Proximal Causal Inference for Complex Longitudinal Studies

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Summary. A standard assumption for causal inference about the joint effects of time-varying treatment is that one has measured sufficient covariates to ensure that within covariate strata, subjects are exchangeable across observed treatment values, also known as “sequential randomization assumption (SRA)”. SRA is often criticized as it requires one to accurately measure all confounders. Realistically, measured covariates can rarely capture all confounders with certainty. Often covariate measurements are at best proxies of confounders, thus invalidating inferences under SRA. In this paper, we extend the proximal causal inference (PCI) framework of Miao et al. (2018) to the longitudinal setting under a semiparametric marginal structural mean model (MSMM). PCI offers an opportunity to learn about joint causal effects in settings where SRA based on measured time-varying covariates fails, by formally accounting for the covariate measurements as imperfect proxies of underlying confounding mechanisms. We establish nonparametric identification with a pair of time-varying proxies and provide a corresponding characterization of regular and asymptotically linear estimators of the parameter indexing the MSMM, including a rich class of doubly robust estimators, and establish the corresponding semiparametric efficiency bound for the MSMM. Extensive simulation studies and a data application illustrate the finite sample behavior of proposed methods.

Keywords: Proximal causal inference; Marginal structural mean model; Unmeasured confounding; Semiparametric theory; Double robustness; Longitudinal data.

1. Introduction

A common assumption for causal inference from observational longitudinal data is the so-called “sequential randomization assumption (SRA)” (Robins, 1986, 1987, 1997, 1998, 1999), which states that at each follow-up time, one has measured a sufficiently rich set of covariates to ensure that conditional on covariate and treatment history, subjects are exchangeable across observed treatment values received at that time point. This
fundamental assumption is inherently untestable empirically, without introducing a different untestable assumption, and therefore must be taken on faith even with substantial subject matter knowledge at hand. For this reason, SRA is often the subject of much skepticism, mainly because it hinges on an assumed ability of the investigator to accurately measure covariates relevant to the various confounding mechanisms potentially present in the observational study. Realistically, confounding mechanisms can rarely if ever, be learned with certainty from measured covariates. Therefore, practically in a given observational study, one can at most hope that covariate measurements are proxies of the true underlying confounding mechanism. Such acknowledgement invalidates any causal claim made on the basis of SRA.

1.1. Proximal Causal Inference Framework

Instead of relying on SRA on the basis of measured covariates, proximal causal inference essentially requires that the analyst has measured covariates, that can be classified into three bucket types: 1) variables that may be common causes of the treatment and outcome variables; 2) potential treatment-inducing confounding proxies; and 3) potential outcome-inducing confounding proxies. A proxy of type 2) is a potential cause of the treatment which is related with the outcome only through an unmeasured common cause for which the variable is a proxy; while a proxy of type 3) is a potential cause of the outcome which is related with the treatment only through an unmeasured common cause for which the variable is a proxy. Proxies that are neither causes of treatment or outcome variables can belong to either bucket type 2) or 3). An illustration of proxies of types 1) - 3) is given for a simple point exposure case in Figure 1.

Fig. 1. Directed Acyclic Graphs illustrating treatment- and outcome-inducing proxies in a simple point exposure case, where we temporarily term $A$ as the treatment, $Y$ as the outcome, $X$ as the type 1) proxy, $Z$ as the type 2) proxy, $W$ as the type 3) proxy, $U$, $U_1$, $U_2$, $U_3$ as some unmeasured confounders.

Negative control treatment and outcome variables form a prominent class of proxies that has in recent years received growing interest; e.g. see Lipsitch et al. (2010); Kuroki
With the exception of Tchetgen Tchetgen et al. (2020), prior literature on proxies has largely focused on point exposure studies and not considered joint effects of longitudinal treatments. The current paper builds on initial results obtained in Tchetgen Tchetgen et al. (2020) and like the latter, departs from the current practice of assuming that sequential randomization can be attained upon adjusting for measured time-varying covariates. Instead, we leverage an investigator’s ability to classify measured time varying covariates as proxies of types 1), 2) or 3) of unmeasured time-varying factors that would in principle suffice to account for time-varying confounding. This condition is formalized using the potential outcomes framework in Section 2.

Here we briefly introduce the data application we will later analyze, which we use throughout as a running example; additional examples of longitudinal proxies are discussed in supplementary material, also see Tchetgen Tchetgen et al. (2020). In this paper, we aim to evaluate the joint causal effects of the disease-modifying anti-rheumatic therapy Methotrexate (MTX) over time among patients with rheumatoid arthritis (RA). The outcome is the average number of tender joints at end of follow-up, a well-established measure of disease progression. Although prior studies have established the effectiveness of MTX against premature mortality in RA patients (Choi et al., 2002), prior analyses relied on SRA and therefore may be susceptible to bias due to residual confounding of time-varying use of MTX by a patient’s evolving health status and her potential health-seeking behavior. Fortunately, the available data include important covariates known to be associated with both MTX uptake and disease progression, including demographic, clinical, laboratory, other medication use, and self-reported health status updated over time. Among measured covariates, RA activity measures such as health assessment questionnaire, number of tender joints, patient’s global assessment, and erythrocyte sedimentation rate stand out as likely subject to reporting or measurement error and therefore may be viewed as good candidate proxies of a patient’s underlying state of recent disease progression at the source of confounding. Such proxies seldom constitute a common cause of both treatment allocation (MTX use) and disease progression (increased number of tender joints), but may be strongly associated with both treatment and outcome variables to the extent that they share an unmeasured common cause corresponding to the patient’s underlying health status and her inherent health-seeking behavior (e.g. health assessment questionnaire, being a measure for quality of life, is a proxy of underlying health status). Thus, such variables provide a candidate set of proxies of type 2) and 3) as we argue throughout the paper and leverage in Section 6 in order to obtain more credible causal estimates of the joint effects of MTX on disease progression.

1.2. Related Literature and Our Contributions

As mentioned in the previous section, the proximal causal inference framework is closely related to recent literature on the use of negative control variables to identify and sometimes mitigate confounding bias in the analysis of observational data, see Lipsitch et al. (2010); Kuroki and Pearl (2014); Miao et al. (2018); Shi et al. (2020); Shi et al. (2020). Initial results on point identification of causal effects leveraging negative control variables relied on fairly restrictive assumptions such as linear models for the outcome and unmeasured confounding variables (Flanders et al., 2011; Gagnon-Bartsch and Speed,
A. Ying, W. Miao, X. Shi and E.J. Tchetgen Tchetgen (2012; Flanders et al., 2017; Wang et al., 2017), rank preservation (Tchetgen Tchetgen, 2014), monotonicity (Sofer et al., 2016), or categorical unmeasured confounders (Shi et al., 2020). Miao et al. (2018) were first to establish sufficient conditions for nonparametric identification of causal effects using a pair of proxies (including negative control variables) in the point treatment setting.

Building upon Miao et al. (2018), recently Tchetgen Tchetgen et al. (2020) introduced a potential outcome framework for proximal causal inference, which offers an opportunity to learn about causal effects in point treatment or time-varying treatment settings where the assumption of no unmeasured confounding or sequential randomization on the basis of measured covariates fails. In their work, identification hinges on a longitudinal generalization of Miao et al. (2018), which relies on an assumption that certain Fredholm integral equations of the first kind involving the observed outcome process, admit a solution. For estimation and inference, Tchetgen Tchetgen et al. (2020) focused primarily on so-called proximal g-computation, a generalization of Robins’ g-computation algorithm which may be viewed essentially as a maximum likelihood estimator, requiring a correctly specified model restricting the observed data joint distribution. Notably, they propose a proximal recursive two-stage least squares algorithm for point and time-varying treatments. The algorithm remains consistent provided a key linear model restricting the observed data distribution for the outcome holds, even if a linear model restricting the distribution of the time-varying proxies is incorrect. However, recursive two-stage least squares fails to be consistent if the linear outcome model is misspecified. In the point treatment case, Cui et al. (2020) proposed an alternative set of conditions for nonparametric proximal identification of the average treatment effect and effect on the treated under the assumption that a certain Fredholm integral equation of the first kind involving the treatment data generating mechanism admits a solution. They also developed semiparametric theory for proximal estimation of the average treatment effect (and the treatment effect for the treated), including efficiency bounds for key semiparametric models of interest and characterized proximal doubly robust and locally efficient estimators of the average treatment effect. Deaner (2020) proposed identification results of the so-called “conditional average structural function” (CASF), thus independently establishing identification conditions for the effect of treatment on the treated in the case of point exposure. For longitudinal data, Deaner (2020) leveraged a Markov condition that lagged treatments have a null causal effect on the outcome. Importantly, unlike Tchetgen Tchetgen et al. (2020) who avoid the assumption that past treatments do not have a direct effect on future outcomes, Deaner’s Markov conditions essentially reduce a potentially complex longitudinal study involving time-varying treatments, into a series of point exposure studies with past treatment and outcome variables providing a rich source of potential proxies. Estimation in Deaner (2020) is performed using a penalized sieve minimum distance estimator for the outcome process. Tenen Holtz et al. (2020) recently investigated proximal identification in off-policy evaluation for time series, where similar to Deaner (2020) they leverage Markov restrictions to generate proxies.

In this paper, we aim to develop proximal causal inference and semiparametric theory for complex longitudinal studies when SRA fails to hold due to unmeasured time-varying confounding. Notably, as mentioned above, similar to Tchetgen Tchetgen et al. (2020), we do not impose the Markov condition of Deaner (2020); Tenen Holtz et al. (2020)
on the effect of lagged treatments, and thus, we allow time-varying confounders (both measured and unmeasured) to mediate the causal effects of past treatment, a widely recognized challenge of complex longitudinal studies routinely encountered in health and social sciences. In this vein, we aim to make inferences about the parameters indexing a marginal structural mean model (MSMM) (Robins, 1998, 1999, 2000; Robins et al., 2000), a well-established class of counterfactual models for the joint causal effects of time-varying treatments subject to time-varying confounding. In recent work, Tchetgen Tchetgen et al. (2020) gave sufficient conditions for proximal nonparametric identification of the joint effects of time-varying treatments, therefore establishing that one could in principle, sample size permitting, estimate saturated MSMs using the proposed proximal framework, simultaneously accounting for measured and unmeasured time-varying confounding. Their results which we briefly review in the next sections is based on so-called outcome confounding bridge functions, a natural extension of Robins’ foundational g-formula to the proximal framework. In this paper, we further this line of work by proposing an alternative identification result via the so-called treatment confounding bridge functions, a longitudinal generalization of an approach proposed in Cui et al. (2020) in the point treatment setting. A major contribution of the paper is to provide a general semiparametric theory for proximal inference about MSMM parameters in longitudinal settings leveraging time-varying proxies. Specifically, we derive a rich class of estimators including proximal outcome regression (POR) estimators, proximal inverse probability weighted (IPW) estimators, and proximal doubly robust (PDR) estimators, which extend existing OR estimators, IPW estimators, and DR estimators derived under SRA (Robins, 1998) and generalize Cui et al. (2020)’s semiparametric estimators to the longitudinal setting. Furthermore, we establish the semiparametric efficiency bound for the parameters of an MSMM assuming the observed data distribution is otherwise unrestricted, and we provide a one-step update estimator which is locally efficient in the sense that it attains the efficiency bound at the intersection submodel where all posited models are correctly specified. We emphasize that the contributions made in this paper are non-trivial developments that extend the proximal causal inference framework to one of the most challenging settings encountered in epidemiology and related sciences: complex longitudinal studies with time-varying treatment and, both measured and unmeasured time-varying confounders potentially affected by prior treatment.

Thus, our paper contributes to the growing literature on the identification and inference of MSMM parameters under endogeneity. Recently, Tchetgen Tchetgen et al. (2018) developed an instrumental variables approach to identify and estimate MSM parameters without SRA (Cui and Tchetgen Tchetgen, 2021; Michael et al., 2020). A key assumption in their work entails an “independent compliance type”, which rules out any additive interaction between instrument and unmeasured confounders in a longitudinal model for the treatment process. No such restriction is needed in the proximal causal framework.

The remainder of the article is organized as follows. We introduce notation and key assumptions in Section 2. We provide proximal identification results in Section 3. In Section 4, we derive the set of influence functions under a semiparametric MSMM. Furthermore, we derive the efficient influence function and thus the semiparametric efficiency bound for the MSMM parameters. In Section 5, we propose three practical classes of estimators including a rich class of doubly robust estimators. We further apply our proposed
estimators to the data application evaluating the joint causal effects of anti-rheumatic therapy Methotrexate (MTX) use over time among patients with rheumatoid arthritis in Section 6. We end the paper with a discussion in Section 7. Proofs, additional regularity conditions, additional theoretical results, and extensive simulations are provided in the supplementary material.

2. Preliminaries

2.1. Notation

For the sake of clarity in the exposition, we restrict the presentation of all results to the two-occasion longitudinal case, and we relegate results and proofs for the general case of arbitrary length of follow-up to the supplementary material. Importantly, this simplification is without loss of generality as the two-occasion case captures the essential complexities of the general case. In this vein, suppose that one has observed n i.i.d. copies of longitudinal data \((Y, \overline{A}(1), \overline{L}(1))\), where \(Y\) is a measure of an outcome at end of follow-up, \(\overline{A}(1) = (A(0), A(1))\) represents a binary treatment process up to time 1 and \(\overline{L}(1)\) are observed covariates up to time 1. We aim to investigate the joint effects of \(\overline{A}(1)\) on the outcome \(Y\) through an MSMM. Let \(\mathcal{A} = \{(0, 0), (0, 1), (1, 0), (1, 1)\}\) denote the set of possible treatment allocations and \(Y_{\overline{A}(1)}\), \(\pi(1) \in \mathcal{A}\) denote the potential outcome (Robins, 1986, 1987) that would be observed if the treatment process were, possibly contrary to fact, set to \(\overline{a}(1)\). We make the following standard consistency assumption that \(Y = Y_{\overline{A}(1)}\) almost surely, which links observed outcomes and potential outcomes via the observed treatment process.

The sequential randomization assumption of Robins (1986, 1987, 1997) is expressed as, \(Y_{\overline{A}(1)} \perp A(0)|L(0)\) and \(Y_{\overline{A}(1)} \perp A(1)|A(0), \overline{L}(1)\), which essentially requires that \(L(0)\) includes all common causes of \(Y\) and \(A(0)\), and \(A(0), \overline{L}(1)\) include all common causes of \(Y\) and \(A(1)\). It is well known that under consistency, SRA and the positivity assumption, the counterfactual mean \(E(Y_{\overline{A}(1)})\) is nonparametrically identified from the observed data distribution by the \(g\)-formula of Robins (1986) \(E(Y_{\overline{A}(1)}) = E\{E(Y|\pi(1), \overline{L}(1))|a(0), L(0)\}\).

Below, we discuss the proximal causal inference framework which offers an alternative set of identification conditions that allows for nonparametric identification of the counterfactual mean \(E(Y_{\overline{A}(1)})\), even when SRA fails to hold due to possible time-varying unmeasured confounding.

To formally introduce the longitudinal proximal causal inference framework, analogous to Tchetgen Tchetgen et al. (2020), suppose that the observed covariates \(\overline{L}(1)\) consists of three types \((\overline{X}(1), \overline{Z}(1), \overline{W}(1))\), where \(\overline{X}(1) = (X(0), X(1))\) are common causes of subsequent treatment and outcome variables (type 1)), \(A(1)\) and \(Y\); \(\overline{Z}(1) = (Z(0), Z(1))\) are referred to as sequential treatment-inducing proxies (type 2)); and \(\overline{W}(1) = (W(0), W(1))\) are referred to as sequential outcome-inducing proxies (type 3)) (Tchetgen Tchetgen et al., 2020), which are formally defined below.

We now introduce the class of marginal structural models (MSMs) we wish to make inferences about. Robins and colleagues proposed MSMs (Robins, 1998, 1999, 2000; Robins et al., 2000) that encode the joint causal effects of time-varying treatment subject to time-varying confounding. MSMs model the marginal distribution of counterfactual outcomes, possibly conditional on baseline covariates. A marginal structural mean model (MSMM)
is an MSM that places restrictions solely on the mean of $Y_{a(1)}$ possibly conditional on baseline variables $V \subset X(0)$, or more formally,

$$
\mathbb{E}[Y_{a(1)}|V] = g(\mathbf{\alpha}(1), V; \beta), \text{ for any } \mathbf{\alpha}(1) \in \mathcal{A},
$$

for a known function $g(\cdot, \cdot; \cdot)$ and $p$-dimensional parameter $\beta$. The truth is defined as $\beta_*$, which we aim to make inferences about. For example, a common MSMM is

$$
g(\mathbf{\alpha}(1), V; \beta) = \mu(\beta_0 + \beta_1(a(0) + a(1)) + \beta_2V),
$$

where $\mu$ corresponds to the inverse of an appropriate choice of link function, e.g. identity link when $Y$ is continuous, or logit link function for a binary outcome. A saturated MSMM corresponds to an MSM indexed by a parameter of dimension equal to the total number of possible potential outcomes; in the two-occasion setting, a saturated MSMM for instance is given by

$$
\mathbb{E}(Y_{a(1)}) = \beta_0 + \beta_1a(0) + \beta_2a(1) + \beta_3a(0)a(1);
$$

note that a saturated MSMM is technically a nonparametric model.

### 2.2. Assumptions

In order to describe our identifying assumptions, suppose for a moment that it is possible to conceptualize joint interventions on $(\overline{\mathbf{A}}(1), \overline{\mathbf{Z}}(1))$, such that the following potential outcomes are well defined $(Y_{a(1)}, \pi(1), W_{a(0), z(0)}(0))$ and denote potential outcomes under a hypothetical intervention that sets $\overline{\mathbf{A}}(1)$ and $\overline{\mathbf{Z}}(1)$ to $\pi(1)$, $\pi(1)$, respectively. Also, let $\overline{U}(1) = (U(0), U(1))$ denote time-varying unmeasured variables that confound the causal effect of treatment assigned over time on the outcome measured at the end of follow-up. Throughout, we rely on identification conditions introduced in Tchetgen Tchetgen et al. (2020) which we now describe.

**Assumption 1** (Sequential Potential Outcome-inducing Confounding Proxies).

$$
W_{A(1), Z(1)}(1) = W_{a(0)}(1), \quad \forall \, a(1), \pi(1), \text{ almost surely.}
$$

$$
W_{a(0), z(0)}(0) = W(0), \quad \forall \, a(0), z(0), \text{ almost surely.}
$$

This assumption states that $(A(1), Z(1))$ and $Z(0)$ have no direct effect on $W(1)$ and $W(0)$, respectively. In the MTX study, as suggested in the introduction, because the average number of tender joints at baseline and sixth-month follow-up provide an error prone measurement of underlying disease progression which fully mediates the causal effect of past treatment on the outcome (average number of tender joints at end of follow-up), they may be taken as outcome-inducing confounding proxies. Likewise, a health assessment questionnaire, as a measurement of a patient’s evolving health status, prone to recall bias and other forms of measurement error, which may reflect health-seeking behavior as a determinant of treatment initiation, is a good candidate treatment-inducing confounding proxy.

**Assumption 2** (Sequential Potential Treatment-inducing Confounding Proxies).

$$
Y_{A(1), Z(1)} = Y_{A(1)}, \quad \forall \, a(1), \pi(1) \text{ almost surely.}
$$

This implies that $\overline{Z}(1)$ does not have a direct effect on $Y$ other than through $\overline{A}(1)$. For example, self-reported health status as measured by a health assessment questionnaire does not by itself cause tender joints, but may determine MTX initiation which
in turn may reduce disease progression and subsequent tender joints at end-of follow-up. Furthermore, self-reported health may be associated with disease progression to the extent that it is associated with a patient’s underlying health status (e.g. co-morbidities).

Throughout we make the following standard assumptions: (i) consistency: $Y = Y_{A(1), Z(1)}$, $W(1) = W_{A(1), Z(1)}(1)$, $W(0) = W_{A(0), Z(0)}(0)$ almost surely. That is, a person’s observed outcomes match his/her potential outcomes for the treatment regime he/she did indeed followed; (ii) positivity: $P(A(1) = a|A(0), U(1), L(1)) > 0$ and $P(A(0) = a|U(0), L(0)) > 0$ for $a = 1, 0$ almost surely, that is, for any realized history of treatment and covariates (both observed and unobserved) at each follow up time, there is a non-negligible opportunity to receive either treatment.

**Assumption 3** (Sequential Proximal Latent Randomization Assumption).

$\{Z(1), A(1)\} \perp \{W_{a(0), z(0)}(0), W_{a(1), z(1)}(1), Y_{a(1), z(1)}\} | A(0) = a(0), X(1), U(1),$

$\{Z(0), A(0)\} \perp \{W_{a(0), z(0)}(0), Y_{a(1), z(1)}\} | X(0), U(0).$

This assumption formally states sequential randomization and thus identifiability of the joint effects of $\{Z(1), A(1)\}$ on $Y$ and $W(1)$ given observed treatment history $A(0)$, covariate history $X(1)$ and unmeasured factors $U(1)$.

Assumptions 1–3 together formally define $\overline{Z}(1)$ and $\overline{W}(1)$ as sequential treatment-inducing and outcome-inducing proxies respectively. Technically, the following independence statements implied by Assumptions 1–3 can be taken as primitive conditions for our framework, in place of the above assumptions particularly in settings where one does not wish to entertain potential interventions on $\overline{Z}(1)$.

$\overline{Z}(1) \perp Y | \overline{A}(1), \overline{X}(1), \overline{U}(1), \quad (2)$

$\{\overline{Z}(1), A(1)\} \perp \overline{W}(1) | A(0), \overline{X}(1), \overline{U}(1), \quad (3)$

$\{Z(0), A(0)\} \perp W(0) | X(0), U(0). \quad (4)$

![Fig. 2. A directed acyclic graph with time varying endogenous treatments and time varying proxies when proximal independence assumptions (2), (3) and (4) hold.](image-url)
Figure 2 illustrates a possible data generating mechanism in which assumptions 1–3 and thus (2)–(4) hold, where to simplify the figure time-varying covariates $X(1)$ which are structurally similar to $U(1)$ are suppressed. We also note that alternative DAGs compatible with conditions (2), (3) and (4) can in principle be drawn, although throughout, we take Figure 2 as a canonical graphical representation of key conditional independence conditions.

3. Proximal Causal Identification

In this section, we describe two approaches for nonparametric proximal identification of the counterfactual mean $E(Y_\alpha/V)$ that will later motivate a rich class of estimating equations for the parameters of an MSMM. It is important to note that the results described below do not presume a particular functional form relating a counterfactual outcome mean to its corresponding treatment regime. We describe two identification results in the time-varying treatment setting, the proximal analog of Robins’ $g$-formula (Robins, 1986, 1987; Hernán and Robins, 2020) obtained by Tchetgen Tchetgen et al. (2020) and a novel proximal analog of inverse probability weighting (Robins, 1998; Hernán et al., 2001; Hernán and Robins, 2020).

3.1. Identification via Outcome Confounding Bridge Functions

We first briefly describe the identification result due to Tchetgen Tchetgen et al. (2020) based on outcome confounding bridge functions defined as a solution to certain Fredholm integral equations of the first kind. This approach effectively generalizes results due to Miao et al. (2018); Cui et al. (2020) for the average treatment effect in the point exposure case to the longitudinal treatment setting.

The result relies on the following additional conditions codifying an informational relevance requirement the proxies must fulfill.

