel (M(a), A, Z) \mid U, X \quad \text{(Assumptions \texttt{5} 3, \texttt{4} 4 and 4th axiom)}$$

$$\rightarrow W \parallel (M(a), Z) \mid A, U, X \quad \text{(3rd axiom)}$$

$$\rightarrow W \parallel (M, Z) \mid A, U, X \quad \text{(Assumption \texttt{1})}$$

$$\rightarrow W \parallel Z \mid M, A, U, X \quad \text{(3rd axiom)}$$

$$\rightarrow Z \parallel W \mid M, A, U, X \quad \text{(1st axiom)}$$

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From the previous two results and the 4th axiom, we have $Z \perp (W, M) | A, U, X$. Also,

$$W \perp (M(a), A, Z) | U, X \quad \text{(Assumptions 3, 4 and 4th axiom)}$$

$$\rightarrow W \perp (A, Z) | U, X \quad \text{(2nd axiom)}$$

$$\rightarrow W \perp Z | A, U, X \quad \text{(3rd axiom)}$$

Next,

$$W \perp (M(a), A, Z) | U, X \quad \text{(Assumptions 3, 4 and 4th axiom)}$$

$$\rightarrow W \perp A | U, X \quad \text{(2nd axiom)}$$

Finally,

$$W \perp (M(a), A, Z) | U, X \quad \text{(Assumptions 3, 4 and 4th axiom)}$$

$$\rightarrow W \perp (M(a), A) | U, X \quad \text{(2nd axiom)}$$

$$\rightarrow W \perp M | A, U, X \quad \text{(3rd axiom)}$$

$$\rightarrow W \perp (M, A) | U, X \quad \text{(W \perp A | U, X and 4th axiom)}$$

$$\rightarrow W \perp A | M, U, X \quad \text{(3rd axiom)}$$

**Proof of Theorem 2.1**

*Proof.* Following the proof of Theorem 1 in Miao et al. (2018a):

$$E(Y|z, A = 1, m, x) = \int E(Y|u, z, A = 1, m, x)dF(u|z, A = 1, m, x) \quad \text{(Tower rule)}$$

$$= \int E(Y|u, A = 1, m, x)dF(u|z, A = 1, m, x) \quad \text{(Z \perp Y|M, A, U, X).}$$

Also,

$$E(Y|z, A = 1, m, x)$$

$$= \int h_1(w, m, x)dF(w|z, A = 1, m, x) \quad \text{(by 2)}$$

$$= \int \int h_1(w, m, x)dF(w|u, z, A = 1, m, x)dF(u|z, A = 1, m, x) \quad \text{(Tower rule)}$$

$$= \int \int h_1(w, m, x)dF(w|u, A = 1, m, x)dF(u|z, A = 1, m, x) \quad \text{(Z \perp W|M, A, U, X)}$$
and by the completeness condition 6.1, result (4) follows.

Then

\[ E\{h_1(W, M, x)|z, A = 0, x\} = \int E\{h_1(W, M, x)|u, z, A = 0, x\}dF(u|z, A = 0, x) \quad \text{(Tower rule)} \]

\[ = \int E\{h_1(W, M, x)|u, A = 0, x\}dF(u|z, A = 0, x) \quad \text{($Z \perp\!
\!
\!
\perp (W, M)|A, U, X$)} \]

and

\[ E\{h_1(W, M, x)|z, A = 0, x\} = \int h_0(w, x)dF(w|z, A = 0, x) \quad \text{(by (3))} \]

\[ = \int \int h_0(w, x)dF(w|z, u, A = 0, x)dF(u|z, A = 0, x) \quad \text{(Tower rule)} \]

\[ = \int \int h_0(w, x)dF(w|u, A = 0, x)dF(u|z, A = 0, x) \quad \text{($Z \perp\!
\!
\!
\perp W|A, U, X$)} \]

and by the completeness condition 6.2, we have

\[ E\{h_1(W, M, X)|U, A = 0, X\} = \int h_0(w, X)dF(w|U, A = 0, X). \quad \text{(10)} \]
Finally, it follows from the above results that

\[
\psi = \int \int E[Y \{1, M(0)\}|u, x]dF(u|x)dF(x)
\]

\[
= \int \int \int E\{Y(1, m)|u, M(0) = m, x\}dF_M(0)(m|u, x)dF(u|x)dF(x) \quad \text{(Tower rule)}
\]

\[
= \int \int \int E\{Y(1, m)|u, x\}dF_M(0)(m|u, x)dF(u|x)dF(x) \quad \text{(Assumption 4)}
\]

\[
= \int \int \int E\{Y(1, m)|u, A = 1, x\}dF_M(0)(m|u, x)dF(u|x)dF(x) \quad \text{(Assumption 3.1)}
\]

\[
= \int \int \int E\{Y|u, A = 1, m, x\}dF_M(0)(m|u, x)dF(u|x)dF(x) \quad \text{(Assumption 3.2)}
\]

\[
= \int \int \int E\{Y|u, A = 1, m, x\}dF_M(0)(m|u, x)dF(u|x)dF(x) \quad \text{(Assumption 1)}
\]

\[
= \int \int \int \int h_1(w, m, x)dF(w|u, A = 1, m, x)dF_M(0)(m|u, A = 0, x)dF(u|x)dF(x) \quad \text{(by (4))}
\]

\[
= \int \int \int \int h_1(w, m, x)dF(w|u, A = 0, x)dF(u|x)dF(x) \quad \text{(W \perp\!
\perp A|M, U, X)}
\]

\[
= \int \int \int \int h_0(w, x)dF(w|u, A = 0, x)dF(u|x)dF(x) \quad \text{(W \perp\!
\perp A|U, X)}
\]

\[
= \int \int h_0(w, x)dF(w|x)dF(x) \quad \text{(Tower rule)}
\]

where we index by \(M(0)\) to indicate that the integration is done over the counterfactual \(M(0)\) rather than the observed \(M\).

**Proof of Theorem 2.2**

Assumption 8. (*Completeness*)
1. For any function $g(u)$, if $E\{g(U)|W = w, A = 1, M = m, X = x\} = 0$ for any $w$, $m$ and $x$ almost surely, then $g(U) = 0$ almost surely.

2. For any function $g(u)$, if $E\{g(U)|W = w, A = 0, X = x\} = 0$ for any $w$ and $x$ almost surely, then $g(U) = 0$ almost surely.

Proof. Result (7) follows directly from Theorem 2.2 of Cui et al. (2020), but is reproduced here for completeness. First,

$$
\frac{1}{f(A = 0|w, x)} = \int \frac{1}{f(A = 0|w, x)} dF(u|w, x)
= \int \frac{1}{f(A = 0|u, w, x)} dF(u|w, A = 0, x)
= \int \frac{1}{f(A = 0|u, x)} dF(u|w, A = 0, x) \quad (W \perp A|U, X)
$$

and also

$$
\frac{1}{f(A = 0|w, x)} = E\{q_0(Z, x)|w, A = 0, x\} \quad \text{(by (6))}
= \int \int q_0(Z, x) dF(z|u, w, A = 0, x) dF(u|w, A = 0, x) \quad \text{(Tower rule)}
= \int \int q_0(Z, x) dF(z|u, A = 0, x) dF(u|w, A = 0, x) \quad (Z \perp W|A, U, X)
$$
and by Assumption 8.2, we have (7). Further

\[
\psi = \int \int \int E(Y|u, A = 1, m, x) dF(m|u, A = 0, x) dF(u|x) dF(x) \quad \text{(Assumptions 1, 3 and 1)}
\]

\[
= \int \int \int E(Y|u, A = 1, m, x) dF(m|u, A = 0, x) \frac{f(A = 0|u, x)}{f(A = 0|u, x)} dF(u|x) dF(x)
\]

\[
= E \left\{ \frac{I(A = 0)}{f(A = 0|U, X)} E(Y|U, A = 1, M, X) \right\} \quad \text{(Tower rule)}
\]

\[
= E \left[ I(A = 0) E\{q_0(Z, X)|U, A = 0, X\} E(Y|U, A = 1, M, X) \right] \quad \text{by (7)}
\]

\[
= E \left[ I(A = 0) E\{q_0(Z, X)|U, A = 0, M, X\} E(Y|U, A = 1, M, X) \right] \quad (Z \perp M|A, U, X)
\]

\[
= E \left[ I(A = 0) E\{q_0(Z, X)|U, A, M, X\} E(Y|U, A = 1, M, X) \right]
\]

\[
= E \left\{ I(A = 0) q_0(Z, X) E(Y|U, A = 1, M, X) \right\} \quad \text{(Tower rule)}
\]

\[
= E \left[ I(A = 0) q_0(Z, X) E\{h_1(W, M, X)|U, A = 1, M, X\} \right] \quad \text{by (4)}
\]

\[
= E \left[ I(A = 0) q_0(Z, X) E\{h_1(W, M, X)|U, A = 0, M, X\} \right] \quad (W \perp A|M, U, X)
\]

\[
= E \left[ I(A = 0) q_0(Z, X) E\{h_1(W, M, X)|Z, U, A = 0, M, X\} \right] \quad (Z \perp W|M, A, U, X)
\]

\[
= E \left[ I(A = 0) q_0(Z, X) h_1(W, M, X) \right] \quad \text{(Law of iterated expectation.)}
\]

