Semiparametric Estimation for Causal Mediation Analysis with Multiple Causally Ordered Mediators[*]

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Abstract

Causal mediation analysis concerns the pathways through which a treatment affects an outcome. While most of the mediation literature focuses on settings with a single mediator, a flourishing line of research has examined settings involving multiple mediators, under which path-specific effects (PSEs) are often of interest. We consider estimation of PSEs when the treatment effect operates through $K(\geq 1)$ causally ordered, possibly multivariate mediators. In this setting, the PSEs for many causal paths are not nonparametrically identified, and we focus on a set of PSEs that are identified under Pearl's nonparametric structural equation model. These PSEs are defined as contrasts between the expectations of 2^{K+1} potential outcomes and identified via what we call the generalized mediation functional (GMF). We introduce an array of regression-imputation, weighting, and "hybrid" estimators, and, in particular, two $K+2$-robust and locally semiparametric efficient estimators for the GMF. The latter estimators are well suited to the use of data-adaptive methods for estimating their nuisance functions. We establish the rate conditions required of the nuisance functions for semiparametric efficiency. We also discuss how our framework applies to several estimands that may be of particular interest in empirical applications. The proposed estimators are illustrated with a simulation study and an empirical example.

Keywords: causal inference, mediation, path-specific effects, multiple robustness, semiparametric efficiency

1 Introduction

Causal mediation analysis aims to disentangle the pathways through which a treatment affects an outcome. While traditional approaches to mediation analysis have relied on linear structural equation models, along with their stringent parametric assumptions, to define and estimate direct and indirect effects (e.g., Baron and Kenny 1986), a large body of research has emerged within the causal inference literature that disentangles the tasks of definition, identification, and estimation in the study of causal mechanisms. Using the potential outcomes framework (Neyman 1923; Rubin 1974), this body of research has provided model-free definitions of direct and indirect effects (Robins and Greenland 1992; Pearl 2001), established the assumptions needed for nonparametric identification (Robins and Greenland 1992; Pearl 2001; Robins 2003; Petersen *et al.* 2006; Imai *et al.* 2010; Hafeman and VanderWeele 2011; VanderWeele 2015), and developed an array of imputation, weighting, and multiply robust methods for estimation (e.g., Goetgeluk *et al.* 2009; Albert 2012; Tchetgen Tchetgen and Shpitser 2012; Vansteelandt *et al.* 2012; Zheng and van der Laan 2012; Tchetgen Tchetgen 2013; VanderWeele 2015; Wodtke and Zhou 2020).

While the bulk of the causal mediation literature focuses on settings with a single mediator (or a set of mediators considered as a whole), a flourishing line of research has studied settings that involve multiple causally dependent mediators, under which a set of path-specific effects (PSEs) are often of interest (Avin *et al.* 2005; Albert and Nelson 2011; Shpitser 2013; VanderWeele and Vansteelandt 2014; VanderWeele *et al.* 2014; Daniel *et al.* 2015; Lin and VanderWeele 2017; Miles *et al.* 2017; Steen *et al.* 2017; Vansteelandt and Daniel 2017; Miles *et al.* 2020). In particular, Daniel *et al.* (2015) demonstrated a large number of ways in which the total effect of a treatment can be decomposed into PSEs, established the assumptions under which a subset of these PSEs are identified, and provided a parametric method for estimating these effects (see also Albert and Nelson 2011). More recently, for a particular PSE in the case of two causally ordered mediators, Miles *et al.* (2020) offered an in-depth discussion of alternative estimation methods, and, utilizing the efficient influence function of its identification formula, developed a triply robust and locally semiparametric efficient estimator. This estimator, by virtue of its multiple robustness, is well suited to the use of data-adaptive methods for estimating its nuisance functions.

To date, most of the literature on PSEs has focused on the case of two mediators, and it

remains underexplored how the estimation methods developed in previous studies, such as those in VanderWeele *et al.* (2014) and Miles *et al.* (2020), generalize to the case of $K (\geq 1)$ causally ordered mediators. This article aims to bridge this gap. First, we observe that despite a multitude of ways in which a PSE can be defined for each causal path from the treatment to the outcome, most of these PSEs are not identified under Pearl's nonparametric structural equation model. This observation leads us to focus on the much smaller set of PSEs that *can be* nonparametrically identified. These PSEs are defined as contrasts between the expectations of 2^{K+1} potential outcomes, which, in turn, are identified through a formula that can be viewed as an extension of Pearl's (2001) and Daniel *et al.*'s (2015) mediation formulae to the case of K causally ordered mediators. Following Tchetgen Tchetgen and Shpitser (2012), we refer to the identification formula for these expected potential outcomes as the *generalized mediation functional* (GMF).

We then show that the GMF can be estimated via an array of regression, weighting, and "hybrid" estimators. More important, building on its efficient influence function (EIF), we develop two multiply robust and locally semiparametric efficient estimators for the GMF. Both of these estimators are $K + 2$-robust, in the sense that they are consistent provided that one of $K + 2$ sets of nuisance functions is correctly specified and consistently estimated. These multiply robust estimators are well suited to the use of data-adaptive methods for estimating the nuisance functions. We establish rate conditions for consistency and semiparametric efficiency when data-adaptive methods and cross-fitting (Zheng and van der Laan 2011; Chernozhukov *et al.* 2018) are used to estimate the nuisance functions.

Compared with existing estimators that have been proposed for causal mediation analysis, the methodology proposed in this article is distinct in its generality. In fact, the doubly robust estimator for the mean of an incomplete outcome (Scharfstein *et al.* 1999), the triply robust estimator developed by Tchetgen Tchetgen and Shpitser (2012) for the mediation functional in the one-mediator setting (see also Zheng and van der Laan 2012), and the estimator proposed by Miles *et al.* (2020) for their particular PSE, can all be viewed as special cases of the $K + 2$-robust estimators — when $K = 0, 1, 2$, respectively. Yet, our framework also encompasses important estimands for which semiparametric estimators have not been proposed. To demonstrate the generality of our framework, we show how our multiply robust semiparametric estimators apply to several estimands that may be of particular interest in empirical applications, including the natural direct effect (NDE),

the natural/total indirect effect (NIE/TIE), the natural path-specific effect (nPSE), and the cumulative path-specific effect (cPSE). In Supplementary Material E, we discuss how our framework can also be employed to estimate noncausal decompositions of between-group disparities that are widely used in social science research (Fortin *et al.* 2011).

Before proceeding, we note that in a separate strand of literature, the term "multiple robustness" has been used to characterize a class of estimators for the mean of incomplete data that are consistent if one of several working models for the propensity score or one of several working models for the outcome is correctly specified (e.g., Han and Wang 2013; Han 2014). In this paper, we use "V-robustness" to characterize estimators that require modeling *multiple parts of the observed data likelihood* and are consistent provided that one of V sets of the corresponding models is correctly specified, in keeping with the terminology in the causal mediation literature. This definition of "multiple robustness" does not imply that a "$K + 2$-robust" estimator is necessarily more robust than, for example, a "$K + 1$-robust" estimator. First, they may correspond to different estimands that require modeling different parts of the likelihood. For example, the doubly robust estimator of the average treatment effect only involves a propensity score model and an outcome model; it is thus less demanding than Tchetgen Tchetgen and Shpitser's (2012) triply robust estimator of the mediation functional, which involves an additional model for the mediator. Second, for our semiparametric estimators of the GMF, the "$K + 2$-robustness" property is not "sharp" because it can be tightened in various special cases. As we demonstrate in Section 4 and Supplementary Material E, such a tightening may result in a lower V (as in the case of NDE, NIE/TIE, nPSE, and cPSE), or a higher V (as in the case of noncausal decompositions of between-group disparities).

The rest of the paper is organized as follows. In Section 2, we define the PSEs of interest, lay out their identification assumptions, and introduce the GMF. In Section 3, we introduce a range of regression-imputation, weighting, "hybrid," and multiply robust estimators for the GMF, and present several techniques that could be used to improve the finite sample performance of the multiply robust estimators. In Section 4, we discuss how our results apply to a number of special cases such as the NDE, NIE/TIE, nPSE, and cPSE. A simulation study and an empirical example are given in Section 5 and Section 6 to illustrate the proposed estimators. Proofs of Theorems 1-4 are given in Supplementary Materials A, C, and D. Replication data and code for the simulation study and the empirical example are available at https://doi.org/10.7910/DVN/5TBUM3.
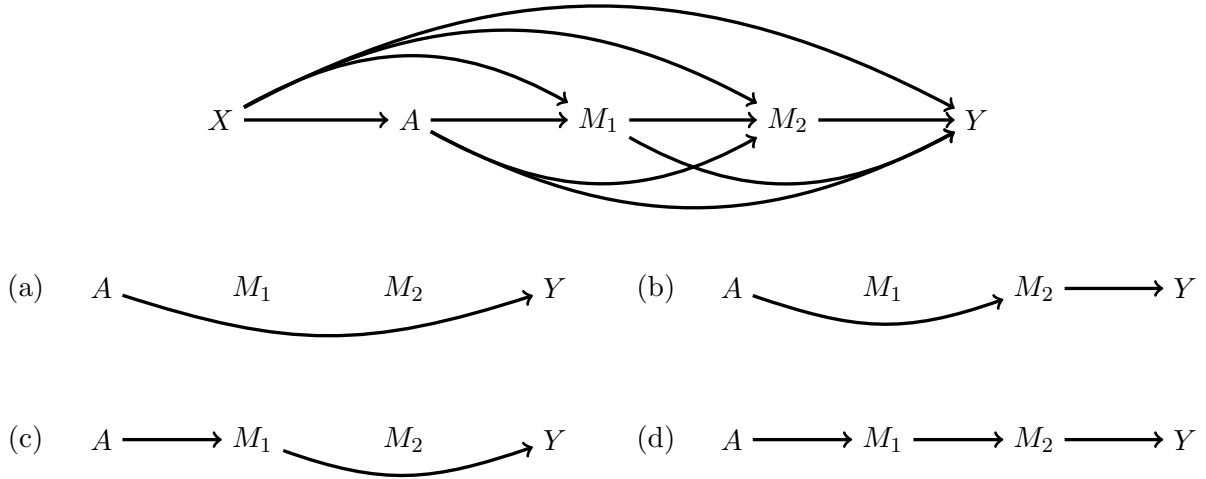
Figure 1: Causal relationships with two causally ordered mediators.

Note: A denotes the treatment, Y denotes the outcome of interest, X denotes a vector of pretreatment covariates, and M_1 and M_2 denote two causally ordered mediators.

2 Notation, Definitions, and Identification

To ease exposition, we start with the case of two causally ordered mediators before moving onto the general setting of K mediators.

2.1 The Case of Two Causally Ordered Mediators

Let A denote a binary treatment, Y an outcome of interest, and X a vector of pretreatment covariates. In addition, let M_1 and M_2 denote two causally ordered mediators, and assume M_1 precedes M_2. We allow each of these mediators to be multivariate, in which case the causal relationships among the component variables are left unspecified. A directed acyclic graph (DAG) representing the relationships between these variables is given in the top panel of Figure 1. In this DAG, four possible causal paths exist from the treatment to the outcome, as shown in the lower panels: (a) $A \to Y$; (b) $A \to M_2 \to Y$; (c) $A \to M_1 \to Y$; and (d) $A \to M_1 \to M_2 \to Y$.

A formal definition of path-specific effects (PSEs) requires the potential-outcomes notation for both the outcome and the mediators. Specifically, let $Y(a, m_1, m_2)$ denote the potential outcome under treatment status a and mediator values $M_1 = m_1$ and $M_2 = m_2$, $M_2(a, m_1)$ the potential value of the mediator M_2 under treatment status a and mediator value $M_1 = m_1$, and $M_1(a)$ the

potential value of the mediator M_1 under treatment status a. This notation allows us to define nested counterfactuals in the form of $Y\big(a, M_1(a_1), M_2(a_2, M_1(a_{12}))\big)$, where a, a_1, a_2, and a_{12} can each take 0 or 1. For example, $Y\big(1, M_1(0), M_2(0, M_1(0))\big)$ represents the potential outcome in the hypothetical scenario where the subject was treated but the mediators M_1 and M_2 were set to values they would have taken if the subject had not been treated. Further, if we let $Y(a)$ denote the potential outcome when treatment status is set to a and the mediators M_1 and M_2 take on their "natural" values under treatment status a (i.e., $M_1(a)$ and $M_2(a, M_1(a))$), we have $Y(a) = Y\big(a, M_1(a), M_2(a, M_1(a))\big)$ by construction. This is sometimes referred to as the "composition" assumption (VanderWeele 2009).

Under the above notation, for each of the causal paths shown in Figure 1, its PSE can be defined in eight different ways, depending on the reference levels chosen for A for each of the other three paths (Daniel *et al.* 2015). For example, the average direct effect of A on Y, i.e., the portion of the treatment effect that operates through the path $A \to Y$, can be defined as

$$\tau_{A \to Y}(a_1, a_2, a_{12}) = \mathbb{E}[Y\big(1, M_1(a_1), M_2(a_2, M_1(a_{12}))\big) - Y\big(0, M_1(a_1), M_2(a_2, M_1(a_{12}))\big)],$$

where a_1, a_2, and a_{12} can each take 0 or 1. In particular, $\tau_{A \to Y}(0, 0, 0)$ corresponds to the natural direct effect (NDE; Pearl 2001) or pure direct effect (PDE; Robins and Greenland 1992) if the mediators M_1 and M_2 are considered as a whole. In a similar vein, the PSEs via $A \to M_2 \to Y$, $A \to M_1 \to Y$, and $A \to M_1 \to M_2 \to Y$ can be defined as

$$\tau_{A \to M_2 \to Y}(a, a_1, a_{12}) = \mathbb{E}[Y\big(a, M_1(a_1), M_2(1, M_1(a_{12}))\big) - Y\big(a, M_1(a_1), M_2(0, M_1(a_{12}))\big)],$$

$$\tau_{A \to M_1 \to Y}(a, a_2, a_{12}) = \mathbb{E}[Y\big(a, M_1(1), M_2(a_2, M_1(a_{12}))\big) - Y\big(a, M_1(0), M_2(a_2, M_1(a_{12}))\big)],$$

$$\tau_{A \to M_1 \to M_2 \to Y}(a, a_1, a_2) = \mathbb{E}[Y\big(a, M_1(a_1), M_2(a_2, M_1(1))\big) - Y\big(a, M_1(a_1), M_2(a_2, M_1(0))\big)].$$

In addition, if we use $A \to M_1 \rightsquigarrow Y$ to denote the combination of the causal paths $A \to M_1 \to Y$ and $A \to M_1 \to M_2 \to Y$, the corresponding PSE for this "composite path" can be defined as

$$\tau_{A \to M_1 \rightsquigarrow Y}(a, a_2) = \mathbb{E}[Y\big(a, M_1(1), M_2(a_2, M_1(1))\big) - Y\big(a, M_1(0), M_2(a_2, M_1(0))\big)].$$

This quantity reflects the portion of the treatment effect that operates through M_1, regardless of whether it further operates through M_2 or not. In particular, $\tau_{A \to M_1 \rightsquigarrow Y}(0, 0)$ is often referred to as

the natural indirect effect (NIE; Pearl 2001) or the pure indirect effect (PIE; Robins and Greenland 1992) for M_1, whereas $\tau_{A \to M_1 \leadsto Y}(1,1)$ is sometimes called the total indirect effect (TIE; Robins and Greenland 1992) for M_1. Note, however, that the term NIE has also been used to denote $\tau_{A \to M_1 \leadsto Y}(1,1)$ (e.g., Tchetgen Tchetgen and Shpitser 2012). To avoid ambiguity, we use NIE and TIE to denote $\tau_{A \to M_1 \leadsto Y}(0,0)$ and $\tau_{A \to M_1 \leadsto Y}(1,1)$, respectively. By definition, these PSEs are identified if the corresponding expected potential outcomes, i.e., $\mathbb{E}[Y(a, M_1(a_1), M_2(a_2, M_1(a_{12})))]$, are identified. Below, we review the assumptions under which these expected potential outcomes are identified from observed data.

Following Pearl (2009), we use a DAG to encode a nonparametric structural equation model (NPSEM) with mutually independent errors. In this framework, the top panel of Figure 1 implies no unobserved confounding for any of the treatment-mediator, treatment-outcome, mediator-mediator, and mediator-outcome relationships. Formally, we invoke the following assumptions.

Assumption 1. *Consistency of A on M_1, (A, M_1) on M_2, and (A, M_1, M_2) on Y: For any unit and any a, m_1, m_2, $M_1 = M_1(a)$ if $A = a$; $M_2 = M_2(a, m_1)$ if $A = a$ and $M_1 = m_1$; and $Y = Y(a, m_1, m_2)$ if $A = a$, $M_1 = m_1$, and $M_2 = m_2$.*

Assumption 2. *Conditional independence among treatment and potential outcomes: for any $a, a_1, a_2, m_1, m_1^*, m_2$, $\big(M_1(a_1), M_2(a_2, m_1), Y(a, m_1, m_2)\big) \perp\!\!\!\perp A | X$; $\big(M_2(a_2, m_1), Y(a, m_1, m_2)\big) \perp\!\!\!\perp M_1(a_1) | X, A$, and $Y(a, m_1, m_2) \perp\!\!\!\perp M_2(a_2, m_1^*) | X, A, M_1$.*

Assumption 3. *Positivity: $p_{A|X}(a|x) > \epsilon > 0$ whenever $p_X(x) > 0$; $p_{A|X,M_1}(a|x, m_1) > \epsilon > 0$ whenever $p_{X,M_1}(x, m_1) > 0$, and $p_{A|X,M_1,M_2}(a|x, m_1, m_2) > \epsilon > 0$ whenever $p_{X,M,M_2}(x, m_1, m_2) > 0$, where $p(\cdot)$ denotes a probability density/mass function.*

Note that Assumption 2 involves conditional independence relationships between the so-called cross-world counterfactuals, such as $\big(M_2(a_2, m_1), Y(a, m_1, m_2)\big) \perp\!\!\!\perp M_1(a_1) | X, A$. This assumption is a direct consequence of Pearl's NPSEM with mutually independent errors. It implies, but is not implied by, the sequential ignorability assumption that Robins (2003) invokes in interpreting causal diagrams (see Robins and Richardson 2010 for an in-depth discussion). In addition, we note that Assumption 2 does not rule out all forms of unobserved confounding for the causal effects of X on its descendants. For example, unobserved variables are permitted (although not shown) in Figure 1 that affect both X and Y.

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Under Assumptions 1-3, it can be shown that $\mathbb{E}[Y\big(a, M_1(a_1), M_2(a_2, M_1(a_{12})))]$ is identified if and only if $a_{12} = a_1$ (Avin *et al.* 2005; Albert and Nelson 2011; Daniel *et al.* 2015). Consequently, none of the PSEs for the path $A \rightarrow M_1 \rightarrow Y$ is identified because given a_{12}, either $\mathbb{E}[Y\big(a, M_1(1), M_2(a_2, M_1(a_{12})))]$ or $\mathbb{E}[Y\big(a, M_1(0), M_2(a_2, M_1(a_{12})))]$ is unidentified. Similarly, none of the PSEs for the path $A \rightarrow M_1 \rightarrow M_2 \rightarrow Y$ is identified. Interestingly, the PSEs for the composite path $A \rightarrow M_1 \rightsquigarrow Y$ are all identified, even if $a \neq a_2$. These results echo the recanting witness criterion developed by Avin *et al.* (2005), which implies that the PSE for a (possibly composite) path from A to Y when A is set to 0 (or 1) for all other paths is identified if and only if the path of interest contains no "recanting witness" — a variable W that has an additional path to Y that is not contained in the path of interest. Thus the PSE $\tau_{A \rightarrow M_1 \rightarrow Y}(0, 0, 0)$ is not identified because M_1 has an additional path to Y $(M_1 \rightarrow M_2 \rightarrow Y)$ that is not contained in $A \rightarrow M_1 \rightarrow Y$, but the PSE $\tau_{A \rightarrow M_1 \rightsquigarrow Y}(0, 0)$ is identified because all possible paths from M_1 to Y is contained in $A \rightarrow M_1 \rightsquigarrow Y$.

Because $\mathbb{E}[Y\big(a, M_1(a_1), M_2(a_2, M_1(a_{12})))]$ is identified if and only if $a_1 = a_{12}$, we restrict our attention to cases where $a_1 = a_{12}$ and use the following notation:

$$\psi_{a_1,a_2,a} \triangleq \mathbb{E}\big[Y\big(a, M_1(a_1), M_2(a_2, M_1(a_1)))\big].$$

Under Assumptions 1-3, $\psi_{a_1,a_2,a}$ is identified via the following formula:

$$\psi_{a_1,a_2,a} = \iiint \mathbb{E}[Y|x, a, m_1, m_2]dP(m_2|x, a_2, m_1)dP(m_1|x, a_1)dP(x). \tag{1}$$

For a proof of the above formula, see Daniel *et al.* (2015). Equation (1) can be seen as an extension of Pearl's (2001) mediation formula to the case of two causally ordered mediators.

It should be noted that Assumptions 1-3 constitute a sufficient set of conditions that allow us to identify $\psi_{a_1,a_2,a}$ for arbitrary combinations of a_1, a_2, and a. For specific combinations of a_1, a_2, and a, Assumption 2 can be relaxed. For example, ψ_{100} is still identified via equation (1) when unobserved confounding exists for the M_2-Y relationship, and ψ_{010} is still identified via equation (1) when unobserved confounding exists for the M_1-Y relationship (Shpitser 2013; Miles *et al.* 2020).

2.2 The Case of $K(\geq 1)$ Causally Ordered Mediators

We now generalize the preceding results to the setting where the treatment effect of A on Y operates through K causally ordered, possibly multivariate mediators, $M_1, M_2, \ldots M_K$. We assume that for any $k < k'$, M_k precedes $M_{k'}$, such that no component of $M_{k'}$ causally affects any component of M_k. In a DAG that is consistent with this setup, a directed path from the treatment to the outcome can pass through any combination of the K mediators, resulting in 2^K possible paths. Among the 2^K paths, each can be switched "on" or "off," creating 2^{2^K} potential outcomes. Also, for each of the 2^K paths, the corresponding PSE can be defined in 2^{2^K-1} different ways, depending on whether each of the other $2^K - 1$ paths is switched "on" or "off." For example, when $K = 3$, for each causal path from A to Y, its PSE can be defined in $2^{2^3-1} = 128$ different ways.

As we will see, despite the exponential growth of possible causal paths and the double exponential growth of possible PSEs, most of these PSEs are not identified under the assumptions associated with Pearl's NPSEM. To fix ideas, let an overbar denote a vector of variables, so that $\overline{M}_k = (M_1, M_2, \ldots M_k)$, $\overline{m}_k = (m_1, m_2, \ldots m_k)$, and $\overline{a}_k = (a_1, a_2, \ldots a_k)$, where $\overline{M}_l = \overline{m}_l = \overline{a}_l = \varnothing$ if $l \leq 0$. In addition, let $[K]$ denote the set $\{1, 2, \ldots K\}$, and let a_{K+1}, instead of a, denote the treatment status set to the path $A \to Y$. Assumptions 1-3 can now be generalized as below.

Assumption 1*. *Consistency: For any unit, $M_k = M_k(a_k, \overline{m}_{k-1})$ if $A = a_k$ and $\overline{M}_{k-1} = \overline{m}_{k-1}$, $\forall k \in [K]$; and $Y = Y(a_{K+1}, \overline{m}_K)$ if $A = a_{K+1}$ and $\overline{M}_K = \overline{m}_K$.*

Assumption 2*. *Conditional independence among treatment and potential outcomes: $\big(M_1(a_1), M_2(a_2, \overline{m}_1), \ldots Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp A|X$; and $\big(M_{k+1}(a_{k+1}, \overline{m}_k), \ldots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_k(a_k, \overline{m}^*_{k-1})|X, A, \overline{M}_{k-1}, \forall k \in [K].$*

Assumption 3*. *Positivity: $p_{A|X}(a|x) > \epsilon > 0$ whenever $p_X(x) > 0$; $p_{A|X,\overline{M}_k}(a|x, \overline{m}_k) > \epsilon > 0$ whenever $p_{X,\overline{M}_k}(x, \overline{m}_k) > 0$, $\forall k \in [K].$*

Before giving the identification results, we introduce the following notational shorthands:

$$\overline{M}_k(\overline{a}_k) \triangleq \big(\overline{M}_{k-1}(\overline{a}_{k-1}), M_k(a_k, \overline{M}_{k-1}(\overline{a}_{k-1}))\big), \forall k \in [K],$$

$$\psi_{\overline{a}} \triangleq \mathbb{E}[Y(a_{K+1}, \overline{M}_k(\overline{a}_k))],$$

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where $\overline{M}_k(\overline{a}_k)$ is defined iteratively, with the assumption that $\overline{M}_0(\overline{a}_0) = \varnothing$. For example, when $K = 3$,

$$\psi_{\overline{a}} = \mathbb{E}\big[Y\big(a_4, M_1(a_1), M_2(a_2, M_1(a_1)), M_3(a_3, M_1(a_1), M_2(a_2, M_1(a_1)))\big)\big].$$

Theorem 1 states that $\psi_{\overline{a}}$ is identified under Assumptions 1*-3*.