**Assumption 4** (Sequential Proxy Relevance for Outcome Confounding Bridge Functions).

(a) For any $\overline{\alpha}(1), \overline{x}(1)$, and any square-integrable function $\nu$,

$$E[\nu\{U(1)|\overline{\alpha}(1), \overline{x}(1), \overline{\pi}(1)\} = 0 \text{ if and only if } \nu\{U(1)\} = 0 \text{ almost surely,}$$

$$E[\nu\{U(0)|\alpha(0), Z(0), x(0)\} = 0 \text{ if and only if } \nu\{U(0)\} = 0 \text{ almost surely.}$$

(b) For any $\overline{\alpha}(1), \overline{x}(1)$, and any square-integrable function $\nu$,

$$E[\nu\{Z(1)|\overline{\alpha}(1), \overline{W}(1), \overline{\pi}(1)\} = 0 \text{ if and only if } \nu\{Z(1)\} = 0 \text{ almost surely,}$$

$$E[\nu\{Z(0)|\alpha(0), W(0), x(0)\} = 0 \text{ if and only if } \nu\{Z(0)\} = 0 \text{ almost surely.}$$

These conditions are formally known as completeness conditions which can accommodate both categorical, discrete and continuous variables. Completeness is essential to ensure existence of a solution to a certain integral equation we consider below, as well as identification of the MSMM. Here one may interpret the first completeness condition
(5) as a requirement relating the range of $\mathcal{U}(1)$ to that of $\mathcal{Z}(1)$ which essentially states that the set of proxies must have sufficient variability relative to variability of $\mathcal{U}(1)$. In order to gain intuition about the condition, consider the special case of categorical \( \{U(t), Z(t), W(t) : t\} \), with constant cardinality over time \( d_u, d_z \) and \( d_w \) respectively, where the cardinality is defined as the product of the cardinalities of each component in the vector. In this case, completeness requires that

$$\min(d_z, d_w) \geq d_u,$$

which states that $\mathcal{Z}(1)$ and $\mathcal{W}(1)$ must each have at least as many categories as $\mathcal{U}(1)$. Intuitively, condition (6) states that proximal causal inference can potentially account for unmeasured confounding in the categorical case as long as the number of categories of $\mathcal{U}(1)$ is no larger than that of either proxies $\mathcal{Z}(1)$ and $\mathcal{W}(1)$ (Miao et al., 2018; Shi et al., 2020; Tchetgen Tchetgen et al., 2020; Cui et al., 2020). Completeness is a familiar technical condition central to the study of sufficiency in the foundational theory of statistical inference. Many commonly-used parametric and semiparametric models such as the semiparametric exponential family (Newey and Powell, 2003) and semiparametric location-scale family (Hu and Shiu, 2018) satisfy the completeness condition. For nonparametric regression models, results of D'Haultfoeuille (2011) and Darolles et al. (2011) can be used to justify the completeness condition, although their primary focus is on a nonparametric instrumental variable model, where completeness plays a central role. In order to supplement the more succinct discussion given here, a more extensive discussion of the completeness condition is provided in the supplementary material for the interested reader. Also, see Chen et al. (2014), Andrews (2017) and references therein for an excellent overview of the role of completeness in nonparametric causal inference.

**Lemma 1.** Under Assumption 4(b) and regularity Conditions B.1(a, b, c) given in the supplementary material, there exist functions $H_1\{\pi(1)\} = h_1\{\mathcal{W}(1), \mathcal{Z}(1), X(1)\}$ and $H_0\{\pi(1)\} = h_0\{W(0), \mathcal{Z}(1), X(0)\}$ such that

$$\mathbb{E}\{Y|\pi(1), \pi(1), \pi(1)\} = \mathbb{E}[H_1\{\pi(1)\}|\pi(1), \pi(1), \pi(1)],$$

and

$$\mathbb{E}[H_1\{\pi(1)\}|a(0), z(0), x(0)] = \mathbb{E}[H_0\{\pi(1)\}|a(0), z(0), x(0)].$$

Equations (7) and (8) define Fredholm integral equations of the first kind. Lemma 1 provides sufficient conditions for existence of a solution to these integral equations, however they do not ensure uniqueness of such solutions. Interestingly as noted by Tchetgen Tchetgen et al. (2020), any set of functions \((h_1, h_0)\) satisfying (7) and (8) uniquely identify $\mathbb{E}(Y_{\pi(1)}|V)$ as formally stated in the theorem below. A remarkable result of proximal causal inference is that it offers a genuine opportunity to account for $\mathcal{U}(k)$ without either measuring $\mathcal{U}(k)$ directly or estimating its distribution provided that the set of proxies, though imperfect, is sufficiently rich so that the integral equations (7) and (8) admit a solution.

**Theorem 1** (Tchetgen Tchetgen et al. (2020)). Under assumptions 1, 2, 3 and 4(a), for $h_1$ and $h_0$ satisfying (7) and (8), we have that

$$\mathbb{E}\{Y_{\pi(1)}|\pi(1), \pi(1), \pi(1)\} = \mathbb{E}[H_1\{\pi(1)\}|\pi(1), \pi(1), \pi(1)],$$
and
\[ \mathbb{E}\{Y_{\pi(1)}|a(0), u(0), x(0)\} = \mathbb{E}\{H_0\{\pi(1)\}|a(0), u(0), x(0)\}. \]

It follows that
\[ \mathbb{E}\{Y_{\pi(1)}|a(0), \pi(1)\} = \mathbb{E}\{H_1\{\pi(1)\}|a(0), \pi(1)\}, \]
\[ \mathbb{E}\{Y_{\pi(1)}|x(0)\} = \mathbb{E}\{H_0\{\pi(1)\}|x(0)\}, \]
and therefore
\[ \mathbb{E}\{Y_{\pi(1)}|V\} = \mathbb{E}\{H_0\{\pi(1)\}|V\} = \mathbb{E}\{h_0\{W(0), \pi(1), X(0)\}|V\}. \]

Remark 1. Under SRA given \( L(1) = (X(1), W(1)) \), such that we may take \( Z(1) = W(1) \), (7) and (8) simplify to
\[ h_1\{\pi(1), l(1)\} = \mathbb{E}\{Y|\pi(1), l(1)\}, \]
and
\[ h_0\{\pi(1), l(0)\} = \mathbb{E}\{h_1\{\pi(1), L(1)\}|a(0), L(0) = l(0)\}, \]
recovering Robins’ well-established g-formula (Robins, 1986, 1987; Hernán and Robins, 2020).

3.2. Identification via Treatment Confounding Bridge Functions
We now provide new identification results that complement the results given in the last subsection. Specifically, we introduce and leverage so-called treatment confounding bridge functions for identification, an alternative to the outcome confounding bridge function approach. The approach provides a longitudinal generalization of the identification result for the average treatment effect obtained by Cui et al. (2020).

Our result relies on an alternative set of completeness conditions.

**Assumption 5** (Sequential Proxy Relevance for Treatment Confounding Bridge Functions).

(a) For any \( \pi(1), \bar{\pi}(1) \), and any square-integrable function \( \nu \),
\[ \mathbb{E}\{\nu\{U(1)\}|\pi(1), W(1), \bar{\pi}(1)\} = 0 \text{ if and only if } \nu\{U(1)\} = 0 \text{ almost surely}, \]
\[ \mathbb{E}\{\nu\{U(0)\}|a(0), W(0), x(0)\} = 0 \text{ if and only if } \nu\{U(0)\} = 0 \text{ almost surely}. \]

(b) For any \( \pi(1), \bar{\pi}(1) \), and any square-integrable function \( \nu \),
\[ \mathbb{E}\{\nu\{W(1)\}|\pi(1), Z(1), \bar{\pi}(1)\} = 0 \text{ if and only if } \nu\{W(1)\} = 0 \text{ almost surely}, \]
\[ \mathbb{E}\{\nu\{W(0)\}|a(0), Z(0), x(0)\} = 0 \text{ if and only if } \nu\{W(0)\} = 0 \text{ almost surely}. \]

**Lemma 2.** Under Assumption 5(b) and regularity Conditions B.1(a, d, e) in the supplementary material, there exist functions \( Q_0\{a(0)\} = q_0\{Z(0), a(0), X(0)\} \), \( Q_1\{\pi(1)\} = q_1\{Z(1), \pi(1), X(1)\} \) such that
\[ \frac{1}{\mathbb{P}\{A(0) = a(0)|w(0), x(0)\}} = \mathbb{E}\{Q_0\{a(0)\}|a(0), w(0), x(0)\}, \quad (9) \]
and
\[ \frac{\mathbb{E}\{Q_0\{a(0)\}|a(0), \bar{\pi}(1), \bar{\pi}(1)\}}{\mathbb{P}\{A(0) = a(1)|a(0), \bar{\pi}(1), \bar{\pi}(1)\}} = \mathbb{E}\{Q_1\{\pi(1)\}|\bar{\pi}(1), \pi(1), \bar{\pi}(1)\}. \quad (10) \]
We then have the following identification result.

**Theorem 2.** Under assumptions 1, 2, 3 and 5(a), any functions $q_0$ and $q_1$ satisfying (9) and (10) satisfy

$$\frac{1}{\mathbb{P}\{A(0) = a(0)|u(0), x(0)\}} = \mathbb{E}[Q_0\{a(0)\}|a(0), u(0), x(0)],$$

and

$$\frac{\mathbb{E}[Q_0\{a(0)\}|a(0), \bar{\pi}(1), \bar{x}(1)]}{\mathbb{P}\{A(1) = a(1)|a(0), \bar{\pi}(1), \bar{x}(1)\}} = \mathbb{E}[Q_1\{\bar{\pi}(1)\}|\bar{\pi}(1), \bar{x}(1)].$$

Therefore

$$\mathbb{E}\{Y_{\bar{\pi}(1)}|V\} = \mathbb{E}[Y 1\{\bar{A}(1) = \bar{\pi}(1)\}Q_1\{\bar{\pi}(1)\}|V] = \mathbb{E}[Y 1\{\bar{A}(1) = \bar{\pi}(1)\}q_1\{\bar{\pi}(1), \bar{\pi}(1), \bar{x}(1)\}|V].$$

**Remark 2.** Under the SRA considered in Remark 1, (9) and (10) simplify to

$$q_0\{a(0), l(0)\} = \frac{1}{\mathbb{P}\{A(0) = a(0)|l(0)\}},$$

and

$$q_1\{\bar{\pi}(1), \bar{l}(1)\} = \frac{1}{\mathbb{P}\{a(1)|a(0), \bar{l}(1)\} \mathbb{P}\{A(0) = a(0)|l(0)\}}.$$

recovering standard inverse probability weighting (Robins, 1998).

4. Semiparametric Theory under MSMM

In the previous section, we established that the joint effects of a time-varying treatment can in fact be identified nonparametrically despite unmeasured time-varying confounding, provided proxies satisfy certain conditions. In principle one may wish to estimate the treatment effects under a nonparametric MSMM, however, in practice in order to manage the curse of dimensionality, it is customary to conduct inferences under a parametric or semiparametric MSMM. In this section, we derive the set of regular and asymptotically linear estimators and the efficiency lower bound of the parameters of an MSMM under a semiparametric model which is otherwise unrestricted. Note that the MSMM restriction (1), is equivalent to the moment restriction that for any $p$-dimensional measurable functions $d\{\bar{\pi}(1), V\},$

$$\mathbb{E}\left(\sum_{\bar{\pi}(1) \in A} d\{\bar{\pi}(1), V\} [\mathbb{E}(Y_{\bar{\pi}(1)}|V) - g\{\bar{\pi}(1), V; \beta\}]\right) = 0.$$

Clearly, these moment equations cannot be evaluated empirically and are therefore infeasible due to dependence on potential outcomes that are not observable, however, under Theorem 1 an observable analog of these moment equations can be obtained, mainly:

$$\mathbb{E}\{D(\beta, d)\} = 0,$$

(11)
where $D(\beta, d) = \sum_{\pi(1) \in \mathcal{A}} d(\pi(1), V) \{ H_0(\pi(1)) - g(\pi(1), V; \beta) \}$ and $H_0(\pi(1))$ is the outcome confounding bridge function defined in (8). To proceed with inference, let $\mathcal{M}$ denote the semiparametric model consisting of all observed data distributions for which integral equations (7), (8) admit a solution that satisfies the MSMM for the proximal g-formula given by (11). Note that this semiparametric model is quite rich, including data-generating mechanisms for which the conditions of Lemma 1 hold. Let $L^1(S)$ and $L^2(S)$ be spaces of all integrable and all square-integrable functions of a random variable $S$, respectively. That is,

$$L^1(S) = \left\{ f : \int |f(S)| d\mathbb{P}(S) < \infty \right\},$$

$$L^2(S) = \left\{ f : \int f^2(S) d\mathbb{P}(S) < \infty \right\}.$$

Define $T_1 : L^2(\overline{W}(1), A(0), \overline{X}(1)) \to L^2(Z(0), A(0), X(0))$, $T_0 : L^2(W(0), A(0), X(0)) \to L^2(Z(0), A(0), X(0))$ as the $L^2$ extension of conditional expectation operators, namely, when restricting $T_1$ to $s \in L^1(\overline{W}(1), A(0), \overline{X}(1)) \cap L^2(\overline{W}(1), A(0), \overline{X}(1))$,

$$T_1(s) = \mathbb{E}[s(\overline{W}(1), A(0), \overline{X}(1)) | Z(0), A(0), X(0)],$$

when restricting $T_0$ to $s \in L^1(W(0), A(0), X(0)) \cap L^2(W(0), A(0), X(0))$,

$$T_0(s) = \mathbb{E}[s(W(0), A(0), X(0)) | Z(0), A(0), X(0)].$$

$$T_1 = \{ S \in L_{2,0}(\mathcal{O}) : \mathbb{E}\{(Y - H_1) S(\mathcal{O}) | a(0), z(0), x(0) \in \text{range}(T_1) \},$$

and

$$T_0 = \{ S \in L_{2,0}(\mathcal{O}) : \mathbb{E}\{(H_1 - H_0) S(\mathcal{O}) | a(0), z(0), x(0) \in \text{range}(T_0) \}.$$

**Theorem 3.** Any regular and asymptotically linear estimator $\hat{\beta}$ of $\beta_*$ in $\mathcal{M}$, at a law where (9) and (10) admit a solution, must satisfy the following:

$$n^{1/2}(\hat{\beta} - \beta_*) = n^{1/2} \mathbb{P}_n(S) + o_p(1),$$

where $S \in \text{closure}\left[ \left\{ k(d) \right\}^{-1} R(\beta_*, d) + T_1^{-1} + T_0^{-1} : \text{for any } d \right\}.$

The theorem provides a characterization of all influence functions of regular and asymptotically linear estimators of MSMM parameters. An important special case we later leverage, arises when the following assumption holds.

**Assumption 6.** $T_1$ and $T_0$ are surjective.

The assumption essentially states that $L^2(\overline{W}(1), A(0), \overline{X}(1))$ and $L^2(W(0), A(0), X(0))$ are sufficiently rich so that mapping them onto $L^2(Z(0), A(0), X(0))$ via conditional expectation operator can generate all elements of the latter space.

**Corollary 1.** Any regular and asymptotically linear estimator $\hat{\beta}$ of $\beta_*$ in $\mathcal{M}$, at a law where (9) and (10) admit a solution and Assumption 6 holds, must satisfy the following:

$$n^{1/2}(\hat{\beta} - \beta_*) = n^{1/2} \left\{ k(d) \right\}^{-1} \mathbb{P}_n\{ R(\beta_*, d) \} + o_p(1),$$
where $\mathbb{P}_n$ is the sample mean,

$$ R(\beta, d) = \sum_{\pi(1) \in A} d(\bar{\pi}(1), V) \Xi(\beta)\pi(1), $$

for some $p$-dimensional measurable function $d(\bar{A}(1), V)$,

$$ \Xi(\beta)\pi(1) := \mathbb{1}\{\bar{A}(1) = \bar{\pi}(1)\} Q_1{\bar{\pi}(1)}[Y - H_1{\bar{\pi}(1)}] $$

$$ + \mathbb{1}\{A(0) = a(0)\} Q_0{\bar{\pi}(1)}[H_1{\bar{\pi}(1)} - H_0{\bar{\pi}(1)}] $$

$$ + H_0{\bar{\pi}(1)} - g{\bar{\pi}(1), V; \beta}, $$

and

$$ k(d) = -\mathbb{E}\left\{\frac{\partial R(\beta, d)}{\partial \beta}\right\} = -\mathbb{E}\left\{\frac{\partial D(\beta, d)}{\partial \beta}\right\}. $$

Furthermore, the optimal index $d_{eff}$ of $d$ and thus the semiparametric efficiency bound for $\mathcal{M}$ are given by equations (B.15) and (B.16) of the supplementary material.

5. Proximal Estimation under MSMM

It is straightforward to prove that $\hat{\beta}$ in Theorem 3 can in fact be obtained (up to asymptotic equivalence) under the conditions given in the theorem by solving $\mathbb{P}_n[R(\beta, d)] = 0$; however, clearly such an estimator is technically not feasible as it depends crucially on complicated functions of the true (unknown) observed data distribution, mainly $(h_1, h_0)$ and $(q_1, q_0)$ that satisfy (7), (8) and (9), (10). Empirical solutions to these integral equations are notoriously challenging to compute due to the ill-posedness nature of the problem, typically requiring a form of regularization. In the point treatment case, parametric (Tchetgen Tchetgen et al., 2020), semiparametric (Shi et al., 2020; Miao et al., 2018; Cui et al., 2020), and nonparametric approaches (Cui et al., 2020; Shi et al., 2020; Kallus et al., 2021; Ghassami et al., 2022; Mastouri et al., 2021; Deaner, 2020) have recently been considered for estimation and inference about causal effects using the proximal framework. The results of Ghassami et al. (2022) suggest that root-$n$ estimation of $\beta_*$ may not be attainable even in the point treatment case in moderate to high dimensional settings primarily due to necessarily slow convergence rates of nonparametric estimation of confounding bridge functions, further aggravated by the potential ill-posedness of moment equations defining them. Our current longitudinal setting is considerably more challenging than considered in these prior works, as the number of bridge functions and their dimensionality expand significantly over time, rendering nonparametric estimation practically infeasible. In order to resolve this difficulty, we consider a practical approach to constructing feasible moment estimating equations for $\beta_*$ under low dimensional smooth working models for the nuisance parameters $(h_1, h_0, q_1, q_0)$. Nevertheless, as we establish below we can mitigate concerns about model dependence to some extent, as our approach enjoys some degree of robustness against misspecification of working models for confounding bridge functions as our moment equations for the underlying MSMM of primary scientific interest are in fact doubly robust.

We first detail our proposed approach to estimate $(h_1, h_0, q_1, q_0)$. Let $h_1(\cdot) = h_1(\cdot; b_1)$, $h_0(\cdot) = h_0(\cdot; b_0)$, $q_1(\cdot) = q_1(\cdot; t_1)$, $q_0(\cdot) = q_0(\cdot; t_0)$ denote parametric working models
indexed by low dimensional parameters \((b_1, b_0, t_1, t_0)\), respectively. Let \(M_1 = m_1(Z(1), \overline{A}(1), \overline{X}(1))\), \(M_0 = m_0(Z(0), A(0), X(0))\) for some measurable functions \(m_1(\cdot)\), \(m_0(\cdot)\) that are of the same dimensions as \(b_1\) and \(b_0\). Also, write \(N_1 = n_1(W(1), \overline{A}(1), \overline{X}(1))\), \(N_0 = n_0(W(0), A(0), X(0))\) for some measurable function \(n_1(\cdot)\), \(n_0(\cdot)\) that are of the same dimensions as \(t_1\) and \(t_0\). We also denote \(N_{1,+} = n_1(W(1), A(1) = 1, A(0), \overline{X}(1))\) + \(n_1(W(1), A(1) = 0, A(0), \overline{X}(1))\) and \(N_{0,+} = n_0(W(0), A(0) = 1, X(0)) + n_0(W(0), A(0) = 0, X(0))\). By Theorem E.1 in the supplementary material, estimators of \((\overline{b}_1, \overline{b}_0, \overline{q}_1, \overline{q}_0)\) can be obtained by solving the following estimating equations

\[
\begin{align*}
\mathbb{P}_n\{[Y - H_1(\overline{A}(1); b_1)]M_1\} & = 0, \\
\mathbb{P}_n\{[H_1\{a(1), A(0); \overline{b}_1\} - H_0\{a(1), A(0); b_0\}]M_0\} & = 0, \\
\mathbb{P}_n\{Q_0\{A(0); t_0\}N_0 - N_{0,+}\} & = 0, \\
\mathbb{P}_n\{Q_1\{\overline{A}(1); t_1\}N_1 - Q_0\{A(0); \overline{t}_0\}N_{1,+}\} & = 0.
\end{align*}
\]

Simple working models of parameterization of confounding bridge are as following

\[
\begin{align*}
h_1(W(1), \overline{A}(1), \overline{X}(1); b_1) & = b_{1,0} + b_{1,a}^t \overline{A}(1) + b_{1,w}^t W(1) + b_{1,x}^t \overline{X}(1), \\
h_0(W(0), \overline{A}(1), X(0); b_0) & = b_{0,0} + b_{0,a}^t \overline{A}(1) + b_{0,w} W(0) + b_{0,x} X(0), \\
q_0\{Z(0), A(0), X(0); t_0\} & = 1 + \exp\left[-(1)^{-A(0)}\{t_{0,0} + t_{0,a} A(0) + t_{0,x} X(0)\}\right],
\end{align*}
\]

and

\[
\begin{align*}
q_1\{\overline{Z}(1), \overline{A}(1), \overline{X}(1); t_1\} \\
& = 1 + q_0\{Z(0), A(0), X(0); t_0\} \\
& + \exp\left[-(1)^{-A(1)}\{t_{1,0} + t_{1,a}^t \overline{A}(1) + t_{1,w}^t \overline{Z}(1) + t_{1,x}^t \overline{X}(1)\}\right] \\
& + q_0\{Z(0), A(0), X(0); t_0\} \exp\left[-(1)^{-A(1)}\{t_{1,0} + t_{1,a}^t \overline{A}(1) + t_{1,w}^t \overline{Z}(1) + t_{1,x}^t \overline{X}(1)\}\right].
\end{align*}
\]

Under SRA considered in Remark 1, the working models considered above correspond to imposing linear models on \(\mathbb{E}\{Y|A(1), L(1)\}, \mathbb{E}\{Y|a(1), A(0), L(1)|A(0), L(0)\}\), and logistic models on \(\mathbb{P}\{A(1)|A(0), L(1)\}, \mathbb{P}\{A(0)|L(0)\}\). Our selection of working models generalizes those considered in Cui et al. (2020). In this case, a natural choice sets \(M_1 = \{1, \overline{A}(1), \overline{Z}(1), \overline{X}(1)\}^\top\), \(M_0 = \{1, A(0), Z(0), X(0)\}^\top\) and \(N_1 = (-1)^{-A(1)}\{1, \overline{A}(1), \overline{W}(1), \overline{X}(1)\}^\top\), \(N_0 = (-1)^{-A(0)}\{1, A(0), W(0), X(0)\}^\top\). In fact, (12), (13), (14) and (15) become

\[
\begin{align*}
\mathbb{P}_n\{[Y - H_1(\overline{A}(1); b_1)]\{1, \overline{Z}(1), \overline{A}(1), \overline{X}(1)\}^\top\} & = 0, \\
\mathbb{P}_n\{[H_1\{a(1), A(0); \overline{b}_1\} - H_0\{a(1), A(0); b_0\}]\{1, Z(0), A(0), X(0)\}^\top\} & = 0, \\
\mathbb{P}_n\{(-1)^{-A(0)}Q_0\{A(0); t_0\}\{1, W(0), A(0), X(0)\}^\top - \{0, 0, p_{w(0)}, 1, 0, 0, p_{w(0)}\}^\top\} & = 0, \\
\mathbb{P}_n\{(-1)^{-A(1)}Q_1\{\overline{A}(1); t_1\}\{1, \overline{W}(1), A(0), A(1), \overline{X}(1)\}^\top \\
- \{0, 0, p_{w(1)}, 0, Q_0\{A(0); \overline{t}_0\}, 0, 0, p_{w(1)}\}^\top\} & = 0,
\end{align*}
\]
where \( p_w(0), p_x(0), p_w(1) \) and \( p_x(1) \) denote dimension of \( W(0), X(0), W(1) \) and \( X(1) \), respectively.