For the second part of Theorem 2.2

\[
E\{q_0(Z, x)|w, A = 0, m, x\} \frac{f(A = 0|w, m, x)}{f(A = 1|w, m, x)}
\]

\[
= \frac{1}{f(A = 1|w, m, x)} \int E\{q_0(Z, x)|u, w, A = 0, m, x\} f(A = 0|w, m, x) dF(u|w, A = 0, m, x)
\]

(Tower rule)

\[
= \frac{1}{f(A = 1|w, m, x)} \int E\{q_0(Z, x)|u, w, A = 0, m, x\} f(A = 0|u, w, m, x) dF(u|w, m, x)
\]

\[
= \int E\{q_0(Z, x)|u, w, A = 0, m, x\} \frac{f(A = 0|u, w, m, x)}{f(A = 1|u, w, m, x)} dF(u|w, A = 1, m, x)
\]

\[
= \int E\{q_0(Z, x)|u, w, A = 0, m, x\} \frac{f(A = 0|u, m, x)}{f(A = 1|u, m, x)} dF(u|w, A = 1, m, x) \quad (W \perp A|M, U, X)
\]

\[
= \int E\{q_0(Z, x)|u, A = 0, m, x\} \frac{f(A = 0|u, m, x)}{f(A = 1|u, m, x)} dF(u|w, A = 1, m, x) \quad (Z \perp W|M, A, U, X)
\]
where for the third equality, we use that
\[ f(U|W, A = 1, M, X) f(A = 1|W, M, X) = f(A = 1|U, W, M, X) f(U|W, M, X) \]
and so
\[ \frac{f(U|W, A = 1, M, X)}{f(A = 1|U, W, M, X)} = \frac{f(U|W, M, X)}{f(A = 1|W, M, X)}. \]

Also
\[
E\{q_0(Z, x)|w, A = 0, m, x\} \frac{f(A = 0|w, m, x)}{f(A = 1|w, m, x)} \\
= \int q_1(z, m, x) dF(z|w, A = 1, m, x) \quad \text{(by (9))}
\]
\[
= \int \int q_1(z, m, x) dF(z|u, w, A = 1, m, x) dF(u|w, A = 1, m, x) \quad \text{(Tower rule)}
\]
\[
= \int \int q_1(z, m, x) dF(z|u, A = 1, m, x) dF(u|w, A = 1, m, x) \quad (Z \perp W|M, A, U, X)
\]
Hence
\[
E\{q_0(Z, X)|U, A = 0, M, X\} \frac{f(A = 0|U, M, X)}{f(A = 1|U, M, X)} = E\{q_1(Z, M, X)|U, A = 1, M, X\} \quad (11)
\]
follows from Assumption S.1. Finally,

\[
\psi = E \left\{ \frac{I(A = 0)}{f(A = 0 | U, X)} E(Y | U, A = 1, M, X) \right\} \quad \text{(Assumptions 1, 3, and 4)}
\]

\[
= E \left[ I(A = 0) E\{q_0(Z, X) | U, A = 0, X \} E(Y | U, A = 1, M, X) \right] \quad \text{(by (7))}
\]

\[
= E \left\{ I(A = 0) q_0(Z, X) E(Y | U, A = 1, M, X) \right\} \quad \text{(Tower rule)}
\]

\[
= E \left\{ I(A = 0) q_0(Z, X) E(Y | Z, U, A = 1, M, X) \right\} \quad \text{(Tower rule)}
\]

\[
= \int \int q_0(z, x) E(Y | z, u, A = 1, m, x) f(A = 0 | u, m, z, x) dF(u, m, z|x) dF(x) \quad \text{(Tower rule)}
\]

\[
= \int \int q_0(z, x) E(Y | u, A = 1, m, x) f(A = 0 | u, m, z, x) dF(u, m, z|x) dF(x) \quad \text{(Tower rule)}
\]

\[
= E \left[ E\left\{q_0(Z, X) | U, A = 0, M, X \right\} E(Y | U, A = 1, M, X) f(A = 0 | U, M, X) \right] \quad \text{(Tower rule)}
\]

\[
= E \left[ I(A = 1) Y E\{q_1(Z, M, X) | U, A = 1, M, X \} \right] \quad \text{(Tower rule)}
\]

\[
= E \left[ I(A = 1) Y q_1(Z, M, X) \right] \quad \text{(Tower rule)}
\]

Proof of Theorem 3.1

Proof. In order to first obtain an influence function for \( \psi \) under the semiparametric model \( M_{sp} \), one can find the mean zero random variable \( G \) for which

\[
\frac{\partial \psi}{\partial t}|_{t=0} = E\{GS(O; t)\}|_{t=0}
\]

where \( S(O; t) = \partial \log f(O; t) / \partial t \). Here, we take a derivative with respect to the parameter \( t \) indexing a one-dimensional parametric submodel in \( M_{sp} \), which returns true density \( f(O) \) at \( t = 0 \).

After noting the moment restrictions

\[
E\{Y - h_1(W, M, X) | Z, A = 1, M, X \} = 0
\]

\[
E\{h_1(W, M, X) - h_0(W, X) | Z, A = 0, X \} = 0
\]

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implied by (2) and (3), then letting $E_1 = Y - h_1(W, M, X)$ and $E_0 = h_1(W, M, X) - h_0(W, X)$, it follows that

$$E \left\{ \frac{\partial}{\partial t} h_0(W, X)|_{t=0} \right\} Z, A = 0, X \right\}$$

$$= E \{ E_0 S(W, M | Z, A = 0, X)|Z, A = 0, X \} + E \left\{ \frac{\partial}{\partial t} h_1(W, M, X)|_{t=0} \right\} Z, A = 0, X \right\}$$

(12)

and

$$E \left\{ \frac{\partial}{\partial t} h_1(W, M, X)|_{t=0} \right\} Z, A = 1, M, X \right\} = E \{ E_1 S(Y, W | Z, A = 1, M, X)|Z, A = 1, M, X \} .$$

(13)

Then

$$\frac{\partial \psi |_{t=0}}{\partial t} = \frac{\partial}{\partial t} E_t[h_0(W, X)]|_{t=0} = E[h_0(W, X) S(W, X)] + E \left\{ \frac{\partial}{\partial t} h_0(W, X)|_{t=0} \right\}$$

$$= E[\{h_0(W, X) - \psi\} S(O)] + E \left\{ \frac{\partial}{\partial t} h_0(W, X)|_{t=0} \right\}$$