Theorem 1. *Under Assumptions 1*-3*, we have*

$$\psi_{\overline{a}} = \int_x \int_{\overline{m}_K} \mathbb{E}[Y|x, a_{K+1}, \overline{m}_K]\big[\prod_{k=1}^{K} dP(m_k|x, a_k, \overline{m}_{k-1})\big] dP(x). \tag{2}$$

The above equation extends Pearl's (2001) and Daniel *et al.*'s (2015) mediation formula to the case of K causally ordered mediators. Following the terminology of Tchetgen Tchetgen and Shpitser (2012), we refer to the right-hand side of equation (1) as the generalized mediation functional (GMF). Theorem 1 echoes Avin *et al.*'s (2005) recanting witness criterion: a potential outcome is identified (in expectation) if the value that a mediator M_k takes, i.e., $M_k(a_k)$, is carried over to all future mediators. This result leads us to focus on the set of expected potential outcomes and PSEs that are nonparametrically identified. For example, to assess the mediating role of M_k, we focus on the composite causal path $A \to M_k \rightsquigarrow Y$, where, as before, the squiggle arrow encompasses all possible causal paths from M_k to Y. An identifiable PSE for this path can be expressed as

$$\tau_{A \to M_k \rightsquigarrow Y}(\overline{a}_{k-1}, \cdot, \underline{a}_{k+1}) = \psi_{\overline{a}_{k-1}, 1, \underline{a}_{k+1}} - \psi_{\overline{a}_{k-1}, 0, \underline{a}_{k+1}},$$

where $\underline{a}_{k+1} \overset{\Delta}{=} (a_{k+1}, \dots a_{K+1})$. The notation $\psi_{\overline{a}}$ makes it clear that the average total effect (ATE) of A on Y can be decomposed into $K+1$ identifiable PSEs corresponding to $A \to Y$ and $A \to M_k \rightsquigarrow Y$ $(k \in [K])$:

$$\text{ATE} = \psi_{\overline{1}} - \psi_{\overline{0}} = \underbrace{\psi_{\overline{0}_K, 1} - \psi_{\overline{0}_{K+1}}}_{A \to Y} + \sum_{k=1}^{K} \underbrace{\big(\psi_{\overline{0}_{k-1}, \underline{1}_k} - \psi_{\overline{0}_k, \underline{1}_{k+1}}\big)}_{A \to M_k \rightsquigarrow Y}. \tag{3}$$

To be sure, equation (3) is not the only way of decomposing the ATE. Depending on the order in which the paths $A \to Y$ and $A \to M_k \rightsquigarrow Y$ $(k \in [K])$ are considered, there are $(K+1)!$ different ways of decomposing the ATE. In the above decomposition, $\psi_{\overline{0}_K, 1} - \psi_{\overline{0}_{K+1}}$ corresponds to the NDE if the mediators $\overline{M}_K$ are considered as a whole.

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3 Estimation

In this section, we focus on the estimation of the GMF, i.e., the right-hand side of equation (2). When Assumptions 1*-3* hold, the GMF is equal to the causal parameter $\psi_{\overline{a}}$, but otherwise, it is still a well-defined statistical parameter of potential scientific interest. To distinguish it from the causal parameter $\psi_{\overline{a}}$, we henceforth denote the GMF by $\overline{\theta}_a$.

3.1 MLE, Regression-Imputation, and Weighting

Equation (2) suggests that $\theta_{\overline{a}}$ can be estimated via maximum likelihood (MLE) (Miles *et al.* 2017). Specifically, we can fit a parametric model for each $p(m_k|x, a_k, \overline{m}_{k-1})$ ($k \in [K]$) and for $\mathbb{E}[Y|x, a_{K+1}, \overline{m}_K]$, and then estimate the GMF via the following equation:

$$\hat{\theta}_{\overline{a}}^{\mathrm{mle}} = \mathbb{P}_n \Big[\int_{\overline{m}_K} \hat{\mathbb{E}}[Y|X, a_{K+1}, \overline{m}_K] \Big(\prod_{k=1}^{K} \hat{p}(m_k|x, a_k, \overline{m}_{k-1}) d\nu(m_k) \Big) \Big], \tag{4}$$

where $\mathbb{P}_n[\cdot] = n^{-1} \sum_i [\cdot]_i$ and $\nu(\cdot)$ is an appropriate dominating measure. This approach works best when the mediators $M_1, M_2, \ldots M_K$ are all discrete and the covariates X are low-dimensional, in which case the working models for $p(m_k|x, a_k, \overline{m}_{k-1})$ are simply models for the conditional probabilities of M_k that can be reliably estimated. When some of the mediators are continuous/multivariate or when the covariates X are high-dimensional, estimates of the corresponding conditional density/probability functions can be unstable and sensitive to model misspecification. This problem could be mitigated by imposing highly constrained functional forms on the conditional means of the mediators and the outcome. For example, when $\mathbb{E}[M_k|x, a_k, \overline{m}_{k-1}]$ and $\mathbb{E}[Y|x, a_{K+1}, \overline{m}_K]$ are all assumed to be linear with no higher-order or interaction terms, $\hat{\theta}_{\overline{a}}^{\mathrm{mle}}$ will reduce to a simple function of regression coefficients (e.g., Alwin and Hauser 1975). Yet, the assumptions of linearity and additivity are unrealistic in many applications, which may lead to biased estimates of $\theta_{\overline{a}}$. Below, we describe several imputation- and weighting-based strategies for estimating $\theta_{\overline{a}}$.

First, we observe that the GMF can be written as

$$\theta_{\overline{a}} = \mathbb{E}_X \Big[\mathbb{E}_{M_1|X,a_1} \cdots \mathbb{E}_{M_K|X,a_K,\overline{M}_{K-1}} \underbrace{\mathbb{E}[Y|X,a_{K+1},\overline{M}_K]}_{\triangleq \mu_K(X,\overline{M}_K)} \Big]. \tag{5}$$

This expression suggests that $\theta_{\overline{a}}$ can be estimated via an iterated regression-imputation (RI) approach (Zhou and Yamamoto 2020):

1. Estimate $\mu_K(X, \overline{M}_K)$ by fitting a parametric model for the conditional mean of Y given $(X, A, \overline{M}_K)$ and then setting $A = a_{K+1}$ for all units;

2. For $k = K - 1, \ldots 0$, estimate $\mu_k(X, \overline{M}_k)$ by fitting a parametric model for the conditional mean of $\mu_{k+1}(X, \overline{M}_{k+1})$ and then setting $A = a_{k+1}$ for all units;

3. Estimate $\theta_{\overline{a}}$ by averaging the fitted values $\hat{\mu}_0(X)$ among all units:

$$\hat{\theta}_{\overline{a}}^{\mathrm{ri}} = \mathbb{P}_n \big[\hat{\mu}_0(X) \big]. \tag{6}$$

The regression-imputation estimator can be seen as an extension of the imputation strategy proposed by Vansteelandt *et al.* (2012) for estimating the NDE and NIE in the one-mediator setting. Since this approach requires modeling only the conditional means of observed/imputed outcomes given different sets of mediators, it is more flexible to use with continuous/multivariate mediators than MLE. Nonetheless, because $\mu_k(x, \overline{m}_k)$ is estimated iteratively, correct specification of all of the outcome models is required for $\hat{\theta}_{\overline{a}}^{\mathrm{ri}}$ to be consistent. Thus, in practice, when parametric models are used to estimate $\mu_k(x, \overline{m}_k)$, care should be taken to ensure that the outcome models used to estimate these functions are mutually compatible. For example, if $\mu_1(X, M_1)$ follows a linear model that includes X and X^2 as predictors, then the model used to estimate $\mu_0(X) = \mathbb{E}[\mu_1(X, M_1)|X, A = a_1]$ should also include X and X^2 in the predictor set.

The GMF can also be written as

$$\theta_{\overline{a}} = \mathbb{E}\Big[\frac{\mathbb{I}(A = a_{K+1})}{p(a_{K+1}|X)} \Big(\prod_{k=1}^{K} \frac{p(M_k|X, a_k, \overline{M}_{k-1})}{p(M_k|X, a_{K+1}, \overline{M}_{k-1})} \Big) Y \Big].$$

This expression suggests a weighting estimator of $\theta_{\overline{a}}$:

$$\hat{\theta}_{\overline{a}}^{\text{w-m}} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A = a_{K+1})}{\hat{p}(a_{K+1}|X)} \Big(\prod_{k=1}^{K} \frac{\hat{p}(M_k|X, a_k, \overline{M}_{k-1})}{\hat{p}(M_k|X, a_{K+1}, \overline{M}_{k-1})} \Big) Y \Big]. \tag{7}$$

This estimator can be seen as an extension of the weighting estimator proposed in VanderWeele *et al.* (2014) for the case of two mediators. It shares a limitation of $\hat{\theta}_{\overline{a}}^{\text{mle}}$ in that it requires estimates of the conditional densities/probabilities of the mediators, which tend to be noisy if the mediators are continuous or multivariate. This problem, however, can be sidestepped by recasting the mediator density ratios, via Bayes' rule, as odds ratios in terms of the treatment variable:

$$\frac{p(M_k|X, a_k, \overline{M}_{k-1})}{p(M_k|X, a_{K+1}, \overline{M}_{k-1})} = \frac{p(a_k|X, \overline{M}_k)/p(a_{K+1}|X, \overline{M}_k)}{p(a_k|X, \overline{M}_{k-1})/p(a_{K+1}|X, \overline{M}_{k-1})}.$$

This observation leads to an alternative weighting estimator based on estimates of the conditional probabilities of treatment given different sets of mediators:

$$\hat{\theta}_{\overline{a}}^{\text{w-a}} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A = a_{K+1})}{\hat{p}(a_1|X)} \Big(\prod_{k=1}^{K} \frac{\hat{p}(a_k|X, \overline{M}_k)}{\hat{p}(a_{k+1}|X, \overline{M}_k)} \Big) Y \Big]. \tag{8}$$

In applications where the mediators are continuous/multivariate, $\hat{\theta}_{\overline{a}}^{\text{w-a}}$ should be easier to work with than $\hat{\theta}_{\overline{a}}^{\text{w-m}}$. Yet, the parameters for $p(a|x, \overline{m}_k)$ are not variationally independent across different values of k. As in the case of the regression-imputation estimator, care should be taken to ensure the compatibility of the models specified for $p(a|x, \overline{m}_k)$ (see Miles *et al.* 2020 for some practical recommendations).

The regression-imputation approach and the weighting approach can be combined to form various "hybrid estimators" of $\theta_{\overline{a}}$. For example, in the case of $K = 2$, one can use regression-imputation to estimate $\mu_2(x, m_1, m_2)$, another regression-imputation step to estimate $\mu_1(x, m_1)$, and weighting to estimate $\theta_{\overline{a}}$, yielding an "RI-RI-W" estimator:

$$\hat{\theta}_{\overline{a}}^{\text{ri-ri-w}} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A = a_1)}{\hat{p}(a_1|X)} \hat{\mu}_1(X, M_1) \Big]. \tag{9}$$

One can also use regression-imputation to estimate $\mu_2(x, m_1, m_2)$ and then employ appropriate weights to estimate $\theta_{\overline{a}}$, which leads to an "RI-W-W" estimator:

$$\hat{\theta}_{\overline{a}}^{\text{ri-w-w}} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A = a_2)}{\hat{p}(a_2|X)} \frac{\hat{p}(M_1|X, a_1)}{\hat{p}(M_1|X, a_2)} \hat{\mu}_2(X, M_1, M_2) \Big]. \tag{10}$$

In fact, with K mediators, there are 2^{K+1} different ways to combine regression-imputation and weighting, each of which involves estimating $K+1$ nuisance functions, which entail a choice between $p(a|x)$ and $\mu_0(x)$ and a choice between $p(m_k|x, a, \overline{m}_{k-1})$ and $\mu_k(x, \overline{m}_k)$ for each $k \in [K]$ (see Supplementary Material B for detailed expressions of these hybrid estimators in the case of $K = 2$). As with $\hat{\theta}_{\overline{a}}^{\mathrm{mle}}$, $\hat{\theta}_{\overline{a}}^{\mathrm{ri}}$, $\hat{\theta}_{\overline{a}}^{\mathrm{w\text{-}m}}$, and $\hat{\theta}_{\overline{a}}^{\mathrm{w\text{-}a}}$, each of these hybrid estimators will be consistent only if the corresponding nuisance functions are all correctly specified and consistently estimated. In applications where the pretreatment covariates X and/or the mediators have many components, all of the above estimators will be prone to model misspecification bias.

3.2 Multiply Robust and Semiparametric Efficient Estimation

Henceforth, let $O = (X, A, \overline{M}_K, Y)$ denote the observed data, and $\mathcal{P}_{\mathrm{np}}$ a nonparametric model over O wherein all laws P satisfy the positivity assumption described in Section 2.2. In addition, define $\mu_k(X, \overline{M}_k)$ iteratively as in equation (5):

$$\mu_K(X, \overline{M}_K) \triangleq \mathbb{E}[Y|X, a_{K+1}, \overline{M}_K]$$

$$\mu_k(X, \overline{M}_k) \triangleq \mathbb{E}[\mu_{k+1}(X, \overline{M}_{k+1})|X, a_{k+1}, \overline{M}_k], \quad k = K - 1, \ldots, 0.$$

Theorem 2. *The efficient influence function (EIF) of $\theta_{\overline{a}}$ in $\mathcal{P}_{\mathrm{np}}$ is given by*

$$\varphi_{\overline{a}}(O) = \sum_{k=0}^{K+1} \varphi_k(O), \tag{11}$$

where

$$\varphi_0(O) = \mu_0(X) - \theta_{\overline{a}},$$

$$\varphi_k(O) = \frac{\mathbb{I}(A = a_k)}{p(a_k|X)}\left(\prod_{j=1}^{k-1} \frac{p(M_j|X, a_j, \overline{M}_{j-1})}{p(M_j|X, a_k, \overline{M}_{j-1})}\right)\left(\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1})\right), \quad k \in [K],$$

$$\varphi_{K+1}(O) = \frac{\mathbb{I}(A = a_{K+1})}{p(a_{K+1}|X)}\left(\prod_{j=1}^{K} \frac{p(M_j|X, a_j, \overline{M}_{j-1})}{p(M_j|X, a_{K+1}, \overline{M}_{j-1})}\right)\left(Y - \mu_K(X, \overline{M}_K)\right).$$

The semiparametric efficiency bound for any regular and asymptotically linear estimator of $\theta_{\overline{a}}$ in $\mathcal{P}_{\mathrm{np}}$ is therefore $\mathbb{E}\left[\left(\varphi_{\overline{a}}(O)\right)^2\right]$.

We now present two estimators of $\theta_{\overline{a}}$ based on the EIF. First, consider the factorized likelihood of O: $p(O) = p(X)p(A|X)\left(\prod_{k=1}^{K} p(M_k|X, A, \overline{M}_{k-1})\right)p(Y|X, A, \overline{M}_K)$. Suppose we have estimated

$K + 2$ nuisance functions, each of which corresponds to a component of $p(O)$: $\hat{\pi}_0(a|x)$ for $p(a|x)$, $\hat{f}_k(m_k|x, a, \overline{m}_{k-1})$ for $p(m_k|x, a, \overline{m}_{k-1})$, and $\hat{\mu}_K(x, \overline{m}_K)$ for $\mathbb{E}[Y|x, a_{K+1}, \overline{m}_K]$. The GMF can now be estimated as

$$
\begin{aligned}
\hat{\theta}_{\overline{a}}^{\text{eif}_1} =\mathbb{P}_n\Big[& \frac{\mathbb{I}(A = a_{K+1})}{\hat{\pi}_0(a_{K+1}|X)} \Big(\prod_{j=1}^{K} \frac{\hat{f}_j(M_j|X, a_j, \overline{M}_{j-1})}{\hat{f}_j(M_j|X, a_{K+1}, \overline{M}_{j-1})} \Big) \big(Y - \hat{\mu}_K(X, \overline{M}_K) \big) \\
& + \sum_{k=1}^{K} \frac{\mathbb{I}(A = a_k)}{\hat{\pi}_0(a_k|X)} \Big(\prod_{j=1}^{k-1} \frac{\hat{f}_j(M_j|X, a_j, \overline{M}_{j-1})}{\hat{f}_j(M_j|X, a_k, \overline{M}_{j-1})} \Big) \big(\hat{\mu}_k^{\text{mle}}(X, \overline{M}_k) - \hat{\mu}_{k-1}^{\text{mle}}(X, \overline{M}_{k-1}) \big) \\
& + \hat{\mu}_0^{\text{mle}}(X) \Big],
\end{aligned}
\tag{12}
$$

where $\hat{\mu}_K^{\text{mle}}(X, \overline{M}_K) = \hat{\mu}_K(X, \overline{M}_K)$ and $\hat{\mu}_k^{\text{mle}}(X, \overline{M}_k)$ is iteratively constructed as

$$
\hat{\mu}_k^{\text{mle}}(X, \overline{M}_k) = \int \hat{\mu}_{k+1}^{\text{mle}}(X, \overline{M}_k, m_{k+1}) \hat{f}_{k+1}(m_{k+1}|X, a_{k+1}, \overline{M}_k) d\nu(m_{k+1}), \quad k = K - 1, \ldots 0. \tag{13}
$$

When M_{k+1} involves continuous components, equation (13) can be evaluated via Monte Carlo simulation.

When some of the mediators are continuous/multivariate, it can be difficult to estimate the conditional distributions $p(m_k|x, a, \overline{m}_{k-1})$. In such cases, it is often preferable to estimate the mediator density ratios using the corresponding odds ratios of the treatment variable, and estimate the functions $\mu_k(x, \overline{m}_k)$ using the regression-imputation approach. Specifically, suppose we have estimated $2(K + 1)$ nuisance functions: $\hat{\pi}_0(a|x)$ for $p(a|x)$, $\hat{\pi}_k(a|x, \overline{m}_k)$ for $p(a|x, \overline{m}_k)$ ($k \in [K]$), and $\hat{\mu}_k(x, \overline{m}_k)$ for $\mu_k(x, \overline{m}_k)$ ($k \in \{0, 1, \ldots K\}$), where for $k < K$, $\mu_k(x, \overline{m}_k)$ is estimated iteratively by fitting a model for the conditional mean of $\hat{\mu}_{k+1}(X, \overline{M}_{k+1})$ given $(X, A, \overline{M}_k)$ and then setting $A = a_{k+1}$ for all units. The GMF can then be estimated as

$$
\begin{aligned}
\hat{\theta}_{\overline{a}}^{\text{eif}_2} =\mathbb{P}_n\Big[& \frac{\mathbb{I}(A = a_{K+1})}{\hat{\pi}_0(a_1|X)} \Big(\prod_{j=1}^{K} \frac{\hat{\pi}_j(a_j|X, \overline{M}_j)}{\hat{\pi}_j(a_{j+1}|X, \overline{M}_j)} \Big) \big(Y - \hat{\mu}_K(X, \overline{M}_K) \big) \\
& + \sum_{k=1}^{K} \frac{\mathbb{I}(A = a_k)}{\hat{\pi}_0(a_1|X)} \Big(\prod_{j=1}^{k-1} \frac{\hat{\pi}_j(a_j|X, \overline{M}_j)}{\hat{\pi}_j(a_{j+1}|X, \overline{M}_j)} \Big) \big(\hat{\mu}_k(X, \overline{M}_k) - \hat{\mu}_{k-1}(X, \overline{M}_{k-1}) \big) \\
& + \hat{\mu}_0(X) \Big].
\end{aligned}
\tag{14}
$$

The multiple robustness and semiparametric efficiency of $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ are given below.

Theorem 3. *Let $\eta_1 = \{\pi_0, f_1, \ldots f_K, \mu_K\}$ denote the $K + 2$ nuisance functions involved in $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$, and $\eta_2 = \{\pi_0, \ldots \pi_K, \mu_0, \ldots \mu_K\}$ denote the $2(K + 1)$ nuisance functions involved in $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$. Suppose*

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that Assumption 3* (positivity) and suitable regularity conditions for estimating equations (e.g., Newey and McFadden 1994, p. 2148) hold. In addition, suppose that $\mu_K(x, \overline{m}_K)$ is bounded over the support of $(X, \overline{M}_K)$. Then, when the elements of η_1 and η_2 are estimated via parametric models,

1. *$\hat{\theta}_{\overline{a}}^{\mathrm{eif}_1}$ is consistent and asymptotically normal (CAN) if $K+1$ of the $K+2$ nuisance functions in η_1 are correctly specified and their parameter estimates are $\sqrt{n}$-consistent; it is semiparametric efficient if all of the $K+2$ nuisance functions in η_1 are correctly specified and their parameter estimates are $\sqrt{n}$-consistent.*

2. *$\hat{\theta}_{\overline{a}}^{\mathrm{eif}_2}$ is CAN if $\exists k \in \{0, \ldots K+1\}$, the first k treatment models $\pi_0, \ldots \pi_{k-1}$ and the last $K+1-k$ outcome models $\mu_k, \ldots \mu_K$ in η_2 are correctly specified and their parameter estimates are $\sqrt{n}$-consistent; it is semiparametric efficient if all of the treatment and outcome models in η_2 are correctly specified and their parameter estimates are $\sqrt{n}$-consistent.*

Both $\hat{\theta}_{\overline{a}}^{\mathrm{eif}_1}$ and $\hat{\theta}_{\overline{a}}^{\mathrm{eif}_2}$ are $K + 2$-robust in the sense that they are CAN provided that one of $K + 2$ sets of nuisance functions is correctly specified and the corresponding parameter estimates are $\sqrt{n}$-consistent. Several special cases are worth noting. First, in the degenerate case where $K = 0$, it is clear that both $\hat{\theta}_{\overline{a}}^{\mathrm{eif}_1}$ and $\hat{\theta}_{\overline{a}}^{\mathrm{eif}_2}$ reduce to the standard doubly robust estimator for $\mathbb{E}[Y(a)]$ (Scharfstein *et al.* 1999). Second, when $K = 1$, $\hat{\theta}_{01}^{\mathrm{eif}_1}$ coincides with Tchetgen Tchetgen and Shpitser's (2012) triply robust estimator for $\mathbb{E}[Y(1, M(0))]$. Finally, when $K = 2$, $\hat{\theta}_{010}^{\mathrm{eif}_1}$ is identical to Miles *et al.*'s (2020) estimator for θ_{010}. For this case, however, Miles *et al.* provide a slightly weaker condition than that implied by Theorem 3 for $\hat{\theta}_{010}^{\mathrm{eif}_1}$ to be CAN. Specifically, they showed that $\hat{\theta}_{010}^{\mathrm{eif}_1}$ remains CAN even if both f_1 and μ_2 are misspecified. In Section 4, we show that the conditions for $\hat{\theta}_{\overline{a}}^{\mathrm{eif}_2}$ to be CAN can also be relaxed for several particular types of PSEs, including the natural path-specific effect (nPSE), of which $\psi_{010} - \psi_{000}$ is a special case. For the $K = 2$ case, Miles *et al.* also noted that the mediator density ratios in $\hat{\theta}_{010}^{\mathrm{eif}_1}$ can be indirectly estimated through models for π_1 and π_2. Clearly, this approach will result in $\hat{\theta}_{010}^{\mathrm{eif}_2}$ if the $\mu_k(x, \overline{m}_k)$ functions are in the meanwhile estimated through regression-imputation. The $K + 2$-robustness of $\hat{\theta}_{\overline{a}}^{\mathrm{eif}_1}$ and $\hat{\theta}_{\overline{a}}^{\mathrm{eif}_2}$, interestingly, resembles the multiple robustness of the Bang-Robins (2005) estimator for the mean of a potential outcome with time-varying treatments and time-varying confounders (Luedtke *et al.* 2017; Molina *et al.* 2017; Rotnitzky *et al.* 2017).

To gain some intuition as to why $\hat{\theta}_{\overline{a}}^{\mathrm{eif}_1}$ is $K + 2$-robust, consider cases in which only one nuisance

function in η_1 is misspecified. When only π_0 is misspecified, all terms inside $\mathbb{P}_n[\cdot]$ but $\hat{\mu}_0^{\text{mle}}(X)$ will have a zero mean (asymptotically), leaving only $\mathbb{P}_n[\hat{\mu}_0^{\text{mle}}(X)]$ (i.e., the MLE estimator (4)), which is consistent because the corresponding nuisance functions $\{f_1, \ldots f_K, \mu_K\}$ are all correctly specified. When only μ_K is misspecified, all terms involving $\hat{\mu}_K(X, \overline{M}_K)$ and $\hat{\mu}_k^{\text{mle}}(X, \overline{M}_k)$ $(k = 0, 1, \ldots K-1)$ inside $\mathbb{P}_n[\cdot]$ will have a zero mean (asymptotically), leaving only a weighted average of Y (i.e., the weighting estimator (7)), which is consistent because the corresponding nuisance functions $\{\pi_0, f_1, \ldots f_K\}$ are all correctly specified. Finally, when only $f_{k'}$ is misspecified (for some $k' \in [K]$), it can be shown that all terms involving $\hat{f}_{k'}$ and $\hat{\mu}_k^{\text{mle}}(X, \overline{M}_k)$ $(\forall k < k')$ inside $\mathbb{P}_n[\cdot]$ will have a zero mean (asymptotically), leaving only a weighted average of $\hat{\mu}_{k'}^{\text{mle}}(X, \overline{M}_{k'})$. The latter constitutes a "hybrid" estimator similar to those mentioned in the previous section, and it is consistent in this case because its nuisance functions $\{\pi_0, f_1, \ldots f_{k'-1}, f_{k'+1}, \ldots f_K, \mu_K\}$ are all correctly specified.