Resulting estimators \((\hat{h}_1, \hat{h}_0, \hat{q}_1, \hat{q}_0)\) can then be used to construct corresponding substitution estimators of \( \beta_* \). We describe three practical classes of estimators for estimating \( \beta_* \). Specifically, the first approach entails a large class of proximal outcome regression estimators (POR) \( \hat{\beta}_{\text{POR}} = \hat{\beta}_{\text{POR}}(d) \) of \( \beta_* \) defined as solution to

\[
\mathbb{P}_n \left( \sum_{\pi(1) \in A} d(\pi(1), V) [\hat{H}_1(\pi(1)) - \hat{g}(\pi(1), V; \beta)] \right) = 0. \tag{20}
\]

The second class of estimators entail a large class of proximal inverse probability weighted estimators (PIPW) \( \hat{\beta}_{\text{PIPW}} = \hat{\beta}_{\text{PIPW}}(d) \) of \( \beta_* \) defined as solution to

\[
\mathbb{P}_n \left( d(\bar{A}(1), V) \hat{Q}_1(\bar{A}(1)) [Y - \hat{g}(\bar{A}(1), V; \beta)] \right) = 0. \tag{21}
\]

When \( \mathcal{L}(1) \) is high dimensional, one cannot be confident that either set of working model \((h_1, h_0)\) or \((q_1, q_0)\) can be specified correctly, a prerequisite for consistent estimation of the MSMM. It is therefore of interest to develop doubly robust estimators of MSMMs, under parametric/semiparametric restrictions on confounding bridge functions, which are guaranteed to deliver valid inferences about \( \beta_* \) provided that one but not necessarily both low dimensional working models used to estimate \((h_1, h_0)\) and \((q_1, q_0)\) can be specified correctly. To this end, motivated by Theorem 3, a class of proximal doubly robust estimators (PDR) \( \hat{\beta}_{\text{PDR}} = \hat{\beta}_{\text{PDR}}(d) \) of \( \beta_* \) is obtained as solution to estimating equations of form:

\[
\mathbb{P}_n \left[ \sum_{\pi(1) \in A} d(\pi(1), V) \bar{\Xi}(\beta)_{\pi(1)} \right] = 0, \tag{22}
\]

where

\[
\bar{\Xi}(\beta)_{\pi(1)} := 1\{\bar{A}(1) = \pi(1)\} \hat{Q}_1(\pi(1)) [Y - \hat{H}_1(\pi(1))] \\
+ 1\{A(0) = a(0)\} \hat{Q}_0(a(0)) [\hat{H}_1(\pi(1)) - \hat{H}_0(\pi(1))] \\
+ \hat{H}_0(\pi(1)) - \hat{g}(\pi(1), V; \beta).
\]

An algorithmic summary of the steps towards constructing the above estimators is given
in Algorithm 1.

**Algorithm 1:** Computation of the POR, PIPW and PDR estimators

**Step 1:** Nuisance parameters estimation:

Solve
\[
\mathbb{P}_n\{[Y - H_1(\mathcal{A}(1); b_1)] \{1, \mathcal{Z}(1), \mathcal{A}(1), \mathcal{X}(1)\}^\top = 0,
\]
\[
\mathbb{P}_n\{(-1)^{1-A(0)}Q_0(A(0); t_0) \{1, W(0), A(0), X(0)\}^\top - \{0, (0)_{p=(0)}, 1, (0)_{p=(0)}\}^\top = 0,
\]
to get estimates \( \hat{b}_1 \) and \( \hat{t}_0 \). Then solve
\[
\mathbb{P}_n\{[H_1(a(1), A(0); \hat{b}_1) - H_0 \mathbb{P}\{a(1), A(0); b_0]\} \{1, Z(0), A(0), X(0)\}^\top = 0.
\]
\[
\mathbb{P}_n\{(-1)^{1-A(1)}Q_1(\mathcal{A}(1); t_1) \{1, W(1), A(0), A(1), \mathcal{X}(1)\}^\top
\]
\[- [0, (0)_{p=(1)}, 0, Q_0(A(0); \hat{t}_0), (0)_{p=(1)}] = 0.
\]
to get estimates \( \hat{b}_0 \) and \( \hat{t}_1 \). These yield \( (\hat{h}_1, \hat{h}_0) \) and \( (\hat{q}_1, \hat{q}_0) \).

**Step 2:** Estimation of MSMM parameter:
\( \hat{\beta}_{\text{POR}}(d) \) is a solution to
\[
\mathbb{P}_n\left[ \sum_{\pi(1) \in A} d(\overline{\pi}(1), V)(\hat{\beta}_{h_0}(\overline{\pi}(1)) - g(\overline{\pi}(1), V; \beta)) \right] = 0.
\]
\( \hat{\beta}_{\text{PIPW}}(d) \) is a solution to
\[
\mathbb{P}_n[ d(\overline{\mathcal{A}}(1), V) \hat{Q}_1(\mathcal{A}(1))(Y - g(\mathcal{A}(1), V; \beta))] = 0,
\]
and \( \hat{\beta}_{\text{PDR}}(d) \) is a solution to
\[
\mathbb{P}_n\left[ \sum_{\pi(1) \in A} d(\overline{\pi}(1), V) \hat{\beta}(\beta_{\pi(1)}) \right] = 0.
\]

**Remark 3.** In step 1 of the Algorithm 1, one might, for instance, find \( \hat{b}_1 \) by minimizing a corresponding square loss function, that is, letting
\[
S_n = \mathbb{P}_n\{[Y - H_1(\mathcal{A}(1); b_1)] \{1, \mathcal{Z}(1), \mathcal{A}(1), \mathcal{X}(1)\}^\top = 0,
\]
\( \hat{b}_1 \) can be defined as the minimizer of
\[
\min S_n S_n^\top.
\]
This can readily be implemented with the “optim” function of the “stats” package in R.

In step 2 of the Algorithm 1, if a linear MSMM is imposed on \( g \) as in our simulations and data application, one can simply run (weighted) linear regressions to compute \( \hat{\beta} \) by setting \( d = g \).

The following theorem provides the asymptotic behavior of our proposed estimators, using standard large sample arguments. Let \( \mathcal{M}_h \) denote the collection of observed data generating laws under which specified working models \( (h_1(\cdot; b_1), h_0(\cdot; b_0)) \) are correctly specified, and the model is otherwise unrestricted; likewise, let \( \mathcal{M}_q \) denote the collection
of observed data laws under which \((q_1(·; t_1), q_0(·; t_0))\) are correctly specified with unknown parameters \((b_1, b_0)\) and \((t_1, t_0)\) respectively. Specifically,

\[
\mathcal{M}_h = \{h_1\{\overline{W}(1), \overline{A}(1), \overline{X}(1)\} = h_1\{\overline{W}(1), \overline{A}(1), \overline{X}(1); b_1\} \}
\]

for some value of \(b_1\),

\[
\mathcal{M}_q = \{q_1\{\overline{Z}(1), \overline{A}(1), \overline{X}(1)\} = q_1\{\overline{Z}(1), \overline{A}(1), \overline{X}(1); t_1\} \}
\]

for some value of \(t_1\),

\[
\mathcal{M}_h = \{h_0\{W(0), \overline{A}(1), X(0)\} = h_0\{W(0), \overline{A}(1), X(0); b_0\} \}
\]

for some value of \(b_0\),

\[
\mathcal{M}_q = \{q_0\{Z(0), A(0), X(0)\} = q_0\{Z(0), A(0), X(0); t_0\} \}
\]

for some value of \(t_0\),

such that (7) and (8) hold.

\[
\mathcal{M}_h = \{h_0\{W(0), \overline{A}(1), X(0)\} = h_0\{W(0), \overline{A}(1), X(0); b_0\} \}
\]

such that (9) and (10) hold.

**Theorem 4.** Under Assumptions 1–5, the estimators \(\hat{\beta}_{POR}\), \(\hat{\beta}_{PIPW}\) and \(\hat{\beta}_{PDR}\) are consistent for \(\beta_*\) and asymptotically normal under MSMM (1) and \(\mathcal{M}_h, \mathcal{M}_q\) and \(\mathcal{M}_h \cup \mathcal{M}_q\), respectively.

We derive the asymptotic distribution of various proposed estimators which may be used to obtain inferences about the MSMM.

(a) Suppose \(n^{1/2}(\hat{h}_0 - b_0) = n^{-1/2} \sum_{i=1}^n \varepsilon_{b_0,i} + o_p(1)\) and \(b_0\) is the truth, which holds under \(\mathcal{M}_h\), the POR \(\hat{\beta}_{POR}\) obtained by solving

\[
n^{1/2}\{D(\beta, d, \hat{b}_0)\} = n^{1/2} \mathbb{P}_n \left[ \sum_{\pi \in \mathcal{A}} d(\pi, V) \{H_0(\pi; \hat{b}_0) - g(\pi, V; \beta)\} \right] = o_p(1),
\]

is consistent and asymptotically normal for \(\beta_*\), with influence function \(IF_{POR,i}\) given by

\[
\sqrt{n}(\hat{\beta}_{POR} - \beta_*) = \frac{1}{\sqrt{n}} \sum_{i=1}^n IF_{POR,i} + o_p(1)
\]

\[
= \frac{1}{\sqrt{n}} \sum_{i=1}^n \left[ -\mathbb{P} \left( \frac{\partial D(\beta_*, d, b_0^*)}{\partial \beta} \right) \right]^{-1} D_i(\beta_*, d, b_0^*) + \mathbb{P} \left( \frac{\partial D(\beta_*, d, b_0^*)}{\partial b_0} \right) \varepsilon_{b_0,i} + o_p(1).
\]

(b) Suppose \(n^{1/2}(\hat{t}_K - t_0^*) = n^{-1/2} \sum_{i=1}^n \varepsilon_{t_0,i} + o_p(1)\) and \(t_0^*\) is the truth, which holds under \(\mathcal{M}_q\), the PIPW \(\hat{\beta}_{PIPW}\) obtained by solving

\[
n^{1/2} \mathbb{P}_n \{D(\beta, d, \hat{q}_K)\} = n^{1/2} \mathbb{P}_n \left[ d(\overline{A}, V) \overline{Q}_K(\overline{A}) \{Y - g(\overline{A}, V; \beta)\} \right] = o_p(1),
\]

is consistent and asymptotically normal for \(\beta_*\), with influence function \(IF_{PIPW,i}\) given by

\[
\sqrt{n}(\hat{\beta}_{PIPW} - \beta_*) = \frac{1}{\sqrt{n}} \sum_{i=1}^n IF_{PIPW,i} + o_p(1)
\]

\[
= \frac{1}{\sqrt{n}} \sum_{i=1}^n \left[ -\mathbb{P} \left( \frac{\partial D(\beta_*, d, q_K^*)}{\partial \beta} \right) \right]^{-1} D_i(\beta_*, d, q_K^*) + \mathbb{P} \left( \frac{\partial D(\beta_*, d, q_K^*)}{\partial t_1} \right) \varepsilon_{t_0,i} + o_p(1).
\]
(c) Suppose \( n^{1/2} (b_0 - b_0^*) = n^{-1/2} \sum_{i=1}^{n} \varepsilon_{b_0,i} + o_p(1) \), \( n^{1/2} (t_K - t_K^*) = n^{-1/2} \sum_{i=1}^{n} \varepsilon_{t_K,i} + o_p(1) \) and either \( \{b_k^*\} \) or \( \{t_k^*\} \) is the truth, the PDR \( \hat{\beta}_{PDR} \) obtained by solving
\[
n^{1/2} \mathbb{P}_n \{ R(\beta, d, h, q) \} = n^{1/2} \mathbb{P}_n \left\{ \sum_{i=1}^{n} d(\pi, V) \Xi(\beta) \right\} = o_p(1),
\]
is consistent and asymptotically normal for \( \beta_* \), with influence function \( IF_{PDR,i} \) given by
\[
\sqrt{n} (\hat{\beta}_{PDR} - \beta_*) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} IF_{PDR,i} + o_p(1)
\]
\[
= \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \left[ - \mathbb{P} \left\{ \frac{\partial R(\beta_*, d, h^*, q^*)}{\partial \beta} \right\} \right]^{-1} \left\{ R_i(\beta_*, d, h^*, q^*) \right\} + \mathbb{P} \left\{ \frac{\partial R(\beta_*, d, h^*, q^*)}{\partial b_0} \right\} \varepsilon_{b_0,i} + \mathbb{P} \left\{ \frac{\partial R(\beta_*, d, h^*, q^*)}{\partial t_0} \right\} \varepsilon_{t_0,i}
+ \mathbb{P} \left\{ \frac{\partial R(\beta_*, d, h^*, q^*)}{\partial t_1} \right\} \varepsilon_{t_1,i} + o_p(1).
\]
The empirical variance covariance matrices \( \mathbb{P}_n(\mathbb{IF}_{POR} \mathbb{IF}_{POR}^T) \), \( \mathbb{P}_n(\mathbb{IF}_{PPIP} \mathbb{IF}_{PPIP}^T) \), and \( \mathbb{P}_n(\mathbb{IF}_{PDR} \mathbb{IF}_{PDR}^T) \) can be used to provide variance estimates for \( \hat{\beta}_{POR}, \hat{\beta}_{PIP}, \) and \( \hat{\beta}_{PDR} \) by replacing the true parameters and \( \mathbb{P} \) in \( \mathbb{IF}_{POR}, \mathbb{IF}_{PPIP} \), and \( \mathbb{IF}_{PDR} \) by their estimates and \( \mathbb{P}_n \).

6. Causal Effects of Methotrexate on Rheumatoid Arthritis

We reanalyze data from Choi et al. (2002) on the potential protective effects of the anti-rheumatic therapy Methotrexate (MTX) among patients with rheumatoid arthritis. While Choi et al. (2002) focused on survival as an endpoint and using a marginal structural Cox model to quantify joint treatment effects under SRA, here we consider the joint causal effects of MTX on the average of the reported number of tender joints under an MSMM, a crucial measure of disease progression, without appealing to SRA. These causal effects were also examined in Tchetgen Tchetgen et al. (2020) by employing a proximal recursive least squares algorithm, a proximal g-computation algorithm based on linear outcome confounding bridge functions specification.

A thousand and ten patients with rheumatoid arthritis met our inclusion criteria, 183 of them were treated with MTX after six months of follow-up. We have recorded baseline covariates including age, sex, education level, rheumatoid arthritis duration and rheumatoid factor positive (rapos). Time varying covariates include current smoking status (smoking), health assessment questionnaire (haqc), number of tender joints (jc), patient’s global assessment (gsc), erythrocyte sedimentation rate (esrc), number of disease modifying antirheumatic drugs taken (dmrd) and prednisone use (onprd2) at baseline and sixth month. The treatment process of interest is defined as use of MTX at baseline and month-six of follow-up. As in Choi et al. (2002), MTX initiation defines exposure status i.e., once a patient starts MTX therapy, he or she was considered on therapy for the rest of the follow-up. This approach provides a conservative estimate of
MTX efficacy just as intent-to-treat analysis does in randomized clinical trial. Therefore the possible treatment strategies are $A = \{(0, 0), (0, 1), (1, 1)\}$. Similar to Tchetgen Tchetgen et al. (2020), outcome is defined as the average of reported number of tender joints at month-twelve of follow-up.

We selected proxies from available time-varying covariates; excluding dmrd and onprd2 as both are antirheumatic treatments which are more likely to have direct effects on both MTX initiation and disease progression. Candidates proxies included smoking status, haqc, jc, gsc, esrc. Our allocation of covariates to various bucket types was consistent with that of Tchetgen Tchetgen et al. (2020), mainly:

- $\overline{X}(1) = \text{(age, education, sex, smoking, rheumatoid arthritis duration, rheumatoid factor positive (rapos), prednisone use (onprd2), number of disease modifying antirheumatic drugs taken (dmrd))}$, where smoking, dmrd and onprd2 are time varying;
- $\overline{Z}(1) = \text{(health assessment questionnaire (haqc), erythrocyte sedimentation rate (esrc))}$;
- $\overline{W}(1) = \text{(number of tender joints (jc), patient’s global assessment (gsc))}$.

We specified the MSMM

$$E(Y_{a(1)}) = \beta_0 + \beta_1 (1 - a(0)) a(1) + \beta_2 a(0),$$

which is a saturated MSMM. By this definition, $\beta_1$ and $\beta_2$ encode the causal effect of MTX starting on the sixth month and baseline, respectively.

We estimated $\beta_1, \beta_2$ by POR (20), PIPW (21) and PDR (22) with working models for $h_1$, $h_0$, $q_0$, and $q_1$ specified as (16), (17), (18) and (19), as in the simulations reported in the supplementary material. Note that as this MSMM is nonparametric, the PDR estimator is fully efficient at the intersection submodel where all confounding bridge functions are correctly specified. In addition to proximal causal inference, for comparison, we estimated $\beta_1, \beta_2$ via the standard doubly robust estimator (DR) assuming SRA conditional on all baseline and time-varying covariates. The results are given in Table 1.

Point estimates from POR, PIPW and PDR are consistent with each other and therefore by double robustness, there is no evidence of model misspecification. Results reflected by all three proximal estimators indicate a significant protective effect of MTX against disease progression when treatment is initiated at baseline. The corresponding doubly robust SRA-based estimator suggests a substantially smaller protective effect of MTX which fails to meet statistical significance. Results obtained by all four methods yield an effect estimate for initiating MTX at month six that is protective, however all fail to reach statistical significance. Proximal estimates are substantially larger than the DR estimator. Interestingly, the proximal effect estimates for 12 months of MTX therapy are roughly double estimates for MTX therapy initiated at month 6. This result suggests that an MSMM encoding a cumulative treatment effect might be appropriate for these data.

We therefore also estimated the cumulative treatment effect MSMM

$$E\{Y_{\pi(1)}\} = \beta_0 + \beta_1 \{a(0) + a(1)\},$$

which is a saturated MSMM. By this definition, $\beta_1$ and $\beta_2$ encode the causal effect of MTX starting on the sixth month and baseline, respectively.
Table 1. Results of real data application for saturated MSMM (23) and cumulative effect MSMM (24). We report point estimates from POR, PIPW, PDR and standard DR, together with their 95% confidence intervals in parentheses.

|                     | β_1, POR = -0.21(-0.41, 0.01) | β_2, POR = -0.47(-0.67, -0.28) |
|---------------------|---------------------------------|---------------------------------|
| The saturated MSMM (23) | β_1, PIPW = -0.29(-1.12, 0.54) | β_2, PIPW = -0.44(-0.80, -0.07) |
|                     | β_1, PDR = -0.34(-1.11, 0.43)   | β_2, PDR = -0.58(-0.84, -0.31)   |
|                     | β_1, DR = -0.12(-0.91, 1.41)     | β_2, DR = -0.34(-0.91, 0.22)     |
| The cumulative MSMM (24) | β_1, POR = -0.24(-0.33, -0.14)   | β_1, PIPW = -0.22(-0.41, -0.03)   |
|                     | β_1, PDR = -0.29(-0.42, -0.16)   | β_1, DR = -0.17(-0.41, 0.06)     |

with β_1/2 encoding the causal effect of an additional six month since MTX therapy initiation.

We estimated β_1 using the same estimators as above. Results are also summarized in Table 1. Results obtained by fitting (24) are similar to those from (23). All three proximal estimators indicate a significant protective effect of MTX against disease progression over the course of the first year of follow-up. The DR estimator based on SRA again gives a weaker and nonsignificant protective effect of MTX. As noted in the previous model the point estimates of an additional six months on MTX therapy in the cumulative model are indeed aligned with corresponding estimates from the saturated model.

Our analysis reinforces our understanding of the potential protective effects of MTX on disease progression, providing more compelling evidence of such protective effects than an analysis that relies strictly on SRA.

7. Discussion

We have described a novel framework for the analysis of complex longitudinal studies under a marginal structural mean model subject to potential confounding bias. The approach acknowledges that in practice, measured covariates generally fail in observational settings to capture all potential confounding mechanisms and at most may be seen as proxy measurements of underlying confounding factors. Our proximal causal inference framework provides a formal potential outcome framework under which one can articulate conditions to identify causal effects from proxies in complex longitudinal studies.

There are several possible future directions for this line of research. We note that the Cox proportional hazards MSM is widely used for censored survival time endpoints under SRA, proximal identification and inference for this model is a promising area of future research. Another possible direction for future research is to develop nonparametric proximal methods analogous to Ghassami et al. (2022), however, as previously mentioned, this may be particularly challenging due to the curse of dimensionality.
Acknowledgements

Research reported in this publication was supported by the Beijing Natural Science Foundation, China (award Z190001, to Wang Miao), National Natural Science Foundation of China (award 12071015, to Wang Miao), and the National Institutes of Health (award R01GM139926 to Xu Shi, award R01AI27271, R01AG065276, R01GM139926, to Eric J. Tchetgen Tchetgen). Andrew Ying was awarded the David P. Byar Early Career Award under the Biometrics Section of the American Statistical Association at the 2022 Joint Statistical Meetings.

A. Description of the Supplementary Material

In the supplementary material we provide a general treatment of proximal causal identification of MSMM in longitudinal studies of arbitrary follow-up. This material also includes proofs to all results given in the main text of the paper allowing for follow-up of arbitrary length. We also provide more extensive discussion of the completeness conditions used throughout the paper for the unfamiliar reader. An alternative characterization of the set of influence functions of $\beta_*$ which does not impose Assumption 6 is provided. We show the unbiasedness of the estimating equations used for estimating the nuisance parameters $(h_1, h_0)$, $(q_0, q_1)$. An algorithmic summary of the steps towards constructing the proposed estimators $\hat{\beta}_{\text{POR}}$, $\hat{\beta}_{\text{PIPW}}$ and $\hat{\beta}_{\text{PDR}}$ is given. Asymptotic distributions for $\hat{\beta}_{\text{POR}}$, $\hat{\beta}_{\text{PIPW}}$ and $\hat{\beta}_{\text{PDR}}$ are provided. Compatibility of the confounding bridge functions with respect to the data generating process used in simulation studies is proved. Finally, supplemental simulations are summarized in this material, evaluating sensitivity of the proposed methods to violations of identifying conditions.

Code replicating numerical results including all simulations are provided on github. Here is the link: https://github.com/andrewyyp/Proximal_Causal_Inference_for_Complex_Longitudinal_Studies.git.

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Supplementary Material to “Proximal Causal Inference for Complex Longitudinal Studies”

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In this supplementary material, we provide a general treatment of proximal causal identification of MSMM in longitudinal studies of arbitrary follow-up. This material also includes proofs of all results given in the main text of the paper allowing for follow-up of arbitrary length. We also provide a more extensive discussion of the completeness conditions used throughout the paper for the unfamiliar reader. An alternative characterization of the set of influence functions of \( \beta^* \) which does not impose Assumption 6 is provided. We show the unbiasedness of the estimating equations used for estimating the nuisance parameters \((h_1, h_0), (q_0, q_1)\). An algorithmic summary of the steps towards constructing the proposed estimators \( \hat{\beta}_{POR}, \hat{\beta}_{PIPW} \) and \( \hat{\beta}_{PDR} \) is given. Asymptotic distributions for \( \hat{\beta}_{POR}, \hat{\beta}_{PIPW} \) and \( \hat{\beta}_{PDR} \) are provided. Compatibility of the confounding bridge functions with respect to the data generating process used in simulation studies is proved. Finally, supplemental simulations are summarized in this material, examining finite-sample performance and evaluating the sensitivity of the proposed methods to violations of key identifying conditions.

A. Preliminaries

A.1. Notation

Suppose that one has observed \( n \) i.i.d. copies of longitudinal data \((Y, A(K), L(K))\), where \( Y \) is a measure of an outcome at end of follow-up \( k = K \) with time indexed by \( k = 0, \ldots, K \), \( A(k) = (A(0), A(1), \cdots, A(k)) \) represents a binary treatment process up to time \( k \) and \( L(k) \) are observed covariates up to time \( k \). We write \( \overline{A} = A(K), \overline{A}(0) = A(0) \) and \( \overline{A}(-1) = \emptyset \) for convenience (and for other variables as well). Let \( A \) denote the set of possible treatment allocations. To formally introduce the proximal causal inference framework with longitudinal data, we further assume that the observed covariates \( L(k) \) consist of three bucket types \((X(k), Z(k), W(k))\), where \( X(k) \) are common causes of
subsequent treatment and outcome variables, $A(k), A(k+1), \ldots, A(K)$ and $Y, Z(k)$ are referred to as treatment-inducing proxies (type 2) and $W(k)$ are referred to as outcome-inducing proxies (type 3).