For the second term on the right hand side of the final equality,

$$E \left\{ \frac{\partial}{\partial t} h_0(W, X)|_{t=0} \right\} = E \left\{ \frac{I(A = 0)}{f(A = 0|W, X)} \frac{\partial}{\partial t} h_0(W, X)|_{t=0} \right\}$$

$$= E \left\{ I(A = 0) q_0(Z, X)|W, A = 0, X \right\} \frac{\partial}{\partial t} h_0(W, X)|_{t=0} \right\}$$

$$= E \left\{ I(A = 0) q_0(Z, X) \frac{\partial}{\partial t} h_0(W, X)|_{t=0} \right\}$$

$$= E \left[ I(A = 0) q_0(Z, X) E \left\{ \frac{\partial}{\partial t} h_0(W, X)|_{t=0} \right\} Z, A = 0, X \right\}$$

$$= E \left[ I(A = 0) q_0(Z, X) E \{ E_0 S(W, M | Z, A = 0, X)|Z, A = 0, X \} \right]$$

$$+ E \left[ I(A = 0) q_0(Z, X) E \left\{ \frac{\partial}{\partial t} h_1(W, M, X)|_{t=0} \right\} Z, A = 0, X \right\} .$$

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and

\[
E \left[ I(A = 0)q_0(Z, X)E \left\{ \frac{\partial}{\partial t} h_{1t}(W, M, X) \big|_{t=0} \right\} \right] \\
= E \left\{ I(A = 0)q_0(Z, X) \frac{\partial}{\partial t} h_{1t}(W, M, X) \big|_{t=0} \right\} \\
= E \left[ f(A = 0|W, M, X)E\{q_0(Z, X)|W, A = 0, M, X\} \frac{\partial}{\partial t} h_{1t}(W, M, X) \big|_{t=0} \right] \\
= E \left[ I(A = 1) \frac{f(A = 0|W, M, X)}{f(A = 1|W, M, X)} E\{q_0(Z, X)|A = 0, M, W\} \frac{\partial}{\partial t} h_{1t}(W, M, X) \big|_{t=0} \right] \\
= E \left[ I(A = 1)E\{q_1(Z, M, X)|W, A = 1, M, X\} \frac{\partial}{\partial t} h_{1t}(W, M, X) \big|_{t=0} \right] \\
= E \left\{ I(A = 1)q_1(Z, M, X) \frac{\partial}{\partial t} h_{1t}(W, M, X) \big|_{t=0} \right\} \\
= E \left[ I(A = 1)q_1(Z, M, X)E \left\{ \frac{\partial}{\partial t} h_{1t}(W, M, X) \big|_{t=0} \right\} \right] \\
= E \left[ I(A = 1)q_1(Z, M, X)E \left\{ S(Y, W|Z, A = 1, M, X) \right\} \right] \\
= E \left[ I(A = 1)q_1(Z, M, X)E \left\{ \frac{\partial}{\partial t} h_{1t}(W, M, X) \big|_{t=0} \right\} \right]
\]

Putting this together, we have

\[
E \left\{ \frac{\partial}{\partial t} h_{0t}(W, X) \big|_{t=0} \right\} \\
= E \left\{ I(A = 0)q_0(Z, X)E_0S(W, M|Z, A = 0, X) \right\} \\
+ E \left\{ I(A = 1)q_1(Z, M, X)E_1S(Y, W|Z, A = 1, M, X) \right\} \\
= E \left[ I(A = 0)q_0(Z, X)E_0S(O|W, M, Z, A, X) \right] \\
- E \left[ I(A = 0)q_0(Z, X)E_0S(O|Z, A, X) \right] \\
+ E \left[ I(A = 1)q_1(Z, M, X)E_1E(S(O)|Y, W, Z, A, M, X) \right] \\
- E \left[ I(A = 1)q_1(Z, M, X)E_1E(S(O)|Z, A, M, X) \right] \\
= E \left[ I(A = 0)q_0(Z, X)E_0S(O) \right] + E \left[ I(A = 1)q_1(Z, M, X)E_1S(O) \right]
\]

To show that

\[
I(A = 1)q_1(Z, M, X)E_1 + I(A = 0)q_0(Z, X)E_0 + h_0(W, X) - \psi
\]

is the efficient influence function, we need to show that it belongs to the tangent space implied by the restrictions (12) and (13) on the scores. Specifically, by (12) and (13) the
tangent space is comprised of the set of scores $S(O) \in L_2(O)$ that satisfy

$$E \{ \mathcal{E}_1 S(Y, W | Z, A = 1, M, X) | Z, A = 1, M, X \} \in R(T_1)$$
$$E \{ \mathcal{E}_0 S(W, M | Z, A = 0, X) | Z, A = 0, X \} \in R(T_0)$$

where $R()$ denotes the range space of an operator. Following the proof of Theorem 3 in Ying et al. (2021), by Assumption 7 holding at the true law, the tangent space equals $L_2(O)$ and the main result follows.

\[ \square \]

**Proof of Theorem 3.2**

**Proof.** From (8), we have that

$$E \left[ q_1(Z, M, X; \gamma_1) - \kappa(W, M, X; \gamma_0) \right| W, A = 1, M, X] = 0$$

where

$$\kappa(W, M, X; \gamma_0) = E \{ q_0(Z, X; \gamma_0) | W, A = 0, M, X \} \frac{f(A = 0 | W, M, X)}{f(A = 1 | W, M, X)}$$

and therefore

$$\partial E_t \left[ \{ q_1(Z, M, X; \gamma_1_t) - \kappa_t(W, M, X; \gamma_0_t) \} d_1(W, M, X) \right| A = 1 \bigg/ \partial t \big| t = 0 = 0$$

for any $d_1(W, M, X)$ of the same dimension as $\gamma_1$, where

$$\kappa_t(W, M, X; \gamma_0_t) = E_t \{ q_0(Z, X; \gamma_0_t) | W, A = 0, M, X \} \frac{f_t(A = 0 | W, M, X)}{f_t(A = 1 | W, M, X)}.$$
After some algebra and re-arrangement of terms,

\[-\frac{1}{f(A = 1)} E \left\{ \frac{\partial q_1(Z, M, X; \gamma_1)}{\partial \gamma_1} A d_1(W, M, X) \right\} \frac{\partial \gamma_1}{\partial t} \bigg|_{t=0} \]

\[-\frac{1}{f(A = 1)} E \left[ A \{ q_1(Z, M, X; \gamma_1) - \kappa(W, M, X; \gamma_0) \} d_1(W, M, X) S(O) \right] \]

\[-\frac{1}{f(A = 1)} E \left[ \frac{\partial q_0(Z, X; \gamma_0)}{\partial \gamma_0} (1 - A) d_1(W, M, X) \right] \frac{\partial \gamma_0}{\partial t} \bigg|_{t=0} \]

\[-\frac{1}{f(A = 1)} E \left[ (1 - A) q_0(Z, X; \gamma_0) S(Z|W, A, M, X) d_1(W, M, X) \right] \]

\[-E \left[ \frac{\partial f(A = 0|W, M, X)}{f(A = 1|W, M, X)} \bigg|_{t=0} \right] E \{ q_0(Z, X; \gamma_0)|W, A = 0, M, X \} d_1(W, M, X) \bigg|_{A = 1} \]

\[+ E \left[ \frac{\partial f(A = 1|W, M, X)}{f^2(A = 1|W, M, X)} \right] f(A = 0|W, M, X) E \{ q_0(Z; \gamma_0)|W, A = 0, M, X \} d_1(W, M, X) \bigg|_{A = 1} \]

For the third term on the right hand side of the equality,

\[-\frac{1}{f(A = 1)} E \left[ (1 - A) q_0(Z, X; \gamma_0) S(Z|W, A, M, X) d_1(W, M, X) \right] \]

\[-\frac{1}{f(A = 1)} E \left[ (1 - A) [q_0(Z, X; \gamma_0) - E \{ q_0(Z, X; \gamma_0)|W, A = 0, M, X \}] d_1(W, M, X) S(O) \right] \]

For the penultimate term, we have

\[-E \left[ \frac{\partial f(A = 0|W, M, X)}{f(A = 1|W, M, X)} \bigg|_{t=0} \right] E \{ q_0(Z, X; \gamma_0)|W, A = 0, M, X \} d_1(W, M, X) \bigg|_{A = 1} \]

\[-E \left[ E \{ (1 - A) S(A|W, M, X)|W, M, X \} \right] f(A = 1|W, M, X) E \{ q_0(Z, X; \gamma_0)|W, A = 0, M, X \} d_1(W, M, X) \bigg|_{A = 1} \]

\[-\frac{1}{f(A = 1)} E \left[ (1 - A) S(A|W, M, X) q_0(Z, X; \gamma_0) d_1(W, M, X) \right] \]

\[-\frac{1}{f(A = 1)} E \left[ \{(1 - A) - f(A = 0|W, M, X)\} E \{ q_0(Z, X; \gamma_0)|W, A = 0, M, X \} d_1(W, M, X) S(O) \right] \} .