The $K + 2$-robustness of $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ is due to a similar logic to that of $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$. Yet, different from $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$, $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ involves estimating $2(K + 1)$ nuisance functions, $K + 1$ for the conditional probabilities of treatment and $K + 1$ for the conditional means of observed/imputed outcomes. Also, unlike $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$, the treatment models involved in $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ are not variationally independent; neither are the outcome models. For example, when $M_K \perp\!\!\!\perp A | X, \overline{M}_{K-1}$, $\pi_K(A|X, \overline{M}_K)$ should be identical to $\pi_{K-1}(A|X, \overline{M}_{K-1})$; similarly, when $M_K \perp\!\!\!\perp Y | X, A, \overline{M}_{K-1}$, $\mu_K(X, \overline{M}_K)$ should be identical to $\mu_{K-1}(X, \overline{M}_{K-1})$. Thus, in practice, both the treatment and outcome models should be specified in a mutually compatible way, otherwise some of the conditions in Theorem 3 may fail by design.

The local efficiency of $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ is due to the fact that both of the EIF-based estimating equations (12) and (14) have a zero derivative with respect to the nuisance functions at the truth. This property, referred to as "Neyman orthogonality" by Chernozhukov *et al.* (2018), implies that first step estimation of the nuisance functions has no first order effect on the influence functions of $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$. This property suggests that the nuisance functions can be estimated using data-adaptive/machine learning methods or their ensembles. In this case, these estimators will still be consistent as long as the nuisance functions associated with one of the $K + 2$ conditions in Theorem 3 are consistently estimated. For $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$, an added advantage of employing data-adaptive methods to estimate the nuisance functions is that, by exploring a larger space within $\mathcal{P}_{\text{np}}$, the risk of model incompatibility is reduced.

When data-adaptive/machine learning methods are used to estimate the nuisance functions, it

is advisable to use sample splitting to render the empirical process term asymptotically negligible (Zheng and van der Laan 2011; Chernozhukov *et al.* 2018; Newey and Robins 2018). For example, Chernozhukov *et al.* (2018) suggest the method of "cross-fitting," which involves the following steps: (a) randomly partition the sample S into J folds: $S_1, S_2 \ldots S_J$; (b) for each j, obtain a fold-specific estimate of the target parameter using only data from S_j ("main sample"), but with nuisance functions learned from the remainder of the sample (i.e., $S \backslash S_j$; "auxiliary sample"); (c) average these fold-specific estimates to form a final estimate of the target parameter.

When cross-fitting is used, $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\bar{a}}^{\text{eif}_2}$ will be semiparametric efficient if the corresponding nuisance function estimates are all consistent and converge at sufficiently fast rates. For example, a sufficient (but not necessary) condition for $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\bar{a}}^{\text{eif}_2}$ to attain the semiparametric efficiency bound is when all of the nuisance function estimates converge at faster-than-$n^{-1/4}$ rates. More precise conditions are given in Theorem 4.

Theorem 4. *Let $\hat{\eta}_1 = \{\hat{\pi}_0, \hat{f}_1, \ldots \hat{f}_K, \hat{\mu}_K\}$ and $\hat{\eta}_2 = \{\hat{\pi}_0, \ldots \hat{\pi}_K, \hat{\mu}_0, \ldots \hat{\mu}_K\}$ denote estimates of the nuisance functions involved in $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\bar{a}}^{\text{eif}_2}$, respectively. Let $r_n(\cdot)$ denote a mapping from a nuisance function estimator to its $L_2(P)$ convergence rate where P represents the true distribution of $O = (X, A, \overline{M}_K, Y)$. Suppose that Assumption 3* (positivity) holds for both the true distribution P and its estimates implied by $\hat{\eta}_1$ and $\hat{\eta}_2$, and that all other assumptions required for Theorem 3 hold. Then, when the nuisance functions are estimated via data-adaptive methods and cross-fitting,*

1. *$\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ is consistent if $K + 1$ of the $K + 2$ elements in $\hat{\eta}_1$ are consistent in the L_2-norm; it is CAN and semiparametric efficient if all elements in $\hat{\eta}_1$ are consistent in the L_2-norm and*
$$\sum_{u,v \in \hat{\eta}_1; u \neq v} r_n(u) r_n(v) = o(n^{-1/2});$$

2. *$\hat{\theta}_{\bar{a}}^{\text{eif}_2}$ is consistent if $\exists k \in \{0, \ldots K + 1\}$, $\hat{\pi}_0, \ldots \hat{\pi}_{k-1}, \hat{\mu}_k, \ldots \hat{\mu}_K$ are all consistent in the L_2-norm; it is CAN and semiparametric efficient if all elements in $\hat{\eta}_2$ are consistent in the L_2-norm and $\sum_{j=0}^{K} r_n(\hat{\pi}_j) r_n(\hat{\mu}_j) = o(n^{-1/2})$.*

The multiple robustness result for $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ echoes Theorem 3. Moreover, the first part of Theorem 4 states that $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ is CAN and semiparametric efficient if all nuisance functions in η_1 are consistently estimated and, for every two nuisance functions in η_1, the product of their convergence rates is $o(n^{-1/2})$. Thus $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ is CAN and semiparametric efficient if all of the $K + 2$ nuisance function

estimates are consistent and converge at faster-than-$n^{-1/4}$ rates, but it will also attain semiparametric efficiency under alternative conditions. For example, when estimates of the treatment and mediator models $\{\hat{\pi}_0, \hat{f}_1, \ldots \hat{f}_K\}$ all converge to the truth at a rate of $n^{-1/3}$ and estimates of the outcome model $\hat{\mu}_K$ converge to the truth at a rate of $n^{-1/5}$, the product of the convergence rates of any two elements in $\hat{\eta}_1$ is either $O(n^{-1/3})O(n^{-1/3}) = O(n^{-2/3})$ or $O(n^{-1/3})O(n^{-1/5}) = O(n^{-8/15})$, both faster than $O(n^{-1/2})$.

The second part of Theorem 4 states that $\hat{\theta}_{\bar{a}}^{\text{eif}_2}$ is consistent if there exists a k such that the first k treatment models and the last $K+1-k$ outcome models in η_2 are consistently estimated, echoing Theorem 3. As with $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$, $\hat{\theta}_{\bar{a}}^{\text{eif}_2}$ will be CAN and semiparametric efficient if all of the required nuisance functions are consistently estimated and converge at faster-than-$n^{-1/4}$ rates. The rate condition $\sum_{j=0}^{K} r_n(\hat{\pi}_j)r_n(\hat{\mu}_j) = o(n^{-1/2})$ appears to be weaker than that for $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ as it involves the sum of only $K+1$, rather than $\binom{K+2}{2}$, product terms. Because the outcome models are estimated iteratively, the convergence rate of $\hat{\mu}_k$ will in general depend on the convergence rates of $\{\hat{\mu}_{k+1}, \ldots \hat{\mu}_K\}$. That is, if $r_n(\hat{\mu}_{k+1}) = O(n^{\delta})$, $r_n(\hat{\mu}_k)$ is unlikely to be faster than $O(n^{\delta})$. Nonetheless, $\hat{\theta}_{\bar{a}}^{\text{eif}_2}$ will be CAN and semiparametric efficient under relatively weak conditions — for example, when estimates of the treatment models all converge to the truth at a rate of $n^{-1/3}$ and estimates of the outcome models all converge to the truth at a rate of $n^{-1/5}$, in which case $\sum_{j=0}^{K} r_n(\hat{\pi}_j)r_n(\hat{\mu}_j) = \sum_{j=0}^{K} O(n^{-8/15}) = o(n^{-1/2})$.

For inference on $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\bar{a}}^{\text{eif}_2}$, a simple variance estimator can be constructed from the empirical analog of the EIF, i.e., $\mathbb{P}_n[\hat{\varphi}_{\bar{a}}^2(O)]/n$. However, unlike $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\bar{a}}^{\text{eif}_2}$, this variance estimator is not multiply robust — it will be consistent only if the conditions for semiparametric efficiency in Theorem 3 or Theorem 4 are satisfied. Thus, when the nuisance functions are estimated using parametric models, the variance estimator constructed from the empirical EIF may be inconsistent even when the corresponding estimator for $\theta_{\bar{a}}$ is CAN — for example, when only $K+1$ of the $K+2$ nuisance functions involved in $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ are correctly specified. In this case, the nonparametric bootstrap is a convenient approach to more robust inference. When the nuisance functions are estimated using data-adaptive/machine learning methods, however, the nonparametric bootstrap is not theoretically justified, and the EIF-based variance estimator may still be preferred.

3.3 Multiply Robust Regression-Imputation Estimators

Both of the multiply robust estimators described above involve inverse probability weights. When the positivity assumption is nearly violated, the inverse probability weights tend to be highly variable, which may lead to poor finite sample performance (Kang and Schafer 2007; Petersen *et al.* 2012). A variety of methods have been proposed to reduce the influence of highly variable weights on doubly robust and multiply robust estimators in similar settings (e.g., Robins *et al.* 2007; Tchetgen Tchetgen and Shpitser 2012; Seaman and Vansteelandt 2018). Among them, a common strategy is to tailor the estimating equation of the outcome model(s) such that the terms involving inverse probability weights will equal zero, leaving only a regression-imputation or "substitution" estimator that typically resides in the parameter space of the estimand. Below, we briefly describe how this approach can be adapted to $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$.

Let us start with $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$, which can be written as

$$
\begin{aligned}
\hat{\theta}_{\overline{a}}^{\text{eif}_2} = \mathbb{P}_n \big[& \hat{w}_K(X, A, \overline{M}_K)\big(Y - \hat{\mu}_K(X, \overline{M}_K)\big) \\
& + \sum_{k=1}^{K} \hat{w}_{k-1}(X, A, \overline{M}_{k-1})\big(\hat{\mu}_k(X, \overline{M}_k) - \hat{\mu}_{k-1}(X, \overline{M}_{k-1})\big) \\
& + \hat{\mu}_0(X)\big],
\end{aligned}
\tag{15}
$$

where $\hat{w}_k(A, X, \overline{M}_k)$ $(0 \le k \le K)$ are estimates of the corresponding inverse probability weights as displayed in equation (14). Note that the nuisance functions $\hat{\mu}_k(X, \overline{M}_k)$ $(0 \le k \le K)$ here are all estimated via the regression-imputation approach. When the corresponding outcome models are fitted via generalized linear models (GLM) with canonical links, one can either (a) fit weighted GLMs (with an intercept term) for $\hat{\mu}_k(X, \overline{M}_k)$ using $\hat{w}_k(A, X, \overline{M}_k)$ as weights, or (b) add the corresponding inverse probability weight as an additional covariate in these regressions (Robins *et al.* 2007). Either way, the score equations for GLMs will ensure that all terms inside $\mathbb{P}_n[\cdot]$ but $\hat{\mu}_0(X)$ have a sample mean of zero, leaving only $\mathbb{P}_n[\hat{\mu}_0(X)]$, which will reside in the parameter space of $\theta_{\overline{a}}$ if the latter equals the range of the GLM specified for $\mu_0(x)$.

Alternatively, one can use the method of targeted maximum likelihood estimation (TMLE; van Der Laan and Rubin 2006; Zheng and van der Laan 2012), which, by fitting each of the outcome models in two steps, will also ensure a zero sample mean for all terms inside $\mathbb{P}_n[\cdot]$ but $\hat{\mu}_0(X)$. This

approach does not require the first-step models to be GLM and thus can be used with a wider range of outcome models. In our case, it involves the following steps:

1. For $k = K, \ldots 0$

   (a) Using $\hat{\mu}_{k+1}^{\text{tmle}}(X, \overline{M}_{k+1})$ (or, in the case $k = K$, the observed outcome Y) as the response variable, obtain a first-step regression-imputation estimate of $\mu_k(X, \overline{M}_k)$;

   (b) Fit a one-parameter GLM for the conditional mean of $\hat{\mu}_{k+1}^{\text{tmle}}(X, \overline{M}_{k+1})$ (or, in the case $k = K$, the observed outcome Y), using $g(\hat{\mu}_k(X, \overline{M}_k))$ as an offset term and $\hat{w}_k(A, X, \overline{M}_k)$ as the only covariate (without an intercept term), and obtain an updated estimate $\hat{\mu}_k^{\text{tmle}}(X, \overline{M}_k) = g^{-1}\big(g(\hat{\mu}_k(X, \overline{M}_k)) + \hat{\beta}_k \hat{w}_k(A, X, \overline{M}_k)\big)$, where $g(\cdot)$ is the link function for the GLM and $\hat{\beta}_k$ is the estimated coefficient on $\hat{w}_k(A, X, \overline{M}_k)$;

2. Obtain the final estimate $\hat{\theta}_{\overline{a}}^{\text{tmle}} = \mathbb{P}_n[\hat{\mu}_0^{\text{tmle}}(X)]$.

In the one-mediator case, the above estimator is similar to the TMLE estimator proposed by Zheng and van der Laan (2012) for the NDE, i.e., $\psi_{01} - \psi_{00}$. Since Zheng and van der Laan's estimand is the NDE instead of the mediation functional, their TMLE procedure involves fitting a model for the "mediated mean outcome difference" (p. 6), i.e., $\mathbb{E}[\mathbb{E}[Y|X, A = 1, M] - \mathbb{E}[Y|X, A = 0, M]|X, A = 0]$, instead of the conditional mean of the imputed outcome itself, i.e., $\mu_0(X)$.

As with the GLM-based adjustments, the TMLE approach also yields a regression-imputation estimator that resides in the parameter space of $\theta_{\overline{a}}$ if the latter equals the range of the model specified for $\mu_0(x)$. It should be noted that when data-adaptive methods are used to obtain first-step estimates of the nuisance functions, sample splitting should be employed so that steps 1(a) and steps 1(b) are implemented on different subsamples. In cross-fitting, for example, steps 1(a) should be implemented in the auxiliary sample $(S \backslash S_j)$ and steps 1(b) implemented in the main sample S_j. The method of TMLE can also be used to adjust $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$, in which case the first step estimates of $\mu_k(X, \overline{M}_k)$ $(0 \leq k \leq K - 1)$ are based on equation (13), and the weights $\hat{w}_k(A, X, \overline{M}_k)$ $(0 \leq k \leq K)$ reflect the corresponding terms in equation (12).

4 Special Cases

We have so far considered $\theta_{\overline{a}}$ for the unconstrained case where $a_1, \ldots a_{K+1}$ can each take 0 or 1. In many applications, the researcher may be interested in particular causal estimands such as the natural direct effect (NDE), the natural/total indirect effect (NIE/TIE), and natural path-specific effects (nPSE; Daniel *et al.* 2015). Below, we discuss how the multiply robust semiparametric estimators of $\theta_{\overline{a}}$ apply to these estimands. In addition, we discuss a set of cumulative path-specific effects (cPSEs) that together compose the ATE. In Supplementary Material E, we connect these cPSEs to noncausal decompositions of between-group disparities that are widely used in the social sciences. For illustrative purposes, we focus on estimators based on $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$, although similar results hold for those based on $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$. Throughout this section, we maintain Assumptions 1*-3* so that $\theta_{\overline{a}} = \psi_{\overline{a}}$.

4.1 Natural Direct Effect (NDE)

The NDE measures the effect of switching treatment status from 0 to 1 in a hypothetical world where the mediators $(M_1, \ldots M_K)$ were all set to values they would have "naturally" taken for each unit under treatment status $A = 0$. It is thus given by $\psi_{\overline{0}_K, 1} - \psi_{\overline{0}_{K+1}}$. The first row of Figure 2 illustrates the baseline and comparison interventions associated with the NDE for the case of $K = 2$, where the black solid and dashed arrows for $A \to M_1$, $A \to M_2$, and $A \to Y$ denote activated ($A = 1$) and unactivated ($A = 0$) paths, respectively. A semiparametric efficient estimator for the NDE can be constructed as

$$\widehat{\text{NDE}}^{\text{eif}_2} = \hat{\theta}_{\overline{0}_K, 1}^{\text{eif}_2} - \hat{\theta}_{\overline{0}_{K+1}}^{\text{eif}_2}. \tag{16}$$

If we treat $\overline{M}_K = (M_1, \ldots M_K)$ as a whole, $\psi_{\overline{0}_K, 1} - \psi_{\overline{0}_{K+1}}$ coincides with the NDE defined in the single mediator setting. In fact, $\widehat{\text{NDE}}^{\text{eif}_2}$ is akin to the semiparametric estimator of the NDE given in Zheng and van der Laan (2012). By contrast, if we use $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ instead of $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ in equation (16), we obtain Tchetgen Tchetgen and Shpitser's (2012) estimator of the NDE.

Setting $a_1 = \ldots a_{K+1} = 0$ in equation (14), we have

$$\hat{\theta}_{\overline{0}_{K+1}}^{\text{eif}_2} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A = 0)}{\hat{\pi}_0(0|X)} \big(Y - \hat{\mu}_0(X) \big) + \hat{\mu}_0(X) \Big], \tag{17}$$
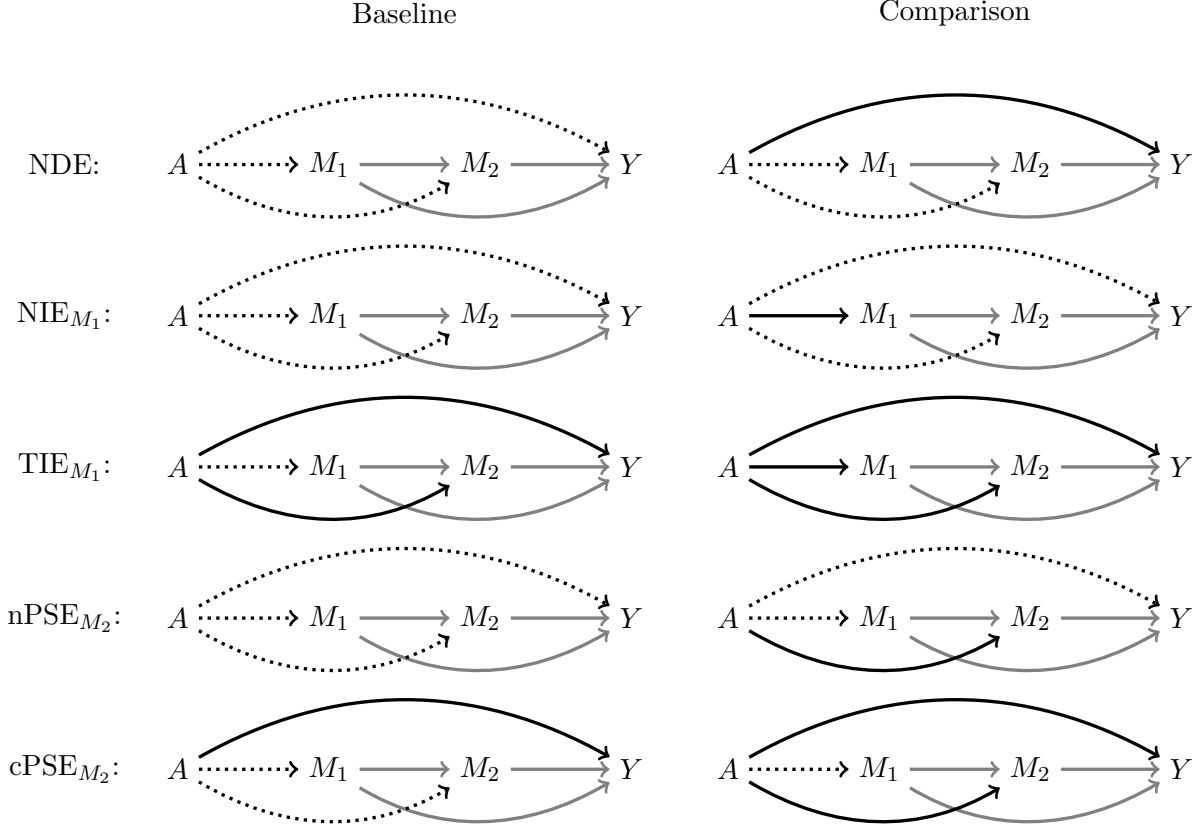
Figure 2: Illustrations of NDE, NIE, TIE, nPSE, and cPSE in the case of two mediators.

Note: A denotes the treatment, Y denotes the outcome of interest, and M_1 and M_2 denote two causally ordered mediators. Solid and dashed arrows for $A \to M_1$, $A \to M_2$, and $A \to Y$ denote activated $(A = 1)$ and unactivated $(A = 0)$ paths, respectively. Gray arrows $M_1 \to M_2$, $M_1 \to Y$, and $M_2 \to Y$ signify that the mediators M_1 and M_2 are not under direct intervention.

where $\mu_0(X) = \mathbb{E}[Y|X, A = 0]$. Not surprisingly, $\hat{\theta}_{\overline{0}_{K+1}}^{\text{eif}_2}$ is the standard doubly robust estimator for $\mathbb{E}[Y(0)]$, which is consistent if either $\hat{\pi}_0(0|X)$ or $\hat{\mu}_0(X)$ is consistent. Similarly, by setting $a_1 = \ldots a_K = 0$ and $a_{K+1} = 1$ in equation (14), we have

$$\hat{\theta}_{\overline{0}_K,1}^{\text{eif}_2} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A=1)}{\hat{\pi}_0(0|X)} \frac{\hat{\pi}_K(0|X, \overline{M}_K)}{\hat{\pi}_K(1|X, \overline{M}_K)} \big(Y - \hat{\mu}_K(X, \overline{M}_K)\big) + \frac{\mathbb{I}(A=0)}{\hat{\pi}_0(0|X)} \big(\hat{\mu}_K(X, \overline{M}_K) - \hat{\mu}_{0,K}(X)\big) + \hat{\mu}_{0,K}(X) \Big].$$

In contrast to the general case where $\overline{a}_K$ is unconstrained, $\hat{\theta}_{\overline{0}_K,1}^{\text{eif}_2}$ involves estimating only four nuisance functions: $\pi_0(a|x)$, $\pi_K(a|x, \overline{m}_K)$, $\mu_{0,K}(x)$, and $\mu_K(x, \overline{m}_K)$, where $\mu_K(x, \overline{m}_K) = \mathbb{E}[Y|x, A = 1, \overline{m}_K]$ and $\mu_{0,K}(x) = \mathbb{E}[\mu_K(X, \overline{M}_K)|x, A = 0]$. Hence $\mu_{0,K}(x)$ can be estimated by fitting a model for the conditional mean of $\hat{\mu}_K(X, \overline{M}_K)$ given (X, A) and then setting $A = 0$ for all units. It follows from Theorem 3 that $\hat{\theta}_{\overline{0}_K,1}^{\text{eif}_2}$ is triply robust in that it is consistent if one of the following

three conditions holds: (a) $\hat{\pi}_0$ and $\hat{\pi}_K$ are consistent; (b) $\hat{\pi}_0$ and $\hat{\mu}_K$ are consistent; and (c) $\hat{\mu}_{0,K}$ and $\hat{\mu}_K$ are consistent. In the meantime, we know that $\hat{\theta}_{\overline{0}_{K+1}}^{\text{eif}_2}$ is consistent if either $\hat{\pi}_0$ or $\hat{\mu}_0$ is consistent. By taking the intersection of the multiple robustness conditions for $\hat{\theta}_{\overline{0}_K,1}^{\text{eif}_2}$ and $\hat{\theta}_{\overline{0}_{K+1}}^{\text{eif}_2}$, we deduce that $\widehat{\text{NDE}}^{\text{eif}_2}$ is also triply robust, as detailed in Corollary 1.

Corollary 1. *Suppose all assumptions required for Theorem 4 hold. When the nuisance functions are estimated via parametric models, $\widehat{\text{NDE}}^{\text{eif}_2}$ is CAN provided that one of the following three sets of nuisance functions is correctly specified and its parameter estimates are $\sqrt{n}$-consistent: $\{\pi_0, \pi_K\}$, $\{\pi_0, \mu_K\}$, $\{\mu_0, \mu_{0,K}, \mu_K\}$. $\widehat{\text{NDE}}^{\text{eif}_2}$ is semiparametric efficient if all of the above nuisance functions are correctly specified and their parameter estimates $\sqrt{n}$-consistent. When the nuisance functions are estimated via data-adaptive methods and cross-fitting, $\widehat{\text{NDE}}^{\text{eif}_2}$ is CAN and semiparametric efficient if all of the nuisance functions are consistently estimated and $r_n(\hat{\pi}_0)r_n(\hat{\mu}_{0,K}) + r_n(\hat{\pi}_K)r_n(\hat{\mu}_K) + r_n(\hat{\pi}_0)r_n(\hat{\mu}_0) = o(n^{-1/2})$.*

4.2 Natural and Total Indirect Effects for M_1

In Section 2.1, we noted that $\psi_{100} - \psi_{000}$ and $\psi_{111} - \psi_{011}$ correspond to the NIE and TIE for the first mediator M_1 (illustrated in the second and third rows of Figure 2). This correspondence extends naturally to the case of K mediators, where the NIE and TIE for M_1 are given by

$$\text{NIE}_{M_1} = \psi_{1,\underline{0}_2} - \psi_{\overline{0}_{K+1}}, \quad \text{TIE}_{M_1} = \psi_{\overline{1}_{K+1}} - \psi_{0,\underline{1}_2},$$

where $\underline{0}_2 = (0, \ldots 0)$ and $\underline{1}_2 = (1, \ldots 1)$ are vectors of length K representing the fact that $a_2 = \ldots = a_{K+1} = 0$ in NIE_{M_1} and $a_2 = \ldots = a_{K+1} = 1$ in TIE_{M_1}. Since TIE_{M_1} can be obtained by switching the 0s and 1s in NIE_{M_1} and then flipping the sign, we focus on NIE_{M_1} below, noting that analogous results hold for TIE_{M_1}.