A.2. Assumptions

Let $(Y_{\pi, \tau}, W_{\pi(k), \tau(k)}(k))$ be the potential outcome under a hypothetical intervention that sets $\overline{A}$ and $\overline{Z}$ to $\overline{a}$, $\overline{\tau}$. Also, define $U(k)$ as time varying unmeasured confounders that confounds the treatment allocation after (including) time $k$ and potential outcomes.

Assumption A.1 (Sequential Potential Outcome-inducing Confounding Proxies).

$W_{\pi(k), \tau(k)}(k) = W_{\pi(k-1), \tau(k)}(k), \forall \overline{a}(k), \overline{\tau}(k), 0 \leq k \leq K$ almost surely.

Assumption A.2 (Sequential Potential Treatment-inducing Confounding Proxies).

$Y_{\pi, \tau} = Y_{\pi}, \forall \overline{a}, \overline{\tau}$ almost surely.

Throughout, we make the following standard assumptions: (i) consistency: $Y = Y_{\overline{A}, \overline{Z}}, W(k) = W_{\overline{A}(k), \overline{Z}(k)}(k)$ almost surely. That is, a person’s observed outcome matches his/her potential outcome for the treatment regime he/she did follow; (ii) positivity: $P(A(k) = a|\overline{A}(k-1), U(k), \overline{Z}(k)) > 0$ for $a = 1, 0$ almost surely, that is, for any realized history of treatment and covariates (both observed and unobserved) at each follow up time, there is a non-negligible opportunity to receive either treatment.

Assumption A.3 (Sequential Proximal Latent Exchangeability Assumption).

$(\overline{Z}(k), A(k)) \perp (W_{\pi(k), \tau(k)}(k), Y_{\pi, \tau}) | \overline{A}(k-1) = \overline{a}(k-1), \overline{X}(k), U(k)$.

This assumption formally states sequential randomization and thus identifiability of the joint effects of $(\overline{Z}(k), A(k))$ on $Y$ and $W(k)$ given observed treatment history $\overline{A}(k-1)$, covariate history $\overline{X}(k)$ and unmeasured factors $U(k)$.

Assumptions A.1 - A.3 together imply the following independences that can be taken as primitive conditions for our framework, in place of assumptions A.1 - A.3 particularly in settings where one might not wish to entertain potential interventions on $\overline{Z}(k)$.

$Z \perp Y | \overline{A}, \overline{X}, U$.

$(\overline{Z}(k), A(k)) \perp W(k) | \overline{A}(k-1), \overline{X}(k), U(k)$.

Suppose we are interested in an MSMM

$E(Y_{\pi}|V) = g(\overline{a}, V; \beta)$,

for a known function $g(\cdot, \cdot; \cdot)$ and $p$-dimensional parameter $\beta$. The truth is defined as $\beta^\ast$. 
B. Proofs of the Main Results

To provide sufficient conditions for existence of confounding bridge function, consider the singular value decomposition (Carrasco et al., 2007, Theorem 2.41) of compact operators to characterize conditions for existence of a solution to Equations (B.2), (B.3), (B.9) and (B.10). Similar conditions were considered by Miao et al. (2018) and Cui et al. (2020) in the point treatment setting.

Let $L_2\{F(t)\}$ denote the space of all square integrable functions of $t$ with respect to a cumulative distribution function $F(t)$, which is a Hilbert space with inner product $<g_1, g_2> = \int g_1(t)g_2(t)dF(t)$. Define $T_{\pi(k), \pi(k)}$ as the conditional expectation operator: $L_2\{F(\pi(k)|\pi(k), \pi(k))\} \rightarrow L_2\{F(\pi(k)|\pi(k), \pi(k))\}, T_{\pi(k), \pi(k)}h = E[h(\pi(k))|\pi(k), \pi(k), \pi(k)]$ and let $(\lambda_{\pi(k), \pi(k)}, l, \varphi_{\pi(k), \pi(k)}, l, \phi_{\pi(k), \pi(k)}, l)$ denote a singular value decomposition of $T_{\pi(k), \pi(k)}$. That is, $T_{\pi(k), \pi(k)}\varphi_{\pi(k), \pi(k), l} = \lambda_{\pi(k), \pi(k), l}\phi_{\pi(k), \pi(k), l}$. Also let $T'_{\pi(k), \pi(k)}$ denote the conditional expectation operator: $L_2\{F(\pi(k)|\pi(k), \pi(k))\} \rightarrow L_2\{F(\pi(k)|\pi(k), \pi(k))\}, T_{\pi(k), \pi(k)}q = E[q(\pi(k))|\pi(k), \pi(k), \pi(k)]$ and let $(\lambda'_{\pi(k), \pi(k), l}, \varphi'_{\pi(k), \pi(k), l}, \phi'_{\pi(k), \pi(k), l})$ denote a singular value decomposition of $T'_{\pi(k), \pi(k)}$.

**Assumption B.1.**

\[(a)\]

\[
\sum_{k=0}^{K} \int \mathbb{P}\{w(k)|\pi(k), \pi(k)\} \mathbb{P}\{\pi(k)|w(k), \pi(k)\} dw(k)d\pi(k) < \infty.
\]

\[(b)\]

\[
\sum_{k=0}^{K} \int \mathbb{E}^2\{y_{\pi(k)|\pi(k)}\} \mathbb{P}\{\pi(k)|w(k), \pi(k)\} dw(k)d\pi(k) < \infty.
\]

\[(c)\]

\[
\sum_{k=0}^{\infty} \sum_{l=1}^{\infty} \lambda_{\pi(k), \pi(k), l}^{-2} \left( \mathbb{E}\{y_{\pi(k)|\pi(k)}\}, \phi'_{\pi(k), \pi(k), l} \right)^2 < \infty.
\]

\[(d)\]

\[
\sum_{k=0}^{K} \int \left[ \frac{\mathbb{E}\{Q_{k-1}(\pi(k-1))|w(k), \pi(k-1), \pi(k)\}}{\mathbb{P}\{a(k)|w(k), \pi(k-1), \pi(k)\}} \right]^{-2} \mathbb{P}\{w(k)|\pi(k), \pi(k)\} dw(k) < \infty.
\]

\[(e)\]

\[
\sum_{k=0}^{\infty} \sum_{l=1}^{\infty} \lambda_{\pi(k), \pi(k), l}^{-2} \left( \frac{\mathbb{E}\{Q_{k-1}(\pi(k-1))|w(k), \pi(k-1), \pi(k)\}}{\mathbb{P}\{a(k)|w(k), \pi(k-1), \pi(k)\}}, \phi'_{\pi(k), \pi(k), l} \right)^2 < \infty.
\]

We restate assumption 4 in the general case.

**Assumption B.2 (Sequential Proxy Relevance for Outcome Bridge Functions).**
For any $a(k), x(k)$, and any square-integrable function $\nu$,
\[
\mathbb{E}[\nu(U(k)) \mid \pi(k), \bar{Z}(k), \bar{\pi}(k)] = 0 \text{ if and only if } \nu(U(k)) = 0 \text{ almost surely } 0 \leq k \leq K. \tag{B.1}
\]

(b) For any $\pi(k), x(k)$, and any square-integrable function $\nu$,
\[
\mathbb{E}[\nu(Z(k)) \mid \pi(k), \bar{W}(k), \bar{\pi}(k)] = 0 \text{ if and only if } \nu(Z(k)) = 0 \text{ almost surely } 0 \leq k \leq K.
\]

B.1. Proof of Lemma 1

Lemma B.1. Under assumption B.2(b) and regularity conditions B.1(a, b, c), there exist functions $H_k(\pi) = h_k\{\bar{W}(k), \bar{\pi}, \bar{X}(k)\}$ such that
\[
\mathbb{E}(Y \mid \bar{\pi}, \bar{\pi}, \bar{\pi}) = \mathbb{E}\{H_K(\pi) \mid \bar{\pi}, \bar{\pi}, \bar{\pi}\}, \tag{B.2}
\]
and
\[
\mathbb{E}\{H_k(\pi) \mid \pi(k-1), \bar{\pi}(k-1), \bar{\pi}(k-1)\} = \mathbb{E}\{H_{k-1}(\pi) \mid \pi(k-1), \bar{\pi}(k-1), \bar{\pi}(k-1)\}, \tag{B.3}
\]
for any $1 \leq k \leq K$.

The proof follows immediately from Picard’s theorem (Kress et al., 1989) and Lemma 2 of Miao et al. (2018).

B.2. Proof of Theorem 1

Theorem B.1 (Tchetgen Tchetgen et al. (2020)). Under assumptions A.1, A.2, A.3 and B.2(a), for $h_k$ satisfying (B.2) and (B.3), we have that
\[
\mathbb{E}(Y_{\pi} \mid \bar{\pi}, \bar{\pi}, \bar{\pi}) = \mathbb{E}\{H_{K}(\pi) \mid \bar{\pi}, \bar{\pi}, \bar{\pi}\}, \tag{B.4}
\]
and
\[
\mathbb{E}\{Y_{\pi}(k-1), \pi(k-1), \bar{\pi}(k-1)\} = \mathbb{E}\{H_{k-1}(\pi) \mid \pi(k-1), \bar{\pi}(k-1), \bar{\pi}(k-1)\}, \tag{B.5}
\]
for $1 \leq k \leq K$. It follows that
\[
\mathbb{E}\{Y_{\pi}(k-1), \bar{\pi}(k)\} = \mathbb{E}\{H_{k}(\pi) \mid \pi(k-1), \bar{\pi}(k)\}, \tag{B.6}
\]
for $0 \leq k \leq K$ and therefore
\[
\mathbb{E}(Y_{\pi} \mid V) = \mathbb{E}\{H_{0}(\pi) \mid V\} = \mathbb{E}[h_{0}\{\bar{W}(0), \bar{\pi}, \bar{X}(0)\} \mid V]. \tag{B.7}
\]

Proof. We show that any solution $h_k(-)$ to (B.2) and (B.3) solves (B.4) and (B.5). From (B.2) and (B.3), by law of total expectation and assumptions A.2, A.3, we have
\[
\mathbb{E}_{\pi}\{\mathbb{E}\{Y \mid \pi, \bar{U}, \bar{\pi}\} \mid \bar{\pi}, \bar{\pi}, \bar{\pi}\} = \mathbb{E}(Y \mid \bar{\pi}, \bar{\pi}, \bar{\pi})
\]
\[
= \mathbb{E}\{H_{K}(\pi) \mid \bar{\pi}, \bar{\pi}, \bar{\pi}\} = \mathbb{E}_{\pi}\{\mathbb{E}(H_{K}(\pi) \mid \pi, \bar{U}, \bar{\pi}) \mid \bar{\pi}, \bar{\pi}, \bar{\pi}\},
\]
and

$$\mathbb{E}_{\bar{U}(k-1)}[\mathbb{E}\{Y_{\pi(k-1),\bar{U}(k-1),\bar{X}(k-1)}|\bar{\pi}(k-1),\bar{x}(k-1),\bar{\pi}(k-1)|a(0),w(0),x(0)\}]$$

= $$\mathbb{E}_{\bar{U}(k),A(k),X(k)}[\mathbb{E}\{Y_{\pi(k)}|\bar{A}(k),\bar{U}(k),\bar{X}(k)\}|\bar{\pi}(k-1),\bar{x}(k-1),\bar{\pi}(k-1)]$$

= $$\mathbb{E}_{\bar{U}(k),A(k),X(k)}[\mathbb{E}\{H_k(\bar{\pi})|\bar{a}(k),\bar{U}(k),\bar{X}(k)\}|\bar{\pi}(k-1),\bar{x}(k-1),\bar{\pi}(k-1)]$$

= $$\mathbb{E}_{\bar{U}(k),A(k),X(k)}[\mathbb{E}\{H_k(\bar{\pi})|\bar{a}(k),\bar{U}(k),\bar{X}(k)\}b(k-1),\bar{x}(k-1),\bar{\pi}(k-1)]$$

= $$\mathbb{E}_{\bar{U}(k),A(k),X(k)}[\mathbb{E}\{H_k(\bar{\pi})|\bar{a}(k),\bar{U}(k),\bar{X}(k)\}b(k-1),\bar{x}(k-1),\bar{\pi}(k-1)]$$

= $$\mathbb{E}_{\bar{U}(k),A(k),X(k)}[\mathbb{E}\{H_k(\bar{\pi})|\bar{a}(k),\bar{U}(k),\bar{X}(k)\}b(k-1),\bar{x}(k-1),\bar{\pi}(k-1)]$$

The completeness condition (B.1) implies (B.4) and (B.5). (B.6) and (B.7) are immediate.

We restate assumption 5 in the general case.

**Assumption B.3** (Sequential Proxy Relevance for Treatment Bridge Functions).

(a) For any $\bar{\pi}(k), \bar{\pi}(k)$, and any square-integrable function $\nu$,

$$\mathbb{E}[\nu(\bar{U}(k))|\bar{\pi}(k),\bar{W}(k),\bar{\pi}(k)] = 0 \text{ if and only if } \nu(\bar{U}(k)) = 0 \text{ almost surely } 0 \leq k \leq K. \quad \text{(B.8)}$$

(b) For any $\bar{\pi}(k), \bar{\pi}(k)$, and any square-integrable function $\nu$,

$$\mathbb{E}[\nu(\bar{W}(k))|\bar{\pi}(k),\bar{Z}(k),\bar{\pi}(k)] = 0 \text{ if and only if } \nu(\bar{W}(k)) = 0 \text{ almost surely } 0 \leq k \leq K.$$

**B.3. Proof of Lemma 2**

**Lemma B.2.** Under assumption B.3(b) and regularity conditions B.1(a, d, e), there exist functions $Q_k\{\bar{\pi}(k)\} = q_k\{\bar{Z}(k),\bar{\pi}(k),\bar{X}(k)\}$ such that

$$\frac{1}{\mathbb{P}\{a(0)|w(0),x(0)\}} = \mathbb{E}[Q_0\{a(0)\}|a(0),w(0),x(0)], \quad \text{(B.9)}$$

and

$$\frac{\mathbb{E}[Q_{k-1}\{\bar{\pi}(k-1)\}|\bar{\pi}(k-1),\bar{w}(k),\bar{\pi}(k)]}{\mathbb{P}\{a(k)|\bar{\pi}(k-1),\bar{w}(k),\bar{\pi}(k)\}} = \mathbb{E}[Q_k\{\bar{\pi}(k)\}|\bar{\pi}(k),\bar{w}(k),\bar{\pi}(k)], \quad \text{(B.10)}$$

for any $1 \leq k \leq K$.

The proof follows immediately from Picard’s theorem (Kress et al., 1989) and Lemma 2 of Miao et al. (2018).
Theorem B.2. Under assumptions A.1, A.2, A.3 and B.3(a), any functions $q_k$ satisfying (B.9) and (B.10) satisfy

$$\frac{1}{\mathbb{P}\{a(0)|u(0), x(0)\}} = \mathbb{E}[Q_0\{a(0)\}|a(0), u(0), x(0)],$$

(B.11)

and

$$\frac{\mathbb{E}[Q_{k-1}\{\bar{a}(k-1)\}|\bar{a}(k-1), \bar{u}(k), \bar{x}(k)]}{\mathbb{P}\{a(k)|\bar{a}(k-1), \bar{u}(k), \bar{x}(k)\}} = \mathbb{E}[Q_k\{\bar{a}(k)\}|\bar{a}(k), \bar{u}(k), \bar{x}(k)],$$

(B.12)

for any $1 \leq k \leq K$.

The conditional average $\mathbb{E}(Y_\pi|V)$ for any $\pi$ can be identified by

$$\mathbb{E}(Y_\pi|V) = \mathbb{E}(Y_1|A = \pi)Q_K(\pi)|V = \mathbb{E}(Y_1|A = \pi)q_K(Z, \pi, \bar{x})|V).$$

Proof. We show that any solution $q_k(\cdot)$ to (B.9) and (B.10) solves (B.11) and (B.12). From (B.9) and (B.10), by law of total expectation and assumptions A.1, A.3, we have

$$\mathbb{E}_{U(0)} \left[ \frac{1}{\mathbb{P}\{a(0)|U(0), x(0)\}} \right] a(0), w(0), x(0) = \int \frac{\mathbb{P}\{a(0)|U(0), w(0), x(0)\}}{\mathbb{P}\{a(0)|U(0), w(0), x(0)\}} du(0)$$

$$= \int \frac{\mathbb{P}\{a(0), w(0), x(0)\}}{\mathbb{P}\{a(0), w(0), x(0)\}} du(0)$$

$$= \frac{1}{\mathbb{P}\{a(0)|w(0), x(0)\}} = \mathbb{E}[Q_0\{a(0)\}|a(0), w(0), x(0)] = \mathbb{E}_{U(0)}(\mathbb{E}[Q_0\{a(0)\}|a(0), U(0), x(0)|a(0), w(0), x(0)],$$

and

$$\mathbb{E}_{U(k)} \left( \frac{\mathbb{E}[Q_{k-1}\{\bar{a}(k-1)\}|\bar{a}(k-1), \bar{U}(k), \bar{x}(k)]}{\mathbb{P}\{a(k)|\bar{a}(k-1), \bar{U}(k), \bar{x}(k)\}} \right) \bar{a}(k), \bar{w}(k), \bar{x}(k)$$

$$= \int \frac{\mathbb{E}[Q_{k-1}\{\bar{a}(k-1)\}|\bar{a}(k), \bar{w}(k), \bar{x}(k)}{\mathbb{P}\{\bar{a}(k)|\bar{a}(k-1), \bar{w}(k), \bar{x}(k)\}} \mathbb{P}\{a(k)|\bar{a}(k-1), \bar{w}(k), \bar{x}(k)\} d\bar{a}(k)$$

$$= \int \frac{\mathbb{E}[Q_{k-1}\{\bar{a}(k-1)\}|\bar{a}(k-1), \bar{w}(k), \bar{x}(k}\] \mathbb{P}\{a(k)|\bar{a}(k-1), \bar{w}(k), \bar{x}(k)\} d\bar{a}(k)$$

$$= \mathbb{E}[Q_k\{\bar{a}(k)\}|\bar{a}(k), \bar{w}(k), \bar{x}(k)\] = \mathbb{E}_{U(k)}(\mathbb{E}[Q_k\{\bar{a}(k)\}|\bar{a}(k), \bar{U}(k), \bar{x}(k)|\bar{a}(k), \bar{w}(k), \bar{x}(k).$$

The completeness condition (B.8) implies (B.11) and (B.12).
Base step: when $k = 0$, by assumptions A.2, A.3, IP weighting and (B.11),
\[
\mathbb{E}(Y^e) = \mathbb{E} \left[ Y^e 1 \{ A(0) = a(0) \} \right] = \mathbb{E} \left[ \mathbb{P}(a(0)|U(0), X(0)) \right] = \mathbb{E}(Y^e 1 \{ A(0) = a(0) \} \mathbb{E}[Q_0\{a(0)|a(0), U(0), X(0)] = \mathbb{E}Y^e 1 \{ A(0) = a(0) \} Q_0\{a(0)\}.
\]

Inductive step: when $1 \leq k \leq K$, by assumptions A.2, A.3, IP weighting and (B.12),
\[
\mathbb{E}(Y^e) = \mathbb{E} \left[ Y^e 1 \{ \overline{A}(k - 1) = \overline{\pi}(k - 1) \} Q_{k-1}(\overline{\pi}(k - 1)) \right]
= \mathbb{E} \left\{ Y^e 1 \{ \overline{A}(k - 1) = \overline{\pi}(k - 1) \} \mathbb{E}[Q_{k-1}(\overline{\pi}(k - 1))|\overline{\pi}(k - 1), U(k), \overline{X}(k)] \right\}
= \mathbb{E} \left\{ Y^e 1 \{ \overline{A}(k) = \overline{\pi}(k) \} \mathbb{E}[Q_{k}(\overline{\pi}(k))|\overline{\pi}(k), U(k), \overline{X}(k)] \right\}
= \mathbb{E}Y^e 1 \{ \overline{A}(k) = \overline{\pi}(k) \} Q_k(a(k)).
\]

\hfill \Box

B.5. Proof of Theorem 3

Here we give a formal proof of Theorem 3, the optimal choice $d_{\text{eff}}$ of $d$ therein and thus the semiparametric efficiency bound for $\mathcal{M}$ are given in (B.15) and (B.16) below. Define, for any function $d(\overline{\pi}, V)$,
\[
\mathbb{E}[D(\beta, d)] = \mathbb{E} \left\{ \sum_{\overline{\pi} \in \mathcal{A}} d(\overline{\pi}, V)[H_0(\overline{\pi}) - g(\overline{\pi}, V; \beta)] \right\} = 0, \tag{B.13}
\]
as the observed data MSMM. Let $\mathcal{M}$ be the semiparametric model of the observed data distributions under which (B.2), (B.3) admit a solution and (B.13) holds. Let $L_1()$ and $L_2()$ be spaces of integrable and square integrable functions. Define $T_K : L_2(\overline{W}, \overline{A}, \overline{X}) \rightarrow L_2(\overline{Z}, \overline{A}, \overline{X})$, as the $L_2$ extension of conditional expectation operators, namely, when restricting $T_k$ to $s \in L_1(\overline{W}, \overline{A}, \overline{X}) \cap L_2(\overline{W}, \overline{A}, \overline{X})$,
\[
T_k(s) = \mathbb{E}(s(\overline{W}, \overline{A}, \overline{X})|\overline{Z}, \overline{A}, \overline{X}).
\]

For $0 \leq k \leq K - 1$, define $T_k : L_2(\overline{W}(k + 1), \overline{A}(k), \overline{X}(k + 1)) \rightarrow L_2(\overline{Z}(k), \overline{A}(k), \overline{X}(k))$, as the $L_2$ extension of conditional expectation operators, namely, when restricting $T_k$ to $s \in L_1(\overline{W}(k + 1), \overline{A}(k), \overline{X}(k + 1)) \cap L_2(\overline{W}(k), \overline{A}(k), \overline{X}(k))$,
\[
T_k(s) = \mathbb{E}(s(\overline{W}(k + 1), \overline{A}(k), \overline{X}(k + 1))|\overline{Z}(k), \overline{A}(k), \overline{X}(k)).
\]

Also, define $\varepsilon_K = Y - H_K$ and $\varepsilon_k = H_{k+1} - H_k$ for $0 \leq k \leq K - 1$, in which we abbreviated the dependence on $\overline{\pi}$ when no confusion arises.

Assumption B.4. At the true data generating mechanism, $T_k$ is surjective for each $0 \leq k \leq K$. 