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For the final term

\[
E \left[ \frac{\partial f_t(A = 1 | W, M, X)}{\partial t |_{t=0}} f(A = 0 | W, M, X) E\{q_0(Z, X; \gamma_0) | W, A = 0, M, X\} d_1(W, M, X) \right] \bigg| A = 1
\]

\[
= \frac{1}{f(A = 1)} E \left[ AS(A | W, M, X) \frac{f(A = 0 | W, M, X)}{f(A = 1 | W, M, X)} E\{q_0(Z, X; \gamma_0) | W, A = 0, M, X\} d_1(W, M, X) \right]
\]

\[
= \frac{1}{f(A = 1)} E \left[ \left\{ \frac{A - f(A = 1 | W, M, X)}{f^2(A = 1 | W, M, X)} \right\} \kappa(W, M, X; \gamma_0) d_1(W, M, X) S(O) \right].
\]

Putting this all together, it follows that

\[
- \frac{1}{f(A = 1)} E \left\{ \frac{\partial q_1(Z, M, X; \gamma_1)}{\partial \gamma_1} A d_1(W, M, X) \right\} \frac{\partial \gamma_1}{\partial t} \bigg|_{t=0}
\]

\[
= \frac{1}{f(A = 1)} E \left[ A \{q_1(Z, M, X; \gamma_1) - \kappa(W, M, X; \gamma_0)\} d_1(W, M, X) S(O) \right]
\]

\[
- \frac{1}{f(A = 1)} E \left[ \frac{\partial q_0(Z, X; \gamma_0)}{\partial \gamma_0} (1 - A) d_1(W, M, X) \right] \frac{\partial \gamma_0}{\partial t} \bigg|_{t=0}
\]

\[
- \frac{1}{f(A = 1)} E \left[ (1 - A) \left[q_0(Z; \gamma_0) - E\{q_0(Z, X; \gamma_0) | W, A = 0, M, X\}\right] d_1(W, M, X) S(O) \right]
\]

\[
- \frac{1}{f(A = 1)} E \left[ \{ (1 - A) - f(A = 0 | W, M, X) \} E\{q_0(Z, X; \gamma_0) | W, A = 0, M, X\} d_1(W, M, X) S(O) \right]
\]

\[
+ \frac{1}{f(A = 1)} E \left[ \left\{ \frac{A - f(A = 1 | W, M, X)}{f^2(A = 1 | W, M, X)} \right\} \kappa(W, M, X; \gamma_0) d_1(W, M, X) S(O) \right]
\]

\[
= \frac{1}{f(A = 1)} E \left[ \{A q_1(Z, M, X; \gamma_1) - (1 - A) q_0(Z, X; \gamma_0)\} d_1(W, M, X) S(O) \right]
\]

\[
- \frac{1}{f(A = 1)} E \left[ \frac{\partial q_0(Z, X; \gamma_0)}{\partial \gamma_0} (1 - A) d_1(W, M, X) \right] \frac{\partial \gamma_0}{\partial t} \bigg|_{t=0}
\]
Proof of Theorem 3.3

Proof. Let $\beta_1^*, \beta_0^*, \gamma_1^*$ and $\gamma_0^*$ refer to the population limits of the estimators $\hat{\beta}_1$, $\hat{\beta}_0$, $\hat{\gamma}_1$ and $\hat{\gamma}_0$. Then if $h_1(W, M, X; \beta_1^*)$ and $h_0(W, X; \beta_0^*)$ are correctly specified,

$$
E[I(A = 1)q_1(Z, M, X; \gamma_1^*)\{Y - h_1(W, M, X; \beta_1^*)\}]
+ E[I(A = 0)q_0(Z, X; \gamma_0^*)\{h_1(W, M, X; \beta_1^*) - h_0(W, X; \beta_0^*)\}]
+ E\{h_0(W, X; \beta_0^*)\} - \psi
= E \left[ I(A = 1)q_1(Z, M, X; \gamma_1^*) \left\{ \frac{E(Y|Z, A = 1, M, X) - \int h_1(w, M, X; \beta_1^*)dF(w|Z, A = 1, M, X)}{E(Y|Z, A = 1, M, X)} \right\} \right]
+ E \left[ I(A = 0)q_0(Z, X; \gamma_0^*) \left\{ \frac{E\{h_1(W, M, X; \beta_1^*)\|Z, A = 0, X\} - \int h_0(w, X; \beta_0^*)dF(w|Z, A = 0, X)}{E\{h_1(W, M, X; \beta_1^*)\|Z, A = 0, X\}} \right\} \right]
+ E\{h_0(W, X; \beta_0^*)\} - \psi
= 0
$$

by virtue of (2) and (3). If $h_1(W, M, X; \beta_1^*)$ and $q_0(Z, X; \gamma_0^*)$ are instead correctly specified,

$$
E[I(A = 1)q_1(Z, M, X; \gamma_1^*)\{Y - h_1(W, M, X; \beta_1^*)\}]
+ E[I(A = 0)q_0(Z, X; \gamma_0^*)\{h_1(W, M, X; \beta_1^*) - h_0(W, X; \beta_0^*)\}]
+ E\{h_0(W, X; \beta_0^*)\} - \psi
= E[I(A = 0)q_0(Z, X; \gamma_0^*)h_1(W, M, X; \beta_1^*)]
- E[I(A = 0)q_0(Z, X; \gamma_0^*)h_0(W, X; \beta_0^*)]
+ E\{h_0(W, X; \beta_0^*)\} - \psi
= 0
$$

Now by (3) and (6),

$$
E[I(A = 0)q_0(Z, X; \gamma_0^*)h_1(W, M, X; \beta_1^*)]
= E[I(A = 0)q_0(Z, X; \gamma_0^*)E\{h_1(W, M, X; \beta_1^*)\|Z, A = 0, X\}]
= E[I(A = 0)q_0(Z, X; \gamma_0^*)E\{h_0(W, X)\|Z, A = 0, X\}]
= E[I(A = 0)E\{q_0(Z, X; \gamma_0^*)|W, A = 0, X\}h_0(W, X)]
= E \left\{ \frac{I(A = 0)}{f(A = 0|W, X)}h_0(W, X) \right\}
= \psi
$$

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\[
E\{h_0(W, X; \beta_0^*)\} - E[I(A = 0)q_0(Z, X; \gamma_0^*)h_0(W, X; \beta_0^*)]
= E\{h_0(W, X; \beta_0^*)\} - E \left\{ \frac{I(A = 0)}{f(A = 0|W, X)} h_0(W, X; \beta_0^*) \right\}
= E\{h_0(W, X; \beta_0^*)\} - E\{h_0(W, X; \beta_0^*)\}
= 0
\]

Finally, if \(q_1(Z, M, X; \gamma_1^*)\) and \(q_0(Z, X; \gamma_0^*)\) are instead correctly specified,

\[
E\left[ I(A = 1)q_1(Z, M, X; \gamma_1^*) \{Y - h_1(W, M, X; \beta_1^*)\} \right]
+ E[I(A = 0)q_0(Z, X; \gamma_0^*)\{h_1(W, M, X; \beta_1^*) - h_0(W, X; \beta_0^*)\}] + E\{h_0(W, X; \beta_0^*)\} - \psi
= E\{I(A = 1)q_1(Z, M, X; \gamma_1^*)Y\} - E\{I(A = 1)q_1(Z, M, X; \gamma_1^*)h_1(W, M, X; \beta_1^*)\}
+ E[I(A = 0)q_0(Z, X; \gamma_0^*)h_1(W, M, X; \beta_1^*)]\]