A semiparametric efficient estimator of NIE_{M_1} can be constructed as

$$\widehat{\text{NIE}}_{M_1}^{\text{eif}_2} = \hat{\theta}_{1,\underline{0}_2}^{\text{eif}_2} - \hat{\theta}_{\overline{0}_{K+1}}^{\text{eif}_2}.$$

As shown previously, $\hat{\theta}_{\overline{0}_{K+1}}^{\text{eif}_2}$ is given by the doubly robust estimator (17). Setting $a_1 = 1$ and $a_2 = \ldots a_{K+1} = 0$ in equation (14), we obtain

$$\hat{\theta}_{1,\underline{0}_2}^{\text{eif}_2} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A=0)}{\hat{\pi}_0(1|X)} \frac{\hat{\pi}_1(1|X, M_1)}{\hat{\pi}_1(0|X, M_1)} (Y - \hat{\mu}_1(X, M_1)) + \frac{\mathbb{I}(A=1)}{\hat{\pi}_0(1|X)} (\hat{\mu}_1(X, M_1) - \hat{\mu}_{0,1}(X)) + \hat{\mu}_{0,1}(X) \Big].$$

Like $\hat{\theta}_{\bar{0}_K,1}^{\text{eif}_2}$, $\hat{\theta}_{1,\underline{0}_2}^{\text{eif}_2}$ also involves estimating four nuisance functions: $\pi_0(a|x)$, $\pi_1(a|x,m_1)$, $\mu_{0,1}(x)$, and $\mu_1(x,m_1)$, where $\mu_1(x,m_1) = \mathbb{E}[Y|x, A = 0, m_1]$ and $\mu_{0,1}(x) = \mathbb{E}[\mu_1(X, M_1)|x, A = 1]$. It follows from Theorem 3 that $\hat{\theta}_{1,\underline{0}_2}^{\text{eif}_2}$ is triply robust in that it is consistent if one of the following three conditions holds: (a) $\hat{\pi}_0$ and $\hat{\pi}_1$ are consistent; (b) $\hat{\pi}_0$ and $\hat{\mu}_1$ are consistent; and (c) $\hat{\mu}_{0,1}$ and $\hat{\mu}_1$ are consistent. By taking the intersection of the multiple robustness conditions for $\hat{\theta}_{1,\underline{0}_2}^{\text{eif}_2}$ and $\hat{\theta}_{\bar{0}_{K+1}}^{\text{eif}_2}$, we deduce that $\widehat{\text{NIE}}_{M_1}^{\text{eif}_2}$ is also triply robust, as detailed in Corollary 2.

Corollary 2. *Suppose all assumptions required for Theorem 4 hold. When the nuisance functions are estimated via parametric models, $\widehat{\text{NIE}}_{M_1}^{\text{eif}_2}$ is CAN provided that one of the following three sets of nuisance functions is correctly specified and its parameter estimates are $\sqrt{n}$-consistent: $\{\pi_0, \pi_1\}$, $\{\pi_0, \mu_1\}$, $\{\mu_0, \mu_{0,1}, \mu_1\}$. $\widehat{\text{NIE}}_{M_1}^{\text{eif}_2}$ is semiparametric efficient if all of the above nuisance functions are correctly specified and their parameter estimates $\sqrt{n}$-consistent. When the nuisance functions are estimated via data-adaptive methods and cross-fitting, $\widehat{\text{NIE}}_{M_1}^{\text{eif}_2}$ is semiparametric efficient if all of the nuisance functions are consistently estimated and $r_n(\hat{\pi}_0)r_n(\hat{\mu}_{0,1}) + r_n(\hat{\pi}_1)r_n(\hat{\mu}_1) + r_n(\hat{\pi}_0)r_n(\hat{\mu}_0) = o(n^{-1/2})$.*

4.3 Natural Path-Specific Effects (nPSE) for M_k ($k \geq 2$)

In the same spirit of the NIE for M_1, the natural path-specific effect (nPSE; Daniel *et al.* 2015) for mediator M_k ($k \geq 2$) is defined as

$$\text{nPSE}_{M_k} = \psi_{\bar{0}_{k-1},1,\underline{0}_{k+1}} - \psi_{\bar{0}_{K+1}}.$$

It can be interpreted as the effect of activating the path $A \to M_k \rightsquigarrow Y$ while all other causal paths are "switched off," as shown in the fourth row of Figure 2. A semiparametric efficient estimator of nPSE_{M_k} can be constructed as

$$\widehat{\text{nPSE}}_{M_k}^{\text{eif}_2} = \hat{\theta}_{\bar{0}_{k-1},1,\underline{0}_{k+1}}^{\text{eif}_2} - \hat{\theta}_{\bar{0}_{K+1}}^{\text{eif}_2}.$$

If, instead, we use $\hat{\theta}_{\bar{a}}^{\text{eif}_1}$ in the above equation, the resulting estimator $\widehat{\text{nPSE}}_{M_k}^{\text{eif}_1}$ can be seen as Miles *et al.*'s (2020) estimator of $\theta_{010} - \theta_{000}$ applied to $\widetilde{M}_1 = (M_1, M_2, \ldots M_{k-1})$ and $\widetilde{M}_2 = M_k$.

Again, $\hat{\theta}_{\bar{0}_{K+1}}^{\text{eif}_2}$ is given by the doubly robust estimator (17). Setting $a_1 = \ldots a_{k-1} = a_{k+1} =$

... $a_{K+1} = 0$ and $a_k = 1$ in equation (14), we obtain

$$\hat{\theta}^{\text{eif}_2}_{\overline{0}_{k-1},1,\underline{0}_{k+1}} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A=0)}{\hat{\pi}_0(0|X)} \frac{\hat{\pi}_{k-1}(0|X,\overline{M}_{k-1})}{\hat{\pi}_{k-1}(1|X,\overline{M}_{k-1})} \frac{\hat{\pi}_k(1|X,\overline{M}_k)}{\hat{\pi}_k(0|X,\overline{M}_k)} (Y - \hat{\mu}_k(X,\overline{M}_k)).$$
$$+ \frac{\mathbb{I}(A=1)}{\hat{\pi}_0(0|X)} \frac{\hat{\pi}_{k-1}(0|X,\overline{M}_{k-1})}{\hat{\pi}_{k-1}(1|X,\overline{M}_{k-1})} (\hat{\mu}_k(X,\overline{M}_k) - \hat{\mu}_{k-1,k}(X,\overline{M}_{k-1}))$$
$$+ \frac{\mathbb{I}(A=0)}{\hat{\pi}_0(0|X)} (\hat{\mu}_{k-1,k}(X,\overline{M}_{k-1}) - \hat{\mu}_{0,k-1,k}(X)) + \hat{\mu}_{0,k-1,k}(X) \Big].$$

We can see that $\hat{\theta}^{\text{eif}_2}_{\overline{0}_{k-1},1,\underline{0}_{k+1}}$ involves estimating six nuisance functions: $\pi_0(a|x)$, $\pi_{k-1}(a|x,\overline{m}_{k-1})$, $\pi_k(a|x,\overline{m}_k)$, $\mu_{0,k-1,k}(x)$, $\mu_{k-1,k}(x,\overline{m}_{k-1})$, and $\mu_k(x,\overline{m}_k)$, where $\mu_k(X,\overline{M}_k) = \mathbb{E}[Y|X,A=0,\overline{M}_k]$, $\mu_{k-1,k}(X,\overline{M}_{k-1}) = \mathbb{E}[\mu_k(X,\overline{M}_k)|X,A=1,\overline{M}_{k-1}]$, and $\mu_{0,k-1,k}(X) = \mathbb{E}[\mu_{k-1,k}(X,\overline{M}_{k-1})|X,A=0]$. Hence $\mu_{k-1,k}(x)$ can be estimated by fitting a model for the conditional mean of $\hat{\mu}_k(X,\overline{M}_k)$ given $(X,A,\overline{M}_{k-1})$ and then setting $A=1$ for all units, and $\mu_{0,k-1,k}(x)$ can be estimated by fitting a model for the conditional mean of $\hat{\mu}_{k-1,k}(X,\overline{M}_{k-1})$ given (X,A) and then setting $A=0$ for all units. It follows from Theorem 3 that $\hat{\theta}^{\text{eif}_2}_{\overline{0}_{k-1},1,\underline{0}_{k+1}}$ is quadruply robust in that it is consistent if one of the following four conditions holds: (a) $\hat{\pi}_0$, $\hat{\pi}_{k-1}$, and $\hat{\pi}_k$ are consistent; (b) $\hat{\pi}_0$, $\hat{\pi}_{k-1}$, and $\hat{\mu}_k$ are consistent; (c) $\hat{\pi}_0$, $\hat{\mu}_{k-1,k}$, and $\hat{\mu}_k$ are consistent; and (d) $\hat{\mu}_{0,k-1,k}$, $\hat{\mu}_{k-1,k}$, and $\hat{\mu}_k$ are consistent. By taking the intersection of the multiple robustness conditions for $\hat{\theta}^{\text{eif}_2}_{1,\underline{0}_2}$ and $\hat{\theta}^{\text{eif}_2}_{\overline{0}_{K+1}}$, we deduce that $\widehat{\text{nPSE}}^{\text{eif}_2}_{M_k}$ is also quadruply robust, as detailed in Corollary 3.

Corollary 3. *Suppose all assumptions required for Theorem 4 hold. When the nuisance functions are estimated via parametric models, $\widehat{\text{nPSE}}^{\text{eif}_2}_{M_k}$ is CAN provided that one of the following four sets of nuisance functions is correctly specified and its parameter estimates are $\sqrt{n}$-consistent: $\{\pi_0, \pi_{k-1}, \pi_k\}$, $\{\pi_0, \pi_{k-1}, \mu_k\}$, $\{\pi_0, \mu_{k-1,k}, \mu_k\}$, $\{\mu_0, \mu_{0,k-1,k}, \mu_{k-1,k}, \mu_k\}$. $\widehat{\text{nPSE}}^{\text{eif}_2}_{M_k}$ is semiparametric efficient if all of the above nuisance functions are correctly specified and their parameter estimates $\sqrt{n}$-consistent. When the nuisance functions are estimated via data-adaptive methods and cross-fitting, $\widehat{\text{nPSE}}^{\text{eif}_2}_{M_k}$ is semiparametric efficient if all of the nuisance functions are consistently estimated and $r_n(\hat{\pi}_0)r_n(\hat{\mu}_{0,k-1,k}) + r_n(\hat{\pi}_{k-1})r_n(\hat{\mu}_{k-1,k}) + r_n(\hat{\pi}_k)r_n(\hat{\mu}_k) + r_n(\hat{\pi}_0)r_n(\hat{\mu}_0) = o(n^{-1/2})$.*

4.4 Cumulative Path-Specific Effects (cPSE) for M_k $(k \geq 2)$

The NDE, NIE, and nPSE are all defined as the effect of activating one causal path while keeping all other causal paths "switched off." By contrast, in equation (3), the ATE is decomposed into $K+1$ components, each of which reflects the *cumulative* contribution of a specific mediator to the

ATE. Specifically, the component $\psi_{\overline{0}_K,1} - \psi_{\overline{0}_{K+1}}$ equals the NDE, the component $\psi_{\underline{1}_1} - \psi_{0,\underline{1}_2}$ equals TIE_{M_1}, and the component $\psi_{\overline{0}_{k-1},\underline{1}_k} - \psi_{\overline{0}_k,\underline{1}_{k+1}}$ gauges the additional contribution of the causal path $A \to M_k \rightsquigarrow Y$ after the causal paths $A \to M_{k+1} \rightsquigarrow Y, \ldots A \to M_K \rightsquigarrow Y, A \to Y$ are "switched on." Such a decomposition will be useful in applications where the investigator aims to partition the ATE into its path-specific components.

We define the cumulative path-specific effect (cPSE) for mediator M_k ($k \geq 2$) as

$$\text{cPSE}_{M_k} = \psi_{\overline{0}_{k-1},\underline{1}_k} - \psi_{\overline{0}_k,\underline{1}_{k+1}}.$$

The last row of Figure 2 gives the baseline and comparison interventions associated with cPSE_{M_2} in the case of $K = 2$. A semiparametric efficient estimator for cPSE_{M_k} can be constructed as

$$\widehat{\text{cPSE}}_{M_k}^{\text{eif}_2} = \hat{\theta}_{\overline{0}_{k-1},\underline{1}_k}^{\text{eif}_2} - \hat{\theta}_{\overline{0}_k,\underline{1}_{k+1}}^{\text{eif}_2}.$$

Setting $a_1 = \ldots a_k = 0$ and $a_{k+1} = \ldots = a_{K+1} = 1$ in equation (14), we obtain

$$\hat{\theta}_{\overline{0}_k,\underline{1}_{k+1}}^{\text{eif}_2} = \mathbb{P}_n \Big[\frac{\mathbb{I}(A=1)}{\hat{\pi}_0(0|X)} \frac{\hat{\pi}_k(0|X,\overline{M}_k)}{\hat{\pi}_k(1|X,\overline{M}_k)} \big(Y - \hat{\mu}_k(X,\overline{M}_k) \big) + \frac{\mathbb{I}(A=0)}{\hat{\pi}_0(0|X)} \big(\hat{\mu}_k(X,\overline{M}_k) - \hat{\mu}_{0,k}(X) \big) + \hat{\mu}_{0,k}(X) \Big],$$

(18)

where $\mu_k(X,\overline{M}_k) = \mathbb{E}[Y|X, A = 1, \overline{M}_k]$ and $\mu_{0,k}(X) = \mathbb{E}[\mu_k(X,\overline{M}_k)|X, A = 0]$. It follows from Theorem 3 that $\hat{\theta}_{\overline{0}_k,\underline{1}_{k+1}}^{\text{eif}_2}$ is triply robust in that it is consistent if one of the following three conditions holds: (a) $\hat{\pi}_0$ and $\hat{\pi}_k$ are consistent; (b) $\hat{\pi}_0$ and $\hat{\mu}_k$ are consistent; and (c) $\hat{\mu}_{0,k}$ and $\hat{\mu}_k$ are consistent. By replacing k with $k-1$ in equation (18), we obtain a similar expression for $\hat{\theta}_{\overline{0}_{k-1},\underline{1}_k}^{\text{eif}_2}$, which is also triply robust in that it is consistent if one of the following three conditions holds: (a) $\hat{\pi}_0$ and $\hat{\pi}_{k-1}$ are consistent; (b) $\hat{\pi}_0$ and $\hat{\mu}_{k-1}$ are consistent; and (c) $\hat{\mu}_{0,k-1}$ and $\hat{\mu}_{k-1}$ are consistent. As a result, $\widehat{\text{cPSE}}_{M_k}^{\text{eif}_2}$ involves fitting seven working models — for $\pi_0(a|x)$, $\pi_{k-1}(a|x,\overline{m}_{k-1})$, $\pi_k(a|x,\overline{m}_k)$, $\mu_{k-1}(x,\overline{m}_{k-1})$, $\mu_{0,k-1}(x)$, $\mu_k(x,\overline{m}_k)$, and $\mu_{0,k}(x)$. By taking the intersection of the multiple robustness conditions for $\hat{\theta}_{\underline{1}_k,\underline{0}_{k+1}}^{\text{eif}_2}$ and $\hat{\theta}_{\underline{1}_{k-1},\underline{0}_k}^{\text{eif}_2}$, we deduce that $\widehat{\text{cPSE}}_{M_k}^{\text{eif}_2}$ is quintuply robust in that it is consistent if one of five sets of nuisance functions is correctly specified and consistently estimated, as detailed in Corollary 4.

Corollary 4. *Suppose all assumptions required for Theorem 4 hold. When the nuisance functions are estimated via parametric models, $\widehat{\text{cPSE}}_{M_k}^{\text{eif}_2}$ is CAN provided that one of the fol-*

lowing five sets of nuisance functions is correctly specified and its parameter estimates are $\sqrt{n}$-consistent: $\{\pi_0, \pi_{k-1}, \pi_k\}; \{\pi_0, \pi_{k-1}, \mu_k\}; \{\pi_0, \mu_{k-1}, \pi_k\}; \{\pi_0, \mu_{k-1}, \mu_k\}; \{\mu_{0,k-1}, \mu_{0,k}, \mu_{k-1}, \mu_k\}.$ $\widehat{\text{cPSE}}_{M_k}^{\text{eif}_2}$ *is semiparametric efficient if all of the above nuisance functions are correctly specified and their parameter estimates $\sqrt{n}$-consistent. When the nuisance functions are estimated via data-adaptive methods and cross-fitting,* $\widehat{\text{cPSE}}_{M_k}^{\text{eif}_2}$ *is semiparametric efficient if all of the nuisance functions are consistently estimated and* $r_n(\hat{\pi}_0)r_n(\hat{\mu}_{0,k-1}) + r_n(\hat{\pi}_0)r_n(\hat{\mu}_{0,k}) + r_n(\hat{\pi}_{k-1})r_n(\hat{\mu}_{k-1}) + r_n(\hat{\pi}_k)r_n(\hat{\mu}_k) = o(n^{-1/2}).$

5 A Simulation Study

In this section, we conduct a simulation study to demonstrate the robustness of various estimators under different forms of model misspecification. Specifically, we consider a binary treatment A, a continuous outcome Y, two causally ordered mediators M_1 and M_2, and four pretreatment covariates X_1, X_2, X_3, X_4 generated from the following model:

$$(U_1, U_2, U_3, U_{XY}) \sim N(0, I_4),$$
$$X_j \sim N((U_1, U_2, U_3, U_{XY})\beta_{X_j}, 1), \quad j = 1, 2, 3, 4,$$
$$A \sim \text{Bernoulli}(\text{logit}^{-1}[(1, X_1, X_2, X_3, X_4)\beta_A]),$$
$$M_1 \sim N((1, X_1, X_2, X_3, X_4, A)\beta_{M_1}, 1),$$
$$M_2 \sim N((1, X_1, X_2, X_3, X_4, A, M_1)\beta_{M_2}, 1),$$
$$Y \sim N((1, U_{XY}, X_1, X_2, X_3, X_4, A, M_1, M_2)\beta_Y, 1).$$

The coefficients $\beta_{X_j}(1 \leq j \leq 4)$, β_A, β_{M_1}, β_{M_2}, β_Y are produced from a set of uniform distributions (see Supplementary Material F for more details). Given the coefficients, we generate 1,000 Monte Carlo samples of size 2,000. Note that in the above model, the unobserved variable U_{XY} confounds the X-Y relationship but does not pose an identification threat for $\psi_{\bar{a}}$ and the associated PSEs (i.e., Assumption 2 still holds).

Without loss of generality, we focus on the estimand cPSE_{M_2}, which we estimate by $\hat{\theta}_{011} - \hat{\theta}_{001}$. To highlight the general results stated in Theorem 3, we use only estimators for the generic $\theta_{\bar{a}}$ (i.e., those described in Section 3). First, we consider the weighting estimator $\hat{\theta}_{\bar{a}}^{\text{w-a}}$, the regression-

imputation estimator $\hat{\theta}_{\bar{a}}^{\mathrm{ri}}$, and the hybrid estimators $\hat{\theta}_{\bar{a}}^{\mathrm{ri\text{-}w\text{-}w}}$ and $\hat{\theta}_{\bar{a}}^{\mathrm{ri\text{-}ri\text{-}w}}$, where the mediator density ratio involved in $\hat{\theta}_{\bar{a}}^{\mathrm{ri\text{-}w\text{-}w}}$ is estimated via the corresponding odds ratio of the treatment variable. We then consider four EIF-based estimators $\hat{\theta}_{\bar{a}}^{\mathrm{par,eif}_2}$, $\hat{\theta}_{\bar{a}}^{\mathrm{par}_2,\mathrm{eif}_2}$, $\hat{\theta}_{\bar{a}}^{\mathrm{np,eif}_2}$, and $\hat{\theta}_{\bar{a}}^{\mathrm{tmle,eif}_2}$. For $\hat{\theta}_{\bar{a}}^{\mathrm{par,eif}_2}$ and $\hat{\theta}_{\bar{a}}^{\mathrm{par}_2,\mathrm{eif}_2}$, the nuisance functions are estimated via GLMs. $\hat{\theta}_{\bar{a}}^{\mathrm{par}_2,\mathrm{eif}_2}$ differs from $\hat{\theta}_{\bar{a}}^{\mathrm{par,eif}_2}$ in that the outcome models $\mu_2(x, m_1, m_2)$, $\mu_1(x, m_1)$, and $\mu_0(x)$ are fitted using a set of weighted GLMs such that in equation (15), all terms inside $\mathbb{P}_n[\cdot]$ but $\hat{\mu}_0(X)$ have a zero sample mean, yielding a regression-imputation estimator that may perform better in finite samples.

All of the above estimators are constructed using estimates of six nuisance functions: $\pi_0(a|x)$, $\pi_1(a|x, m_1)$, $\pi_2(a|x, m_1, m_2)$, $\mu_0(x)$, $\mu_1(x, m_1)$, and $\mu_2(x, m_1, m_2)$. To demonstrate the consequences of model misspecification and the multiple robustness of $\hat{\theta}_{\bar{a}}^{\mathrm{par,eif}_2}$ and $\hat{\theta}_{\bar{a}}^{\mathrm{par}_2,\mathrm{eif}_2}$, we generate a set of "false covariates" $Z = \left(X_1, e^{X_2/2}, (X_3/X_1)^{1/3}, X_4/(e^{X_1/2} + 1)\right)$ and use them to fit a misspecified GLM for each of the nuisance functions (with only the main effects of Z_1, Z_2, Z_3, Z_4). We evaluate each of the parametric estimators under five different cases: (a) only π_0, π_1, π_2 are correctly specified; (b) only π_0, π_1, μ_2 are correctly specified; (c) only π_0, μ_1, μ_2 are correctly specified; (d) only μ_0, μ_1, μ_2 are correctly specified; and (e) all of the six nuisance functions are misspecified. In theory, $\hat{\theta}_{\bar{a}}^{\mathrm{w\text{-}a}}$ is consistent in case (a), $\hat{\theta}_{\bar{a}}^{\mathrm{ri\text{-}w\text{-}w}}$ is consistent in case (b), $\hat{\theta}_{\bar{a}}^{\mathrm{ri\text{-}ri\text{-}w}}$ is consistent in case (c), $\hat{\theta}_{\bar{a}}^{\mathrm{ri}}$ is consistent in case (d), and $\hat{\theta}_{\bar{a}}^{\mathrm{par,eif}_2}$ and $\hat{\theta}_{\bar{a}}^{\mathrm{par}_2,\mathrm{eif}_2}$ are consistent in cases (a)-(d). The corresponding estimators of cPSE_{M_2} should follow the same properties.

For the two nonparametric estimators, $\hat{\theta}_{\bar{a}}^{\mathrm{np,eif}_2}$ is based on estimating equation (14), and $\hat{\theta}_{\bar{a}}^{\mathrm{tmle,eif}_2}$ is based on the method of TMLE. Like $\hat{\theta}_{\bar{a}}^{\mathrm{par}_2,\mathrm{eif}_2}$, $\hat{\theta}_{\bar{a}}^{\mathrm{tmle,eif}_2}$ is a regression-imputation estimator, which may have better finite-sample performance than $\hat{\theta}_{\bar{a}}^{\mathrm{np,eif}_2}$. For both $\hat{\theta}_{\bar{a}}^{\mathrm{np,eif}_2}$ and $\hat{\theta}_{\bar{a}}^{\mathrm{tmle,eif}_2}$, the nuisance functions are estimated via a super learner (van der Laan *et al.* 2007) composed of Lasso and random forest, where the feature matrix consists of first-order, second-order, and interaction terms of *the false covariates Z*. The super learner is more flexible than a misspecified GLM consisting of only the main effects of Z, but it remains agnostic about the true nuisance functions, which are either logit or linear models that depend on $X = (Z_1, 2\log(Z_2), Z_1 Z_3^3, (1 + e^{Z_1/2})Z_4)$. We obtain nonparametric estimates of cPSE_{M_2} using both five-fold cross-fitting and no cross-fitting.