Theorem B.3. Any regular and asymptotically linear estimator \( \hat{\beta} \) of \( \beta_* \) in \( \mathcal{M} \), at a law where (B.9), (B.10) admit a solution and Assumption B.4 holds, must satisfy the following:

\[
n^{1/2}(\hat{\beta} - \beta_*) = n^{1/2}(k(d))^{-1} \mathbb{P}_n[R(\beta_*, d)] + o_p(1),
\]

where

\[
R(\beta, d) = \sum_{a \in \mathcal{A}} d(\bar{a}, V) \Xi(\beta)_\pi =: d \Xi(\beta),
\]

for some \( p \)-dimensional measurable function \( d(\bar{A}, V) \),

\[
\Xi(\beta)_\pi := 1(\bar{A} = \bar{a}) Q_K(\bar{a}) [Y - H_K(\bar{a})]
\]

\[
+ \sum_{k=1}^K 1(\bar{A}(k-1) = \bar{a}(k-1)) Q_{k-1}(\bar{a}(k-1))(H_{k}(\bar{a}) - H_{k-1}(\bar{a}))
\]

\[
+ H_0(\bar{a}) - g(\bar{a}, V; \beta_*)].
\]

and

\[
k(d) = -\mathbb{E} \left( \frac{\partial R(\beta_*, d)}{\partial \beta} \right) = -\mathbb{E} \left( \frac{\partial D(\beta_*, d)}{\partial \beta} \right), \tag{B.14}
\]

The efficient score \( S_{\text{eff}, \beta} \) for \( \beta_* \) under \( \mathcal{M} \) is given by \( R(\beta_*, d_{\text{eff}}) \) with:

\[
d_{\text{eff}} = -\mathbb{E} [\nabla_\beta^\top \Xi(\beta_*) | V]^\top \mathbb{E} [\Xi(\beta_*) \Xi(\beta_*)^\top | V]^{-1} \text{ almost surely.} \tag{B.15}
\]

The semiparametric efficiency bound of \( \mathcal{M} \) is given by

\[
\left\{ \mathbb{E}[d_{\text{eff}} \Xi(\beta_*) \Xi(\beta_*)^\top d_{\text{eff}}^\top] \right\}^{-1}. \tag{B.16}
\]

Proof. Let \( \mathcal{M}(d) \) denote the semiparametric model under which (B.2), (B.3) admit a solution and (B.13) holds for a fixed \( d(\bar{a}, V) \). Clearly \( \mathcal{M} = \bigcap_d \mathcal{M}(d) \). Therefore any RAL estimator under \( \mathcal{M}(d) \) remains RAL under \( \mathcal{M} \) and any RAL estimator under \( \mathcal{M} \) is RAL in at least one \( \mathcal{M}(d) \). Therefore to characterize the set of IFs under \( \mathcal{M} \) it suffices to work under \( \mathcal{M}(d) \) and take the union. Note the set of IFs under \( \mathcal{M}(d) \) is of the form

\[
IF + \mathcal{T}(\mathcal{M}(d))^{\perp},
\]

where \( IF \) is an influence function of \( \beta_* \) and \( \mathcal{T}(\mathcal{M}(d))^{\perp} \) is the orthogonal complement of the tangent space \( \mathcal{T}(\mathcal{M}(d)) \) under \( \mathcal{M}(d) \).

To find an IF, it suffices to compute the pathwise derivative (or equivalently, the gradient) of \( \beta \) for the fixed \( d \) at \( \beta_* \). For any regular parametric submodel \( \{ f(O; t) \} \subset \mathcal{M}(d) \) indexed by \( t \) (\( \mathcal{O} = \{ Y, \bar{A}, \bar{X}, \bar{W}, Z \} \) represents the observed data), \( f(O; 0) \) being the true law, we use \( \mathbb{E}_d \) and \( H_{k,t} \) to represent the corresponding expectation and confounding bridge functions under the submodel, such that \( \mathbb{E}_d \sum_{a \in \mathcal{A}} d(\bar{a}, V) [H_{0,t}(\bar{a}) - g(\bar{a}, V; \beta_*)] = 0 \) holds at any \( t \). We write the derivative of \( \beta_* \) at 0 as \( \beta'(0) \) and the score at the true model associated with the parametric submodel as \( S(O) = \partial \log \mathbb{P}(O; t) / \partial t \big|_{t=0} \). The pathwise derivative \( G(d) \) is a mean zero random variable satisfying

\[
\beta'(0) = \mathbb{E}[G(d) S(O)].
\]
Differentiating on both sides of (B.2) at \( t = 0 \) gives

\[
E \left[ \frac{\partial}{\partial t} H_{K,t}(\pi) \bigg|_{t=0} \pi, \tau, \pi \right] = E[\varepsilon_K S(Y, W|\pi, \tau, \pi)|\pi, \tau, \pi]. \tag{B.17}
\]

Similarly, by differentiating both sides of (B.3) at \( t = 0 \), we have

\[
E \left[ \frac{\partial}{\partial t} H_{k,t}(\pi) \bigg|_{t=0} \pi(k), \tau(k), \pi(k) \right] = E[\varepsilon_k S(W(k + 1)|\pi(k), \tau(k))|\pi(k), \tau(k), \pi(k)]
+ E \left[ \frac{\partial}{\partial t} H_{k+1,t}(\pi) \bigg|_{t=0} \pi(k), \tau(k), \pi(k) \right], \tag{B.18}
\]

for any \( 0 \leq k \leq K - 1 \). Differentiating (B.13) with respect to the parametric submodel \( f(O; t) \) yields

\[
\beta'(0) = \left[ E \left( \sum_{\pi \in A} d(\pi, V) \frac{\partial g(\pi, V; \beta_\ast)}{\partial \beta} \right) \right]^{-1} E \left[ \left( \sum_{\pi \in A} d(\pi, V) H_0(\pi) \right) S(W(0), X(0)) \right]
+ \left[ E \left( \sum_{\pi \in A} d(\pi, V) \frac{\partial g(\pi, V; \beta_\ast)}{\partial \beta} \right) \right]^{-1} E \left( \sum_{\pi \in A} d(\pi, V) \frac{\partial}{\partial t} H_{0,t}(\pi) \bigg|_{t=0} \right).
\]

Note that by (B.14),

\[
E \left( \sum_{\pi \in A} d(\pi, V) \frac{\partial g(\pi, V; \beta_\ast)}{\partial \beta} \right) = k(d),
\]

Therefore the first term is equal to

\[
(k(d))^{-1} E \left[ \left( \sum_{\pi \in A} d(\pi, V)(H_0(\pi) - g(\pi, V; \beta_\ast)) \right) S(O) \right].
\]
By (B.18), the second term equals

\[
\begin{align*}
(k(d))^{-1} & \mathbb{E} \left( \sum_{\pi \in A} d(\pi, V) \frac{\partial}{\partial t} H_{0,t}(\pi) \bigg|_{t=0} \right) \\
& = (k(d))^{-1} \mathbb{E} \left( \sum_{\pi \in A} d(\pi, V) \mathbb{1}(A(0) = a(0)) \frac{1}{P(a(0)|W(0), \bar{X}(0))} \frac{\partial}{\partial t} H_{0,t}(\pi) \bigg|_{t=0} \right) \\
& = (k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(A(0) = a(0)) \mathbb{E} \left( Q_0(a(0))|W(0), A(0), \bar{X}(0) \right) \frac{\partial}{\partial t} H_{0,t}(\pi) \bigg|_{t=0} \right] \\
& = (k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(A(0) = a(0)) Q_0(a(0)) \frac{\partial}{\partial t} H_{0,t}(\pi) \bigg|_{t=0} \right] \\
& = (k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(A(0) = a(0)) Q_0(a(0)) \mathbb{E} \left( \frac{\partial}{\partial t} H_{0,t}(\pi) \bigg|_{t=0} \right) \right] \\
& = (k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(A(0) = a(0)) Q_0(a(0)) \mathbb{E} \left( \frac{\partial}{\partial t} H_{1,t}(\pi) \bigg|_{t=0} \right) \right] \\
& = (k(d))^{-1} \mathbb{E} \left( \sum_{\pi \in A} d(\pi, V) \mathbb{1}(A(0) = a(0)) Q_0(a(0)) \mathbb{E} \left( \frac{\partial}{\partial t} H_{1,t}(\pi) \bigg|_{t=0} \right) \right)
\end{align*}
\]

where the last equality follows from (B.3) when \( k = 0 \). By using the above approach repeatedly, with the help of (B.18) and (B.3), we reach

\[
\beta'(0) = (k(d))^{-1} \mathbb{E} \left( \sum_{\pi \in A} d(\pi, V) H_0(\pi) - g(\pi, V; \beta_*) \right) S(\mathcal{O})
\]

\[
+ \sum_{k=0}^{K-1} (k(d))^{-1} \mathbb{E} \left( \sum_{\pi \in A} d(\pi, V) \mathbb{1}(\bar{A}(k) = \bar{a}(k)) Q_k(\bar{a}(k)) \mathbb{E} \left( \frac{\partial}{\partial t} H_{K,t}(\bar{a}) \bigg|_{t=0} \right) \right) S(\mathcal{O})
\]

\[
+ (k(d))^{-1} \mathbb{E} \left( \sum_{\pi \in A} d(\pi, V) \mathbb{1}(\bar{A}(K - 1) = \bar{a}(K - 1)) Q_{K-1}(\bar{a}(K - 1)) \mathbb{E} \left( \frac{\partial}{\partial t} H_{K,t}(\bar{a}) \bigg|_{t=0} \right) \right)
\]
Observe that the last term, by (B.17) is in fact

\[(k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(\overline{A}(K - 1) = \overline{\pi}(K - 1)) Q_{K-1}(\overline{\pi}(K - 1)) \frac{\partial}{\partial t} H_{K,t}(\overline{\pi}) \bigg| t=0 \right] \]

\[= (k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(\overline{A}(K - 1) = \overline{\pi}(K - 1)) \mathbb{E}(Q_{K-1}(\overline{\pi}(K - 1)) | \overline{W}, \overline{A}(K - 1), \overline{X}) \frac{\partial}{\partial t} H_{K,t}(\overline{\pi}) \bigg| t=0 \right] \]

\[= (k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(\overline{A} = \overline{\pi}) \frac{\mathbb{E}(Q_{K-1}(\overline{\pi}(K - 1)) | \overline{W}, \overline{A}(K - 1), \overline{X}) \mathbb{E} \left( \frac{\partial}{\partial t} H_{K,t}(\overline{\pi}) \bigg| t=0 \right)}{\mathbb{P}(\overline{a}(K)| \overline{W}, \overline{A}(K - 1), \overline{X})} \right] \]

\[= (k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(\overline{A} = \overline{\pi}) q_K(\overline{Z}, \overline{\pi}, \overline{Z}) \mathbb{E} \left( \frac{\partial}{\partial t} H_{K,t}(\overline{\pi}) \bigg| t=0 \right) | \overline{Z}, \overline{A}, \overline{X} \right] \]

\[= (k(d))^{-1} \mathbb{E} \left[ \sum_{\pi \in A} d(\pi, V) \mathbb{1}(\overline{A} = \overline{\pi}) q_K(\overline{Z}, \overline{\pi}, \overline{Z}) \mathbb{E}(\varepsilon_K S(Y, \overline{W} | \overline{Z}, \overline{A}, \overline{X}) | \overline{Z}, \overline{A}, \overline{X}) \right] \]

where the last equality follows from (B.2). Now adding and rearranging all terms implies

\[\beta'(0) = (k(d))^{-1} \mathbb{E}[d(\beta_*) S(O)] = (k(d))^{-1} \mathbb{E}[R(\beta_*, d) S(O)].\]

Therefore we find a pathwise derivative \(G(d) = (k(d))^{-1} R(\beta_*, d).\)

By definition of \(\mathcal{M}(d),\) the tangent space \(\mathcal{T}(\mathcal{M}(d))\) is the set of \(S(O) \in L_{2,0}(O)\) satisfying (B.17) and (B.18) (implied by (B.2), (B.3)), rewritten as

\[\mathbb{E}[\varepsilon_K S(O) | \overline{\pi}, \overline{z}, \overline{x}] = \mathbb{E} \left[ \frac{\partial}{\partial t} H_{K,t}(\overline{\pi}) \bigg| t=0 \right] \overline{\pi}, \overline{z}, \overline{x}, \tag{B.19} \]

and

\[\mathbb{E}[\varepsilon_k S(O) | \overline{\pi}(k), \overline{z}(k), \overline{x}(k)] = \mathbb{E} \left[ \frac{\partial}{\partial t} H_{k+1,t}(\overline{\pi}) \bigg| t=0 \right] \overline{\pi}(k), \overline{z}(k), \overline{x}(k) - \mathbb{E} \left[ \frac{\partial}{\partial t} H_{k,t}(\overline{\pi}) \bigg| t=0 \right] \overline{\pi}(k), \overline{z}(k), \overline{x}(k), \tag{B.20} \]

for any \(0 \leq k \leq K - 1.\) The condition that (B.13) holds for the fixed \(d(\pi, V)\) places no restriction on the observed data distribution. By arbitrariness of \(h_k\) and the fact that the true data distribution lies in the submodel given by proxy relevance assumptions B.2(b), B.3(b), the moment conditions (B.19) and (B.20) imply that for any \(S(O) \in \mathcal{T}(\mathcal{M}),\)

\[\mathbb{E}[\varepsilon_k S(O) | \overline{\pi}(k), \overline{z}(k), \overline{x}(k)] \in \text{range}(T_k), \tag{B.21} \]
for any $0 \leq k \leq K$. Denote
$$T_k = \{ S \in L_{2,0}(\mathcal{O}) : S(\mathcal{O}) \text{ satisfies } (B.21) \}.$$  

Therefore, the tangent space $\mathcal{T}(\mathcal{M}(d))$ is
$$\mathcal{T}(\mathcal{M}(d)) = \bigcap_{0 \leq k \leq K} T_k$$

When assumption B.4 holds at the true law, range($T_k$) = $L_2(\mathcal{O})$, $T_k = L_{2,0}(\mathcal{O})$ and hence
$$\mathcal{T}(\mathcal{M}(d)) = L_{2,0}(\mathcal{O}),$$

and the set of IFs is $\{(k(d))^{-1}R(\beta_*, d)\}$ for fixed $d$. Now taking the union over all $d$ yields the set of IFs under $\mathcal{M}$ is $\{(k(d))^{-1}R(\beta_*, d) : d\}$.

Now we characterize the optimal index $d_{\text{eff}}$ of $d$, which yields an RAL estimator with the minimum variance, and therefore establish the semiparametric efficiency of $\mathcal{M}$. By Theorem 5.3 in Newey and McFadden (1994), the optimal estimating equation $R(\beta, d_{\text{eff}})$ in model $\mathcal{M}$ is uniquely characterized by the requirement that for all $R(\beta, d)$,
$$E \left[ R(\beta_*, d)R(\beta_*, d_{\text{eff}})^\top \right] = -E \left[ \nabla_{\beta^\top} R(\beta_*, d) \right].$$

This implies
$$E \left[ d\Xi(\beta_*)\Xi^\top(\beta_*)d_{\text{eff}}^\top \right] = -E \left[ d\nabla_{\beta^\top} \Xi(\beta_*) \right].$$

Since $d(V)$ is measurable and arbitrary in $V$, we have
$$d_{\text{eff}} = -E[\nabla_{\beta^\top} \Xi(\beta_*)][V]^\top E[\Xi(\beta_*)\Xi^\top(\beta_*)][V]^{-1}$$
almost surely.

\[ \square \]

**B.6. Proof of Theorem 4**

The theorem presumes that parametric working models of bridge functions are used to construct estimators POR, PIPW, PDR. Specifically, suppose one has specified parametric working models $h_k(\cdot; b_k)$ and $q_k(\cdot; t_k)$ with unknown finite-dimensional parameters $b_k$ and $t_k$, respectively. Under standard regularity conditions, $b_k$ and $t_k$ converge in probability to $b_k^*$ and $t_k^*$ as sample size goes to infinity, and admit a first order influence function irrespective of whether their corresponding working model is correct. Let $\mathcal{M}_h$ denote the collection of observed data generating laws under which specified working models $(h_1(\cdot; b_1), h_0(\cdot; b_0))$ are correctly specified, and the model is otherwise unrestricted; likewise, let $\mathcal{M}_q$ denote the collection of observed data laws under which $(q_1(\cdot; t_1), q_0(\cdot; t_0))$ are correctly specified with unknown parameters $(b_1, b_0)$ and $(t_1, t_0)$ respectively. Specifically,
$$\mathcal{M}_h = \{ H_k = h_k(\overline{W}(k), \overline{A}(k), \overline{X}(k); b_k), \text{ for some value of } b_k, \ k = 0, \cdots, K \text{ such that } (B.2) \text{ and } (B.3) \text{ holds} \};$$
\( \mathcal{M}_q = \{ Q_k = q_k(\mathbf{Z}(k), \mathbf{A}(k), \mathbf{X}(k); t_k), \text{ for some value of } t_k, \ k = 0, \ldots, K \} \) such that (B.9) and (B.10) holds).

Consequently, under \( \mathcal{M}_h \) (or \( \mathcal{M}_q \)), \( b_k^* \) (or \( t_k^* \)) is the truth. See Section E.1 for a detailed description of estimation and inference about nuisance parameters and the MSMM parameter.

**Theorem B.4.** Under assumptions A.1, A.2, A.3, B.2, B.3,

(a) the estimator \( \hat{\beta}_{\text{POR}} \) is consistent and asymptotically normal for \( \beta_* \) under \( \mathcal{M}_h \);

(b) the estimator \( \hat{\beta}_{\text{PIPW}} \) is consistent and asymptotically normal for \( \beta_* \) under \( \mathcal{M}_q \);

(c) the estimator \( \hat{\beta}_{\text{PDR}} \) is consistent and asymptotically normal for \( \beta_* \) under \( \mathcal{M}_h \cup \mathcal{M}_q \).

**Proof.** Consistency and asymptotic normality of \( \hat{\beta}_{\text{POR}}, \hat{\beta}_{\text{PIPW}} \) and \( \hat{\beta}_{\text{PDR}} \) follows immediately from standard law of large numbers and central limit theorems. Therefore, we need only establish the double robustness of \( \hat{\beta}_{\text{PDR}} \). To show that \( \hat{\beta} \) is doubly robust, it suffices to show that the estimating equation

\[ \mathbb{E}[d^T \Xi(\beta_*)] = 0, \quad \text{(B.22)} \]

under either \( \mathcal{M}_h \) or \( \mathcal{M}_q \). A sufficient condition for (B.22) is

\[ \mathbb{E}[\Xi(\beta_*|\pi)|V] = \mathbb{E}[\{1(\mathbf{A}_K = \mathbf{a})Q_K(\mathbf{a})|Y - H_K(\mathbf{a})]\]

\[ + \sum_{k=1}^{K-1}1(\mathbf{A}_{k-1} = \mathbf{a}_{k-1})Q_{k-1}(\mathbf{a}_{k-1})[H_k(\mathbf{a}) - H_{k-1}(\mathbf{a})] + H_0(\mathbf{a}) - g(\mathbf{a}, V; \beta_*)|V] = 0, \]

under either \( \mathcal{M}_h \) or \( \mathcal{M}_q \) for any \( \mathbf{a} \in \mathcal{A} \), where \( \Xi(\beta_*|\pi) \) represents \( \pi \) entry of \( \Xi(\beta_*) \). Under \( \mathcal{M}_h \), namely, when \( h_k(\cdot) = h_k(\cdot; b_k^*) \) are the true outcome confounding bridge functions, by (B.2) and (B.3),

\[ \mathbb{E}[\Xi(\beta_*|\pi)|V] \]

\[ = \mathbb{E}[\{1(\mathbf{A}_K = \mathbf{a})Q_K(\mathbf{a})|Y - H_K(\mathbf{a})]\] \[ + \sum_{k=1}^{K-1}1(\mathbf{A}_{k-1} = \mathbf{a}_{k-1})Q_{k-1}(\mathbf{a}_{k-1})[H_k(\mathbf{a}) - H_{k-1}(\mathbf{a})] + H_0(\mathbf{a}) - g(\mathbf{a}, V; \beta_*)|V] \]

\[ = \mathbb{E}[\{1(\mathbf{A}_K = \mathbf{a})Q_K(\mathbf{a})|Y - H_K(\mathbf{a})]\] \[ + \sum_{k=1}^K1(\mathbf{A}_{k-1} = \mathbf{a}_{k-1})Q_{k-1}(\mathbf{a}_{k-1})[H_k(\mathbf{a}) - H_{k-1}(\mathbf{a})][\mathbf{a}(k-1), \mathbf{Z}(k-1), \mathbf{X}(k-1)] + H_0(\mathbf{a}) - Y|V] \]

\[ = \mathbb{E}[H_0(\mathbf{a}) - Y|V] = 0. \]

Under \( \mathcal{M}_h \), \( q_k(\cdot) = q_k(\cdot; t_k^*) \) are the true treatment confounding bridge functions, by
re-expressing $\Xi(\beta_*)$, we have

$$E[\Xi(\beta_*) | V]$$

$$= E[1(\overline{A} = \overline{a}) Q_K(\overline{a}) Y]$$

$$- \sum_{k=0}^{K-1} H_k(\overline{a}) 1(\overline{A}(k) = \overline{a}(k)) Q_k(\overline{a}(k)) - 1(\overline{A}(k-1) = \overline{a}(k-1)) Q_{k-1}(\overline{a}(k-1))$$

$$- g(\overline{a}, V; \beta_*) | V]$$

$$= E[1(\overline{A} = \overline{a}) Q_K(\overline{a}) Y - \sum_{k=0}^{K-1} H_k(\overline{a}) 1(\overline{A}(k) = \overline{a}(k)) E[Q_k(\overline{a}(k)) | \overline{a}(k), \overline{W}(k), \overline{X}(k)]$$

$$+ \sum_{k=0}^{K-1} H_k(\overline{a}) 1(\overline{A}(k-1) = \overline{a}(k-1)) Q_{k-1}(\overline{a}(k-1)) - g(\overline{a}, V; \beta_*) | V]$$

$$= E[1(\overline{A} = \overline{a}) Q_K(\overline{a}) Y - g(\overline{a}, V; \beta_*) | V],$$

where $q_{-1}(\cdot) = 1$. \hfill $\square$

### C. More on Completeness Assumptions

In this section, we provide additional background and intuition for completeness conditions used throughout the paper under the label of "sequential proxy relevance assumptions" in the main text.

We first restate the completeness assumptions in a more general form. To simplify notation, within this section, consider random variables (or vectors) $W$ and $Z$, we say that $Z$ is complete with respect to $W$ if for any $h \in L_2(F_W)$,

$$E(h(W) | Z) = 0, \text{ a.s. implies } h(W) = 0, \text{ a.s.} \tag{C.1}$$

This essentially amounts to the conditional expectation projection operator $T : L_2(W) \to L_2(Z)$ is injective ($\text{Null}(T) = \{0\}$). A necessary and sufficient condition for completeness is given by

**Proposition C.1** (Severini and Tripathi (2006); Andrews (2017)). $Z$ is complete with respect to $W$ if and only if every non-constant random variable $\lambda(W) \in L_2(F_W)$ is correlated with some random variable $\phi(Z) \in L_2(F_Z)$.

Intuitively completeness assumptions encode that no information has been lost through the projection operator. Note that in (5) in Assumption 4, $W = (\overline{A}(1), \overline{U}(1), \overline{X}(1)),$
\[ Z = (A(1), Z(1), X(1)) \]. All proxy relevance conditions given in the main text also fit this definition.

Originally, Lehmann and Scheffé (1950, 1955) introduced the concept of completeness and applied it to define estimators with minimal risk within unbiased estimators. They defined completeness as \( \mathbb{E}_\theta[f(X)] = 0 \) for any \( \theta \in \Theta \) implying \( f(X) = 0 \) a.s. with respect to some parameter space \( \Theta \) parameterizing the distribution space. This definition was later adopted in Lehmann and Casella (2006); Lehmann and Romano (2006). Van Der Vaart (1991) considered a similar setup to ours in Section 7 of his paper where he considered semiparametric estimation of a differentiable functional of a mixing distribution, completeness was invoked to ensure identification. Shao et al. (2003) defined completeness with respect to a family of distributions, namely, \( \mathbb{E}_P(f(X)) = 0 \) for any \( P \in \mathcal{P} \) implying \( f(X) = 0 \) a.s. with respect to some family of distributions \( \mathcal{P} \). This provides a connection to our definition of completeness by setting \( \mathcal{P} \) to be a conditional distribution defined in terms of the proxies. To draw a connection between these definitions and (C.1), as pointed by Andrews (2017), one can define a family of distributions \( \mathcal{F} = \{ F_W,\theta : \theta \in \Theta \} \) of the random vector \( W \) to be complete if for any \( h \in L_2(F_W) \), \( \mathbb{E}[h(W)] = 0 \), for any \( F_W,\theta \in \mathcal{F} \) implies that \( h(W) = 0 \), a.s., for any \( \theta \in \Theta \), where the expectation of \( W \) is taken under \( F_W,\theta \). Here, \( \theta \) is a fixed parameter and its parameter space is \( \Theta \), which play the role of \( z \) and the support of \( F_W \), respectively, and \( F_W,\theta \) is the distribution of \( W \), which plays the role of the conditional distribution of \( W \) given \( Z = z \).