By (2), (6) and (8),

\[
E\{I(A = 1)q_1(Z, M, X; \gamma_1^*)Y\}
= E\{I(A = 1)q_1(Z, M, X; \gamma_1^*)E(Y|Z, A = 1, M, X)\}
= E\{I(A = 1)q_1(Z, M, X; \gamma_1^*)h_1(W, M, X)\}
= E[I(A = 1)E\{q_1(Z, M, X; \gamma_1^*)|W, A = 1, M, X\}h_1(W, M, X)]
= E \left[ I(A = 1)E\{q_0(Z, X; \gamma_0^*)|W, A = 0, M, X\} \frac{f(A = 0|W, M, X)}{f(A = 1|W, M, X)} h_1(W, M, X) \right]
= E\{E\{q_0(Z, X; \gamma_0^*)|W, A = 0, M, X\}f(A = 0|W, M, X)h_1(W, M, X)\}
= E[I(A = 0)q_0(Z, X; \gamma_0^*)h_1(W, M, X)]
= \psi
\]
and also

$$E[I(A = 0)q_0(Z, X; \gamma_0)h_1(W, M, X; \beta_1^*)] - E[I(A = 1)q_1(Z, M, X; \gamma_1^*)h_1(W, M, X; \beta_1^*)]$$

$$= E[I(A = 0)q_0(Z, X; \gamma_0)h_1(W, M, X; \beta_1^*)]$$

$$- E[I(A = 1)E\{q_1(Z, M, X; \gamma_1^*)|Z, A = 1, M, X\}h_1(W, M, X; \beta_1^*)]$$

$$= E[I(A = 0)q_0(Z, X; \gamma_0)h_1(W, M, X; \beta_1^*)]$$

$$- E[I(A = 1)E\{q_0(Z, X; \gamma_0)|W, A = 0, M, X\}f(A = 0|W, M, X)h_1(W, M, X; \beta_1^*)]$$

$$= E[I(A = 0)q_0(Z, X; \gamma_0)h_1(W, M, X; \beta_1^*)] - E[I(A = 0)q_0(Z, X; \gamma_0^*)h_1(W, M, X; \beta_1^*)]$$

$$= 0$$

and the first result in Theorem 3.3 follows.

To show (local) semiparametric efficiency, we will show that $\hat{\psi}_{P-MR}$ has an influence function equal to $IF_\psi$ under $M_1 \cap M_2 \cap M_3$. Following a Taylor expansion and standard $M$-estimation arguments, we have that

$$\sqrt{n}(\hat{\psi}_{P-MR} - \psi)$$

$$= \frac{1}{\sqrt{n}} \sum_{i=1}^{n} A_i q_1(Z_i, M_i, X_i; \gamma_1^*)\{Y_i - h_1(W_i, M_i, X_i; \beta_1^*)\}$$

$$+ \frac{1}{\sqrt{n}} \sum_{i=1}^{n} (1 - A_i)q_0(Z_i, X_i; \gamma_0^*)\{h_1(W_i, M_i, X_i; \beta_1^*) - h_0(W_i, X_i; \gamma_0^*)\}$$

$$+ \frac{1}{\sqrt{n}} \sum_{i=1}^{n} h_0(W_i, X_i; \gamma_0^*) - \psi$$

$$+ E\left[I(A = 1)\frac{\partial q_1(Z, M, X; \gamma_1^*)}{\partial \gamma_1^*}\{Y - h_1(W, M, X; \beta_1^*)\}\right]\sqrt{n}(\gamma_1^* - \gamma_1^*)$$

$$+ E\left[I(A = 0)\frac{\partial q_0(Z, X; \gamma_0^*)}{\partial \gamma_0^*}\{h_1(W, M, X; \beta_1^*) - h_0(W, X; \beta_0^*)\}\right]\sqrt{n}(\gamma_0^* - \gamma_0^*)$$

$$+ E\left[\frac{\partial h_1(W, M, X; \beta_1^*)}{\partial \beta_1^*}\{I(A = 0)q_0(Z, X; \gamma_0^*) - I(A = 1)q_1(Z, M, X; \gamma_1^*)\}\right]\sqrt{n}(\beta_1^* - \beta_1^*)$$

$$+ E\left[\frac{\partial h_0(W, X; \beta_0^*)}{\partial \beta_0^*}\{1 - I(A = 0)q_0(Z, X; \gamma_0^*)\}\right]\sqrt{n}(\beta_0^* - \beta_0^*)$$

$$+ o_p(1)$$
Following the previous arguments in this section, under model $M_{\text{union}}$, 

$$
E \left[ I(A = 1) \frac{\partial q_1(Z, M, X; \gamma^*_1)}{\partial \gamma^*_1} \{Y - h_1(W, M, X; \beta^*_1)\} \right] = 0
$$

$$
E \left[ I(A = 0) \frac{\partial q_0(Z, X; \gamma^*_0)}{\partial \gamma^*_0} \{h_1(W, M, X; \beta^*_1) - h_0(W, X; \beta^*_0)\} \right] = 0
$$

$$
E \left[ \frac{\partial h_1(W, M, X; \beta^*_1)}{\partial \beta^*_1} \{I(A = 0)q_0(Z, X; \gamma^*_0) - I(A = 1)q_1(Z, M, X; \gamma^*_1)\} \right] = 0
$$

$$
E \left[ \frac{\partial h_0(W, X; \beta^*_0)}{\partial \beta^*_0} \{1 - I(A = 0)q_0(Z, X; \gamma^*_0)\} \right] = 0
$$

which completes the proof. 

**Randomised trials**

We will consider briefly estimation of $\psi$ in a setting where the exposure $A$ is randomised at baseline. In that case, by virtue of randomisation, there can be no confounding of either the exposure-outcome or exposure-mediator relationship. Nevertheless, we cannot discount the possibility of unmeasured mediator-outcome confounders. Figure 3 describes a setting where there is an unmeasured common cause of $M$ and $Y$, in addition to a measured common cause $X$, but where again we will make progress thanks to proxy variables $Z$ and $W$. Although in Figure 3 encodes the assumption that the are no unmeasured common causes of $A$ and $Y$, or $A$ and $M$, to be sufficiently general the following results allow for $X$ to influence $A$.

**Theorem .1.** (Part a) We will assume that there exist proxies that satisfy Assumptions 2.1, 2.3, 2.4 and $U \perp A|W, X$, and that there exist $h_1$, and $q_1$ that satisfy (2) and

$$
\frac{f(A = 0|W, M, X)}{f(A = 1|W, M, X)} = E \{q_1(Z, M, X)|W, A = 1, X\}. \quad (14)
$$

Suppose furthermore that $Y(a, m) \perp A|X$ for $a = 0, 1$ and each $m \in S$, $M(a) \perp A|X$ for $a = 0, 1$, $Pr(A = a|X) > 0$ almost surely for $a = 0, 1$ and that Assumptions 4, 4.1, 4.2, 4.4 and 8.1 hold. If we define

$$
\eta_0(W, X) = \int h_1(W, m, X)dF(m|W, A = 0, M, X)
$$

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Figure 3: Causal diagram with unmeasured mediator-outcome confounding.

then, we again have results (4),

\[
\frac{f(A = 0|U, M, X)}{f(A = 1|U, M, X)} = E \{q_1(Z, M, X)|U, A = 1, M, X\}
\]  \hspace{1cm} (15)

and we have the three following representations of the proximal mediation formula

\[
\psi = \int \int \eta_0(w, x)dF(w|x)dF(x)
= \int \int \frac{I(a = 0)}{f(a = 0|x)}h_1(w, m, x)dF(w, z, a, m|x)dF(x)
= \int \int \frac{I(a = 1)}{f(a = 1|x)}q_1(z, m, x)y dF(y, z, a, m|x)dF(x)
\]

(Part b) Consider a semiparametric model \( M_{sp}^* \) where \( h_1 \) is assumed to exist at every data law under the model but the observed data distribution is otherwise left unrestricted. Furthermore, \( q_1 \) is assumed to exist at the true data-generating law and Assumption 6.1 is assumed to hold. Then a valid influence function for \( \psi \) under \( M_{sp}^* \) is equal to

\[
IF_{\psi}^* = \frac{I(A = 1)}{f(A = 0|X)}q_1(Z, M, X)\{Y - h_1(W, M, X)\}
+ \frac{I(A = 0)}{f(A = 0|X)}\{h_1(W, M, X) - \eta_0(W, X)\} + \eta_0(W, X) - \psi.
\]

Furthermore, in the submodel where \( h_1 \) and \( q_1 \) are unique and Assumption 7.1 holds, the efficiency bound for \( \psi \) is \( E(IF_{\psi}^{*2}) \). The efficiency bound is also unchanged in the case that \( f(A = 0|X) \) is known.
Proof. For Part a), results (14) follows from the proof of Theorem 2.1, by Assumptions 1, 3.2, 5.1, 5.3, 5.4, 6.1 and the existence of a bridge function that satisfies (2). Similarly, (15) follows from the proof of Theorem 2.2, by Assumptions 1, 3.2, 5.1, 5.3, 5.4, 6.1 and the existence of a bridge function that satisfies (14).