Results from the simulation study are shown in Figure 3, where each panel corresponds to an estimator, and the y axis is recentered at the true value of cPSE_{M_2}. The shaded box plots highlight cases under which a given estimator should be consistent, and the box plots with a lighter shade
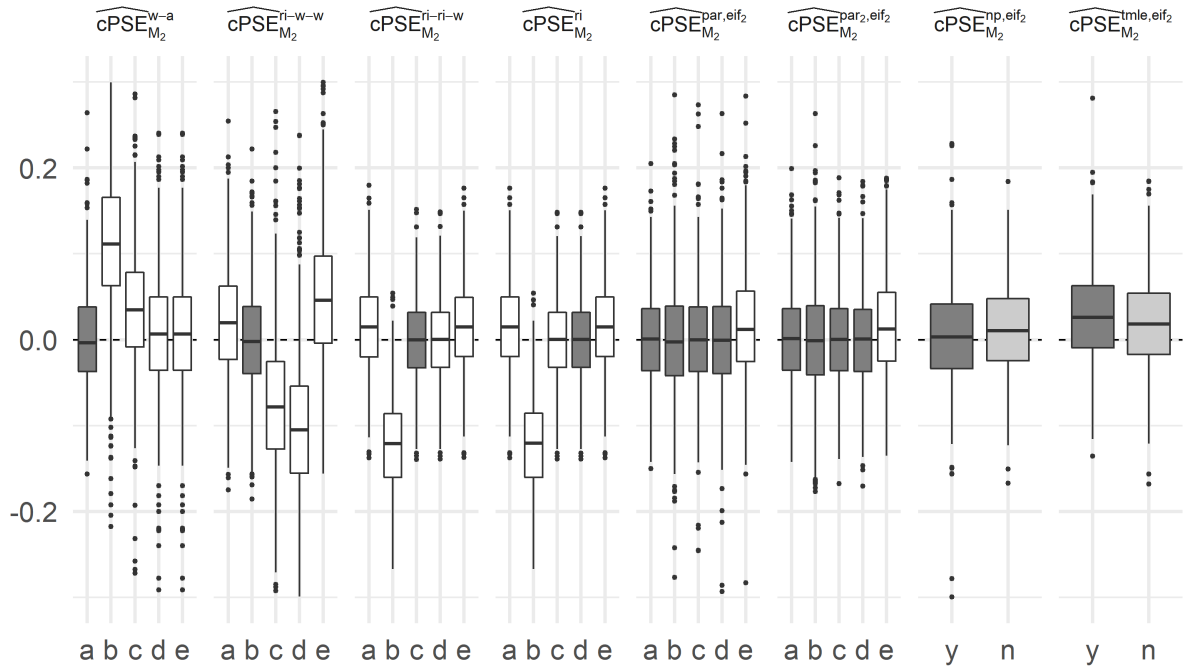
Figure 3: Sampling distributions of eight different estimators for $n = 2,000$. Cases (a)-(e) are described in the main text. The symbols y and n denote whether cross-fitting is used to implement the nonparametric estimators (y = yes, n = no).

in the last two panels denote nonparametric estimators obtained without cross-fitting. From the first four panels, we can see that the weighting, regression-imputation, and hybrid estimators all behave as expected. They center around the true value if the requisite nuisance functions are all correctly specified, and deviate from the truth in most other cases. The next four panels show the box plots of the EIF-based estimators. As expected, both of the parametric EIF-based estimators are quadruply robust, as their sampling distributions roughly concentrate around the true value in all of the four cases from (a) to (d). Moreover, it is reassuring to see that when all of the nuisance functions are misspecified (case (e)), the multiply robust estimators do not show a larger amount of bias than those of the other parametric estimators. Finally, both of the nonparametric EIF-based estimators perform reasonably well. When cross-fitting is used, the estimating equation estimator $\widehat{\mathrm{cPSE}}_{M_2}^{\mathrm{np,eif}_2}$ appears to have a smaller bias than the TMLE estimator $\widehat{\mathrm{cPSE}}_{M_2}^{\mathrm{tmle,eif}_2}$, but it occasionally gives rise to extreme estimates. Their 95% Wald confidence intervals, constructed using the estimated variance $\hat{\mathbb{E}}\big[\big(\hat{\varphi}_{011} - \hat{\varphi}_{001}\big)^2\big]/n$, have close-to-nominal coverage rates — 95.5% for

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$\widehat{\text{cPSE}}_{M_2}^{\text{np,eif}_2}$ and 90.9% for $\widehat{\text{cPSE}}_{M_2}^{\text{tmle,eif}_2}$. Without cross-fitting, the point estimates exhibit similar distributions, but the coverage rates of the corresponding 95% confidence intervals are somewhat lower — 87.3% for $\widehat{\text{cPSE}}_{M_2}^{\text{np,eif}_2}$ and 85.8% for $\widehat{\text{cPSE}}_{M_2}^{\text{tmle,eif}_2}$.

6   An Empirical Application

In this section, we illustrate semiparametric estimation of PSEs by analyzing the causal pathways through which higher education affects political participation. Prior research suggests that college attendance has a substantial positive effect on political participation in the United States (e.g., Dee 2004; Milligan *et al.* 2004). Yet, the mechanisms underlying this causal link remain unclear. The effect of college on political participation may operate through the development of civic and political interest (e.g., Hillygus 2005), through an increase in economic status (e.g., Kingston *et al.* 2003), or through other pathways such as social and occupational networks (e.g., Rolfe 2012). To examine these direct and indirect effects, we consider a causal structure akin to the top panel of Figure 1, where A denotes college attendance, Y denotes political participation, and M_1 and M_2 denote two causally ordered mediators that reflect (a) economic status, and (b) civic and political interest, respectively.

In this model, economic status is allowed to affect civic and political interest but not vice versa, which we consider to be a reasonable approximation to reality. Nonetheless, the conditional independence assumption (Assumption 2) is still strong in this context, as it rules out unobserved confounding for any of the pairwise relationships between college attendance, economic status, civic and political interest, and political participation. Thus, the following analyses should be viewed as an illustration of the proposed methodology rather than a definitive assessment of the PSEs of interest.

We use data from $n = 2,969$ individuals in the National Longitudinal Survey of Youth 1997 (NLSY97) who were age 15-17 in 1997 and had completed high school by age 20. The treatment A is a binary indicator for whether the individual had attended a two-year or four-year college by age 20. The outcome Y is a binary indicator for whether the individual voted in the 2010 general election. We measure economic status (M_1) using the respondent's average annual earnings from 2006 to 2009. To gauge civic and political interest (M_2), we use a set of variables that reflect the

respondent's interest in government and public affairs and involvement in volunteering, donation, community group activities between 2007 and 2010. The overlap of the periods in which M_1 and M_2 were measured is a limitation of this analysis, and it makes our earlier assumption that M_2 does not affect M_1 essential for identifying the direct and path-specific effects.

To minimize potential bias due to unobserved confounding, we include a rich set of pre-college individual and contextual characteristics in the vector of pretreatment covariates X. They include gender, race, ethnicity, age at 1997, parental education, parental income, parental assets, presence of a father figure, co-residence with both biological parents, percentile score on the Armed Services Vocational Aptitude Battery (ASVAB), high school GPA, an index of substance use (ranging from 0 to 3), an index of delinquency (ranging from 0 to 10), whether the respondent had any children by age 18, college expectation among the respondent's peers, and a number of school-level characteristics. Descriptive statistics on these pre-college characteristics as well as the mediators and the outcome are given in Supplementary Material G. Some components of X, M_1, and M_2 contain a small fraction of missing values. They are imputed via a random-forest-based multiple imputation procedure (with ten imputed data sets). The standard errors of our parameter estimates are adjusted using Rubin's (1987) method.

Under Assumptions 1-3 given in Section 2.1, a set of PSEs reflecting the causal paths $A \to Y$, $A \to M_1 \rightsquigarrow Y$, and $A \to M_2 \to Y$ are identified. For illustrative purposes, we focus on the cumulative PSEs (cPSEs) defined in Section 4.4:

$$\text{ATE} = \underbrace{\psi_{001} - \psi_{000}}_{A \to Y} + \underbrace{\psi_{011} - \psi_{001}}_{A \to M_2 \to Y} + \underbrace{\psi_{111} - \psi_{011}}_{A \to M_1 \rightsquigarrow Y}. \tag{19}$$

Here, the first component is the NDE of college attendance, and the second and third components reflect the amounts of treatment effect that are additionally mediated by civic/political interest and economic status, respectively. Since M_2 is multivariate, it would be difficult to model its conditional distributions directly. We thus estimate the PSEs using the estimator $\hat{\theta}^{\text{eif}_2}_{a_1, a_2, a}$. Each of the nuisance functions is estimated using a super learner composed with Lasso and random forest. For computational reasons, the feature matrix supplied to the super learner consists of only first-order terms of the corresponding variables. As in our simulation study, we implement two versions of this EIF-based estimator, one based on the original estimating equation ($\hat{\theta}^{\text{np,eif}_2}_{\bar{a}}$), and one based

Table 1: Estimates of total and path-specific effects of college attendance on voting.

	Estimating equation ($\hat{\theta}_{\bar{a}}^{\text{np,eif}_2}$)	TMLE ($\hat{\theta}_{\bar{a}}^{\text{tmle,eif}_2}$)
Average total effect	0.152 (0.022)	0.156 (0.023)
Through economic status ($A \to M_1 \rightsquigarrow Y$)	0.007 (0.005)	0.002 (0.005)
Through civic/political interest ($A \to M_2 \to Y$)	0.042 (0.008)	0.049 (0.008)
Direct effect ($A \to Y$)	0.103 (0.021)	0.105 (0.021)

Note: Numbers in parentheses are estimated standard errors, which are constructed using sample variances of the estimated efficient influence functions and adjusted for multiple imputation via Rubin's (1987) method.

on the method of TMLE ($\hat{\theta}_{\bar{a}}^{\text{tmle,eif}_2}$). Five-fold cross-fitting is used to obtain the final estimates.

The results are shown in Table 1. We can see that the two estimators yield similar estimates of the total and path-specific effects. By $\hat{\theta}_{\bar{a}}^{\text{np,eif}_2}$, for example, the estimated total effect of college attendance on voting is 0.152, meaning that, on average, college attendance increases the likelihood of voting in 2010 by about 15 percentage points. The estimated PSE via M_2 is 0.042, suggesting that a small fraction of the college effect operates through the development of civic and political interest. By contrast, the estimated PSE via economic status is substantively negligible and statistically insignificant. A large portion of the college effect appears to be "direct," i.e., operating neither through increased economic status nor through increased civic and political interest.

7 Concluding Remarks

By considering the general case of $K(\geq 1)$ causally ordered mediators, this paper offers several new insights into the identification and estimation of PSEs. First, under the assumptions associated with Pearl's NPSEM with mutually independent errors, we have defined a set of PSEs as contrasts between the expectations of 2^{K+1} potential outcomes, which are identified via what we call the generalized mediation functional (GMF). Second, building on its efficient influence function, we have developed two $K + 2$-robust and semiparametric efficient estimators for the GMF. By virtue of their multiple robustness, these estimators are well suited to the use of data-adaptive methods for estimating their nuisance functions. For such cases, we have established the rate conditions required of the nuisance functions for consistency and semiparametric efficiency.

As we have seen, our proposed methodology is general in that the GMF encompasses a variety of causal estimands such as the NDE, NIE/TIE, nPSE, cPSE. Nonetheless, it does not accommodate PSEs that are not identified under Pearl's NPSEM, some of which may be scientifically important. For example, social and biomedical scientists are often interested in testing hypotheses about "serial mediation," i.e., the degree to which the effect of a treatment operates through multiple mediators sequentially, such as that reflected in the causal path $A \rightarrow M_1 \rightarrow M_2 \rightarrow Y$ (e.g., Jones *et al.* 2015). Given that the corresponding PSEs are not nonparametrically identified under Pearl's NPSEM, previous research has proposed strategies that involve either additional assumptions (Albert and Nelson 2011) or alternative estimands (Lin and VanderWeele 2017). We consider semiparametric estimation and inference for these alternative approaches a promising direction for future research.

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Supplementary Materials

A   Proof of Theorem 1

Assumption 2* implies that for any $k \in \{2, \dots K\}$ and any $j \in \{1, \dots k-1\}$,

$$
\big(M_k(a_k, \overline{m}_{k-1}), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_{k-j}(a_{k-j}, \overline{m}^*_{k-j-1})|X, A, \overline{M}_{k-j-1}
$$
$$
\Rightarrow \big(M_k(a_k, \overline{m}_{k-1}), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_{k-j}(a_{k-j}, \overline{m}^*_{k-j-1})|X, A = a_{k-j}, \overline{M}_{k-j-1} = \overline{m}^*_{k-j-1}
$$
$$
\Rightarrow \big(M_k(a_k, \overline{m}_{k-1}), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_{k-j}|X, A = a_{k-j}, \overline{M}_{k-j-1} = \overline{m}^*_{k-j-1}
$$
$$
\Rightarrow \big(M_k(a_k, \overline{m}_{k-1}), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_{k-j}|X, A, \overline{M}_{k-j-1}. \tag{20}
$$

Setting $\overline{m}^*_{k-1} = \overline{m}_{k-1}$, Assumption 2* also implies that for any $k \in [K]$,

$$
\big(M_{k+1}(a_{k+1}, \overline{m}_k), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_k(a_k, \overline{m}_{k-1})|X, A, \overline{M}_{k-1}. \tag{21}
$$

Now suppose that for some $j \in \{1, \dots k-1\}$,

$$
\big(M_{k+1}(a_{k+1}, \overline{m}_k), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_k(a_k, \overline{m}_{k-1})|X, A, \overline{M}_{k-j}. \tag{22}
$$

By the contraction rule of conditional independence, the relationships (20) and (22) imply

$$
\big(M_{k+1}(a_{k+1}, \overline{m}_k), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_k(a_k, \overline{m}_{k-1})|X, A, \overline{M}_{k-j-1}.
$$

Hence, by the initial relationship (21) and mathematical induction, we have

$$
\big(M_{k+1}(a_{k+1}, \overline{m}_k), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp M_k(a_k, \overline{m}_{k-1})|X, A, \quad \forall k \in [K]. \tag{23}
$$

In the meantime, because $\big(M_{k+1}(a_{k+1}, \overline{m}_k), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp A|X$, we have (by the contraction rule)

$$
\big(M_{k+1}(a_{k+1}, \overline{m}_k), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big) \perp\!\!\!\perp \big(A, M_k(a_k, \overline{m}_{k-1})\big)|X, \quad \forall k \in [K].
$$

Thus the components in $\big(A, M_1(a_1), \dots M_K(a_K, \overline{m}_{K-1}), Y(a_{K+1}, \overline{m}_K)\big)$ are mutually independent given X. Therefore,

$$
\psi_{\overline{a}} = \mathbb{E}[Y(a_{K+1}, \overline{M}_K(\overline{a}_K))]
$$
$$
= \int_x \int_{\overline{m}_K} \mathbb{E}[Y(a_{K+1}, \overline{m}_K)|X = x, A = a_{K+1}, M_1(a_1) = m_1, \dots M_K(a_K, \overline{m}_{K-1}) = m_K]
$$
$$
\big(\prod_{k=1}^K dP_{M_k(a_k, \overline{m}_{k-1})|X, A, M_1(a_1), \dots M_{k-1}(a_{k-1}, \overline{m}_{k-2})}(m_k|x, a_{K+1}, \overline{m}_{k-1})\big) dP_X(x)
$$

$$= \int_x \int_{\overline{m}_K} \mathbb{E}[Y(a_{K+1}, \overline{m}_K)|X = x, A = a_{K+1}] \Big(\prod_{k=1}^K dP_{M_k(a_k, \overline{m}_{k-1})|X}(m_k|x) \Big) dP_X(x)$$

$$= \int_x \int_{\overline{m}_K} \mathbb{E}[Y(a_{K+1}, \overline{m}_K)|x, a_{K+1}, \overline{M}_K = \overline{m}_K] \Big(\prod_{k=1}^K dP_{M_k(a_k, \overline{m}_{k-1})|X,A,\overline{M}_{k-1}}(m_k|x, a_k, \overline{m}_{k-1}) \Big) dP_X(x)$$

$$= \int_x \int_{\overline{m}_K} \mathbb{E}[Y|x, a_{K+1}, \overline{m}_K] \Big(\prod_{k=1}^K dP_{M_k|X,A,\overline{M}_{k-1}}(m_k|x, a_k, \overline{m}_{k-1}) \Big) dP_X(x).$$

B   Hybrid Estimators of $\theta_{a_1,a_2,a}$

For notational brevity, let us use the following shorthands:

$$\lambda_0^j(A|X) \triangleq \frac{\mathbb{I}(A = a_j)}{p(a_j|X)}$$

$$\lambda_1^j(M_1|X) \triangleq \frac{p(M_1|X, a_1)}{p(M_1|X, a_j)}$$

$$\lambda_2^j(M_2|X, M_1) \triangleq \frac{p(M_2|X, a_2, M_1)}{p(M_2|X, a_j, M_1)},$$

In addition, define $\lambda_0(A|X) = \mathbb{I}(A = a)/p(a|X)$, $\lambda_1(M_1|X) = p(M_1|X, a_1)/p(M_1|X, a)$ and $\lambda_2(M_2|X, M_1) = p(M_2|X, a_2, M_1)/p(M_2|X, a, M_1)$. With the above notation, the iterated conditional means $\mu_1(X, M_1)$, $\mu_0(X)$, and $\theta_{a_1,a_2,a}$ can each be written in several different forms:

$$\mu_1(X, M_1) = \begin{cases} \mathbb{E}[\mu_2(X, M_1, M_2)|X, a_2, M_1] \\ \mathbb{E}[\lambda_2(M_2|X, M_1)Y|X, a, M_1] \end{cases}$$

$$\mu_0(X) = \begin{cases} \mathbb{E}[\mu_1(X, M_1)|X, a_1] = \begin{cases} \mathbb{E}\big[\mathbb{E}[\mu_2(X, M_1, M_2)|X, a_2, M_1]|X, a_1\big] \\ \mathbb{E}\big[\mathbb{E}[\lambda_2(M_2|X, M_1)Y|X, a, M_1]|X, a_1\big] \end{cases} \\ \mathbb{E}[\lambda_1^2(M_1|X)\mu_2(X, M_1, M_2)|X, a_2] \\ \mathbb{E}[\lambda_1(M_1|X)\lambda_2(X, M_1, M_2)Y|X, a] \end{cases}$$

$$\theta_{a_1,a_2,a} = \begin{cases} \mathbb{E}[\mu_0(X)] = \begin{cases} \mathbb{E}\Big[\mathbb{E}\big[\mathbb{E}[\mu_2(X, M_1, M_2)|X, a_2, M_1]|X, a_1\big]\Big] & \text{(RI-RI-RI)} \\ \mathbb{E}\Big[\mathbb{E}\big[\mathbb{E}[\lambda_2(M_2|X, M_1)Y|X, a, M_1]|X, a_1\big]\Big] & \text{(W-RI-RI)} \\ \mathbb{E}\Big[\mathbb{E}[\lambda_1^2(M_1|X)\mu_2(X, M_1, M_2)|X, a_2]\Big] & \text{(RI-W-RI)} \\ \mathbb{E}\Big[\mathbb{E}[\lambda_1(M_1|X)\lambda_2(X, M_1, M_2)Y|X, a]\Big] & \text{(W-W-RI)} \end{cases} \\ \mathbb{E}[\lambda_0^1(A|X)\mu_1(X, M_1)] = \begin{cases} \mathbb{E}\big[\lambda_0^1(A|X)\mathbb{E}[\mu_2(X, M_1, M_2)|X, a_2, M_1]\big] & \text{(RI-RI-W)} \\ \mathbb{E}\big[\lambda_0^1(A|X)\mathbb{E}[\lambda_2(M_2|X, M_1)Y|X, a, M_1]\big] & \text{(W-RI-W)} \end{cases} \\ \mathbb{E}[\lambda_0^2(A|X)\lambda_1^2(M_1|X)\mu_2(X, M_1, M_2)] & \text{(RI-W-W)} \\ \mathbb{E}[\lambda_0(A|X)\lambda_1(M_1|X)\lambda_2(M_2|X, M_1)Y] & \text{(W-W-W)} \end{cases}$$

The first set of equations suggest two different ways of estimating $\mu_1(x, m_1)$: (a) fit a model for the conditional mean of $\hat{\mu}_2(X, M_1, M_2)$ given X, A, M_1 and then set $A = a_2$ for all units; (b) fit a model for the conditional mean of $\hat{\lambda}_2(M_2|X, M_1)Y$ given X, A, and M_1 and then set $A = a$ for all units. Similarly, the second set of equations suggest four different ways of estimating $\mu_0(x)$, and the last set of equations point to eight different ways of estimating $\theta_{a_1, a_2, a}$. Each of these eight estimators corresponds to a unique combination of regression-imputation and weighting.

C Proof of Theorem 2

To show that equation (11) is the EIF of $\theta_{\overline{a}}$ in $\mathcal{P}_{\mathrm{np}}$, it suffices to show

$$\left.\frac{\partial \theta_{\overline{a}}(t)}{\partial t}\right|_{t=0} = \mathbb{E}[\varphi_{\overline{a}}(O)S_0(O)], \tag{24}$$

where $S_0(O)$ is the score function for any one-dimensional submodel $P_t(O)$ evaluated at $t = 0$. We first note that $S_t(O)$ can be written as $S_t(O) = S_t(X) + S_t(A|X) + \sum_{k=1}^{K} S_t(M_k|X, A, \overline{M}_{k-1}) + S_t(Y|X, A, \overline{M}_K)$, where $S_t(u|v) = \partial \log p_t(u|v)/\partial t$ and $p_t(u|v)$ is the conditional probability density/mass function of U given V. Using equation (2) and the product rule, the left-hand side of equation (24) can be written as

$$\left.\frac{\partial \theta_{\overline{a}}(t)}{\partial t}\right|_{t=0} = \left.\frac{\partial \iiint y\, dP_t(y|x, a_{K+1}, \overline{m}_K)\big[\prod_{k=1}^{K} dP_t(m_k|x, a_k, \overline{m}_{k-1})\big] dP_t(x)}{\partial t}\right|_{t=0}$$

$$= \underbrace{\iiint y S_0(x) dP_0(y|x, a_{K+1}, \overline{m}_K)\Big[\prod_{k=1}^{K} dP_0(m_k|x, a_k, \overline{m}_{k-1})\Big] dP_0(x)}_{=:\phi_0}$$

$$+ \underbrace{\sum_{k=1}^{K} \iiint y S_0(m_k|x, a_k, \overline{m}_{k-1}) dP_0(y|x, a_{K+1}, \overline{m}_K)\Big[\prod_{k=1}^{K} dP_0(m_k|x, a_k, \overline{m}_{k-1})\Big] dP_0(x)}_{=:\phi_k}$$

$$+ \underbrace{\iiint y S_0(y|x, a_{K+1}, \overline{m}_K) dP_0(y|x, a_{K+1}, \overline{m}_K)\Big[\prod_{k=1}^{K} dP_0(m_k|x, a_k, \overline{m}_{k-1})\Big] dP_0(x)}_{=:\phi_{K+1}}$$

$$= \sum_{k=0}^{K+1} \phi_k$$

where the second equality follows from the fact that $\partial dP_t(u|v)/\partial t = S_t(u|v) dP_t(u|v)$. Below, we verify that $\phi_k = \mathbb{E}[\varphi_k(O)S_0(O)]$ for all $k \in \{0, \ldots K+1\}$, where $\varphi_k(O)$ is defined in Theorem 2. First,

$$\mathbb{E}[\varphi_0(O)S_0(O)]$$
$$= \mathbb{E}[(\mu_0(X) - \theta_{\overline{a}})S_0(O)]$$

$$=\mathbb{E}[\mu_0(X)S_0(O)]$$

$$=\mathbb{E}\big[\mu_0(X)\big(S_0(X)+S_0(A|X)+\sum_{k=1}^{K}S_0(M_k|X,A,\overline{M}_{k-1})+S_0(Y|X,A,\overline{M}_K)\big)\big]$$

$$=\mathbb{E}\big[\mu_0(X)S_0(X)\big]+\mathbb{E}\Big[\mu_0(X)\underbrace{\mathbb{E}\big[S_0(A|X)|X\big]}_{=0}\Big]+\sum_{k=1}^{K}\mathbb{E}\Big[\mu_0(X)\underbrace{\mathbb{E}\big[S_0(M_k|X,A,\overline{M}_{k-1})|X,A,\overline{M}_{k-1}\big]}_{=0}\Big]$$

$$+\mathbb{E}\Big[\mu_0(X)\underbrace{\mathbb{E}\big[S_0(Y|X,A,\overline{M}_K)|X,A,\overline{M}_K\big]}_{=0}\Big]$$

$$=\int \mu_0(x)S_0(x)dP_0(x)$$

$$=\iiint yS_0(x)dP_0(y|x,a_{K+1},\overline{m}_K)\big[\prod_{k=1}^{K}dP_0(m_k|x,a_k,\overline{m}_{k-1})\big]dP_0(x)$$

$$=\phi_0.$$

Second, for $k\in[K]$,

$$\mathbb{E}[\varphi_k(O)S_0(O)]$$

$$=\mathbb{E}\big[\varphi_k(O)\big(S_0(X)+S_0(A|X)+\sum_{j=1}^{K}S_0(M_j|X,A,\overline{M}_{j-1})+S_0(Y|X,A,\overline{M}_K)\big)\big]$$

$$=\mathbb{E}\Big[\mathbb{E}\big[\varphi_k(O)\big(S_0(X)+S_0(A|X)+\sum_{j=1}^{k-1}S_0(M_j|X,A,\overline{M}_{j-1}))|X,A,\overline{M}_{k-1}\big]\Big]+\mathbb{E}\big[\varphi_k(O)S_0(M_k|X,A,\overline{M}_{k-1}))\big]$$

$$+\sum_{j=k+1}^{K}\mathbb{E}\Big[\varphi_k(O)\underbrace{\mathbb{E}\big[S_0(M_j|X,A,\overline{M}_{j-1})|X,A,\overline{M}_{j-1}\big]}_{=0}\Big]+\mathbb{E}\Big[\varphi_k(O)\underbrace{\mathbb{E}\big[S_0(Y|X,A,\overline{M}_K)|X,A,\overline{M}_K\big]}_{=0}\Big]$$