Recently, the completeness assumption has been used in the econometrics literature to obtain global and local identification conditions for a variety of nonparametric and semiparametric models, including nonparametric models with instrumental variables (Newey and Powell, 2003; Ai and Chen, 2003; Chernozhukov and Hansen, 2005; Hall et al., 2005; Blundell et al., 2007; Chernozhukov et al., 2007; Darolles et al., 2011; Horowitz, 2011; Chen and Christensen, 2018), measurement error models (Hu and Schennach, 2008; An and Hu, 2012; Carroll et al., 2010; Chen and Hu, 2006), dynamic models (Hu and Shum, 2012; Shiu and Hu, 2013), panel data models (Freyberger, 2018), and auction models. Proxy measurements essentially can be seen as measurements of the hidden confounders subject to error and bias. Therefore our work also connects to measurement error literature (Hu and Schennach, 2008; An and Hu, 2012; Carroll et al., 2010; Chen and Hu, 2006; Kuroki and Pearl, 2014), in which the completeness assumption has been invoked quite widely.

Although completeness is widely considered a technical condition that can be hard to fully appreciate, a number of papers do provide more intuitive conditions for completeness by exhibiting distributions for which the assumption can formally be shown to hold. Lehmann and Romano (2006); Newey and Powell (2003) gave sufficient conditions for completeness of distributions with discrete finite support and exponential parametric families. Andrews (2017) constructed broad (nonparametric) classes of distributions that are complete, for instance, bivariate density functions. The distributions can have any marginal distributions and a wide range of strengths of dependence. They also provided examples of incomplete distributions. As pointed out by the Hu et al. (2017), injectivity of integral operators is related to completeness conditions of their corresponding kernel functions. Hu et al. (2017) relied on known results regarding a Volterra equation to provide sufficient conditions for completeness conditions for densities with compact support.
Freyberger (2017) provided positive testability results for the completeness condition in a nonparametric instrumental variable model.

D. More on Semiparametric Theory

We provide a more general characterization of the set of influence functions for the MSMM under $\mathcal{M}$ which does not require Assumption B.4. Define $\Omega_k = P_{L_2(\mathcal{Z}(k),\mathcal{X}(k))}(\varepsilon_k^2)$ and $\bar{\Omega}_k = \Omega_k^{-1}$. We write $(T_k \bar{\Omega}_k T_k)^+$ as the Moore-Penrose inverse (Engl et al., 2000) of $T_k \bar{\Omega}_k T_k$.

**Assumption D.1.**

$$0 < \min_{0 \leq k \leq K} \inf \Omega_k \leq \max_{0 \leq k \leq K} \sup \Omega_k < \infty.$$  

Define, like in proof of Theorem B.3,

$$T_k = \{ S(\mathcal{O}) \in L_{2,0}(\mathcal{O}) \text{ satisfies } (B.21) \text{ for a fixed } k \}.$$  

The following lemma is immediate from (Severini and Tripathi, 2012, Lemma B.2).

**Lemma D.1.** Under Assumption D.1,

$$T_k = \{ S(\mathcal{O}) \in L_{2,0}(\mathcal{O}) : T_k^\prime \bar{\Omega}_k P_{L_2(\mathcal{Z}(k),\mathcal{X}(k))}(\varepsilon_k S) \in \text{range}(T_k^\prime \bar{\Omega}_k T_k) \text{ and } (I - T_k(T_k^\prime \bar{\Omega}_k T_k)^+ T_k^\prime \bar{\Omega}_k)P_{L_2(\mathcal{Z}(k),\mathcal{X}(k))}(\varepsilon_k S) = 0 \}.$$  

**Theorem D.1.** The set of influence functions in $\mathcal{M}$, at a submodel where (B.9), (B.10) admit a solution, is

$$\text{closure}((k(d))^{-1}R(\beta_s, d) + \sum_{k=0}^K T_k^\perp),$$  

(D.1)

for any $d$. In particular, if Assumption D.1 holds, then

$$T_k^\perp = \text{closure}\{ s \in L_{2,0}(\mathcal{O}) : \varepsilon_k(I - \bar{\Omega}_k T_k(T_k \bar{\Omega}_k T_k)^+ T_k^\prime \bar{\Omega}_k P_{L_2(\mathcal{Z}(k),\mathcal{X}(k))}(\varepsilon_k s)) \}.$$  

**Proof.** We first show (D.1), for any $G \in (k(d))^{-1}R(\beta_s, d) + \text{closure}(\sum_{k=0}^K T_k^\perp)$, there exists a sequence $\{ G_m : m \} \subset (k(d))^{-1}R(\beta_s, d) + \sum_{k=0}^K T_k^\perp$ such that $||G_m - G||_2 \to 0$ as $m \to \infty$. By the proof of Theorem B.3, $G_m$ are pathwise derivatives and thus IFs, satisfying

$$\beta'(0) = \mathbb{E}[G_m S(\mathcal{O})],$$  

for any $S(\mathcal{O}) \in T(\mathcal{M})$. We need to prove $G$ is also a pathwise derivative, which can be accomplished by an application of triangular inequality and Cauchy-Schwarz inequality. Indeed, for any fixed $S(\mathcal{O}) \in T(\mathcal{M}),$

$$|\mathbb{E}[G_m S(\mathcal{O})] - \beta'(0)| \leq |\mathbb{E}[(G - G_m) S(\mathcal{O})] - \beta'(0)| + |\mathbb{E}[G_m S(\mathcal{O})] - \beta'(0)| \leq ||G - G_m||_2 ||S(\mathcal{O})||_2 \to 0.$$  

Therefore

$$\beta'(0) = \mathbb{E}[GS(\mathcal{O})],$$
and hence (D.1).

Now we prove the explicit representation of \( \mathcal{T}_k^\perp \). One can show that for any \( s \in L_{2,0}(\mathcal{O}) \), its projection onto \( \mathcal{T}_k \) is

\[
P_{\mathcal{T}_k}(s) = s - \varepsilon_k(I - \hat{\theta}_k T_k(T_k \hat{\theta}_k T_k) + T_k' \hat{\theta}_k P_{L_2}(\mathcal{Z}(k), \mathcal{X}(k), \mathcal{X}(k)) (\varepsilon_k s)).
\]

First, it is immediate that \( P_{\mathcal{T}_k}(s) \) satisfies (B.21) for \( k \). In fact,

\[
\mathbb{E}[\varepsilon_k P_{\mathcal{T}_k}(s) | \mathcal{O}(k), \mathcal{X}(k)] = \mathbb{E}[\varepsilon_k s | \mathcal{O}(k), \mathcal{X}(k)] - \mathbb{E}[\varepsilon_k^2 | \mathcal{O}(k), \mathcal{X}(k)] (I - \hat{\theta}_k T_k(T_k \hat{\theta}_k T_k) + T_k' \hat{\theta}_k P_{L_2}(\mathcal{Z}(k), \mathcal{X}(k), \mathcal{X}(k)) (\varepsilon_k s))
\]

Next, we show \( s - P_{\mathcal{T}_k}(s) \perp \mathcal{T}_k \). For any \( s' \in \mathcal{T}_k \),

\[
\mathbb{E}[(s - P_{\mathcal{T}_k}(s)) s'] = \varepsilon_k(I - \hat{\theta}_k T_k(T_k \hat{\theta}_k T_k) + T_k' \hat{\theta}_k P_{L_2}(\mathcal{Z}(k), \mathcal{X}(k), \mathcal{X}(k)) (\varepsilon_k s), s') > 0.
\]

By Lemma D.1, \( (I - \hat{\theta}_k T_k(T_k \hat{\theta}_k T_k) + T_k' \hat{\theta}_k P_{L_2}(\mathcal{Z}(k), \mathcal{X}(k), \mathcal{X}(k)) (\varepsilon_k s)) = 0 \), hence \( s - P_{\mathcal{T}_k}(s) \perp \mathcal{T}_k \).

E. Supplemental Material for Proximal Estimation

E.1. Unbiasedness of the Estimating Equations in Section 5

We repeat the definition of \( \mathcal{M}_h \) and \( \mathcal{M}_q \) for convenience. Let model \( \mathcal{M}_h \) denote the collection of data generating laws under working models \( h_k(\cdot ; b_k) \) and \( \mathcal{M}_q \) denotes the collection of data generating laws under working models \( q_k(\cdot ; t_k) \) with unknown parameters \( b_k \) and \( t_k \) respectively. Namely,

\[
\mathcal{M}_h = \{ h_k = h_k(W(k), \bar{A}(k), \bar{X}(k)) ; b_k \} \text{ for some value of } b_k, k = 0, \ldots, K \text{ such that (B.2) and (B.3) holds};
\]

\[
\mathcal{M}_q = \{ q_k = q_k(\bar{Z}(k), \bar{A}(k), \bar{X}(k)) ; t_k \} \text{ for some value of } t_k, k = 0, \ldots, K \text{ such that (B.9) and (B.10) holds}.
\]

The following result is analogous to Theorem 3.2 in Cui et al. (2020) and provides a characterization of the set of influence functions of \( b_k \) and \( t_k \) in \( \mathcal{M}_h \) and \( \mathcal{M}_q \) respectively, which implies the unbiasedness of the estimating equations in Section 5.
Theorem E.1. 
a) Influence functions of regular and asymptotically linear estimators of \( b = (b_K, \cdots, b_0) \) under \( \mathcal{M}_h \) are of the form:

\[
k_h^{-1} \varepsilon_h,
\]

where

\[
\varepsilon_h = ((Y - H_K(\bar{A}; b_K))^T, \cdots, (H_1(\bar{A}; b_1) - H_0(\bar{A}; b_0))^T)^T,
\]

and

\[
k_h = \begin{pmatrix}
\mathbb{E} \left[ \frac{\partial H_k(\bar{A})}{\partial b_k} M_K \right] & 0 & \cdots & 0 \\
- \mathbb{E} \left[ \frac{\partial H_{k-1}(\bar{A})}{\partial b_{k-1}} M_{K-1} \right] & \mathbb{E} \left[ \frac{\partial H_{k-1}(\bar{A})}{\partial b_{k-1}} M_{K-1} \right] & \cdots & 0 \\
\vdots & \ddots & \ddots & \vdots \\
0 & \cdots & \cdots & - \mathbb{E} \left[ \frac{\partial H_1(\bar{A})}{\partial b_1} M_0 \right] + \mathbb{E} \left[ \frac{\partial H_1(\bar{A})}{\partial b_1} M_0 \right]
\end{pmatrix},
\]

where we write \( M_k = m_k(\bar{A}(k), \bar{Z}(k), \bar{X}(k)) \) for simplicity for some measurable function \( m_k(\bar{A}(k), \bar{Z}(k), \bar{X}(k)) \) of the same dimension as \( b_k \).

b) Influence functions of regular and asymptotically linear estimators of \( t = (t_0, \cdots, t_K) \) under \( \mathcal{M}_q \) are of the form:

\[
k_q^{-1} \varepsilon_q,
\]

where

\[
\varepsilon_q = (N_{0,+}-Q_0(A(0); t_0)N_0)^T, \cdots, (Q_{K-1}(\bar{A}(K-1); t_{K-1})N_{K,+} - Q_K(\bar{A}; t_K)N_K)^T)^T,
\]

and

\[
k_q = \begin{pmatrix}
\mathbb{E} \left[ \frac{\partial Q_0(A(0))}{\partial t_0} N_0 \right] & 0 & \cdots & 0 \\
- \mathbb{E} \left[ \frac{\partial Q_0(A(0))}{\partial t_0} N_1 \right] & \mathbb{E} \left[ \frac{\partial Q_1(A(1))}{\partial t_1} N_1 \right] & \cdots & 0 \\
\vdots & \ddots & \ddots & \vdots \\
0 & \cdots & \cdots & - \mathbb{E} \left[ \frac{\partial Q_{K-1}(A(K-1))}{\partial t_{K-1}} N_{K,+} \right] + \mathbb{E} \left[ \frac{\partial Q_K(A)}{\partial t_K} N_K \right]
\end{pmatrix},
\]

where we write \( N_k = n_k(\bar{A}(k), \bar{W}(k), \bar{X}(k)) \) for simplicity for some measurable function \( n_k(\bar{A}(k), \bar{W}(k), \bar{X}(k)) \) of the same dimension as \( t_k \). We also denote \( N_{K,+} = n_k(A(k) = 1, \bar{A}(k-1), \bar{W}(k), \bar{X}(k)) + n_k(A(k) = 0, \bar{A}(k-1), \bar{W}(k), \bar{X}(k)) \).

Proof. (a) under the assumed models, (B.2) and (B.3) become

\[
\mathbb{E}_s(Y | \bar{a}, \bar{z}, \bar{w}) = \mathbb{E}_s[H_K(\bar{a}; b_{K,s}) | \bar{a}, \bar{z}, \bar{w}],
\]

and

\[
\mathbb{E}_s[H_k(\bar{a}; b_{k,s}) | \bar{a}(k-1), \bar{z}(k-1), \bar{w}(k-1)] = \mathbb{E}_s[H_{k-1}(\bar{a}; b_{k-1,s}) | \bar{a}(k-1), \bar{z}(k-1), \bar{w}(k-1)],
\]

for any \( 1 \leq k \leq K \) under any regular parametric submodel \( \{p_s : s\} \). Furthermore, these moment conditions are equivalent to

\[
\mathbb{E}_s[(Y - H_K(\bar{A}; b_{K,s}))^2] = 0,
\]
and
\[ E_s[(H_k(a(k), \overline{A}(k-1); b_{k,s}) - H_{k-1}(a(k), \overline{A}(k-1); b_{k-1,s}))M_{k-1}] = 0, \]
for any measurable function \( m_k \) of the same dimension as \( b_k \). We write \( M_k = m_K(\overline{A}(k), \overline{Z}(k), \overline{X}(k)) \) for simplicity. Differentiating at \( s = 0 \) yields
\[ E \left[ \frac{\partial H_k(\overline{A}; b_K)}{\partial b_K} M_K \right] \frac{\partial b_{K,s}}{\partial s} \bigg|_{s=0} = E[(Y - H_k(\overline{A}; b_K))M_KS(O)], \]
and
\[ E \left[ \frac{\partial H_{k-1}(a(k), \overline{A}(k-1); b_{k-1})}{\partial b_{k-1}} M_{k-1} \right] \frac{\partial b_{k-1,s}}{\partial s} \bigg|_{s=0} - E \left[ \frac{\partial H_k(a(k), \overline{A}(k-1); b_k)}{\partial b_k} M_{k-1} \right] \frac{\partial b_{k,s}}{\partial s} \bigg|_{s=0} = E[(H_k(a(k), \overline{A}(k-1); b_k) - H_{k-1}(a(k), \overline{A}(k-1); b_{k-1}))M_{k-1}S(O)]. \]
Therefore we have the canonical gradient
\[ \frac{\partial b_s}{\partial s} \bigg|_{s=0} = E(k_h^{-1} \varepsilon_h S(O)), \]
with \( k_h \) and \( \varepsilon_h \) given in the theorem.

(b) Under the assumed models, (B.9) and (B.10) become
\[ \frac{1}{P_s(A(0) = a(0)|w(0), x(0))} = E_s[Q(a(0); t_{0,s})|a(0), w(0), x(0)], \]
and
\[ E_s[Q_{k-1}(a(k-1); t_{k-1,s})|\pi(k-1), \overline{w}(k), \overline{x}(k)] \frac{1}{P_s(A(k) = a(k)|\pi(k-1), \overline{w}(k), \overline{x}(k))} = E_s[Q_k(\pi(k); t_{k,s})|\pi(k), \overline{w}(k), \overline{x}(k)], \]
for any \( 1 \leq k \leq K \) under any regular parametric submodel \( \{p_s : s\} \). Furthermore, these moment conditions are equivalent to
\[ E_s \left[ \left( \frac{1}{P_s(A(0)|\overline{w}(0), \overline{x}(0))} - Q_0(A(0); t_{0,s}) \right) N_0 \right] = E_s [N_0(1) + N_0(0) - Q_0(A(0); t_{0,s})N_0] = 0, \]
and
\[ E_s \left[ \left( \frac{E_s(Q_{k-1}(a(k-1); t_{k-1,s})|\pi(k-1), \overline{w}(k), \overline{x}(k))}{P_s(A(k)|\overline{A}(k-1), \overline{w}(k), \overline{x}(k))} - Q_k(\overline{A}(k); t_{k,s}) \right) N_k \right] = E_s \left[ Q_{k-1}(A(k-1); t_{k-1,s})(N_k(1) + N_k(0)) - Q_k(\overline{A}(k); t_{k,s})N_k \right] = 0, \]
for any measurable function \( n_k \) of the same dimension as \( t_k \). Recall that \( N_k = n_k(\overline{A}(k), \overline{w}(k), \overline{x}(k)) \) and \( N_{k,+} = n_k(a(k) = 1, \overline{A}(k-1), \overline{w}(k), \overline{x}(k)) + n_k(a(k) = 0, \overline{A}(k-1), \overline{w}(k), \overline{x}(k)) \). Differentiating at \( s = 0 \) yields
\[ E \left( \frac{\partial Q_0(A(0); t_0)}{\partial t_0} N_0 \right) \frac{\partial t_{0,s}}{\partial s} = E [(N_{0,+} - Q_0(A(0); t_0)N_0)S(O)], \]
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and

$$E \left[ \frac{\partial Q_k(A(k); t_k)}{\partial t_k} N_k \right] \frac{\partial t_{k,s}}{\partial s} - E \left[ \frac{\partial Q_{k-1}(a(k-1); t_{k-1}) N_{k,+}}{\partial t_{k-1}} \right] \frac{\partial t_{k-1,s}}{\partial s}$$

$$= E_s \left[ (Q_{k-1}(A(k-1); t_{k-1}) N_{k,+} - Q_k(A(k); t_k) N_k) S(\mathcal{O}) \right].$$

Therefore we have the canonical gradient

$$\frac{\partial t_s}{\partial s} \bigg|_{s=0} = E(k_q^{-1} \varepsilon_q S(\mathcal{O})),$$

with $k_q$ and $\varepsilon_q$ given in the theorem.

We derive the asymptotic distribution of various proposed estimators which may be used to obtain inferences about the MSMM.

(a) Suppose $n^{1/2}(b_0 - b_0^*) = n^{-1/2} \sum_{i=1}^n \varepsilon_{b_0,i} + o_p(1)$ and $b_0^*$ is the truth, which holds under $\mathcal{M}_h$, the PDR $\hat{\beta}_{PDR}$ obtained by solving

$$n^{1/2} \{D(\beta, d, \hat{b}_0)\} = n^{1/2} \mathbb{P}_n \left\{ \sum_{a \in A} d(\pi, V) [\hat{H}_p(\pi; \hat{b}_0) - g(\pi, V; \beta)] \right\} = o_p(1),$$

is consistent and asymptotically normal for $\beta_*$, with influence function $IF_{PDR,i}$ given by

$$\sqrt{n}(\hat{\beta}_{PDR} - \beta_*) = \frac{1}{\sqrt{n}} \sum_{i=1}^n IF_{PDR,i} + o_p(1)$$

$$= \frac{1}{\sqrt{n}} \sum_{i=1}^n \left[ -\mathbb{P} \left( \frac{\partial D(\beta_*, d, b_0^*)}{\partial \beta} \right) \right]^{-1} \left[ D_i(\beta_*, d, b_0^*) + \mathbb{P} \left( \frac{\partial D(\beta_*, d, b_0^*)}{\partial b_0} \right) \varepsilon_{b_0,i} \right] + o_p(1).$$

(b) Suppose $n^{1/2}(\hat{t}_K - \hat{t}_K^*) = n^{-1/2} \sum_{i=1}^n \varepsilon_{t_K,i} + o_p(1)$ and $t_K^*$ is the truth, which holds under $\mathcal{M}_q$, the PIPW $\hat{\beta}_{PIPW}$ obtained by solving

$$n^{1/2} \mathbb{P}_n \{D(\beta, d, \hat{q}_K)\} = n^{1/2} \mathbb{P}_n \left\{ d(\bar{A}, V) \hat{Q}_K(\bar{A}) [g(\bar{A}, V; \beta) - \bar{g}(\bar{A}, V; \beta)] \right\} = o_p(1),$$

is consistent and asymptotically normal for $\beta_*$, with influence function $IF_{PIPW,i}$ given by

$$\sqrt{n}(\hat{\beta}_{PIPW} - \beta_*) = \frac{1}{\sqrt{n}} \sum_{i=1}^n IF_{PIPW,i} + o_p(1)$$

$$= \frac{1}{\sqrt{n}} \sum_{i=1}^n \left[ -\mathbb{P} \left( \frac{\partial D(\beta_*, d, q_K^*)}{\partial \beta} \right) \right]^{-1} \left[ D_i(\beta_*, d, q_K^*) + \mathbb{P} \left( \frac{\partial D(\beta_*, d, q_K^*)}{\partial q_K} \right) \varepsilon_{q_K,i} \right] + o_p(1).$$

(c) Suppose $n^{1/2}(\hat{b}_0 - b_0^*) = n^{-1/2} \sum_{i=1}^n \varepsilon_{b_0,i} + o_p(1)$, $n^{1/2}(\hat{t}_K - t_K^*) = n^{-1/2} \sum_{i=1}^n \varepsilon_{t_K,i} + o_p(1)$ and either $\{b_k^*\}$ or $\{t_k^*\}$ is the truth, the PDR $\hat{\beta}_{PDR}$ obtained by solving

$$n^{1/2} \mathbb{P}_n \{R(\beta, d, \hat{h}, \hat{q})\} = n^{1/2} \mathbb{P}_n \left\{ \sum_{\pi \in A} d(\pi, V) \hat{\Xi}(\beta) \pi \right\} = o_p(1),$$

where $\hat{\Xi}(\beta)$ is the influence function for $\beta$. 

\[\square\]
is consistent and asymptotically normal for \( \beta^* \), with influence function \( \text{IF}_{PDR,i} \) given by

\[
\sqrt{n}(\hat{\beta}_{PDR} - \beta^*) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \text{IF}_{PDR,i} + o_p(1)
\]

\[
= \frac{1}{\sqrt{n}} \sum_{i=1}^{n} [ -P \left( \frac{\partial R(\beta^*, d, h^*, q^*)}{\partial \beta} \right)^{-1} \left[ R_i(\beta^*, d, h^*, q^*) \right] + \sum_{k=0}^{K} P \left( \frac{\partial R(\beta^*, d, h^*, q^*)}{\partial b_k} \right) \epsilon_{b_k,i} + \sum_{k=0}^{K} P \left( \frac{\partial R(\beta^*, d, h^*, q^*)}{\partial t_k} \right) \epsilon_{t_k,i}] + o_p(1).
\]

The empirical variance covariance matrices \( \mathbb{P}_n(\text{IF}_{POR}\text{IF}_{POR}^\top) \), \( \mathbb{P}_n(\text{IF}_{PIPW}\text{IF}_{PIPW}^\top) \) and \( \mathbb{P}_n(\text{IF}_{PDR}\text{IF}_{PDR}^\top) \) can be used to provide variance estimates for \( \hat{\beta}_{POR} \), \( \hat{\beta}_{PIPW} \) and \( \hat{\beta}_{PDR} \) by replacing the true parameters and \( \mathbb{P} \) therein by their estimates and \( \mathbb{P}_n \). Next, we provide an algorithm (Algorithm 1) to compute POR, PIPW, and PDR estimators in the arbitrary follow-up setting.
Algorithm 1: Computation of the POR, PIPW, and PDR estimators

Step 1: Nuisance parameters estimation.
Solve
\[ P_n \{ Y - H_1(A(1); b_1)][1, Z(1), A(1), X(1)]\top = 0, \]
\[ P_n \{ (-1)^{1-A(0)}Q_0(A(0); t_0)(1, W(0), A(0), X(0))\top - (0, (0)p_w(0), 1, (0)p_x(0))\top = 0, \]
to get estimates \( \hat{b}_1 \) and \( \hat{t}_0 \). Then iteratively solve
\[ P_n \{ H_{k+1}(\pi(k+1), A(k); \hat{b}_{k+1}) - H_k(\pi(k), A(k); b_k)(1, Z(k), A(k), X(k))\top = 0. \]
\[ P_n \{ (-1)^{1-A(k+1)}Q_{k+1}(A(k+1); t_{k+1})(1, W(k+1), A(k+1), X(k+1))\top - (0, (0)p_w(k+1), 0, Q_k(A(k); \hat{t}_k), (0)p_x(k+1))\top = 0. \]
to get estimates \( \hat{b}_k \) and \( \hat{t}_k \). These yield \( \{ \hat{h}_k \} \) and \( \{ \hat{q}_k \} \).