Then

\[ E(Y|u, A = 1, m, x) = \int h_1(w, M, X)dF(w|u, A = 1, M, X) \]

following the proof of Theorem 2.1 and

\[ \psi = \int \int \int E(Y|u, A = 1, m, x)dF(m|u, A = 0, x)dF(u|x)dF(x) \quad \text{(Assumptions 1-4)} \]

\[ = \int \int \int \int h_1(w, m, x)dF(w|u, A = 1, m, x)dF(m|u, A = 0, x)dF(u|x)dF(x) \quad \text{(by (14))} \]

\[ = \int \int \int \int h_1(w, m, x)dF(w|u, A = 0, m, x)dF(m|u, A = 0, x)dF(u|x)dF(x) \quad \text{(W \perp A|M, U, X)} \]

\[ = \int \int \int \int h_1(w, m, x)dF(m|u, A = 0, m, x)dF(w|u, x)dF(u|x)dF(x) \quad W \perp A|U, X \]

\[ = \int \int \int \int h_1(w, m, x)dF(m|u, A = 0, m, x)dF(u|w, x)dF(w|x)dF(x) \]

\[ = \int \int \int \int h_1(w, m, x)dF(m|u, A = 0, w, x)dF(u|w, A = 0, x)dF(w|x)dF(x) \quad \text{(U \perp A|W, X)} \]

\[ = \int \int \int h_1(w, m, x)dF(m|A = 0, w, x)dF(w|x)dF(x) \]

and we note that \( W \perp A|U, X \) and \( W \perp A|M, U, X \) follows from Assumptions 1, 3 and 5, by application of the graphoid axioms.

Part b) follows along the lines of similar arguments to the proof of Theorem 3.1 and is omitted for brevity. We nevertheless clarify that \( IF^*_\psi \) is orthogonal to the scores \( S(A|X) \). First, using the law of iterated expectations,

\[ E \left[ \frac{A}{f(A = 1|X)} q_1(Z, M, X) \{Y - h_1(W, M, X)\} S(A|X) \right] \]

\[ = E \left[ \frac{A}{f(A = 1|X)} q_1(Z, M, X) E\{Y - h_1(W, M, X)|Z, A = 1, M, X\} S(A|X) \right] = 0 \]
by virtue of (2). Next,
\[
E \left[ \frac{(1 - A)}{f(A = 0|X)} \{h_1(W, M, X) - \eta_0(W, X)\} S(A|X) \right] \\
= E \left[ \frac{(1 - A)}{f(A = 0|X)} E\{h_1(W, M, X) - \eta_0(W, X)|A = 0, W, X\} S(A|X) \right] = 0
\]
by the definition of \( \eta_0(W, X) \). Finally, by the (conditional) randomisation of \( A \),
\[
E [\{\eta_0(W, X) - \psi\} S(A|X)] \\
E [\{\eta_0(W, X) - \psi\} E\{S(A|X)|X\}] = 0
\]
and hence we have shown that \( E\{IF^\psi S(A|X)\} = 0 \).
\[
\square
\]

**Model compatibility**

By Bayes’ theorem
\[
f(M|U, A = 0, X) = \frac{f(A = 0|U, M, X)}{f(A = 1|U, M, X)} \times \frac{f(A = 0|U, X)}{f(A = 0|U, X)}.
\]

Suppose that
\[
M|U, A, X \sim N(\tau_0 + \tau_a A + \tau_u U + \tau_x X, \sigma^2_{m|u,a,x});
\]
then one can show that
\[
\log \frac{f(M|U, A = 0, X)}{f(M|U, A = 1, X)} = \frac{\tau_a}{\sigma^2_{m|u,a,x}} \left\{ \frac{\tau_a}{2} - (M - \tau_0 - \tau_u U - \tau_x X) \right\}
\]
which is linear in \( U \) and \( X \). Further, if
\[
\frac{1}{f(A = 0|U, X)} = 1 + \exp\{- (\alpha_{0,0} + \alpha_{0,u} U + \alpha_{0,x} X)\}
\]
then
\[
\log \frac{f(A = 0|U, M, X)}{f(A = 1|U, M, X)} = \log \frac{f(M|U, A = 0, X)}{f(M|U, A = 1, X)} + \log \frac{f(A = 0|U, X)}{f(A = 1|U, X)}
\]
\[
= \frac{\tau_a}{\sigma^2_{m|u,a,x}} \left\{ \frac{\tau_a}{2} - (M - \tau_0 - \tau_u U - \tau_x X) \right\}
\]
\[
+ \alpha_{0,0} + \alpha_{0,u} U + \alpha_{0,x} X
\]
\[
= \alpha_{1,0} + \alpha_{1,m} M + \alpha_{1,u} U + \alpha_{1,x} X
\]

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where
\[ \alpha_{1,0} = \frac{\tau_a}{\sigma^2_{m|u,a,x}} \left( \frac{\tau_a}{2} + \tau_0 \right) + \alpha_{0,0}, \]
\[ \alpha_{1,m} = -\tau_a/\sigma^2_{m|u,a,x}, \quad \alpha_{1,u} = \tau_u/\sigma^2_{m|u,a,x} + \alpha_{0,u} \quad \text{and} \quad \alpha_{1,x} = \tau_x/\sigma^2_{m|u,a,x} + \alpha_{0,x}. \]

Next, suppose that \( Z|U,A,X \sim \mathcal{N}(\epsilon_0 + \epsilon_u U + \epsilon_A A + \epsilon_x X, \sigma^2_{z|u,a,x}) \), and consider the choice of bridge function
\[ q_0(Z, X) = 1 + \exp\{-\gamma_{0,0} + \gamma_{0,z}Z + \gamma_{0,x}X\}, \]
then
\[ E\{q_0(Z, X)|U, A = 0, X\} = 1 + \exp(-\gamma_{0,0} - \gamma_{0,x}X) \int \exp(-\gamma_{0,z}z)dF(z|U, A = 0, X) \]
\[ = 1 + \exp \left\{ -\gamma_{0,0} - \gamma_{0,x}X - \gamma_{0,z}(\epsilon_0 + \epsilon_u U + \epsilon_x X) + \frac{\gamma_{0,z}^2\sigma^2_{z|u,a,x}}{2} \right\} \]
such that for
\[ \gamma_{0,0} = \alpha_{0,0} - \frac{\alpha_{0,u}}{\epsilon_u} \left\{ \epsilon_0 - \frac{(\alpha_{0,u}/\epsilon_u)\sigma^2_{z|u,a,x}}{2} \right\} \]
\[ \gamma_{0,z} = \frac{\alpha_{0,u}}{\epsilon_u} \]
\[ \gamma_{0,x} = \alpha_{0,x} - \frac{\alpha_{0,u}\epsilon_x}{\epsilon_u} \]
we have the equality
\[ \frac{1}{f(A = 0|U, X)} = \int q_0(z, x)dF(z|U, A = 0, X) \]
To show this choice of \( q_0(Z, X) \) also lead to equality (6), since \( W \perp A|U, X \) we have that
\[ \frac{1}{f(A = 0|W, X)} = \int \frac{1}{f(A = 0|u, X)}dF(u|W, A = 0, X) \]
\[ = 1 + \exp(-\alpha_{0,0} - \alpha_{0,x}X) \int \exp(-\alpha_{0,u}u)dF(u|W, A = 0, X) \]
Also,

\[ E\{q_0(Z, X)|W, A = 0, X\} = E\{E\{q_0(Z, X)|U, A = 0, X\}|W, A = 0, X\} \]

\[ = 1 + \exp(-\alpha_{0,0} - \alpha_{0,x}X) \int \exp(-\alpha_{0,u}u)dF(u|W, A = 0, X) \]

by \( Z \perp W|U, A, X \) (which follows from Assumption 5) and equality (6).