$$=\mathbb{E}\Big[\big(S_0(X)+S_0(A|X)+\sum_{j=1}^{k-1}S_0(M_j|X,A,\overline{M}_{j-1})\big)\underbrace{\mathbb{E}\big[\varphi_k(O)|X,A,\overline{M}_{k-1}\big]}_{=0}\Big]+\mathbb{E}\big[\varphi_k(O)S_0(M_k|X,A,\overline{M}_{k-1}))\big]$$

$$=\mathbb{E}\big[\varphi_k(O)S_0(M_k|X,A,\overline{M}_{k-1}))\big]$$

$$=\mathbb{E}\Big[\mathbb{E}\big[\frac{\mathbb{I}(A=a_k)}{p(a_k|X)}\big(\prod_{j=1}^{k-1}\frac{p(M_j|X,a_j,\overline{M}_{j-1})}{p(M_j|X,a_k,\overline{M}_{j-1})}\big)\big(\mu_k(X,\overline{M}_k)-\mu_{k-1}(X,\overline{M}_{k-1})\big)S_0(M_k|X,A,\overline{M}_{k-1}))|X,A,\overline{M}_{k-1}\big]\Big]$$

$$=\mathbb{E}\big[\frac{\mathbb{I}(A=a_k)}{p(a_k|X)}\big(\prod_{j=1}^{k-1}\frac{p(M_j|X,a_j,\overline{M}_{j-1})}{p(M_j|X,a_k,\overline{M}_{j-1})}\big)\mu_k(X,\overline{M}_k)S_0(M_k|X,A,\overline{M}_{k-1}))\big]$$

$$=\mathbb{E}_X\mathbb{E}\big[\big(\prod_{j=1}^{k-1}\frac{p(M_j|X,a_j,\overline{M}_{j-1})}{p(M_j|X,a_k,\overline{M}_{j-1})}\big)\mu_k(X,\overline{M}_k)S_0(M_k|X,A,\overline{M}_{k-1}))|X,A=a_k\big]$$

$$=\iiint S_0(m_k|x,a_k,\overline{m}_{k-1})\Big(\int_y\int_{\overline{m}_K}ydP_0(y|x,a_{K+1},\overline{m}_K)\prod_{j=k+1}^{K}dP_0(m_j|x,a_j,\overline{m}_{j-1})\Big)$$

$$\cdot dP_0(m_k|x, a_k, \overline{m}_{k-1}) \Big(\prod_{j=1}^{k-1} \frac{p(m_j|x, a_j, \overline{m}_{j-1})}{p(m_j|x, a_k, \overline{m}_{j-1})} \Big) \Big(\prod_{j=1}^{k-1} dP_0(m_j|x, a_k, \overline{m}_{j-1}) \Big) dP_0(x)$$

$$= \iiint y S_0(m_k|x, a_k, \overline{m}_{k-1}) dP_0(y|x, a_{K+1}, \overline{m}_K) \Big(\prod_{j=1}^{K} dP_0(m_j|x, a_j, \overline{m}_{j-1}) \Big) dP_0(x)$$

$$= \phi_k,$$

where the fourth equality is due to the fact that

$$\mathbb{E}\big[\varphi_k(O)|X, A, \overline{M}_{k-1}\big]$$

$$= \mathbb{E}\big[\frac{\mathbb{I}(A = a_k)}{p(a_k|X)} \Big(\prod_{j=1}^{k-1} \frac{p(M_j|X, a_j, \overline{M}_{j-1})}{p(M_j|X, a_k, \overline{M}_{j-1})} \Big) \big(\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1}) \big) | X, A, \overline{M}_{k-1} \big]$$

$$= \mathbb{E}\big[\Big(\prod_{j=1}^{k-1} \frac{p(M_j|X, a_j, \overline{M}_{j-1})}{p(M_j|X, a_k, \overline{M}_{j-1})} \Big) \big(\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1}) \big) | X, A = a_k, \overline{M}_{k-1} \big]$$

$$= \Big(\prod_{j=1}^{k-1} \frac{p(M_j|X, a_j, \overline{M}_{j-1})}{p(M_j|X, a_k, \overline{M}_{j-1})} \Big) \underbrace{\mathbb{E}\big[\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1})|X, A = a_k, \overline{M}_{k-1} \big]}_{=0}$$

$$= 0.$$

Finally,

$$\mathbb{E}[\varphi_{K+1}(O) S_0(O)]$$

$$= \mathbb{E}\big[\varphi_{K+1}(O) \big(S_0(X) + S_0(A|X) + \sum_{j=1}^{K} S_0(M_j|X, A, \overline{M}_{j-1}) + S_0(Y|X, A, \overline{M}_K) \big) \big]$$

$$= \mathbb{E}\Big[\mathbb{E}\big[\varphi_{K+1}(O) \big(S_0(X) + S_0(A|X) + \sum_{j=1}^{K} S_0(M_j|X, A, \overline{M}_{j-1}) \big) | X, A, \overline{M}_K \big] \Big] + \mathbb{E}\big[\varphi_{K+1}(O) S_0(Y|X, A, \overline{M}_K) \big]$$

$$= \mathbb{E}\Big[\big(S_0(X) + S_0(A|X) + \sum_{j=1}^{K} S_0(M_j|X, A, \overline{M}_{j-1}) \big) \underbrace{\mathbb{E}\big[\varphi_{K+1}(O)|X, A, \overline{M}_K \big]}_{=0} \Big] + \mathbb{E}\big[\varphi_{K+1}(O) S_0(Y|X, A, \overline{M}_K) \big]$$

$$= \mathbb{E}\big[\varphi_{K+1}(O) S_0(Y|X, A, \overline{M}_K) \big]$$

$$= \mathbb{E}\Big[\mathbb{E}\big[\frac{\mathbb{I}(A = a_{K+1})}{p(a_{K+1}|X)} \Big(\prod_{j=1}^{K} \frac{p(M_j|X, a_j, \overline{M}_{j-1})}{p(M_j|X, a_{K+1}, \overline{M}_{j-1})} \Big) \big(Y - \mu_K(X, \overline{M}_K) \big) S_0(Y|X, A, \overline{M}_K) | X, A, \overline{M}_K \big] \Big]$$

$$= \mathbb{E}\Big[\mathbb{E}\big[\frac{\mathbb{I}(A = a_{K+1})}{p(a_{K+1}|X)} \Big(\prod_{j=1}^{K} \frac{p(M_j|X, a_j, \overline{M}_{j-1})}{p(M_j|X, a_{K+1}, \overline{M}_{j-1})} \Big) Y S_0(Y|X, A, \overline{M}_K) | X, A, \overline{M}_K \big] \Big]$$

$$= \mathbb{E}\Big[\mathbb{E}\big[\frac{\mathbb{I}(A = a_{K+1})}{p(a_{K+1}|X)} \Big(\prod_{j=1}^{K} \frac{p(M_j|X, a_j, \overline{M}_{j-1})}{p(M_j|X, a_{K+1}, \overline{M}_{j-1})} \Big) Y S_0(Y|X, A, \overline{M}_K) | X, A \big] \Big]$$

$$=\mathbb{E}_X\Big[\mathbb{E}\big[\Big(\prod_{j=1}^{K}\frac{p(M_j|X,a_j,\overline{M}_{j-1})}{p(M_j|X,a_{K+1},\overline{M}_{j-1})}\Big)YS_0(Y|X,A,\overline{M}_K))|X,A=a_{K+1}\big]\Big]$$

$$=\iiint yS_0(y|x,a_{K+1},\overline{m}_K)dP_0(y|x,a_{K+1},\overline{m}_K)\Big(\prod_{j=1}^{K}\frac{p(m_j|x,a_j,\overline{m}_{j-1})}{p(m_j|x,a_{K+1},\overline{m}_{j-1})}\Big)\Big(\prod_{j=1}^{K}dP_0(m_j|x,a_{K+1},\overline{m}_{j-1})\Big)dP_0(x)$$

$$=\iiint yS_0(y|x,a_{K+1},\overline{m}_K)dP_0(y|x,a_{K+1},\overline{m}_K)\Big(\prod_{j=1}^{K}dP_0(m_j|x,a_j,\overline{m}_{j-1})\Big)dP_0(x)$$

$$=\phi_{K+1},$$

where the third equality is due to the fact that

$$\mathbb{E}\big[\varphi_{K+1}(O)|X,A,\overline{M}_K\big]$$

$$=\mathbb{E}\big[\frac{\mathbb{I}(A=a_{K+1})}{p(a_{K+1}|X)}\Big(\prod_{j=1}^{K}\frac{p(M_j|X,a_j,\overline{M}_{j-1})}{p(M_j|X,a_{K+1},\overline{M}_{j-1})}\Big)\big(Y-\mu_K(X,\overline{M}_K)\big)|X,A,\overline{M}_K\big]$$

$$=\frac{p(a_{K+1}|X,\overline{M}_K)}{p(a_{K+1}|X)}\Big(\prod_{j=1}^{K}\frac{p(M_j|X,a_j,\overline{M}_{j-1})}{p(M_j|X,a_{K+1},\overline{M}_{j-1})}\Big)\underbrace{\mathbb{E}\big[Y-\mu_K(X,\overline{M}_K)|X,A=a_{K+1},\overline{M}_K\big]}_{=0}$$

$$=0.$$

Since $\phi_k=\mathbb{E}[\varphi_k(O)S_0(O)]$ for all $k\in\{0,\ldots K+1\}$, we have

$$\frac{\partial\theta_{\overline{a}}(t)}{\partial t}\Big|_{t=0}=\sum_{k=0}^{K+1}\phi_k=\mathbb{E}\big[\big(\sum_{k=0}^{K+1}\varphi_k(O)\big)S_0(O)\big]=\mathbb{E}\big[\varphi_{\overline{a}}(O)S_0(O)\big].$$

D   Proof of Theorems 3 and 4

D.1   Parametric Estimation of Nuisance Parameters

In this subsection, we prove the multiple robustness of $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ and $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ for the case where parametric models are used to estimate the corresponding nuisance functions. The local efficiency of these estimators is implied by our proof in Section D.2, which considers the case where data-adaptive methods and cross-fitting are used to estimate the nuisance functions.

Let us start with $\hat{\theta}_{\overline{a}}^{\text{eif}_1}=\mathbb{P}_n[m_1(O;\hat{\eta}_1)]$, where $m_1(O;\hat{\eta}_1)$ denotes the quantity inside $\mathbb{P}_n[\cdot]$ in equation (12), and $\hat{\eta}_1=(\hat{\pi}_0,\hat{f}_1,\ldots\hat{f}_K,\hat{\mu}_K)$. In the meantime, let $\eta_1=(\pi_0,f_1,\ldots f_K,\mu_K)$ denote the truth and $\eta_1^*=(\pi_0^*,f_1^*,\ldots f_K^*,\mu_K^*)$ the probability limit of $\hat{\eta}_1$. A first-order Taylor expansion of $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ yields

$$\hat{\theta}_{\overline{a}}^{\text{eif}_1}=\mathbb{P}_n\big[m_1(O;\eta_1^*)\big]+o_p(1).$$

Hence it suffices to show $\mathbb{E}[m_1(O;\eta_1^*)]=\theta_{\overline{a}}$ whenever all but one elements in η_1^* equal the truth. Consistency follows from the law of large numbers. By treating $\hat{\theta}_{\overline{a}}^{\text{eif}_1}=\mathbb{P}_n[m_1(O;\hat{\eta}_1)]$ as a two-

stage M-estimator, asymptotic normality follows from standard regularity conditions for estimating equations (e.g., Newey and McFadden 1994, p. 2148).

First, if $\eta_1^* = (\pi_0^*, f_1, \ldots f_K, \mu_K)$, the MLE of μ_k $(0 \leq k \leq K-1)$ will also be consistent. Thus,

$$
\mathbb{E}[m_1(O; \eta_1^*)]
$$

$$
= \mathbb{E}\Big[\frac{\mathbb{I}(A = a_{K+1})}{\pi_0^*(a_{K+1}|X)}\Big(\prod_{j=1}^{K} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_{K+1}, \overline{M}_{j-1})}\Big)\big(Y - \mu_K(X, \overline{M}_K)\big)
$$

$$
+ \sum_{k=1}^{K} \frac{\mathbb{I}(A = a_k)}{\pi_0^*(a_k|X)}\Big(\prod_{j=1}^{k-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_k, \overline{M}_{j-1})}\Big)\big(\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1})\big)
$$

$$
+ \mu_0(X)\Big]
$$

$$
= \mathbb{E}\Big[\frac{\pi_0(a_{K+1}|X, \overline{M}_K)}{\pi_0^*(a_{K+1}|X)}\Big(\prod_{j=1}^{K} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_{K+1}, \overline{M}_{j-1})}\Big)\underbrace{\mathbb{E}\big[Y - \mu_K(X, \overline{M}_K)\big|X, A = a_{K+1}, \overline{M}_K\big]}_{=0}
$$

$$
+ \sum_{k=1}^{K} \frac{\pi_0(a_k|X, \overline{M}_{k-1})}{\pi_0^*(a_k|X)}\Big(\prod_{j=1}^{k-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_k, \overline{M}_{j-1})}\Big)\underbrace{\mathbb{E}\big[\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1})\big|X, A = a_k, \overline{M}_{k-1}\big]}_{=0}
$$

$$
+ \mu_0(X)\Big]
$$

$$
= \mathbb{E}[\mu_0(X)]
$$

$$
= \theta_{\overline{a}}.
$$

Second, if $\eta_1^* = (\pi_0, f_1, \ldots f_{k'-1}, f_{k'}^*, f_{k'+1}, \ldots f_K, \mu_K)$, the MLE of μ_k for any $k \geq k'$ will also be consistent. Thus,

$$
\mathbb{E}[m_1(O; \eta_1^*)]
$$

$$
= \mathbb{E}\Big[\frac{\mathbb{I}(A = a_{K+1})}{\pi_0(a_{K+1}|X)}\Big(\prod_{j=1}^{K} \frac{f_j^*(M_j|X, a_j, \overline{M}_{j-1})}{f_j^*(M_j|X, a_{K+1}, \overline{M}_{j-1})}\Big)\big(Y - \mu_K(X, \overline{M}_K)\big)
$$

$$
+ \sum_{k=k'+1}^{K} \frac{\mathbb{I}(A = a_k)}{\pi_0(a_k|X)}\Big(\prod_{j=1}^{k-1} \frac{f_j^*(M_j|X, a_j, \overline{M}_{j-1})}{f_j^*(M_j|X, a_k, \overline{M}_{j-1})}\Big)\big(\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1})\big)
$$

$$
+ \frac{\mathbb{I}(A = a_{k'})}{\pi_0(a_{k'}|X)}\Big(\prod_{j=1}^{k'-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_{k'}, \overline{M}_{j-1})}\Big)\big(\mu_{k'}(X, \overline{M}_{k'}) - \mu_{k'-1}^*(X, \overline{M}_{k'-1})\big)
$$

$$
+ \sum_{k=1}^{k'-1} \frac{\mathbb{I}(A = a_k)}{\pi_0(a_k|X)}\Big(\prod_{j=1}^{k-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_k, \overline{M}_{j-1})}\Big)\big(\mu_k^*(X, \overline{M}_k) - \mu_{k-1}^*(X, \overline{M}_{k-1})\big)
$$

$$
+ \mu_0^*(X)\Big]
$$

$$
= \mathbb{E}\Big[\frac{\pi_0(a_{K+1}|X, \overline{M}_K)}{\pi_0(a_{K+1}|X)}\Big(\prod_{j=1}^{K} \frac{f_j^*(M_j|X, a_j, \overline{M}_{j-1})}{f_j^*(M_j|X, a_{K+1}, \overline{M}_{j-1})}\Big)\underbrace{\mathbb{E}\big[Y - \mu_K(X, \overline{M}_K)\big|X, A = a_{K+1}, \overline{M}_K\big]}_{=0}
$$

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$$+ \sum_{k=k'+1}^{K} \frac{\pi_0(a_k|X, \overline{M}_{k-1})}{\pi_0(a_k|X)} \left(\prod_{j=1}^{k-1} \frac{f_j^*(M_j|X, a_j, \overline{M}_{j-1})}{f_j^*(M_j|X, a_k, \overline{M}_{j-1})} \right) \underbrace{\mathbb{E}\left[\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1}) \big| X, A = a_k, \overline{M}_{k-1} \right]}_{=0}$$

$$+ \frac{\mathbb{I}(A = a_{k'})}{\pi_0(a_{k'}|X)} \left(\prod_{j=1}^{k'-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_{k'}, \overline{M}_{j-1})} \right) \mu_{k'}(X, \overline{M}_{k'})$$

$$+ \sum_{k=1}^{k'-1} \mu_k^*(X, \overline{M}_k) \mathbb{E}\left[\left(\frac{\mathbb{I}(A = a_k)}{\pi_0(a_k|X)} \prod_{j=1}^{k-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_k, \overline{M}_{j-1})} - \frac{\mathbb{I}(A = a_{k+1})}{\pi_0(a_{k+1}|X)} \prod_{j=1}^{k} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_{k+1}, \overline{M}_{j-1})} \right) \big| X, \overline{M}_k \right]$$

$$+ \mu_0^*(X) \underbrace{\mathbb{E}\left[1 - \frac{\mathbb{I}(A = a_1)}{\pi_0(a_1|X)} \big| X \right]}_{=0} \Bigg]$$

$$= \mathbb{E}\left[\frac{\mathbb{I}(A = a_{k'})}{\pi_0(a_{k'}|X)} \left(\prod_{j=1}^{k'-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_{k'}, \overline{M}_{j-1})} \right) \mu_{k'}(X, \overline{M}_{k'}) \right]$$

$$+ \mathbb{E}\left[\sum_{k=1}^{k'-1} \mu_k^*(X, \overline{M}_k) \left(\frac{\pi_k(a_k|X, \overline{M}_k)}{\pi_0(a_k|X)} \prod_{j=1}^{k-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_k, \overline{M}_{j-1})} - \frac{\pi_k(a_{k+1}|X, \overline{M}_k)}{\pi_0(a_{k+1}|X)} \prod_{j=1}^{k} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_{k+1}, \overline{M}_{j-1})} \right) \right]$$

$$= \underbrace{\mathbb{E}\left[\frac{\mathbb{I}(A = a_{k'})}{\pi_0(a_{k'}|X)} \left(\prod_{j=1}^{k'-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_{k'}, \overline{M}_{j-1})} \right) \mu_{k'}(X, \overline{M}_{k'}) \right]}_{=\theta_{\overline{a}}}$$

$$+ \mathbb{E}\left[\sum_{k=1}^{k'-1} \mu_k^*(X, \overline{M}_k) \underbrace{\left(\prod_{j=1}^{k} \frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_{j-1}(a_j|X, \overline{M}_{j-1})} - \prod_{j=1}^{k} \frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_{j-1}(a_j|X, \overline{M}_{j-1})} \right)}_{=0} \right]$$

$$= \theta_{\overline{a}},$$

where the penultimate equality is due to the fact that

$$\frac{\pi_k(a_k|X, \overline{M}_k)}{\pi_0(a_k|X)} \prod_{j=1}^{k-1} \frac{f_j(M_j|X, a_j, \overline{M}_{j-1})}{f_j(M_j|X, a_k, \overline{M}_{j-1})}$$

$$= \frac{\pi_k(a_k|X, \overline{M}_k)}{\pi_0(a_k|X)} \prod_{j=1}^{k-1} \left(\frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_j(a_k|X, \overline{M}_j)} \cdot \frac{\pi_{j-1}(a_k|X, \overline{M}_{j-1})}{\pi_{j-1}(a_j|X, \overline{M}_{j-1})} \right)$$

$$= \frac{\pi_k(a_k|X, \overline{M}_k)}{\pi_0(a_k|X)} \prod_{j=1}^{k-1} \left(\frac{\pi_{j-1}(a_k|X, \overline{M}_{j-1})}{\pi_j(a_k|X, \overline{M}_j)} \right) \prod_{j=1}^{k-1} \left(\frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_{j-1}(a_j|X, \overline{M}_{j-1})} \right)$$

$$= \frac{\pi_k(a_k|X, \overline{M}_k)}{\pi_{k-1}(a_k|X, \overline{M}_{k-1})} \prod_{j=1}^{k-1} \left(\frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_{j-1}(a_j|X, \overline{M}_{j-1})} \right)$$

$$= \prod_{j=1}^{k} \frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_{j-1}(a_j|X, \overline{M}_{j-1})}$$

and that

$$\frac{\pi_k(a_{k+1}|X,\overline{M}_k)}{\pi_0(a_{k+1}|X)}\prod_{j=1}^{k}\frac{f_j(M_j|X,a_j,\overline{M}_{j-1})}{f_j(M_j|X,a_{k+1},\overline{M}_{j-1})}$$

$$=\frac{\pi_k(a_{k+1}|X,\overline{M}_k)}{\pi_0(a_{k+1}|X)}\prod_{j=1}^{k}\Big(\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{k+1}|X,\overline{M}_j)}\cdot\frac{\pi_{j-1}(a_{k+1}|X,\overline{M}_{j-1})}{\pi_{j-1}(a_j|X,\overline{M}_{j-1})}\Big)$$

$$=\frac{\pi_k(a_{k+1}|X,\overline{M}_k)}{\pi_0(a_{k+1}|X)}\prod_{j=1}^{k}\Big(\frac{\pi_{j-1}(a_{k+1}|X,\overline{M}_{j-1})}{\pi_j(a_{k+1}|X,\overline{M}_j)}\Big)\prod_{j=1}^{k}\Big(\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_{j-1}(a_j|X,\overline{M}_{j-1})}\Big)$$

$$=\prod_{j=1}^{k}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_{j-1}(a_j|X,\overline{M}_{j-1})}.$$

Finally, if $\eta_1^* = (\pi_0, f_1, \ldots f_K, \mu_K^*)$, we have

$$\mathbb{E}[m_1(O;\eta_1^*)]$$

$$=\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{K+1})}{\pi_0(a_{K+1}|X)}\Big(\prod_{j=1}^{K}\frac{f_j(M_j|X,a_j,\overline{M}_{j-1})}{f_j(M_j|X,a_{K+1},\overline{M}_{j-1})}\Big)(Y-\mu_K^*(X,\overline{M}_K))$$

$$+\sum_{k=1}^{K}\frac{\mathbb{I}(A=a_k)}{\pi_0(a_k|X)}\Big(\prod_{j=1}^{k}\frac{f_j(M_j|X,a_j,\overline{M}_{j-1})}{f_j(M_j|X,a_k,\overline{M}_{j-1})}\Big)(\mu_k^*(X,\overline{M}_k)-\mu_{k-1}^*(X,\overline{M}_{k-1}))+\mu_0^*(X)\Big]$$

$$=\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{K+1})}{\pi_0(a_{K+1}|X)}\Big(\prod_{j=1}^{K}\frac{f_j(M_j|X,a_j,\overline{M}_{j-1})}{f_j(M_j|X,a_{K+1},\overline{M}_{j-1})}\Big)Y$$

$$+\sum_{k=1}^{K}\mu_k^*(X,\overline{M}_k)\underbrace{\mathbb{E}\Big[\Big(\frac{\mathbb{I}(A=a_k)}{\pi_0(a_k|X)}\prod_{j=1}^{k-1}\frac{f_j(M_j|X,a_j,\overline{M}_{j-1})}{f_j(M_j|X,a_k,\overline{M}_{j-1})}-\frac{\mathbb{I}(A=a_{k+1})}{\pi_0(a_{k+1}|X)}\prod_{j=1}^{k}\frac{f_j(M_j|X,a_j,\overline{M}_{j-1})}{f_j(M_j|X,a_{k+1},\overline{M}_{j-1})}\Big)|X,\overline{M}_k\Big]}_{=0 \quad\text{(same as the previous case)}}$$

$$+\mu_0^*(X)\underbrace{\mathbb{E}\Big[1-\frac{\mathbb{I}(A=a_1)}{\pi_0(a_1|X)}||X\Big]}_{=0}\Big]$$

$$=\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{K+1})}{\pi_0(a_{K+1}|X)}\Big(\prod_{j=1}^{K}\frac{f_j(M_j|X,a_j,\overline{M}_{j-1})}{f_j(M_j|X,a_{K+1},\overline{M}_{j-1})}\Big)Y\Big]$$

$$=\theta_{\overline{a}}.$$

Now consider $\hat{\theta}_{\overline{a}}^{\text{eif}_2} = \mathbb{P}_n[m_2(O;\hat{\eta}_2)]$, where $m_2(O;\hat{\eta}_2)$ denotes the quantity inside $\mathbb{P}_n[\cdot]$ in equation (14), and $\hat{\eta}_2 = (\hat{\pi}_0, \ldots \hat{\pi}_K, \hat{\mu}_0, \ldots \hat{\mu}_K)$. In the meantime, let $\eta_2 = (\pi_0, \ldots \pi_K, \mu_0, \ldots \mu_K)$ denote the truth and $\eta_2^* = (\pi_0^*, \ldots \pi_K^*, \mu_0^*, \ldots \mu_K^*)$ denote the probability limit of $\hat{\eta}_2$. A first-order Taylor expansion of $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ yields

$$\hat{\theta}_{\overline{a}}^{\text{eif}_2} = \mathbb{P}_n\big[m_2(O;\eta_2^*)\big] + o_p(1).$$

Hence it suffices to show $\mathbb{E}[m_2(O; \eta_2^*)] = \theta_{\overline{a}}$ if

$$\eta_2^* = (\pi_0, \ldots \pi_{k'-1}, \pi_{k'}^*, \ldots \pi_K^*, \mu_0^*, \ldots \mu_{k'-1}^*, \mu_{k'}, \ldots \mu_K)$$

for every $k' \in \{0, \ldots K+1\}$.