Step 2: Estimation of \( \beta^* \).
\( \hat{\beta}_{POR}(d) \) is a solution to
\[ P_n \left[ \sum_{\pi \in A} d(\pi, V)(\tilde{H}_0(\pi) - g(\pi, V; \beta)) \right] = 0. \]
\( \hat{\beta}_{PIPW}(d) \) is a solution to
\[ P_n [d(\pi, V)\hat{Q}_K(\pi)(Y - g(\pi, V; \beta))] = 0, \]
and \( \hat{\beta}_{PDR}(d) \) is a solution to
\[ P_n \left[ \sum_{\pi \in A} d(\pi, V)\tilde{\Xi}(\beta)\pi \right] = 0. \]

F. Supplemental Material for Simulation

F.1. Main Simulation
In this section, we investigate the finite-sample performance of POR, PIPW and PDR estimators when confounding bridge functions are correctly specified under the parameterization given by equations (16), (17), (18) and (19). We also investigate their robustness under partial misspecification of a subset of confounding bridge functions. for comparison, we also implement the standard doubly robust estimator which relies on SRA given \( \bar{L}(1) \).

Data-generating mechanisms: We generate data \( (Y, W(1), A(1), Z(1), U(1), X(1)) \) as followed:
\[ X(0) \sim \mathcal{N}(-0.35, 0.5^2), \]
\[ U(0) \sim \mathcal{N}(0.35, 0.5^2), \]
\[ \mathbb{P}(A(0)|X(0), U(0)) = \frac{1}{1 + \exp((-1)^{1-A(0)}(0.5 - 0.35 \cdot X(0) + 0.35 \cdot U(0))))} \]
\[ Z(0) \sim \mathcal{N}(0.2 + 0.5 \cdot A(0) + 0.5 \cdot X(0) + 0.75 \cdot U(0), 0.5^2), \]
\[ W(0) \sim \mathcal{N}(0.2 + 0.5 \cdot X(0) - 0.95 \cdot U(0), 0.5^2), \]
\[ X(1) \sim \mathcal{N}(0.2 + 0.7 \cdot A(0) + 0.7 \cdot X(0), 0.5^2), \]
\[ U(1) \sim \mathcal{N}(0.2 + 0.7 \cdot A(0) + 0.7 \cdot U(0), 0.5^2), \]

\[
\mathbb{P}(A(1)|A(0), X(1), U(1)) \]
\[
= \frac{1}{1 + \exp((-1)^{1-A(1)}(0.5 - 0.5 \cdot A(0) - 0.35 \cdot (X(0) + X(1)) - 0.35 \cdot (U(0) + U(1))))}, \quad \text{(F.1)}
\]
\[ Z(1) \sim \mathcal{N}(0.2 + 0.5 \cdot (A(1) + A(0)) + 0.5 \cdot (X(1) + X(0)) - 0.75 \cdot (U(1) + U(0)), 0.5^2), \quad \text{(F.2)}
\]
\[ W(1) \sim \mathcal{N}(0.35 + 0.45 \cdot (X(1) + X(0)) - 0.85 \cdot (U(1) + U(0))), 0.5^2), \]
\[ Y \sim \mathcal{N}(-1.3 + 1 \cdot A(1) + 1.14 \cdot A(0) + 0.5 \cdot X(1) - 0.7 \cdot U(1) + 0.2 \cdot X(0) - 0.7 \cdot U(0), 0.5^2). \]

We verify in Section F.2 in the supplementary material that this data generating mechanism is compatible with (16), (17), (18) and (19) of \((h_1, h_0, q_1, q_0)\).

**Estimand:** Our estimand is \( \beta \) from the following MSMM

\[
E[Y_{\pi(1)}] = \beta_0 + \beta_1(a(0) + a(1)), \quad \text{(F.3)}
\]

which can be interpreted as the average treatment effect.

**Methods:** Following Kang et al. (2007), we evaluate the performance of the proposed estimators in situations where either or both confounding bridge functions are mis-specified by considering a model based on a nonlinear transformation of observed variables. In particular, each simulated dataset is analyzed using

- The POR estimator \( \hat{\beta}_{\text{POR}} \) with correctly specified working models of \((h_1, h_0)\) given in (16) and (17);
- The POR estimator \( \hat{\beta}_{\text{POR}, \text{WOR}} \) with incorrectly specified \((h_1, h_0)\). \( W(1)^* = 1/\{1 + \exp(-5 * W(1))\} \), \( W(0)^* = 1/\{1 + \exp(-5 * W(0))\} \) instead of \((W(1), W(0))\) are used in (16) and (17);
- The PIPW estimator \( \hat{\beta}_{\text{PIPW}} \) with correctly specified working models of \((q_1, q_0)\) given in (18) and (19);
- The PIPW estimator \( \hat{\beta}_{\text{PIPW}, \text{WIPW}} \) with incorrectly specified \((q_1, q_0)\). \( Z(1)^* = 1/\{1 + \exp(-5 * Z(1))\} \), \( Z(0)^* = 1/\{1 + \exp(-5 * Z(0))\} \) instead of \((Z(1), Z(0))\) are used in (18) and (19);
- The PDR estimator \( \hat{\beta}_{\text{PDR}} \) with both \((h_1, h_0)\) and \((q_1, q_0)\) being correctly specified as in (16), (17), (18), and (19);
- The PDR estimator \( \hat{\beta}_{\text{PDR}, \text{WOR}} \) with incorrectly specified \((h_1, h_0)\) and correctly specified \((q_1, q_0)\) as in (18) and (19). \( W(1)^* = 1/\{1 + \exp(-5 * W(1))\} \), \( W(0)^* = 1/\{1 + \exp(-5 * W(0))\} \) instead of \((W(1), W(0))\) are used in (16) and (17);
The PDR estimator $\hat{\beta}_{\text{PDR, WIPW}}$ with correctly specified $(h, h_0)$ as in (16) and (17) and incorrectly specified $(q_1, q_0)$. $Z(1)^* = 1/(1 + \exp(-5 * Z(1)))$, $Z(0)^* = 1/(1 + \exp(-5 * Z(0)))$ instead of $Z(1)$, $Z(0)$ are used in (18) and (19);

- The PDR estimator $\hat{\beta}_{\text{PDR, BW}}$ with both $(h, h_0)$ and $(q_1, q_0)$ incorrectly specified. $W(1)^* = 1/(1 + \exp(-5 * W(1)))$, $W(0)^* = 1/(1 + \exp(-5 * W(0)))$ instead of $(W(1), W(0))$ are used in (16) and (17). $Z(1)^* = 1/(1 + \exp(-5 * Z(1)))$, $Z(0)^* = 1/(1 + \exp(-5 * Z(0)))$ instead of $Z(1)$, $Z(0)$ are used in (18) and (19);

- The standard DR estimator $\hat{\beta}_{\text{DR}}$ (Robins, 1998), which takes covariates $\tilde{L}(1) = (\tilde{X}(1), \tilde{Z}(1), \tilde{W}(1))$, assumes SRA and ignores the unmeasured confounder, as a comparison.

$\hat{\beta}_{\text{POR}}, \hat{\beta}_{\text{PIPW}}$ and $\hat{\beta}_{\text{PDR}}$ are expected to perform well. $\hat{\beta}_{\text{PDR, WOR}}$ and $\hat{\beta}_{\text{PDR, WIPW}}$ are also anticipated to work well by double robustness. $\hat{\beta}_{\text{POR, WOR}}, \hat{\beta}_{\text{PIPW, WIPW}}, \hat{\beta}_{\text{PDR, BW}}$ and $\hat{\beta}_{\text{DR}}$ are expected to fail since their corresponding modeling assumptions are violated.

**Performance measures:** We examine the performance of these estimators by reporting biases, empirical standard errors (SEE), average estimated standard errors (SD), and coverage probabilities (95% CP) of 95% confidence intervals using biases, empirical standard errors (SEE), average estimated standard errors (SD), and coverage probabilities (95% CP) of 95% confidence intervals using $N = 500, 1000, 4000, 8000$. The results are given in Table 1, 2, 3, and 4.

As the simulation results illustrate, $\hat{\beta}_{\text{POR}}, \hat{\beta}_{\text{PIPW}}$ and $\hat{\beta}_{\text{PDR}}$ perform well with small biases regardless of sample size when the underlying model of the required bridge functions are correctly specified; thus confirming our theoretical results. Variance estimates for $\hat{\beta}_{\text{PIPW}}$ and $\hat{\beta}_{\text{PDR}}$ appear to be conservative at small to moderate sample sizes $N = 500, 1000$. This is because in a few small Monte Carlo samples, near-degenerate Jacobian matrices yielded conservative variance estimates. The resulting coverage probabilities are near the nominal levels confirming that only a tiny portion of variance estimates deviated from the truth. As expected from theory, variance estimates approached the Monte Carlo variance as sample size increased to $N = 4000, 8000$. Confidence intervals of $\hat{\beta}_{\text{POR}}, \hat{\beta}_{\text{PIPW}}$ and $\hat{\beta}_{\text{PDR}}$ attain their nominal levels with improved coverage with a larger sample size. $\hat{\beta}_{\text{POR, WOR}}$ has a substantial bias when the outcome confounding bridge functions are misspecified, which does not vanish as sample gets larger. $\hat{\beta}_{\text{PIPW, WIPW}}$ has substantial bias and over-coverage of confidence intervals when the treatment confounding bridge functions are not correctly specified. $\hat{\beta}_{\text{PDR, WOR}}$ and $\hat{\beta}_{\text{PDR, WIPW}}$ remain consistent and have satisfactory coverage rates, thus confirming double robustness property of PDR. $\hat{\beta}_{\text{PDR, BW}}$ is severely biased under misspecification of both sets of confounding bridge functions because the true data generating mechanism does not fall within the specified union model $\mathcal{M}_h \cup \mathcal{M}_q$. Likewise, $\hat{\beta}_{\text{DR}}$ is substantially biased regardless of sample size, because SRA does not hold.

In the later sections, we also examine the finite-sample performance of $\hat{\beta}_{\text{POR}}, \hat{\beta}_{\text{PIPW}}$ and $\hat{\beta}_{\text{PDR}}$ under relative minor to more substantial violations to proximal independence assumptions (2), (3), (4) or proxy relevance Assumptions 4, 5, which reveal that our proposed approaches can tolerate minor deviation from the key proximal independence assumptions and proxy relevance assumptions, but quickly incur substantial bias and break down when violations become more severe.
Table 1. Simulation results of POR, PIPW and PDR estimators. We report bias ($\times 10^{-3}$), empirical standard error (SEE) ($\times 10^{-3}$), average estimated standard error (SD) ($\times 10^{-3}$), and coverage probability of 95% confidence intervals (95% CP) of POR with correctly specified outcome confounding bridge functions ($\hat{\beta}_{POR}$), POR with incorrectly specified outcome confounding bridge functions ($\hat{\beta}_{POR, WOR}$), PIPW with correctly specified treatment confounding bridge functions ($\hat{\beta}_{PIPW}$), PIPW with incorrectly specified treatment confounding bridge functions ($\hat{\beta}_{PIPW, WIPW}$), PDR with both outcome and treatment confounding bridge functions correctly specified ($\hat{\beta}_{PDR}$), PDR with incorrectly specified outcome confounding bridge functions ($\hat{\beta}_{PDR, WOR}$), PDR with incorrectly specified treatment confounding bridge functions ($\hat{\beta}_{PDR, WIPW}$), PDR with both outcome and treatment confounding bridge functions wrongly put ($\hat{\beta}_{PDR, BW}$) and a standard doubly robust estimator ($\hat{\beta}_{DR}$) for $\beta$ in model (F.3), for sample size $N = 500$ and $B = 1000$ Monte Carlo samples.

|                | Bias  | SEE   | SD    | 95% CP |
|----------------|-------|-------|-------|--------|
| $\hat{\beta}_{0, POR}$ | -1.62 | 64.80 | 64.70 | 94.60  |
| $\hat{\beta}_{1, POR}$ | 1.82  | 52.60 | 51.80 | 94.30  |
| $\hat{\beta}_{0, POR, WOR}$ | -5.89 | 72.00 | 104.00| 94.70  |
| $\hat{\beta}_{1, POR, WOR}$ | 12.20 | 60.60 | 90.60 | 94.70  |
| $\hat{\beta}_{0, PIPW}$  | -0.15 | 76.90 | 7720.00| 97.60  |
| $\hat{\beta}_{1, PIPW}$  | 2.66  | 60.00 | 5970.00| 96.70  |
| $\hat{\beta}_{0, PIPW, WIPW}$ | 31.10 | 73.20 | 3380.00| 97.70  |
| $\hat{\beta}_{1, PIPW, WIPW}$ | -10.20| 56.50 | 1640.00| 96.70  |
| $\hat{\beta}_{0, PDR}$    | -1.88 | 71.20 | 5730.00| 97.20  |
| $\hat{\beta}_{1, PDR}$    | 1.96  | 56.10 | 4200.00| 95.80  |
| $\hat{\beta}_{0, PDR, WOR}$ | 0.02  | 79.70 | 6010.00| 96.50  |
| $\hat{\beta}_{1, PDR, WOR}$ | 1.95  | 65.20 | 4640.00| 95.90  |
| $\hat{\beta}_{0, PDR, WIPW}$ | -0.88 | 70.10 | 2060.00| 97.30  |
| $\hat{\beta}_{1, PDR, WIPW}$ | 1.19  | 57.50 | 2050.00| 96.90  |
| $\hat{\beta}_{0, DR}$     | 15.50 | 78.80 | 1250.00| 98.00  |
| $\hat{\beta}_{1, DR}$     | -3.91 | 65.20 | 2310.00| 98.40  |
| $\hat{\beta}_{0, DR}$     | 25.80 | 77.20 | 100.00 | 98.40  |
| $\hat{\beta}_{1, DR}$     | -421.00| 58.90 | 75.20  | 1.20   |
**Table 2.** Simulation results of POR, PIPW and PDR estimators. We report bias ($\times 10^{-3}$), empirical standard error (SEE) ($\times 10^{-3}$), average estimated standard error (SD) ($\times 10^{-3}$), and coverage probability of 95% confidence intervals (95% CP) of POR with correctly specified outcome confounding bridge functions ($\hat{\beta}_{POR}$), POR with incorrectly specified outcome confounding bridge functions ($\hat{\beta}_{POR, WOR}$), PIPW with correctly specified treatment confounding bridge functions ($\hat{\beta}_{PIPW}$), PIPW with incorrectly specified treatment confounding bridge functions ($\hat{\beta}_{PIPW, WIPW}$), PDR with both outcome and treatment confounding bridge functions correctly specified ($\hat{\beta}_{PDR}$), PDR with incorrectly specified outcome confounding bridge functions ($\hat{\beta}_{PDR, WOR}$), PDR with incorrectly specified treatment confounding bridge functions ($\hat{\beta}_{PDR, WIPW}$), PDR with both outcome and treatment confounding bridge functions wrongly put ($\hat{\beta}_{PDR, BW}$) and a standard doubly robust estimator ($\hat{\beta}_{DR}$) for $\beta$ in model (F.3), for sample size $N = 1000$ and $B = 1000$ Monte Carlo samples.

|                | Bias  | SEE   | SD    | 95% CP |
|----------------|-------|-------|-------|--------|
| $\hat{\beta}_{0, POR}$ | 0.63  | 44.70 | 44.90 | 94.80  |
| $\hat{\beta}_{1, POR}$ | -0.30 | 35.60 | 35.60 | 95.40  |
| $\hat{\beta}_{0, POR, WOR}$ | -4.15 | 48.30 | 50.00 | 95.20  |
| $\hat{\beta}_{1, POR, WOR}$ | 10.60 | 41.10 | 41.90 | 94.80  |
| $\hat{\beta}_{0, PIPW}$ | 0.39  | 50.20 | 1500.00 | 96.10 |
| $\hat{\beta}_{1, PIPW}$ | -0.73 | 40.30 | 595.00 | 96.10 |
| $\hat{\beta}_{0, PIPW, WIPW}$ | 27.00 | 47.60 | 151.00 | 95.50 |
| $\hat{\beta}_{1, PIPW, WIPW}$ | -11.90 | 38.40 | 124.00 | 95.20 |
| $\hat{\beta}_{0, PDR}$ | 0.20  | 47.80 | 2150.00 | 96.20 |
| $\hat{\beta}_{1, PDR}$ | -0.56 | 38.20 | 2390.00 | 96.70 |
| $\hat{\beta}_{0, PDR, WOR}$ | 1.24  | 51.80 | 2170.00 | 96.20 |
| $\hat{\beta}_{1, PDR, WOR}$ | -0.57 | 44.30 | 1060.00 | 96.10 |
| $\hat{\beta}_{0, PDR, WIPW}$ | -0.58 | 47.30 | 145.00 | 97.10 |
| $\hat{\beta}_{1, PDR, WIPW}$ | -0.49 | 38.00 | 89.90 | 96.80 |
| $\hat{\beta}_{0, PDR, BW}$ | 17.00 | 49.50 | 172.00 | 96.50 |
| $\hat{\beta}_{1, PDR, BW}$ | -6.47 | 43.50 | 123.00 | 97.20 |
| $\hat{\beta}_{0, DR}$ | 30.00 | 52.30 | 60.30 | 94.70 |
| $\hat{\beta}_{1, DR}$ | -423.00 | 40.00 | 45.30 | 0.00 |
Table 3. Simulation results of POR, PIPW and PDR estimators. We report bias \((\times 10^{-3})\), empirical standard error (SEE) \((\times 10^{-3})\), average estimated standard error (SD) \((\times 10^{-3})\), and coverage probability of 95% confidence intervals (95% CP) of POR with correctly specified outcome confounding bridge functions \(\hat{\beta}_{\text{POR}}\), POR with incorrectly specified outcome confounding bridge functions \(\hat{\beta}_{\text{POR, WOR}}\), PIPW with correctly specified treatment confounding bridge functions \(\hat{\beta}_{\text{PIPW}}\), PIPW with incorrectly specified treatment confounding bridge functions \(\hat{\beta}_{\text{PIPW, WIPW}}\), PDR with both outcome and treatment confounding bridge functions correctly specified \(\hat{\beta}_{\text{PDR}}\), PDR with incorrectly specified outcome confounding bridge functions \(\hat{\beta}_{\text{PDR, WOR}}\), PDR with incorrectly specified treatment confounding bridge functions \(\hat{\beta}_{\text{PDR, WIPW}}\), PDR with both outcome and treatment confounding bridge functions wrongly put \(\hat{\beta}_{\text{PDR, BW}}\) and a standard doubly robust estimator \(\hat{\beta}_{\text{DR}}\) for \(\beta\) in model (F.3), for sample size \(N = 4000\) and \(B = 1000\) Monte Carlo samples.

| \(\hat{\beta}_{0}\) | \(\hat{\beta}_{1}\) | \(\hat{\beta}_{0}\) | \(\hat{\beta}_{1}\) |
|---------------------|-------------------|---------------------|-------------------|
| POR | POR | POR | POR |
| POR | WOR | POR | WOR |
| PIPW | PIPW | PIPW | PIPW |
| PIPW | WIPW | PIPW | WIPW |
| PDR | PDR | PDR | PDR |
| PDR | WOR | PDR | WOR |
| PDR | WIPW | PDR | WIPW |
| PDR | BW | PDR | BW |
| DR | DR | DR | DR |

| Bias | SEE | SD | 95% CP |
|------|-----|----|--------|
| -0.628 | 22.4 | 22.2 | 95.4 |
| 0.699 | 17.4 | 17.6 | 95.3 |
| -4.69 | 25.2 | 24.6 | 93.3 |
| 10.7 | 20.9 | 20.5 | 92.0 |
| -0.215 | 24.2 | 24.6 | 95.1 |
| 0.152 | 18.8 | 19.3 | 94.6 |
| 21.8 | 23.8 | 26.4 | 88.0 |
| -11.8 | 17.7 | 18.7 | 90.6 |
| -0.391 | 23.1 | 23.4 | 95.8 |
| 0.0221 | 18.0 | 18.4 | 95.1 |
| 0.0457 | 25.6 | 25.6 | 95.5 |
| -0.235 | 21.1 | 21.2 | 95.1 |
| 0.0457 | 23.4 | 23.6 | 95.7 |
| 0.212 | 18.1 | 18.5 | 95.3 |
| 18.6 | 25.4 | 27.0 | 90.3 |
| -7.23 | 20.9 | 23.0 | 95.6 |
| 28.7 | 25.8 | 25.9 | 78.6 |
| -421. | 19.9 | 19.8 | 0 |
Table 4. Simulation results of POR, PIPW and PDR estimators. We report bias ($\times 10^{-3}$), empirical standard error (SEE) ($\times 10^{-3}$), average estimated standard error (SD) ($\times 10^{-3}$), and coverage probability of 95% confidence intervals (95% CP) of POR with correctly specified outcome confounding bridge functions ($\hat{\beta}_{POR}$), POR with incorrectly specified outcome confounding bridge functions ($\hat{\beta}_{POR, WOR}$), PIPW with correctly specified treatment confounding bridge functions ($\hat{\beta}_{PIPW}$), PIPW with incorrectly specified treatment confounding bridge functions ($\hat{\beta}_{PIPW, WIPW}$), PDR with both outcome and treatment confounding bridge functions correctly specified ($\hat{\beta}_{PDR}$), PDR with incorrectly specified outcome confounding bridge functions ($\hat{\beta}_{PDR, WOR}$), PDR with incorrectly specified treatment confounding bridge functions ($\hat{\beta}_{PDR, WIPW}$), PDR with both outcome and treatment confounding bridge functions wrongly put ($\hat{\beta}_{PDR, BW}$) and a standard doubly robust estimator ($\hat{\beta}_{DR}$) for $\beta$ in model (F.3), for sample size $N = 8000$ and $B = 1000$ Monte Carlo samples.

|   | Bias  | SEE  | SD   | 95% CP |
|---|-------|------|------|--------|
| $\hat{\beta}_0$, POR | -0.0433 | 15.5 | 15.7 | 95.9   |
| $\hat{\beta}_1$, POR | 0.359  | 12.1 | 12.4 | 95.3   |
| $\hat{\beta}_0$, POR, WOR | -4.29  | 17.4 | 17.3 | 95.1   |
| $\hat{\beta}_1$, POR, WOR | 10.5   | 14.5 | 14.5 | 89.1   |
| $\hat{\beta}_0$, PIPW | -0.0637 | 16.8 | 16.9 | 95.0   |
| $\hat{\beta}_1$, PIPW | -0.160 | 13.1 | 13.3 | 95.7   |
| $\hat{\beta}_0$, PIPW, WIPW | 20.1   | 16.7 | 17.3 | 79.8   |
| $\hat{\beta}_1$, PIPW, WIPW | -12.0  | 12.4 | 12.8 | 82.9   |
| $\hat{\beta}_0$, PDR | -0.123 | 16.1 | 16.3 | 95.2   |
| $\hat{\beta}_1$, PDR | -0.120 | 12.6 | 12.8 | 94.3   |
| $\hat{\beta}_0$, PDR, WOR | -0.0418 | 17.6 | 17.9 | 95.5   |
| $\hat{\beta}_1$, PDR, WOR | -0.189 | 14.5 | 14.8 | 95.1   |
| $\hat{\beta}_0$, PDR, WIPW | -0.100 | 16.0 | 16.4 | 95.7   |
| $\hat{\beta}_1$, PDR, WIPW | -0.134 | 12.7 | 12.9 | 95.5   |
| $\hat{\beta}_0$, PDR, BW | 18.7   | 17.1 | 18.5 | 83.3   |
| $\hat{\beta}_1$, PDR, BW | -7.59  | 14.3 | 16.0 | 94.2   |
| $\hat{\beta}_0$, DR | 29.3   | 18.3 | 17.9 | 63.2   |
| $\hat{\beta}_1$, DR | -421.  | 14.3 | 13.7 | 0      |
F.2. Compatibility

In order to confirm model compatibility of the data generating mechanism described in Section F.1 we must show that assumptions 1, 2, 3, 4, 5 hold with \((h_k, q_k)\) correctly specified. The data generating time ordering used throughout is \(X(0), U(0), A(0), W(0), Z(0), X(1), U(1), A(1), W(1), Z(1), Y\). The outcome proxy \(W(0)\) is generated solely conditional on \(X(0)\) and \(U(0)\), therefore intervening on \(A(0)\) and \(Z(0)\) does not have a causal effect on \(W(0)\), in other words, \(W(0) = W_{a(0),z(0)}(0)\). The outcome \(W(1)\) is generated conditional on \(A(0), X(1)\) and \(U(1)\), whereas we do not allow \(Z(0)\) to have a direct effect on \(X(1)\) and \(U(1)\), therefore \(W_{a(1),z(1)}(1) = W_{a(0)}(1)\). Similarly, \(Y_{\pi(1),\pi(1)}(1) = Y_{\pi(1)}\). Upon conditioning on \(A(0), X(1), U(1)\) and intervening on \(A(1), (Z(1), A(1)) \perp (Y_{\pi(1)}, W)|A(0), X(1), U(1)\). Upon conditioning on \(X(0), U(0)\) and intervening on \(A(0)\), all paths from \(A(0)\) to \(Y\) are blocked and thus \(A(0)\) and \(Y_{\pi(1)}\) independent given \(X(0), U(0)\). Hence assumptions 1, 2 and 3 hold.