Moving onto \( q_1 \), consider the choice of bridge function

\[ q_1(Z, M, X) = \exp\{\gamma_{1,0} + \gamma_{1,z}Z + \gamma_{1,m}M + \gamma_{1,x}X\} \]

\[ \times \left[ 1 + \exp(-\gamma_{0,0} - \gamma_{0,z}Z - \gamma_{0,x}X) \exp\{\gamma_{0,z}(\epsilon_a + \gamma_{1,z}\sigma^2_{z|u,a,x})\} \right] \]

Noting that by \( Z \perp M|U, A, X \),

\[ E\{q_1(Z, M, X)|U, A = 1, M, X\} \]

\[ = \exp \left\{ \gamma_{1,0} + \frac{\gamma_{1,z}^2\sigma^2_{z|u,a,x}}{2} + \gamma_{1,z}E(Z|U, A = 1, X) + \gamma_{1,m}M + \gamma_{1,x}X \right\} \]

\[ + \exp \left\{ (\gamma_{1,0} - \gamma_{0,0}) + \gamma_{0,z}(\epsilon_a + \gamma_{1,z}\sigma^2_{z|u,a,x}) + \gamma_{1,m}M + (\gamma_{1,x} - \gamma_{0,x})X \right\} \]

\[ \times \left[ 1 + \exp(-\gamma_{0,0} - \gamma_{0,z}Z - \gamma_{0,x}X) \exp\{\gamma_{0,z}(\epsilon_a + \gamma_{1,z}\sigma^2_{z|u,a,x})\} \right] \]

\[ = \exp \left\{ \gamma_{1,0} + \frac{\gamma_{1,z}^2\sigma^2_{z|u,a,x}}{2} + \gamma_{1,z}E(Z|U, A = 1, X) + \gamma_{1,m}M + \gamma_{1,x}X \right\} \]

\[ + \exp \left\{ (\gamma_{1,0} - \gamma_{0,0}) + \gamma_{0,z}(\epsilon_a + \gamma_{1,z}\sigma^2_{z|u,a,x}) + \gamma_{1,m}M + (\gamma_{1,x} - \gamma_{0,x})X \right\} \]

\[ \times \exp \left\{ (\gamma_{1,z} - \gamma_{0,z})E(Z|U, A = 1, X) + \frac{\gamma_{1,z}^2\sigma^2_{z|u,a,x}}{2} + \frac{\gamma_{0,z}^2\sigma^2_{z|u,a,x}}{2} - \gamma_{1,z}\gamma_{0,z}\sigma^2_{z|u,a,x} \right\} \]

\[ = \exp \left\{ \gamma_{1,0} + \frac{\gamma_{1,z}^2\sigma^2_{z|u,a,x}}{2} + \gamma_{1,z}E(Z|U, A = 1, X) + \gamma_{1,m}M + \gamma_{1,x}X \right\} \]

\[ \times \left[ 1 + \exp \left\{ -\gamma_{0,0} - \gamma_{0,x}X - \gamma_{0,z}(\epsilon_0 + \epsilon_{0U} + \epsilon_{z}X) + \frac{\gamma_{0,z}^2\sigma^2_{z|u,a,x}}{2} \right\} \right] \]

\[ = \exp \left\{ \gamma_{1,0} + \frac{\gamma_{1,z}^2\sigma^2_{z|u,a,x}}{2} + \gamma_{1,z}E(Z|U, A = 1, X) + \gamma_{1,m}M + \gamma_{1,x}X \right\} E\{q_0(Z, X)|U, A = 0, X\} \]
Therefore, it follows that this choice of \( q_1(Z, M, X) \) satisfies the equality

\[
E\{q_0(Z, X)\|U, A = 0, M, X\} \frac{f(A = 0\|U, M, X)}{f(A = 1\|W, M, X)} = E\{q_1(Z, M, X)\|U, A = 1, M, X\}
\]

at the parameter values

\[
\begin{align*}
\gamma_{1,0} &= \alpha_{1,0} - \frac{\alpha_{1,u}}{\epsilon_u} \left\{ \frac{\alpha_{1,u} \sigma^2_{u,a,x}}{2 \epsilon_u} + \epsilon_0 + \epsilon_a \right\} \\
\gamma_{1,m} &= \alpha_{1,m} \\
\gamma_{1,z} &= \alpha_{1,u} \\
\gamma_{1,x} &= \alpha_{1,x} - \frac{\alpha_{1,u} \epsilon_x}{\epsilon_u}
\end{align*}
\]

It furthermore follows that under the constraint that

\[
\epsilon_a + \frac{\sigma^2_{u,a,x}}{\epsilon_u} \left\{ \frac{\tau_a \tau_u}{\sigma^2_{m,u,a,x}} + \alpha_{0,u} \right\} = 0
\]

that this choice of bridge function simplifies to

\[
q_0(Z, X) \exp\{\gamma_{1,0} + \gamma_{1,z} Z + \gamma_{1,m} M + \gamma_{1,x} X\}.
\]

It also follows from previous reasoning that this choice of bridge also leads to the equality (\( \Box \)).
Additional simulation results

Data analysis: additional information

The information below follows the AGReMA statement (Lee et al., 2021), which are guidelines for good practice for conducting and reporting mediation analysis in randomised trials and observational studies.

1. Title: The Job Corps study.

2. Abstract: To what extent is the effect of attending class at the beginning of the study on criminal activity mediated by employment?

3. Background and rationale: Using data from the Job Corps study, Schochet et al. (2001) and Schochet et al. (2008) consider the total effect of program assignment on multiple outcomes; their results suggest that being assigned to the program leads to a reduction in criminal activity for some years after the program. Flores & Flores-Lagunes (2009) and Huber (2014) see positive direct effects of assignment/attendance on earnings/health outcomes with the mediator employment. Using an IV design, Frölich & Huber (2017) find evidence of an indirect rather than direct effect of attendance on earnings, as mediated by employment. Less is known about the role of employment as a mediator in the relationship between program attendance and criminal activity.

4. Objectives: Estimate the direct and indirect effects of program attendance (rather than assignment) on number of arrests at year four, with the number of hours worked at year two being the mediator.

5. Study registration: No protocol or study registration available for the mediation analysis.

6. Study design: Job Corps was a randomised controlled trial carried out at 119 separate centres, across 48 states and the District of Columbia. Eligible individuals between the ages of 16-24 were assigned at random either to receive an offer of participation in the Job Corps program or to be declined access to participation in the program for the following three years. Survey data on relevant variables was collected from participants around 2 and 4 years after randomisation. See Schochet et al. (2001) and Schochet et al. (2008) for further details.
Table 3: Simulation results from experiments 5-9. Exp: experiment; Est: estimator; MSE: mean squared error; Bias: Monte Carlo bias; Med. Bias: Median estimate minus true value; Coverage: 95% confidence interval (CI) coverage; Mean Length: average 95% CI length; Med. length: median 95% CI length.