First, if $k' = 0$, then all the outcome models are correctly specified, which implies

$$
\begin{aligned}
&\mathbb{E}[m_2(O; \eta_2^*)] \\
=&\mathbb{E}\Big[\frac{\mathbb{I}(A = a_{K+1})}{\pi_0^*(a_1|X)}\Big(\prod_{j=1}^{K} \frac{\pi_j^*(a_j|X, \overline{M}_j)}{\pi_j^*(a_{j+1}|X, \overline{M}_j)}\Big)\big(Y - \mu_K(X, \overline{M}_K)\big) \\
&+ \sum_{k=1}^{K} \frac{\mathbb{I}(A = a_k)}{\pi_0^*(a_1|X)}\Big(\prod_{j=1}^{k-1} \frac{\pi_j^*(a_j|X, \overline{M}_j)}{\pi_j^*(a_{j+1}|X, \overline{M}_j)}\Big)\big(\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1})\big) \\
&+ \mu_0(X)\Big] \\
=&\mathbb{E}\Big[\frac{\mathbb{I}(A = a_{K+1})}{\pi_0^*(a_1|X)}\Big(\prod_{j=1}^{K} \frac{\pi_j^*(a_j|X, \overline{M}_j)}{\pi_j^*(a_{j+1}|X, \overline{M}_j)}\Big)\underbrace{\mathbb{E}\big[Y - \mu_K(X, \overline{M}_K)\big|X, A = a_{K+1}, \overline{M}_K\big]}_{=0} \\
&+ \sum_{k=1}^{K} \frac{\mathbb{I}(A = a_k)}{\pi_0^*(a_1|X)}\Big(\prod_{j=1}^{k-1} \frac{\pi_j^*(a_j|X, \overline{M}_j)}{\pi_j^*(a_{j+1}|X, \overline{M}_j)}\Big)\underbrace{\mathbb{E}\big[\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1})\big|X, A = a_k, \overline{M}_{k-1}\big]}_{=0} \\
&+ \mu_0(X)\Big] \\
=&\mathbb{E}[\mu_0(X)] \\
=&\theta_{\overline{a}}.
\end{aligned}
$$

Second, if $k' \in \{1, \ldots K-1\}$, we have

$$
\begin{aligned}
&\mathbb{E}[m_2(O; \eta_2^*)] \\
=&\mathbb{E}\Big[\frac{\mathbb{I}(A = a_{K+1})}{\pi_0^*(a_1|X)}\Big(\prod_{j=1}^{K} \frac{\pi_j^*(a_j|X, \overline{M}_j)}{\pi_j^*(a_{j+1}|X, \overline{M}_j)}\Big)\big(Y - \mu_K(X, \overline{M}_K)\big) \\
&+ \sum_{k=k'+1}^{K} \frac{\mathbb{I}(A = a_k)}{\pi_0^*(a_1|X)}\Big(\prod_{j=1}^{k-1} \frac{\pi_j^*(a_j|X, \overline{M}_j)}{\pi_j^*(a_{j+1}|X, \overline{M}_j)}\Big)\big(\mu_k(X, \overline{M}_k) - \mu_{k-1}(X, \overline{M}_{k-1})\big) \\
&+ \frac{\mathbb{I}(A = a_{k'})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k'-1} \frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_j(a_{j+1}|X, \overline{M}_j)}\Big)\big(\mu_{k'}(X, \overline{M}_{k'}) - \mu_{k'-1}^*(X, \overline{M}_{k'-1})\big) \\
&+ \sum_{k=1}^{k'-1} \frac{\mathbb{I}(A = a_k)}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k-1} \frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_j(a_{j+1}|X, \overline{M}_j)}\Big)\big(\mu_k^*(X, \overline{M}_k) - \mu_{k-1}^*(X, \overline{M}_{k-1})\big) \\
&+ \mu_0^*(X)\Big]
\end{aligned}
$$

$$
=\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{K+1})}{\pi_0^*(a_1|X)}\Big(\prod_{j=1}^{K}\frac{\pi_j^*(a_j|X,\overline{M}_j)}{\pi_j^*(a_{j+1}|X,\overline{M}_j)}\Big)\underbrace{\mathbb{E}\big[Y-\mu_K(X,\overline{M}_K)\big|X,A=a_{K+1},\overline{M}_K\big]}_{=0}
$$

$$
+\sum_{k=k'+1}^{K}\frac{\mathbb{I}(A=a_k)}{\pi_0^*(a_1|X)}\Big(\prod_{j=1}^{k-1}\frac{\pi_j^*(a_j|X,\overline{M}_j)}{\pi_j^*(a_{j+1}|X,\overline{M}_j)}\Big)\underbrace{\mathbb{E}\big[\mu_k(X,\overline{M}_k)-\mu_{k-1}(X,\overline{M}_{k-1})\big|X,A=a_k,\overline{M}_{k-1}\big]}_{=0}
$$

$$
+\frac{\mathbb{I}(A=a_{k'})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k'-1}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)\mu_{k'}(X,\overline{M}_{k'})
$$

$$
+\sum_{k=1}^{k'-1}\mu_k^*(X,\overline{M}_k)\mathbb{E}\Big[\frac{\mathbb{I}(A=a_k)}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k-1}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)-\frac{\mathbb{I}(A=a_{k+1})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)\big|X,\overline{M}_k\Big]
$$

$$
+\mu_0^*(X)\underbrace{\mathbb{E}\Big[1-\frac{\mathbb{I}(A=a_1)}{\pi_0(a_1|X)}\big|X\Big]}_{=0}\Big]
$$

$$
=\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{k'})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k'-1}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)\mu_{k'}(X,\overline{M}_{k'})\Big]
$$

$$
+\mathbb{E}\Big[\sum_{k=1}^{k'-1}\mu_k^*(X,\overline{M}_k)\Big(\frac{\pi_k(a_k|X,\overline{M}_k)}{\pi_0(a_1|X)}\prod_{j=1}^{k-1}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}-\frac{\pi_k(a_{k+1}|X,\overline{M}_k)}{\pi_0(a_1|X)}\prod_{j=1}^{k}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)\Big]
$$

$$
=\underbrace{\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{k'})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k'-1}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)\mu_{k'}(X,\overline{M}_{k'})\Big]}_{=\theta_{\overline{a}}}
$$

$$
+\mathbb{E}\Big[\sum_{k=1}^{k'-1}\mu_k^*(X,\overline{M}_k)\underbrace{\Big(\prod_{j=1}^{k}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_{j-1}(a_j|X,\overline{M}_{j-1})}-\prod_{j=1}^{k}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_{j-1}(a_j|X,\overline{M}_{j-1})}\Big)}_{=0}\Big]
$$

$$
=\theta_{\overline{a}}.
$$

Finally, if $k'=K$, we have

$$
\mathbb{E}[m_2(O;\eta_2^*)]
$$

$$
=\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{K+1})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{K}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)\big(Y-\mu_K^*(X,\overline{M}_K)\big)
$$

$$
+\sum_{k=1}^{K}\frac{\mathbb{I}(A=a_k)}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k-1}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)\big(\mu_k^*(X,\overline{M}_k)-\mu_{k-1}^*(X,\overline{M}_{k-1})\big)+\mu_0^*(X)\Big]
$$

$$
=\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{K+1})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{K}\frac{\pi_j(a_j|X,\overline{M}_j)}{\pi_j(a_{j+1}|X,\overline{M}_j)}\Big)Y
$$

$$+ \sum_{k=1}^{K} \mu_k^*(X, \overline{M}_k) \, \mathbb{E}\Big[\Big(\frac{\mathbb{I}(A=a_k)}{\pi_0(a_1|X)} \prod_{j=1}^{k-1} \frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_j(a_{j+1}|X, \overline{M}_j)} - \frac{\mathbb{I}(A=a_{k+1})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{k+1} \frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_j(a_{j+1}|X, \overline{M}_j)}\Big)\Big)|X, \overline{M}_k\Big]$$

$$\underbrace{\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad}_{=0 \quad \text{(same as the previous case)}}$$

$$+ \mu_0^*(X) \underbrace{\mathbb{E}\Big[1 - \frac{\mathbb{I}(A=a_1)}{\pi_0(a_1|X)}||X\Big]}_{=0}\Big]$$

$$=\mathbb{E}\Big[\frac{\mathbb{I}(A=a_{K+1})}{\pi_0(a_1|X)}\Big(\prod_{j=1}^{K} \frac{\pi_j(a_j|X, \overline{M}_j)}{\pi_j(a_{j+1}|X, \overline{M}_j)}\Big)Y\Big]$$

$$=\theta_{\overline{a}}.$$

D.2 Data-Adaptive Estimation of Nuisance Parameters

Let us start with $\hat{\theta}_{\overline{a}}^{\mathrm{eif2}} = \mathbb{P}_n[m_2(O; \hat{\eta}_2)]$. Let $\tilde{\eta}_2 = (\hat{\pi}_0, \dots \hat{\pi}_K, \mu_0, \dots \mu_K)$ denote a combination of estimated treatment models $\hat{\pi}_j$ and true outcome models μ_j $(0 \le j \le K+1)$, and let $Pg = \int g dP$ denote the expectation of a function g of observed data O at the true model P. As before, denote by η_2^* the probability limit of $\hat{\eta}_2$. $\theta_{\overline{a}}^{\mathrm{eif2}}$ can now be written as

$$\hat{\theta}_{\overline{a}}^{\mathrm{eif2}} - \theta_{\overline{a}}$$

$$=\mathbb{P}_n[m_2(O; \hat{\eta}_2)] - P[m_2(O; \eta_2)]$$

$$=(\mathbb{P}_n - P)m_2(O; \eta_2^*) + P[m_2(O; \hat{\eta}_2) - m_2(O; \eta_2)] + (\mathbb{P}_n - P)[m_2(O; \hat{\eta}_2) - m_2(O; \eta_2^*)] \qquad (25)$$

$$=(\mathbb{P}_n - P)\underbrace{[m_2(O; \eta_2^*) - \theta_{\overline{a}}]}_{\triangleq \varphi_{\overline{a}}(O; \eta_2^*)} + P[m_2(O; \hat{\eta}_2) - m_2(O; \eta_2)] + (\mathbb{P}_n - P)[m_2(O; \hat{\eta}_2) - m_2(O; \eta_2^*)] \quad (26)$$

$$=\mathbb{P}_n\varphi_{\overline{a}}(O; \eta_2^*) - P\varphi_{\overline{a}}(O; \eta_2^*) + \underbrace{P[m_2(O; \hat{\eta}_2) - m_2(O; \eta_2)]}_{\triangleq R_2(\hat{\eta}_2)} + (\mathbb{P}_n - P)[m_2(O; \hat{\eta}_2) - m_2(O; \eta_2^*)] \quad (27)$$

In equation (27), the last term is an empirical process term that will be $o_p(n^{-1/2})$ either when parametric models are used to estimate the nuisance functions or when cross-fitting is used to induce independence between $\hat{\eta}_2$ and O (Chernozhukov *et al.* 2018). Thus it remains to analyze the first three terms: $\mathbb{P}_n\varphi_{\overline{a}}(O; \eta_2^*)$, $P\varphi_{\overline{a}}(O; \eta_2^*)$, and $R_2(\hat{\eta}_2) = P[m_2(O; \hat{\eta}_2) - m_2(O; \eta_2)]$.

First, from our proofs in Section D.1, we know that when $\eta_2^* = (\pi_0, \dots \pi_{k'-1}, \pi_{k'}^*, \dots \pi_K^*, \mu_0^*, \dots \mu_{k'-1}^*, \mu_{k'}, \dots \mu_K)$ for some k', i.e., when the first k' treatment models and the last $K - k' + 1$ outcome models are consistently estimated, $P\varphi_{\overline{a}}(O; \eta_2^*) = 0$. Because in this case, $\mathbb{P}_n\varphi_{\overline{a}}(O; \eta_2^*) \xrightarrow{p} P\varphi_{\overline{a}}(O; \eta_2^*) = 0$ by the law of large numbers, it suffices to show $R_2(\hat{\eta}_2) = o_p(1)$ to establish the consistency of $\hat{\theta}_{\overline{a}}^{\mathrm{eif2}}$. Second, in the case where $\eta_2^* = \eta_2$, i.e., when all of the $2(K+1)$ nuisance functions are consistently estimated, the first two terms in equation (27) reduces to $\mathbb{P}_n\varphi_{\overline{a}}(O; \eta_2)$, i.e., the sample average of the efficient influence function, which has an asymptotic variance of $\mathbb{E}[(\varphi_{\overline{a}}(O))^2]$. Thus, in this case, $\hat{\theta}_{\overline{a}}^{\mathrm{eif2}}$ will be asymptotically normal and semiparametric efficient as long as $R_2(\hat{\eta}_2) = o_p(n^{-1/2})$.

To analyze $R_2(\hat{\eta}_2)$, we first observe that

$$P[m_2(O;\tilde{\eta}_2)] = P\Big[\frac{\mathbb{I}(A=a_{K+1})}{\hat{\pi}_0(a_1|X)}\Big(\prod_{j=1}^{K}\frac{\hat{\pi}_j(a_j|X,\overline{M}_j)}{\hat{\pi}_j(a_{j+1}|X,\overline{M}_j)}\Big)\big(Y-\mu_K(X,\overline{M}_K)\big)$$

$$+\sum_{k=1}^{K}\frac{\mathbb{I}(A=a_k)}{\hat{\pi}_0(a_1|X)}\Big(\prod_{j=1}^{k-1}\frac{\hat{\pi}_j(a_j|X,\overline{M}_j)}{\hat{\pi}_j(a_{j+1}|X,\overline{M}_j)}\Big)\big(\mu_k(X,\overline{M}_k)-\mu_{k-1}(X,\overline{M}_{k-1})\big)+\mu_0(X)\Big]$$

$$= P\Big[\frac{\pi_0(a_{K+1}|X,\overline{M}_K)}{\hat{\pi}_0(a_1|X)}\Big(\prod_{j=1}^{K}\frac{\hat{\pi}_j(a_j|X,\overline{M}_j)}{\hat{\pi}_j(a_{j+1}|X,\overline{M}_j)}\Big)\underbrace{\mathbb{E}\big[Y-\mu_K(X,\overline{M}_K)\big|X,A=a_{K+1},\overline{M}_K\big]}_{=0}$$

$$+\sum_{k=1}^{K}\frac{\pi_0(a_k|X,\overline{M}_{k-1})}{\hat{\pi}_0(a_1|X)}\Big(\prod_{j=1}^{k-1}\frac{\hat{\pi}_j(a_j|X,\overline{M}_j)}{\hat{\pi}_j(a_{j+1}|X,\overline{M}_j)}\Big)\underbrace{\mathbb{E}\big[\mu_k(X,\overline{M}_k)-\mu_{k-1}(X,\overline{M}_{k-1})\big|X,A=a_k,\overline{M}_{k-1}\big]}_{=0}$$

$$+\mu_0(X)\Big]$$

$$= P[\mu_0(X)]$$

$$= P[m_2(O;\eta_2)].$$

Then, by substituting $m_2(O;\tilde{\eta}_2)$ for $m_2(O;\eta_2)$ in $R_2(\hat{\eta}_2)$, rearranging terms, and applying the Cauchy-Schwartz inequality, we obtain

$$R_2(\hat{\eta}_2) = P[m_2(O;\hat{\eta}_2)-m_2(O;\tilde{\eta}_2)]$$

$$= P\Big[\frac{\big(\hat{\pi}_0(a_1|X)-\pi_0(a_1|X)\big)\big(\hat{\mu}_0(X)-\mu_0(X)\big)}{\hat{\pi}_0(a_1|X)}\Big]$$

$$+\sum_{k=1}^{K}P\Big[\Big(\prod_{j=1}^{k}\frac{\hat{\pi}_j(a_j|X,\overline{M}_j)}{\hat{\pi}_j(a_{j+1}|X,\overline{M}_j)}\Big)\frac{\big(\hat{\pi}_k(a_{k+1}|X,\overline{M}_k)-\pi_k(a_{k+1}|X,\overline{M}_k)\big)\big(\hat{\mu}_k(X,\overline{M}_k)-\mu_k(X,\overline{M}_k)\big)}{\hat{\pi}_0(a_1|X)}\Big]$$

$$-\sum_{k=1}^{K}P\Big[\Big(\prod_{j=1}^{k-1}\frac{\hat{\pi}_j(a_j|X,\overline{M}_j)}{\hat{\pi}_j(a_{j+1}|X,\overline{M}_j)}\Big)\frac{\big(\hat{\pi}_k(a_k|X,\overline{M}_k)-\pi_k(a_k|X,\overline{M}_k)\big)\big(\hat{\mu}_k(X,\overline{M}_k)-\mu_k(X,\overline{M}_k)\big)}{\hat{\pi}_0(a_1|X)}\Big]$$

$$=\sum_{k=0}^{K}O_p\big(\|\hat{\pi}_k(a_{k+1}|X,\overline{M}_k)-\pi_k(a_{k+1}|X,\overline{M}_k)\|\cdot\|\hat{\mu}_k(X,\overline{M}_k)-\mu_k(X,\overline{M}_k)\|\big)$$

$$+\sum_{k=1}^{K}O_p\big(\|\hat{\pi}_k(a_k|X,\overline{M}_k)-\pi_k(a_k|X,\overline{M}_k)\|\cdot\|\hat{\mu}_k(X,\overline{M}_k)-\mu_k(X,\overline{M}_k)\|\big) \tag{28}$$

where $\|g\| = (\int g^T g\,dP)^{1/2}$. The last equality uses the positivity assumption that $\hat{\pi}_k(a|X,\overline{M}_k)$ is bounded away from zero for all k and a. Thus, assuming that the empirical process term is on the order of $o_p(n^{-1/2})$ (e.g., via cross-fitting), we can write equation (27) as

$$\hat{\theta}_{\overline{a}}^{\text{eif2}}-\theta_{\overline{a}} = \mathbb{P}_n\varphi_{\overline{a}}(O;\eta_2^*)-P\varphi_{\overline{a}}(O;\eta_2^*)+\sum_{k=0}^{K}O_p(\|\hat{\pi}_k-\pi_k\|)\cdot O_p(\|\hat{\mu}_k-\mu_k\|)+o_p(n^{-1/2}),$$

where $\pi_k = (\pi_k(0|X, \overline{M}_k), \pi_k(1|X, \overline{M}_k))^T$. Clearly, when there exists a k' such that the first k' treatment models and the last $K - k' + 1$ outcome models are consistently estimated, $\sum_{k=0}^{K} O_p(\|\hat{\pi}_k - \pi_k\|) \cdot O_p(\|\hat{\mu}_k - \mu_k\|) = o_p(1)$. In this case, since $\mathbb{P}_n \varphi_{\overline{a}}(O; \eta_2^*) - P \varphi_{\overline{a}}(O; \eta_2^*) = \mathbb{P}_n \varphi_{\overline{a}}(O; \eta_2^*) = o_p(1)$, $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ is consistent. When $\eta_2^* = \eta_2$ and $\sum_{k=0}^{K} O_p(\|\hat{\pi}_k - \pi_k\|) \cdot O_p(\|\hat{\mu}_k - \mu_k\|) = o_p(n^{-1/2})$, we have $\hat{\theta}_{\overline{a}}^{\text{eif}_2} - \theta_{\overline{a}} = \mathbb{P}_n \varphi_{\overline{a}}(O; \eta_2) + o_p(n^{-1/2})$, implying that $\hat{\theta}_{\overline{a}}^{\text{eif}_2}$ is CAN and semiparametric efficient. If the nuisance functions are estimated via parametric models and their parameter estimates are all $\sqrt{n}$-consistent, $\sum_{k=0}^{K} O_p(\|\hat{\pi}_k - \pi_k\|) \cdot O_p(\|\hat{\mu}_k - \mu_k\|) = \sum_{k=0}^{K} O_p(n^{-1/2}) \cdot O_p(n^{-1/2}) = o_p(n^{-1/2})$, hence the second part of Theorem 3.

Now let us consider $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$. In a similar vein, we can write $\hat{\theta}_{\overline{a}}^{\text{eif}_1} - \theta_{\overline{a}}$ as

$$\hat{\theta}_{\overline{a}}^{\text{eif}_1} - \theta_{\overline{a}} = \mathbb{P}_n \varphi_{\overline{a}}(O; \eta_1^*) - P \varphi_{\overline{a}}(O; \eta_1^*) + \underbrace{\sum_{k=0}^{K} O_p(\|\check{\pi}_k - \pi_k\|) \cdot O_p(\|\check{\mu}_k - \mu_k\|)}_{\triangleq R_2(\hat{\eta}_1)} + o_p(n^{-1/2}),$$

where $\check{\pi}_k$ and $\check{\mu}_k$ are estimates of π_k and μ_k constructed from $\hat{\eta}_1 = \{\hat{\pi}_0, \hat{f}_1, \dots \hat{f}_K, \hat{\mu}_K\}$. First, from our proofs in Section D.1, we know that when $K + 1$ of the $K + 2$ nuisance functions in η_1 are consistently estimated, $P \varphi_{\overline{a}}(O; \eta_1^*) = 0$. Since in this case $\mathbb{P}_n \varphi_{\overline{a}}(O; \eta_1^*) \xrightarrow{p} P \varphi_{\overline{a}}(O; \eta_1^*) = 0$, it suffices to show $R_2(\hat{\eta}_1) = o_p(1)$ to establish the consistency of $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$. Second, in the case where $\eta_1^* = \eta_1$, i.e., when all of the $K + 2$ nuisance functions are consistently estimated, the first two terms in equation (27) reduces to $\mathbb{P}_n \varphi_{\overline{a}}(O; \eta_1)$, i.e., the sample average of the efficient influence function, which has an asymptotic variance of $\mathbb{E}[(\varphi_{\overline{a}}(O))^2]$. Thus, in this case, $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ will be asymptotically normal and semiparametric efficient as long as $R_2(\hat{\eta}_1) = o_p(n^{-1/2})$.