Assumptions 4, 5 are immediate as \(U(0), W(0), Z(0), U(1), W(1), Z(1)\) are all one-dimensional, continuous and mutually dependent.

Next we show that \(h_0, h_1\) satisfy the functional forms (16) and (17). By our DGP, 
\[
\mathbb{E}(Y|\bar{A}(1), \bar{X}(1), \bar{U}(1)) \quad \text{and} \quad \mathbb{E}(W(1)|\bar{A}(1), \bar{X}(1), \bar{U}(1)) = \mathbb{E}(W(1)|\bar{X}(1), \bar{U}(1))
\]
are linear in \((\bar{A}(1), \bar{X}(1), \bar{U}(1))\). It is easy to see that \(W(0) \perp (X(1), U(1), \bar{A}(1))|X(0), U(0)\) and therefore \(\mathbb{E}(W(0)|\bar{A}(1), \bar{X}(1), \bar{U}(1)) = \mathbb{E}(W(0)|X(0), U(0))\) is also linear. Hence clearly there exists a linear function \(h_1\) so that (16) holds. Now since \(W(1)\) and \(X(1)\) are linear in \((A(0), X(0), U(0))\), \(h_0\) is also linear and (17) holds.

Finally, we prove that \(q_0, q_1\) satisfy the functional forms (18) and (19). Since
\[
\mathbb{E}(Q_0(A_0)|A(0), X(0), U(0)) = \frac{1}{\mathbb{P}(A(0)|X(0), U(0))} = 1 + \exp((-1)^{1-A(0)}(-0.25 - 0.5 * X(0) - U(0))), \quad (F.4)
\]
and \(Z(0)\) is normal given \(A(0), X(0), U(0)\), from the moment generating function of a normal distribution,
\[
\mathbb{E}(Q_0(A(0)|A(0), X(0), U(0)) = 1 + \exp((-1)^{1-A(0)}(t_{0,0} + t_{0,a(0)}A(0) + t_{0,x(0)}X(0)]
\times \mathbb{E}(\exp((-1)^{1-A(0)}t_{0,z(0)}Z(0))|A(0), X(0), U(0))
= 1 + \exp((-1)^{1-A(0)}t_{0,0} + t_{0,a(0)}A(0) + t_{0,x(0)}X(0)
\times \mathbb{E}(Z(0)|A(0), X(0), U(0)) + \frac{t_{0,z(0)}^2}{2} \text{Var}(Z(0)|A(0), X(0), U(0)) \quad (F.5)
\]
Note that \(\mathbb{E}(Z(0)|A(0), X(0), U(0))\) and \(\text{Var} Z(0)|A(0), X(0), U(0)\) are both linear in \((A(0), X(0), U(0))\) by our DGP. One can find \(t_0\) such that (F.5) equals (F.4) and hence
is correctly specified. We also have 
\[ q_0 \] is correctly specified. We also have 
\[ Z(0) \perp (X(1), U(1)) | A(0), X(0), U(0) \] and hence
\[
E(Q_1(\bar{A}(1) | \bar{A}(1), \bar{X}(1), \bar{U}(1)) = \frac{E(Q_0(A(0)|A(0), X(0), U(0)))}{P(A(1)|A(0), \bar{X}(1), \bar{U}(1))}
\]
\[
= \frac{1}{P(A(1)|A(0), \bar{X}(1), \bar{U}(1))} \frac{1 - P(A(0)|X(0), U(0))}{P(A(0)|X(0), U(0))} + \frac{1 - P(A(1)|A(0), \bar{X}(1), \bar{U}(1))}{P(A(1)|A(0), \bar{X}(1), \bar{U}(1))} \frac{1 - P(A(0)|X(0), U(0))}{P(A(0)|X(0), U(0))} \frac{1 - P(A(1)|A(0), \bar{X}(1), \bar{U}(1))}{P(A(1)|A(0), \bar{X}(1), \bar{U}(1))},
\]
written in terms of odds. Note that by (F.5) and the same reasoning when proving that 
(F.5) equals (F.4), conditioning (19) on 
\( (A(0), \bar{X}(1), \bar{U}(1)) \),
\[
E[\exp((-1)^{1-A(0)}(t_0^T (1, A(0), Z(0), X(0))))|A(0), \bar{X}(1), \bar{U}(1)]
= \frac{1 - P(A(0)|X(0), U(0))}{P(A(0)|X(0), U(0))},
\]
and
\[
E[\exp((-1)^{1-A(1)}(t_1^T (1, \bar{A}(1), \bar{Z}(1), \bar{X}(1))))|A(0), \bar{X}(1), \bar{U}(1)]
= \frac{1 - P(A(1)|A(0), \bar{X}(1), \bar{U}(1))}{P(A(1)|A(0), \bar{X}(1), \bar{U}(1))}.
\]
It remains to show that
\[
E[\exp((-1)^{1-A(0)}(t_0^T (1, A(0), Z(0), X(0))) + (-1)^{1-A(1)}(t_1^T (1, \bar{A}(1), \bar{Z}(1), \bar{X}(1))))|A(0), \bar{X}(1), \bar{U}(1)]
= \frac{1 - P(A(1)|A(0), \bar{X}(1), \bar{U}(1))}{P(A(1)|A(0), \bar{X}(1), \bar{U}(1))} 1 - P(A(1)|A(0), \bar{X}(1), \bar{U}(1)) \frac{1 - P(A(1)|A(0), \bar{X}(1), \bar{U}(1))}{P(A(1)|A(0), \bar{X}(1), \bar{U}(1))}.
\]
Note that (F.1) and (F.2) are indeed functions of \( U(1) + U(0) \), implying that \( t_{1,z(0)} = 0 \).
Now since 
\( Z(1) \perp Z(0) | A(0), \bar{X}(1), \bar{U}(1), \)
\[
E[\exp((-1)^{1-A(0)}(t_0^T (1, A(0), Z(0), X(0))) + (-1)^{1-A(1)}(t_1^T (1, \bar{A}(1), \bar{Z}(1), \bar{X}(1))))|A(0), \bar{X}(1), \bar{U}(1)]
= E[\exp((-1)^{1-A(0)}(t_0^T (1, A(0), Z(0))) + (-1)^{1-A(1)}(t_1^T (1, \bar{A}(1), \bar{Z}(1))))|A(0), \bar{X}(1), \bar{U}(1)]
= \exp[\mathbb{E}((-1)^{1-A(0)}(t_0^T (1, A(0), Z(0)))|A(0), \bar{X}(1), \bar{U}(1)]
= \exp[\mathbb{E}((-1)^{1-A(0)}(t_0^T (1, A(0), Z(0)))|A(0), \bar{X}(1), \bar{U}(1)]
+ \text{Var} (-1)^{1-A(0)}(t_0^T (1, A(0), Z(0))|A(0), \bar{X}(1), \bar{U}(1)]
= \exp[\mathbb{E}((-1)^{1-A(0)}(t_0^T (1, A(0), Z(0)))|A(0), \bar{X}(1), \bar{U}(1)]
\cdot \mathbb{E}((-1)^{1-A(1)}(t_1^T (1, A(0), Z(0)))|A(0), \bar{X}(1), \bar{U}(1)]
+ \text{Var} (-1)^{1-A(1)}(t_1^T (1, A(0), Z(0))|A(0), \bar{X}(1), \bar{U}(1)]
It follows that \( q_1 \) is correctly specified.
F.3. Simulation when Sequential Proximal Independence Assumptions Fail

We investigate the finite-sample performance of POR, PIPW and PDR estimators when longitudinal proximal independence assumptions (2), (3) and (4) are violated.

Data-generating mechanisms: We generated data \((Y, \overline{W}(1), \overline{A}(1), \overline{Z}(1), \overline{U}(1), \overline{X}(1))\) as follows (we write \(c(\overline{X}(1)) = X(0) + X(1)\), also for \(c(\overline{U}(1))\)):

\[
X(0) \sim \mathcal{N}(-0.35, 0.5^2),
\]

\[
U(0) \sim \mathcal{N}(0.35, 0.5^2),
\]

\[
Z(0) \sim \mathcal{N}(0.2 + 0.5X(0) + 0.75U(0), 0.5^2),
\]

\[
W(0) \sim \mathcal{N}(0.2 + 0.5X(0) - 0.75U(0) + \alpha_{W(0)|Z(0)}Z(0), 0.5^2),
\]

\[
\mathbb{P}(A(0)|X(0), U(0), W(0)) = \frac{1}{1 + \exp((-1)^1A(0)(0.5 - 0.2X(0) - 0.25U(0) + \alpha_{A(0)|W(0)}W(0))},
\]

\[
X(1) \sim \mathcal{N}(0.2 + 0.7A(0) + 0.7X(0), 0.5^2),
\]

\[
U(1) \sim \mathcal{N}(0.2 + 0.7A(0) + 0.7U(0), 0.5^2),
\]

\[
Z(1) \sim \mathcal{N}(0.2 + 0.5c(\overline{X}(1)) - 0.75c(\overline{U}(1)), 0.5^2),
\]

\[
W(1) \sim \mathcal{N}(0.35 + 0.2c(\overline{X}(1)) - 0.7c(\overline{U}(1)) + \alpha_{W(1)|Z(0)}Z(0) + \alpha_{W(1)|Z(1)}Z(1), 0.5^2),
\]

\[
\mathbb{P}(A(1)|A(0), \overline{X}(1), \overline{U}(1), \overline{W}(1)) = \frac{1}{1 + \exp((-1)^1A(1)(0.5 - 0.5A(0) - 0.15c(\overline{X}(1)) - 0.25c(\overline{U}(1)) + \alpha_{A(1)|W(0)}W(0) + \alpha_{A(1)|W(1)}W(1))},
\]

\[
Y \sim \mathcal{N}(-1.3 + 1A(1) + 1.14A(0) + 0.5X(1) - 0.7U(1) + 0.2X(0) - 0.7U(0) + \alpha_{Y|Z(0)}Z(0) + \alpha_{Y|Z(1)}Z(1), 0.5^2).
\]

We allow \(Z(0), Z(1), W(0)\) and \(W(1)\) to have direct effect on \((\overline{W}(1), Y), (W(1), Y), \overline{A}(1)\) and \(A(1)\), respectively, therefore breaking the proximal independence assumptions (2), (3) and (4). We vary \((\alpha_{W(0)|Z(0)}, \alpha_{A(0)|W(0)}, \alpha_{W(1)|Z(0)}, \alpha_{W(1)|Z(1)}, \alpha_{A(1)|W(0)}, \alpha_{A(1)|W(1)}, \alpha_{Y|Z(0)}, \alpha_{Y|Z(1)})\) in three cases to reflect minor, moderate and substantial deviations from the proximal independence assumptions. Parameters values under these three cases are summarized in Table 5.

Estimand: Our estimand is \(\beta_1\) from the following MSMM

\[
\mathbb{E}[Y_{\pi(1)}] = \beta_0 + \beta_1(a(0) + a(1)),
\]

which encodes the average treatment effect.

Methods: Each simulated dataset is analyzed using

- The POR estimator \(\hat{\beta}_{POR}\);
- The PIPW estimator \(\hat{\beta}_{PIPW}\);
- The PDR estimator \(\hat{\beta}_{PDR}\).
Table 5. Varying parameters to reflect minor, moderate, and substantial deviations from the proximal independence assumptions.

|                         | Minor | Moderate | Substantial |
|-------------------------|-------|----------|-------------|
| \( \alpha_{W(0)|Z(0)} \) | -0.01 | -0.07    | -0.15       |
| \( \alpha_{A(0)|W(0)} \)  | -0.01 | -0.1     | -0.2        |
| \( \alpha_{W(1)|Z(0)} \)  | -0.01 | -0.07    | -0.15       |
| \( \alpha_{W(1)|Z(1)} \)  | -0.01 | -0.07    | -0.15       |
| \( \alpha_{A(1)|W(0)} \)  | 0.01  | 0.1      | 0.2         |
| \( \alpha_{A(1)|W(1)} \)  | -0.01 | -0.1     | -0.3        |
| \( \alpha_{Y|Z(0)} \)     | -0.01 | -0.05    | -0.1        |
| \( \alpha_{Y|Z(1)} \)     | -0.01 | -0.05    | -0.1        |

However, they are expected to fail since the longitudinal proximal independence assumptions (2), (3) and (4) are violated.

**Performance measures:** We examine the performance of these estimators by reporting bias, empirical standard errors (SEE), average estimated standard errors (SD), and coverage probabilities of 95% confidence intervals using \( B = 1000 \) simulated data sets of size \( N = 4000 \). The results are given in Table 6.

As the simulation results illustrate, \( \hat{\beta}_{\text{POR}} \), \( \hat{\beta}_{\text{PIPW}} \) and \( \hat{\beta}_{\text{PDR}} \) can tolerate minor deviation from proximal independence assumptions, with reasonably small bias and coverage probabilities close to nominal levels. However, they incur a larger bias when the underlying model deviates more, leading to poor coverage probabilities.

**F.4. Simulation when Sequential Proxy Relevance Assumptions Fail**

We investigate the finite-sample performance of POR, PIPW and PDR estimators when sequential proxy relevance assumptions 4(a) and 5(a) are violated.

**Data-generating mechanisms:** We generated data \((Y, W(1), A(1), Z(1), U_1(1), U_2(1), X(1))\) as follows (we write \( c(X(1)) = X(0) + X(1) \), also for \( c(U_1(1)) \)):

\[
X(0) \sim \mathcal{N}(-0.35, 0.5^2),
\]

\[
U_1(0) \sim \mathcal{N}(0.35, 0.5^2),
\]

\[
U_2(0) \sim \mathcal{N}(0.2, 0.5^2),
\]

\[
P(A(0)|X(0), U_1(0), U_2(0)) = \frac{1}{1 + \exp((-1)^{1-A(0)}(0.5 - 0.2X(0) - 0.25U_1(0) + \alpha_{A(0)|U_2(0)}U_2(0)))},
\]

\[
Z(0) \sim \mathcal{N}(0.2 + 0.5A(0) + 0.5X(0) + 0.75U_1(0) + \alpha_{Z(0)|U_2(0)}U_2(0), 0.5^2),
\]

\[
W(0) \sim \mathcal{N}(0.2 + 0.5X(0) - 0.75U_1(0) + \alpha_{W(0)|U_2(0)}U_2(0), 0.5^2),
\]

\[
X(1) \sim \mathcal{N}(0.2 + 0.7A(0) + 0.7X(0), 0.5^2),
\]

\[
U_1(1) \sim \mathcal{N}(0.2 + 0.7A(0) + 0.7U_1(0) + \alpha_{U_1(1)|U_2(0)}U_2(0), 0.5^2),
\]

\[
U_2(1) \sim \mathcal{N}(0.2 + 0.7A(0) + \alpha_{U_2(1)|U_1(0)}U_1(0) + 0.7U_2(0), 0.5^2),
\]
Table 6. Simulation results of POR, PIPW and PDR estimators when longitudinal proximal independence assumptions (2), (3) and (4) are violated. We report bias ($\times 10^{-3}$), empirical standard error (SEE) ($\times 10^{-3}$), average estimated standard error (SD) ($\times 10^{-3}$), and coverage probability of 95% confidence intervals (95% CP) of POR ($\hat{\beta}_{1,\text{POR}}$), PIPW ($\hat{\beta}_{1,\text{PIPW}}$), PDR ($\hat{\beta}_{1,\text{PDR}}$) for $\beta_1$ in model (F.6), for sample size $N = 4000$ and $B = 1000$ Monte Carlo samples.

| N = 4000 | Bias | SEE | SD | 95% CP |
|----------|------|-----|----|--------|
| Minor deviation | | | | |
| $\hat{\beta}_{1,\text{POR}}$ | 2.3 | 19.6 | 19.2 | 94.4 |
| $\hat{\beta}_{1,\text{PIPW}}$ | 3.4 | 20.5 | 20.0 | 94.1 |
| $\hat{\beta}_{1,\text{PDR}}$ | 3.5 | 20.0 | 19.7 | 94.0 |
| Moderate deviation | | | | |
| $\hat{\beta}_{1,\text{POR}}$ | 29.1 | 19.0 | 18.6 | 64.8 |
| $\hat{\beta}_{1,\text{PIPW}}$ | 31.1 | 22.3 | 41.0 | 71.8 |
| $\hat{\beta}_{1,\text{PDR}}$ | 31.6 | 20.2 | 31.4 | 68.6 |
| Substantial deviation | | | | |
| $\hat{\beta}_{1,\text{POR}}$ | 73.0 | 20.0 | 20.1 | 3.9 |
| $\hat{\beta}_{1,\text{PIPW}}$ | 73.9 | 40.0 | 1614 | 60.7 |
| $\hat{\beta}_{1,\text{PDR}}$ | 82.4 | 33.4 | 1179 | 46.6 |

$P(A(1)|A(0), \bar{X}(1), \bar{U}_1(1), \bar{U}_2(1)) = \frac{1}{1 + \exp((-1)^{1-A(1)}(0.5 - 0.5A(0) - 0.15c(\bar{X}(1)) - 0.25c(\bar{U}_1(1)) + \alpha_{A(1)}U_2(0)U_2(0) + \alpha_{A(1)}U_2(1)U_2(1)))}.$

$Z(1) \sim \mathcal{N}(0.2 + 0.5A(1) + 0.5c(\bar{X}(1)) - 0.75c(\bar{U}_1(1)) + \alpha_{Z(1)}U_2(0)U_2(0) + 0.5A(0) + \alpha_{Z(1)}U_2(0)U_2(0), 0.5^2),$  

$W(1) \sim \mathcal{N}(0.35 - 0.5c(\bar{X}(1)) - 0.75c(\bar{U}_1(1)) + \alpha_{W(1)}U_2(1)U_2(1) + \alpha_{W(1)}U_2(0)U_2(0), 0.5^2),$  

$Y \sim \mathcal{N}(-1.3 + 1A(1) + 1.14A(0) + 0.5X(1) + \alpha_{Y|U_1(1)}U_1(1) + \alpha_{Y|U_2(1)}U_2(1) + 0.2X(0) - 0.7U_1(0) + \alpha_{Y|U_2(0)}U_2(0), 0.5^2).$  

We allow two time varying unmeasured confounders ($\bar{U}_1(1), \bar{U}_2(1)$) but only provide one time varying outcome-inducing confounding proxy and one time varying treatment-inducing confounding proxy. It hence follows that the proxy relevance assumption 4(a) and 5(a) are not satisfied. We vary ($\alpha_{A(0)}U_2(0)$, $\alpha_{Z(0)}U_2(0)$, $\alpha_{W(0)}U_2(0)$, $\alpha_{U_1(1)}U_2(0)$, $\alpha_{U_2(1)}U_1(0)$, $\alpha_{A(1)}U_2(0)$, $\alpha_{A(1)}U_2(1)$, $\alpha_{Z(1)}U_2(0)$, $\alpha_{Z(1)}U_2(1)$, $\alpha_{W(1)}U_2(0)$, $\alpha_{W(1)}U_2(1)$, $\alpha_{Y|U_1(1)}U_1(1)$, $\alpha_{Y|U_2(1)}U_2(1)$, $\alpha_{Y|U_2(0)}U_2(0)$) in three cases to reflect minor, moderate and substantial deviations from the proxy relevance assumptions. The parameters chosen in the data generating process under these three cases are summarized in Table 7.

**Estimand:** Our estimand is $\beta_1$ from the following MSMM

$$E[Y_{\pi(1)}] = \beta_0 + \beta_1(a(0) + a(1)),$$  

(F.6)
which encodes the average treatment effect.

**Methods:** Each simulated dataset is analyzed using

- The POR estimator $\hat{\beta}_{POR}$;
- The PIPW estimator $\hat{\beta}_{PIPW}$;
- The PDR estimator $\hat{\beta}_{PDR}$.

However, they are expected to fail since sequential proxy relevance assumptions 4(a) and 5(a) are violated.

**Performance measures:** We examine the performance of these estimators by reporting biases, empirical standard errors (SEE), average estimated standard errors (SD), and coverage probabilities of 95% confidence intervals using $B = 1000$ simulated data sets of size $N = 4000$. The results are given in Table 8.

The simulation results imply that $\hat{\beta}_{POR}$, $\hat{\beta}_{PIPW}$ and $\hat{\beta}_{PDR}$ perform satisfactorily under minor deviation from proxy relevance assumptions, with small biases and accurate coverage probabilities to their nominal levels, though the estimators incur larger bias when the underlying model deviates more from proxy relevance assumptions, which leads to poor coverage probabilities.

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An, Y. and Y. Hu (2012). Well-posedness of measurement error models for self-reported data. *Journal of Econometrics* 168(2), 259–269.
Table 8. We investigate the finite-sample performance of POR, PIPW and PDR estimators when sequential proxy relevance assumptions 4(a) and 5(a) are violated. We report bias ($\times 10^{-3}$), empirical standard error (SEE) ($\times 10^{-3}$), average estimated standard error (SD) ($\times 10^{-3}$), and coverage probability of 95% confidence intervals (95% CP) of POR ($\hat{\beta}_{1,\text{POR}}$), PIPW ($\hat{\beta}_{1,\text{PIPW}}$), PDR ($\hat{\beta}_{1,\text{PDR}}$) for $\beta_1$ in model (F.6), for sample size $N = 4000$ and $B = 1000$ Monte Carlo samples.

| N = 4000 | Bias | SEE | SD  | 95% CP |
|----------|------|-----|-----|--------|
| Minor deviation | | | | |
| $\hat{\beta}_{1,\text{POR}}$ | 5.0  | 18.5| 18.8| 94.0   |
| $\hat{\beta}_{1,\text{PIPW}}$ | 4.1  | 19.6| 19.4| 95.1   |
| $\hat{\beta}_{1,\text{PDR}}$  | 4.1  | 19.3| 19.1| 95.1   |
| Moderate deviation | | | | |
| $\hat{\beta}_{1,\text{POR}}$ | 21.4 | 20.8| 20.6| 81.8   |
| $\hat{\beta}_{1,\text{PIPW}}$ | 22.4 | 22.4| 22.5| 83.4   |
| $\hat{\beta}_{1,\text{PDR}}$  | 22.0 | 20.9| 21.0| 82.1   |
| Substantial deviation | | | | |
| $\hat{\beta}_{1,\text{POR}}$ | 46.0 | 23.8| 24.0| 51.8   |
| $\hat{\beta}_{1,\text{PIPW}}$ | 49.0 | 27.8| 28.8| 61.1   |
| $\hat{\beta}_{1,\text{PDR}}$  | 48.0 | 23.8| 24.6| 49.2   |

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