| Exp | Est       | Bias  | Med. Bias | MSE  | Coverage | Mean Length | Med. Length |
|-----|-----------|-------|-----------|------|----------|-------------|-------------|
| 5   | $\hat{\theta}_{OLS}$ | 0.00  | 0.00      | 0.01 | 0.96     | 0.38        | 0.38        |
|     | $\hat{\theta}_{P-IPW}$ | 0.00  | 0.00      | 0.01 | 0.96     | 0.48        | 0.48        |
|     | $\hat{\theta}_{P-hybrid}$ | 0.00  | 0.00      | 0.01 | 0.96     | 0.48        | 0.48        |
|     | $\hat{\theta}_{P-OR}$ | 0.00  | 0.00      | 0.01 | 0.96     | 0.48        | 0.48        |
|     | $\hat{\theta}_{P-MR}$ | 0.00  | 0.00      | 0.01 | 0.96     | 0.48        | 0.48        |
| 6   | $\hat{\theta}_{OLS}$ | 0.31  | 0.31      | 0.11 | 0.12     | 0.39        | 0.39        |
|     | $\hat{\theta}_{P-IPW}$ | 0.40  | 0.40      | 0.17 | 0.03     | 0.54        | 0.41        |
|     | $\hat{\theta}_{P-hybrid}$ | 0.40  | 0.40      | 0.17 | 0.03     | 0.53        | 0.41        |
|     | $\hat{\theta}_{P-OR}$ | 0.40  | 0.40      | 0.17 | 0.04     | 0.49        | 0.41        |
|     | $\hat{\theta}_{P-MR}$ | 0.40  | 0.40      | 0.17 | 0.03     | 0.54        | 0.41        |
| 7   | $\hat{\theta}_{OLS}$ | 0.26  | 0.27      | 0.08 | 0.24     | 0.39        | 0.39        |
|     | $\hat{\theta}_{P-IPW}$ | -0.34 | -0.34     | 0.14 | 0.37     | 43.97       | 0.57        |
|     | $\hat{\theta}_{P-hybrid}$ | -0.34 | -0.34     | 0.14 | 0.33     | 9.83        | 0.54        |
|     | $\hat{\theta}_{P-OR}$ | -0.34 | -0.33     | 0.13 | 0.33     | 7.11        | 0.54        |
|     | $\hat{\theta}_{P-MR}$ | -0.34 | -0.34     | 0.14 | 0.37     | 43.97       | 0.57        |
| 8   | $\hat{\theta}_{OLS}$ | 0.36  | 0.36      | 0.14 | 0.05     | 0.39        | 0.39        |
|     | $\hat{\theta}_{P-IPW}$ | 0.07  | 0.15      | 1.51 | 0.98     | >1000       | 16.08       |
|     | $\hat{\theta}_{P-hybrid}$ | -0.03 | 0.11      | 42.53 | 0.99     | >1000       | 6.74        |
|     | $\hat{\theta}_{P-OR}$ | -0.16 | 0.08      | 59.27 | 1.00     | >1000       | 9.65        |
|     | $\hat{\theta}_{P-MR}$ | -0.11 | 0.11      | 51.33 | 0.98     | >1000       | 18.24       |
| 9   | $\hat{\theta}_{OLS}$ | 0.14  | 0.14      | 0.04 | 0.87     | 0.6         | 0.60        |
|     | $\hat{\theta}_{P-IPW}$ | 0.04  | 0.05      | 0.60 | 0.97     | >1000       | 14.57       |
|     | $\hat{\theta}_{P-hybrid}$ | 0.28  | 0.04      | 84.41 | 0.99     | >1000       | 1.87        |
|     | $\hat{\theta}_{P-OR}$ | 0.28  | 0.04      | 76.73 | 0.99     | >1000       | 2.38        |
|     | $\hat{\theta}_{P-MR}$ | 0.05  | 0.05      | 1.52 | 0.98     | >1000       | 16.20       |
Participants: Data on 15,386 individuals was collected at baseline; however, many individuals failed to enroll in the program and dropped out of the study. As in other closely related analyses (Colangelo & Lee, 2020; Huber et al., 2020; Singh et al., 2021), we restricted our analysis to the 10,775 individuals for which the mediator and outcome were observed.

Sample size: No sample size calculation was conducted for the mediation analysis.

Effects of interest: Total effects and natural direct and indirect effects.

Assumed causal model: See Figure A.1(a).

Causal assumptions: See Assumptions 1-6 in the main manuscript and Assumption 8.

Measurement and measurement levels: Exposure variable $A$: was any time spent in academic or vocational classes in the 12 months following randomisation according to the survey (binary)? Mediator: proportion of weeks employed in the second year, according to the survey (numeric variable, in percentages). Outcome: number of separate arrests in the fourth year after randomisation, according to the survey (numeric). Confounders: gender (binary), age (numeric), ethnicity (categorical), education status (categorical), native English (binary), marital status (categorical), has children (binary), ever worked (binary), average weekly earnings (numeric), head of household (binary), designated for nonresidential slot (binary), total household gross income (categorical), dad did not work when 14 (binary), welfare receipt during childhood (categorical), poor/fair general health status (binary), received AFDC each month (binary), received public assistance each month (binary), received food stamples (binary), physical emotional problems (binary), ever taken illegal drugs that are not marijuana or hallucinogens (binary), extent of smoking (categorical), extent of alcohol consumption (categorical), ever arrested (binary), times in prison (categorical).

Statistical methods: See main manuscript for outline of analysis and details on models/estimators chosen. We removed several variables that were subject to large amounts of missingness (extent of marijuana use, extend of hallucinogen use), since we hypothesised that any confounding would be accounted for by other variables detailing substance use. We also excluded years of education, household size, mum’s years of education and dad’s years of education, as these also contained missing values and
were strongly correlated with covariates with complete data. As in previous analyses of this sample (Colangelo & Lee, 2020; Huber et al., 2020; Singh et al., 2021), the missing indicator method was used for the remaining covariates that had missing values; see Groenwold et al. (2012) for a discussion of the limitations of this approach. We also removed any individuals with incomplete data on the proxies; a complete case analysis is always unbiased when data is missing completely at random, but can be biased under certain missing at random and missing not at random mechanisms. However, since the proportion of individuals removed was small (less than 3% of the total sample size), we hypothesised that any resulting bias (and efficiency loss) would be negligible. All analyses were performed using R.

14. Sensitivity analysis: A sensitivity analysis for the causal identification assumptions was beyond the scope of the article. Huber et al. (2020) did not find strong evidence of the dependence of missing values of outcome and mediator on treatment.

15. Ethical approval: See Schochet et al. (2001).

16. Participants: See Schochet et al. (2008), Huber et al. (2020), Huber et al. (2020) and other previous analyses of the Job Corps study.

17. Outcomes and estimates: See main manuscript, and table 4.

18. Sensitivity parameters: No sensitivity analysis performed.

19. Limitations: Similar to analyses in Colangelo & Lee (2020); Huber et al. (2020); Singh et al. (2021), results may be sensitive to post-treatment confounding, given that the mediator was assessed two years after randomisation. Results may also be sensitive to bias due to loss to follow up.

20. Interpretation: See main manuscript.

21. Implications: There was no strong evidence that participation in the Job studies program affected the number of arrests; either directly or via an effect on employment. However, based on results e.g. in Huber (2014), its possible that a dose-response relationship occurred for the direct effect, such that in those who participated, attending more hours of class led to a reduction in the number of arrests (outside of any mediation via employment).
22. **Funding and role of sponsor**: Study sponsors are discussed e.g. in Schochet et al. (2001). See Acknowledgements in main paper for information on grants that supported the authors of the mediation analysis. Grant funders had no role in the conduct of the study, writing of the manuscript, and decision to submit for publication.

23. **Conflicts of interest and financial disclosures**: None to report.

24. **Data and code**: Data is freely available at [http://qed.econ.queensu.ca/jae/datasets/hsu001/](http://qed.econ.queensu.ca/jae/datasets/hsu001/). Code is available upon request.

Table 4: Additional results from the analysis of the Job Corps study. CI: confidence interval.

|                          | P-IPW | 95% CI     | P-Hybrid | 95% CI     | P-OR | 95% CI     |
|--------------------------|-------|------------|----------|------------|------|------------|
| $E[Y\{1, M(0)\}] - Y\{0, M(0)\}$ | 0.0946 | 0.0251,0.1641 | 0.0238 | -0.0697,0.1173 | -0.0234 | -0.1233,0.0766 |
| $E[Y\{1, M(1)\}] - Y\{0, M(1)\}$ | -0.0145 | -0.0657,0.0368 | -0.0013 | -0.1511,0.1486 | -0.0351 | -0.1653,0.0951 |
| $E[Y\{1, M(1)\}] - Y\{1, M(0)\}$ | -0.0978 | -0.1547,-0.0408 | -0.0270 | -0.0573,0.0033 | -0.0077 | -0.0289,0.0135 |
| $E[Y\{0, M(1)\}] - Y\{0, M(0)\}$ | 0.0113 | -0.0392,0.0618 | -0.0019 | -0.0935,0.0896 | 0.0040 | -0.0269,0.0349 |