We first note that for any a, $\check{\pi}_k(a|X, \overline{M}_k) - \pi_k(a|X, \overline{M}_k)$ can be decomposed as

$$\check{\pi}_k(a|X, \overline{M}_k) - \pi_k(a|X, \overline{M}_k)$$
$$= \frac{\hat{p}(\overline{M}_k|X, a)\hat{\pi}_0(a|X)}{\sum_{a'} \hat{p}(\overline{M}_k|X, a')\hat{\pi}_0(a'|X)} - \frac{p(\overline{M}_k|X, a)\pi_0(a|X)}{\sum_{a'} p(\overline{M}_k|X, a')\pi_0(a'|X)}$$
$$= \underbrace{\frac{\hat{p}(\overline{M}_k|X, a)(\hat{\pi}_0(a|X) - \pi_0(a|X))}{\sum_{a'} \hat{p}(\overline{M}_k|X, a')\hat{\pi}_0(a'|X)}}_{\triangleq \Delta_\pi^1} + \underbrace{\frac{(\hat{p}(\overline{M}_k|X, a) - p(\overline{M}_k|X, a))\pi_0(a|X)}{\sum_{a'} \hat{p}(\overline{M}_k|X, a')\hat{\pi}_0(a'|X)}}_{\triangleq \Delta_\pi^2} +$$
$$\underbrace{\frac{p(\overline{M}_k|X, a)\pi_0(a|X)\sum_{a'}(p(\overline{M}_k|X, a')\pi_0(a'|X) - \hat{p}(\overline{M}_k|X, a')\hat{\pi}_0(a'|X))}{\sum_{a'} \hat{p}(\overline{M}_k|X, a')\hat{\pi}_0(a'|X) \sum_{a'} p(\overline{M}_k|X, a')\pi_0(a'|X)}}_{\triangleq \Delta_\pi^3}.$$

By the positivity assumption, we have $\|\Delta_\pi^1\| = O_p(\|\hat{\pi}_0 - \pi_0\|)$. Using the factorization $p(\overline{M}_k|X, a) = \prod_{j=1}^{k} p(M_j|X, a, \overline{M}_{j-1})$, $\|\Delta_\pi^2\|$ can be expressed as

$$\|\Delta_\pi^2\| = \left\| \frac{\pi_0(a|X)\left(\prod_{j=1}^{k} \hat{f}_j(M_j|X, a, \overline{M}_{j-1}) - \prod_{j=1}^{k} f_j(M_j|X, a, \overline{M}_{j-1})\right)}{\sum_{a'} \hat{p}(\overline{M}_k|X, a')\hat{\pi}_0(a'|X)} \right\|$$

$$= \left\| \frac{\pi_0(a|X)}{\sum_{a'} \hat{p}(\overline{M}_k|X,a')\hat{\pi}_0(a'|X)} \cdot \right.$$

$$\sum_{l=1}^{k} \left(\prod_{j=1}^{l-1} \hat{f}_j(M_j|X,a,\overline{M}_{j-1}) \prod_{j=l+1}^{k} f_j(M_j|X,a,\overline{M}_{j-1}) \right) \left(\hat{f}_l(M_l|X,a,\overline{M}_{l-1}) - f_l(M_l|X,a,\overline{M}_{l-1}) \right) \Bigg\|$$

$$= \sum_{l=1}^{k} O_p(\|\hat{f}_l - f_l\|),$$

where $f_l = (f_l(M_l|X,0,\overline{M}_{l-1}), f_l(M_l|X,1,\overline{M}_{l-1}))^T$. By a similar logic, $\|\Delta_\pi^3\|$ can be written as

$$\|\Delta_\pi^3\| = O_p(\|\hat{\pi}_0 - \pi_0\|) + \sum_{l=1}^{k} O_p(\|\hat{f}_l - f_l\|).$$

In sum, we have

$$\|\check{\pi}_k - \pi_k\| = O_p(\|\hat{\pi}_0 - \pi_0\|) + \sum_{l=1}^{k} O_p(\|\hat{f}_l - f_l\|). \tag{29}$$

Now consider $\|\check{\mu}_k - \mu_k\|$. Using the fact that

$$\mu_k(x,\overline{m}_k) = \int \mu_K(x,\overline{m}_k) \left(\prod_{j=k+1}^{K} p(m_j|x,a_j,\overline{m}_{j-1}) dm_j \right),$$

we can decompose $\check{\mu}_k(x,\overline{m}_k) - \mu_k(x,\overline{m}_k)$ into

$$\check{\mu}_k(x,\overline{m}_k) - \mu_k(x,\overline{m}_k)$$

$$= \int \left(\hat{\mu}_K(x,\overline{m}_K) - \mu_K(x,\overline{m}_K) \right) \left(\prod_{j=k+1}^{K} \hat{f}_j(m_j|x,a_j,\overline{m}_{j-1}) dm_j \right)$$

$$+ \sum_{l=k+1}^{K} \int \mu_K(x,\overline{m}_K) \left(\left(\hat{f}_l(m_l|x,a_l,\overline{m}_{l-1}) - f_l(m_l|x,a_l,\overline{m}_{l-1}) \right) dm_l \right) \cdot$$

$$\left(\prod_{j=k+1}^{l-1} \hat{f}_j(m_j|x,a_j,\overline{m}_{j-1}) dm_j \right) \left(\prod_{j=l+1}^{K} f_j(m_j|x,a_j,\overline{m}_{j-1}) dm_j \right)$$

$$= \int \left(\hat{\mu}_K(x,\overline{m}_K) - \mu_K(x,\overline{m}_K) \right) \underbrace{\left(\frac{\prod_{j=k+1}^{K} \hat{f}_j(m_j|x,a_j,\overline{m}_{j-1})}{\prod_{j=k+1}^{K} f_j(m_j|x,\overline{m}_{j-1})} \right)}_{\triangleq g(x,\overline{m}_K)} \left(\prod_{j=k+1}^{K} f_j(m_j|x,\overline{m}_{j-1}) dm_j \right)$$

$$+ \sum_{l=k+1}^{K} \int \left(\hat{f}_l(m_l|x,a_l,\overline{m}_{l-1}) - f_l(m_l|x,a_l,\overline{m}_{l-1}) \right)$$

$$\underbrace{\frac{\mu_K(x,\overline{m}_K)\left(\prod_{j=k+1}^{l-1}\hat{f}_j(m_j|x,a_j,\overline{m}_{j-1})\right)\left(\prod_{j=l+1}^{K}f_j(m_j|x,a_j,\overline{m}_{j-1})\right)}{\prod_{j=k+1}^{K}f_j(m_j|x,\overline{m}_{j-1})}}_{\triangleq h_l(x,\overline{m}_K)}\left(\prod_{j=k+1}^{K}f_j(m_j|x,\overline{m}_{j-1})dm_j\right)$$

Using the notation $dP_2 = \prod_{j=k+1}^{K}f_j(m_j|x,\overline{m}_{j-1})dm_j$ and $dP_1 = dP_X(x)\cdot\prod_{j=1}^{k}f_j(m_j|x,\overline{m}_{j-1})dm_j$, we have

$$\|\breve{\mu}_k - \mu_k\|$$

$$=\Big\|\int(\hat{\mu}_K - \mu_K)g\,dP_2 + \sum_{l=k+1}^{K}\int(\hat{f}_l - f_l)h_l\,dP_2\Big\|_{P_1}$$

$$\leq\Big\|\int(\hat{\mu}_K - \mu_K)g\,dP_2\Big\|_{P_1} + \sum_{l=k+1}^{K}\Big\|\int(\hat{f}_l - f_l)h_l\,dP_2\Big\|_{P_1}$$

$$=\Big[\int\Big(\int(\hat{\mu}_K - \mu_K)g\,dP_2\Big)^2 dP_1\Big]^{1/2} + \sum_{l=k+1}^{K}\Big[\int\Big(\int(\hat{f}_l - f_l)h_l\,dP_2\Big)^2 dP_1\Big]^{1/2}$$

$$\leq\Big[\int\Big(\int(\hat{\mu}_K - \mu_K)^2 dP_2\Big)\Big(\int g^2 dP_2\Big)dP_1\Big]^{1/2} + \sum_{l=k+1}^{K}\Big[\int\Big(\int(\hat{f}_l - f_l)^2 dP_2\Big)\Big(\int h_l^2 dP_2\Big)dP_1\Big]^{1/2} \text{ (Cauchy-Schwartz)}$$

$$\leq\Big[\int(\hat{\mu}_K - \mu_K)^2 dP_2 dP_1 \cdot \Big\|\int g^2 dP_2\Big\|_{P_1,\infty}\Big]^{1/2} + \sum_{l=k+1}^{K}\Big[\int(\hat{f}_l - f_l)^2 dP_2 dP_1 \cdot \Big\|\int h_l^2 dP_2\Big\|_{P_1,\infty}\Big]^{1/2}$$

$$=O_p(\|\hat{\mu}_K - \mu_K\|) + \sum_{l=k+1}^{K}O_p(\|\hat{f}_l - f_l\|). \tag{30}$$

The last equality uses the assumption that $\mu_K(X,\overline{M}_K)$ (and hence $\int h_l^2 dP_2$) is bounded.

From equations (29)-(30), we have

$$R_2(\hat{\eta}_1) = \sum_{k=0}^{K}O_p(\|\breve{\pi}_k - \pi_k\|)\cdot O_p(\|\breve{\mu}_k - \mu_k\|)$$

$$= \sum_{k=0}^{K}\Big(O_p(\|\hat{\pi}_0 - \pi_0\|) + \sum_{l=1}^{k}O_p(\|\hat{f}_l - f_l\|)\Big)\Big(O_p(\|\hat{\mu}_K - \mu_K\|) + \sum_{l=k+1}^{K}O_p(\|\hat{f}_l - f_l\|)\Big) \tag{31}$$

Clearly, when $K+1$ of the $K+2$ nuisance functions in η_1 are consistently estimated, $R_2(\hat{\eta}_1) = o_p(1)$. In this case, since $\mathbb{P}_n\varphi_{\overline{a}}(O;\eta_1^*) - P\varphi_{\overline{a}}(O;\eta_1^*) = \mathbb{P}_n\varphi_{\overline{a}}(O;\eta_1^*) = o_p(1)$, $\hat{\theta}_{\overline{a}}^{\text{eif}_1}$ is consistent. Moreover, equation (31) suggests that $R_2(\hat{\eta}_1) = o_p(n^{-1/2})$ if $\sum_{u,v\in\hat{\eta}_1;u\neq v}r_n(u)r_n(v) = o(n^{-1/2})$. If the nuisance functions are estimated via parametric models and their parameter estimates are all $\sqrt{n}$-consistent, $R_2(\hat{\eta}_1) = \sum_{k=0}^{K}O_p(n^{-1/2})\cdot O_p(n^{-1/2}) = o_p(n^{-1/2})$, hence the first part of Theorem 3.

E   Multiply Robust Decomposition of Between-group Disparities

The multiply robust semiparametric estimators can also be used to estimate *noncausal* decompositions of between-group disparities (Fortin *et al.* 2011). For example, social scientists in the United States have a long-standing interest in decomposing the black-white income gap into components that are attributable to racial differences in various ascriptive and achieved characteristics. Using linear structural equation models, Duncan (1968) decomposed the total black-white income gap into components that reflect black-white differences in family background, academic performance (net of family background), educational attainment (net of family background and academic performance), occupational attainment (net of family background, academic performance, and educational attainment), and a "residual" component that cannot be explained by the above characteristics. Although proposed prior to Blinder (1973) and Oaxaca (1973), Duncan's decomposition can be viewed as a generalization of the Blinder-Oaxaca decomposition widely used in labor economics.

Duncan's decomposition is similar in form to equation (3), but it is defined in terms of the statistical parameters $\theta_{\overline{a}}$ rather than the causal parameters $\psi_{\overline{a}}$. Moreover, the left-hand side is now the black-white income gap rather than the average causal effect of a manipulable intervention, and, therefore, there are no pretreatment confounders. It should be noted that this decomposition is different from causal mediation analysis for a randomized trial, in which case pretreatment covariates may still be needed to adjust for potential confounding of the mediator-mediator and mediator-outcome relationships. The components associated with Duncan's decomposition, by contrast, are purely statistical parameters and should not be interpreted causally.

Consequently, in the context of decomposing between-group disparities, the functional $\theta_{\overline{0}_k,\underline{1}_{k+1}}$ can be estimated as

$$\hat{\theta}^{\mathrm{eif}_2}_{\overline{0}_k,\underline{1}_{k+1}} = \mathbb{P}_n\Big[\frac{\mathbb{I}(A=1)}{\hat{\pi}_0(0)}\frac{\hat{\pi}_k(0|\overline{M}_k)}{\hat{\pi}_k(1|\overline{M}_k)}\big(Y - \hat{\mu}_k(\overline{M}_k)\big) + \frac{\mathbb{I}(A=0)}{\hat{\pi}_0(0)}\big(\hat{\mu}_k(\overline{M}_k) - \hat{\mu}_{0,k}\big) + \hat{\mu}_{0,k}\Big], \qquad (32)$$

where $\pi_0(0) = \Pr[A = 0]$, $\mu_k(\overline{M}_k) = \mathbb{E}[Y|A = 1, \overline{M}_k]$, and $\mu_{0,k} = \mathbb{E}[\mu_k(\overline{M}_k)|A = 0]$. Since $\hat{\pi}_0(0)$ can be estimated by the sample average of $1 - A$ and $\mu_{0,k}$ the sample average of $\hat{\mu}_k(\overline{M}_k)$ among units with $A = 0$, equation (32) involves estimating only two nuisance functions: $\hat{\pi}_k(a|\overline{m}_k)$ and $\hat{\mu}_k(\overline{m}_k)$. It follows from Theorem 3 that $\hat{\theta}^{\mathrm{eif}_2}_{\overline{0}_k,\underline{1}_{k+1}}$ is now doubly robust — it is consistent if either $\hat{\pi}_k(a|\overline{m}_k)$ or $\hat{\mu}_k(\overline{m}_k)$ is consistent.

To implement the full decomposition, we need to estimate $\theta_{\overline{0}_k,\underline{1}_{k+1}}$ for each $k \in 0, 1, \dots K + 1$, i.e., estimate the vector-valued parameter $\boldsymbol{\theta}_{\mathrm{decomp}} = (\theta_{\underline{1}_1}, \theta_{0,\underline{1}_2}, \dots \theta_{\overline{0}_K,1}, \theta_{\overline{0}_{K+1}})$. Since $\theta_{\underline{1}_1}$ and $\theta_{\overline{0}_{K+1}}$ can be estimated by the sample analogs of $\mathbb{E}[Y|A = 1]$ and $\mathbb{E}[Y|A = 0]$ and $\hat{\theta}^{\mathrm{eif}_2}_{\overline{0}_k,\underline{1}_{k+1}}$ is doubly robust with respect to $\hat{\pi}_k$ and $\hat{\mu}_k$, the semiparametric estimator $\hat{\boldsymbol{\theta}}^{\mathrm{eif}_2}_{\mathrm{decomp}} = (\hat{\theta}^{\mathrm{eif}_2}_{\underline{1}_1}, \hat{\theta}^{\mathrm{eif}_2}_{0,\underline{1}_2}, \dots \hat{\theta}^{\mathrm{eif}_2}_{\overline{0}_K,1}, \hat{\theta}^{\mathrm{eif}_2}_{\overline{0}_{K+1}})$ is 2^K-robust: it is consistent if for each $k \in [K]$, either $\hat{\pi}_k$ or $\hat{\mu}_k$ is consistent. Note that in this case, the functions $\mu_k(\overline{M}_k) = \mathbb{E}[Y|A = 1, \overline{M}_k]$ are not estimated iteratively, but separately for each k.

Corollary 5. *Define $\hat{\boldsymbol{\theta}}^{\mathrm{eif}_2}_{\mathrm{decomp}} = (\hat{\theta}^{\mathrm{eif}_2}_{\underline{1}_1}, \hat{\theta}^{\mathrm{eif}_2}_{0,\underline{1}_2}, \dots \hat{\theta}^{\mathrm{eif}_2}_{\overline{0}_K,1}, \hat{\theta}^{\mathrm{eif}_2}_{\overline{0}_{K+1}})$. Suppose $X = \varnothing$, and that all assump-*

tions required for Theorem 4 hold. When the nuisance functions $(\hat{\pi}_1, \ldots \hat{\pi}_K, \hat{\mu}_1, \ldots \hat{\mu}_K)$ are estimated via parametric models, $\hat{\boldsymbol{\theta}}_{\text{decomp}}^{\text{eif}_2}$ is CAN if for each $k \in [K]$, either $\hat{\pi}_k$ or $\hat{\mu}_k$ is correctly specified and its estimates are $\sqrt{n}$-consistent. $\hat{\boldsymbol{\theta}}_{\text{decomp}}^{\text{eif}_2}$ is semiparametric efficient if all of the nuisance functions are correctly specified and their parameter estimates $\sqrt{n}$-consistent. When the nuisance functions are estimated via data-adaptive methods and cross-fitting, $\hat{\boldsymbol{\theta}}_{\text{decomp}}^{\text{eif}_2}$ is semiparametric efficient if all of the nuisance functions are consistently estimated and $\sum_{k=1}^{K} r_n(\hat{\pi}_k) r_n(\hat{\mu}_k) = o(n^{-1/2})$.

F   Additional Details of the Simulation Study

The variables $X_1, X_2, X_3, X_4, A, M_1, M_2, Y$ in the simulation study are generated via the following model:

$$(U_1, U_2, U_3, U_{XY}) \sim N(0, I_4),$$
$$X_j \sim N((U_1, U_2, U_3, U_{XY})\beta_{X_j}, 1), \quad j = 1, 2, 3, 4,$$
$$A \sim \text{Bernoulli}\big(\text{logit}^{-1}[(1, X_1, X_2, X_3, X_4)\beta_A]\big),$$
$$M_1 \sim N\big((1, X_1, X_2, X_3, X_4, A)\beta_{M_1}, 1\big),$$
$$M_2 \sim N\big((1, X_1, X_2, X_3, X_4, A, M_1)\beta_{M_2}, 1\big),$$
$$Y \sim N\big((1, U_{XY}, X_1, X_2, X_3, X_4, A, M_1, M_2)\beta_Y, 1\big).$$

The coefficients $\beta_{X_j} (1 \le j \le 4)$ and β_Y are drawn from Uniform$[-1, 1]$, the coefficients β_A are drawn from Uniform$[-0.5, 0.5]$, and the coefficients β_{M_1} and β_{M_2} are drawn from Uniform$[0, 0.5]$. Specifically,

$$\beta_{X_1} = (0.77, -0.86, 0.35, 0.88),$$
$$\beta_{X_2} = (-0.99, -0.72, -0.1, 0.54),$$
$$\beta_{X_3} = (-0.74, 0.1, 0.91, 0.46),$$
$$\beta_{X_4} = (-0.21, -0.43, -0.21, -0.7),$$
$$\beta_A = (-0.36, -0.08, -0.06, 0.4, -0.14),$$
$$\beta_{M_1} = (0, 0.3, 0.42, 0.48, 0.28, 0.41),$$
$$\beta_{M_2} = (0.04, 0.2, 0.09, 0.12, 0.39, 0.34, 0.24),$$
$$\beta_Y = (-0.27, -0.1, 0.25, 0.2, -0.08, 0.78, 0.76, -0.4, 0.96).$$

It can be shown that under the above model, the six nuisance functions $\pi_0(a|x)$, $\pi_1(a|x, m_1)$, $\pi_2(a|x, m_1, m_2)$, $\mu_0(x)$, $\mu_1(x, m_1)$, and $\mu_2(x, m_1, m_2)$ for any $\theta_{a_1, a_2, a}$ can be consistently estimated via the following GLMs:

$$\pi_0(1|X) = \text{logit}^{-1}[(1, X_1, X_2, X_3, X_4)\gamma_0],$$
$$\pi_1(1|X, M_1) = \text{logit}^{-1}[(1, X_1, X_2, X_3, X_4, M_1)\gamma_1],$$

$$\pi_2(1|X, M_1, M_2) = \text{logit}^{-1}[(1, X_1, X_2, X_3, X_4, M_1, M_2)\gamma_2],$$

$$\mathbb{E}[Y|X, A, M_1, M_2] = (1, X_1, X_2, X_3, X_4, A, M_1, M_2)\alpha_2, \quad \mu_2(X, M_1, M_2) = \mathbb{E}[Y|X, A = a, M_1, M_2],$$

$$\mathbb{E}[\mu_2(X, M_1, M_2)|X, A, M_1] = (1, X_1, X_2, X_3, X_4, A, M_1)\alpha_1, \quad \mu_1(X, M_1) = \mathbb{E}[\mu_2(X, M_1, M_2)|X, A = a_2, M_1],$$

$$\mathbb{E}[\mu_1(X, M_1)|X, A] = (1, X_1, X_2, X_3, X_4, A)\alpha_0, \quad \mu_0(X) = \mathbb{E}[\mu_1(X, M_1)|X, A = a_1].$$

To demonstrate the multiple robustness of the EIF-based estimators, we use a set of "false co-variates" $Z = \left(X_1, e^{X_2/2}, (X_3/X_1)^{1/3}, X_4/(e^{X_1/2} + 1)\right)$ to fit a misspecified model for each of the nuisance functions:

$$\pi_0(1|Z) = \text{logit}^{-1}[(1, Z_1, Z_2, Z_3, Z_4)\tilde{\gamma}_0],$$

$$\pi_1(1|Z, M_1) = \text{logit}^{-1}[(1, Z_1, Z_2, Z_3, Z_4, M_1)\tilde{\gamma}_1],$$

$$\pi_2(1|Z, M_1, M_2) = \text{logit}^{-1}[(1, Z_1, Z_2, Z_3, Z_4, M_1, M_2)\tilde{\gamma}_2],$$

$$\mathbb{E}[Y|Z, A, M_1, M_2] = (1, Z_1, Z_2, Z_3, Z_4, A, M_1, M_2)\tilde{\alpha}_2, \quad \mu_2(Z, M_1, M_2) = \mathbb{E}[Y|Z, A = a, M_1, M_2],$$

$$\mathbb{E}[\mu_2(Z, M_1, M_2)|Z, A, M_1] = (1, Z_1, Z_2, Z_3, Z_4, A, M_1)\tilde{\alpha}_1, \quad \mu_1(Z, M_1) = \mathbb{E}[\mu_2(Z, M_1, M_2)|Z, A = a_2, M_1],$$

$$\mathbb{E}[\mu_1(Z, M_1)|Z, A] = (1, Z_1, Z_2, Z_3, Z_4, A)\tilde{\alpha}_0, \quad \mu_0(Z) = \mathbb{E}[\mu_1(Z, M_1)|Z, A = a_1].$$

Each of the five cases described in Section 5 reflects a combination of estimated nuisance functions from these correctly and incorrectly specified models. For example, in case (a), all parametric estimators of cPSE_{M_2} use correctly specified models for $\pi_0(1|x), \pi_1(1|x, m_1), \pi_2(1|x, m_1, m_2)$ and incorrectly specified models for $\mu_0(x)$, $\mu_1(x, m_1)$, and $\mu_2(x, m_1, m_2)$.

G   Additional Details of the NLSY97 Data

The data source for the empirical example comes from the National Longitudinal Survey of Youth, 1997 cohort (NLSY97). The NLSY97 began with a nationally representative sample of 8,984 men and women residing in the United States at ages 12-17 in 1997. These individuals were interviewed annually through 2011 and biennially thereafter. Table G1 reports the sample means of the pretreatment covariates X, the mediators M_1 and M_2, and the outcome Y described in the main text, both overall and separately for treated and untreated units (i.e., college goers and non-college-goers). Parental education is measured using mother's years of schooling; when mother's years of schooling is unavailable, it is measured using father's years of schooling. Parental income is measured as the average annual parental income from 1997 to 2001. The mediator M_2, which gauges civic and political interest, includes four components: volunteerism, community participation, donation activity, and political interest. Volunteerism represents the respondent's self-reported frequency of volunteering work over the past 12 months (1: None; 2: 1 - 4 times; 3: 5 - 11 times; 4: 12 times or more). Community participation represents the respondent's self-reported frequency of attending a meeting or event for a political, environmental, or community group (1: None; 2: 1 - 4 times; 3: 5 - 11 times; 4: 12 times or more). Donation activity is a dichotomous variable indicating whether

the respondent donated money to a political, environmental, or community cause over the past 12 months. Political interest represents the respondent's self-reported frequency of following government and public affairs (1: hardly at all; 2: only now and then; 3: some of the time; 4: most of the time). Volunteerism, community participation, and donation activity were measured in 2007, and political interest was measured in both 2008 and 2010. For simplicity, we use the average of the 2008 and 2010 measures of political interest in our analyses (Treating them as separate variables leads to almost identical results).

To gain a basic understanding of the treatment-mediator and mediator-outcome relationships in this dataset, we fit a linear regression model for each component of the mediators and for the outcome given their antecedent variables (including the pretreatment covariates). These models, if correctly specified, will identify the causal effects of A on M_1, (A, M_1) on M_2, and (A, M_1, M_2) on Y under the conditional independence assumptions described in Section 2.1. The coefficients of these regression models are shown in Table G2. The first column indicates a substantively strong and statistically significant effect of college attendance on log earnings: adjusting for pretreatment covariates, attending college by age 20 is associated with a 44.3 percent increase ($e^{0.367} - 1 = 0.443$) in estimated earnings from 2006 to 2009. The next four columns suggest that the direct effects of college attendance on volunteerism, community participation, and donation activity (i.e., $A \rightarrow M_2$) are relatively small and not statistically significant. The estimated direct effect of college attendance on political interest, by contrast, is much larger and statistically significant. The last column shows statistically significant effects of volunteerism, community participation, and political interest on voting (at the $p < 0.05$ level). The estimated effect of political interest is particularly strong: a one unit increase in the four-point scale of political interest is associated with a 14.8 percentage point increase in the estimated probability of voting. The coefficient of college attendance in the last model can be interpreted as the direct effect of college on voting (i.e., $A \rightarrow Y$), i.e., the effect that operates neither through economic status nor through civic and political interest. The estimate, 11.7 percentage points, is comparable to our semiparametric estimates reported in the main text.

Table G1: Overall and group-specific means in pretreatment covariates, mediators, and outcome.

		Overall	Non-College-Goers	College Goers
	Age at 1997	15.98	16.02	15.96
	Female	0.5	0.42	0.55
	Black	0.16	0.22	0.13
	Hispanic	0.12	0.15	0.1
	Parental Education	13.08	12.05	13.71
	Parental Income	86,520	60,706	102,568
	Parental Assets	119,242	62,573	154,550
	Lived with Both Biological Parents	0.53	0.39	0.62
	Presence of a Father Figure	0.76	0.68	0.8
	Lived in Rural Area	0.27	0.29	0.26
	Lived in the South	0.37	0.39	0.35
	ASVAB Percentile Score	53.4	37.26	62.72
	High School GPA	2.9	2.5	3.16
Pretreatment	Substance Use Index	1.36	1.56	1.23
Covariates	Delinquency Index	1.54	2.06	1.22
(X)	Had Children by Age 18	0.06	0.11	0.02
	75%+ of Peers Expected College	0.56	0.41	0.66
	90%+ of Peers Expected College	0.19	0.12	0.24
	Property Ever Stolen at School	0.24	0.27	0.22
	Ever Threatened at School	0.19	0.27	0.14
	Ever in a Fight at School	0.12	0.18	0.08
Mediator M_1	Average Earnings in 2006-2009	33,600	25,082	38,899
	Volunteerism	1.57	1.46	1.64
	Community Participation	1.26	1.17	1.32
Mediator M_2	Donation Activity	0.3	0.22	0.35
	Political Interest	2.63	2.34	2.81
Outcome (Y)	Voted in the 2010 General Election	0.45	0.3	0.54
Sample Size		2,976	1,240	1,736

Note: All statistics are calculated using NLSY97 sampling weights.

Table G2: Regression models for the mediators and the outcome.

	M_1	M_2				Y
	Log Earnings	Volunteerism	Community Participation	Donation Activity	Political Interest	Voting
College Attendance	0.367 (0.055)	0.038 (0.046)	0.039 (0.028)	0.036 (0.023)	0.259 (0.046)	0.117 (0.023)
Log Earnings		0.001 (0.017)	0.008 (0.011)	0.036 (0.009)	0.050 (0.016)	0.016 (0.009)
Volunteerism						0.028 (0.013)
Community Participation						0.041 (0.019)
Donation Activity						-0.007 (0.024)
Political Interest						0.148 (0.010)

Note: Regression coefficients for the pretreatment covariates are omitted. Numbers in parentheses are heteroskedasticity-robust standard errors, which are adjusted for multiple imputation via Rubin's (1987) method.