Robins (1998) introduced marginal structural models (MSMs), a general class of counterfactual models for the joint effects of time-varying treatment regimes in complex longitudinal studies subject to time-varying confounding. He established identification of MSM parameters under a sequential randomization assumption (SRA), which essentially rules out unmeasured confounding of treatment assignment over time. In this technical report, we consider sufficient conditions for identification of MSM parameters with the aid of a time-varying instrumental variable, when sequential randomization fails to hold due to unmeasured confounding. Our identification conditions essentially require that no unobserved confounder predicts compliance type for the time-varying treatment, the longitudinal generalization of the identifying condition of Wang and Tchetgen Tchetgen (2018). Under this assumption, We derive a large class of semiparametric estimators that extends standard inverse-probability weighting (IPW), the most popular approach for estimating MSMs under SRA, by incorporating the time-varying IV through a modified set of weights. The set of influence functions for MSM parameters is derived under a semiparametric model with sole restriction on observed data distribution given by the MSM, and is shown to provide a rich class of multiply robust estimators, including a local semiparametric efficient estimator.

KEY WORDS: marginal structural models, time-varying endogeneity, instrumental variables, multiple robustness, local efficiency.
1 Introduction

Robins (1998, 1999, 2000a) introduced a new class of counterfactual models known as marginal structural models (MSMs) that encode the joint causal effects of time-varying treatment subject to time-varying confounding. For identification, Robins relied on a sequential randomization assumption (SRA) which essentially rules out unmeasured confounding of the time-varying treatment. In this technical report, we consider sufficient conditions for identification of MSM parameters with the aid of a time-varying instrumental variable, when sequential randomization fails to hold due to unmeasured confounding. Our identification conditions essentially require longitudinal generalizations of (i) IV relevance, (ii) exclusion restriction, and (iii) IV independence assumptions, together with a key assumption (iv) that no unobserved confounder predicts compliance type for the time-varying treatment, a longitudinal generalization of the identification condition of Wang and Tchetgen Tchetgen (2018). Under these assumptions, we derive a large class of semiparametric estimators which extends standard inverse-probability weighting (IPW), the most common approach for estimating MSMs under SRA (Robins et al. 2000, Hernán et al., 2000, 2001), that incorporates the time-varying IV through a modified set of weights. The set of influence functions for MSM parameters under IV identification is derived for a semiparametric model with sole restriction on the observed data distribution given by the MSM, and is shown to provide a rich class of multiply robust estimators, including a locally semiparametric efficient estimator.

Prior to the current work, Robins (1994) developed a general framework for identification and estimation of causal effects of time-varying endogenous treatments using a time-varying instrumental variable under a structural nested model (SNM). As described in Robins (2000a), parameters of an SNM can under certain conditions be interpreted as MSM parameters, in which case, Robins (1994) provides alternative identification conditions to ours. In contrast, the proposed methodology is more general as it directly targets MSM parameters irrespective of whether or not they can be interpreted as parameters of an equivalent SNM.

2 Notation and definitions

Continuous time is denoted by $t$ and is measured in months since the beginning of a subject’s follow-up. The index $j$ is often used when we wish to indicate an integer number of months. $J$ corresponds to the administrative end of follow-up, recorded in whole months. Notice that as staggered entry of participants is a common feature of longitudinal studies, $J$ is considered random. We use capital letters to represent
random variables and lower-case letters to represent possible realizations (values) of random variables. \( A(j) \) denotes a binary treatment taken by a subject in \((j, j+1]\), and \( L(j) \) is a vector of relevant prognostic factors for outcomes \( Y(j+1), \ldots Y(J) \). We assume that recorded data on the treatment and prognostic factors do not change except at these times; moreover, \( L(j) \) temporally precedes \( A(j) \), and \( Y(j) \) is included in \( L(j) \). For any time dependent variable, we use overbars to denote the history of that variable up to and including \( t \); for example, the covariate process through \( t \) is \( \bar{L}(t) = \{ L(0), L(1), \ldots, L(t) \} = \{ L(0), L(1), \ldots, L(\text{int}[t]) \} \) where \( \text{int}[t] \) is the greatest integer less than or equal to \( t \). Note that throughout, unless necessary, we suppress the subscript denoting individual, because we assume that the random vector for each subject is drawn independently from a distribution common to all subjects. We use the symbol \( \perp \) to indicate statistical independence; for example \( A \perp B \mid D \) means that \( A \) is conditionally independent of \( B \) given \( D \). Finally, for any \( O_i \), define \( \mathbb{P}_n[O] = \sum_{i=1}^{n} O_i/n \).

In order to formally define MSMs, we need to introduce counterfactual or potential outcomes. Neyman (1923) was the first to use counterfactual outcomes to analyze the causal effect of time independent treatments in randomized experiments. Later on, Rubin (1974) and Holland (1986) adopted Neyman’s idea and demonstrated the usefulness of counterfactuals in the analysis of the causal effects of time-independent treatments from observational data. Robins (1986,1987) proposed a formal counterfactual theory of causal inference that extended Neyman’s time-independent treatment theory to longitudinal studies with both direct and indirect effects and sequential time-varying treatments and confounders. Throughout, we assume no censoring, although we note that methods to address dependent censoring described in Robins (1998) can easily be adapted to our setting. For a specific fixed treatment history \( \bar{a} = (a(0), a(1), \ldots, a(J-1)) \), \( \bar{L}_\pi \) is defined to be the random vector representing a subject’s covariate process had (possibly contrary to fact) the subject been treated [i.e through time \( J-1 \)] with the particular treatment regime \( \bar{a} \) rather than his or her observed treatment history \( \bar{A} = \bar{A}(J-1) \). Note that \( \bar{a}(t) \) is a possible realization of the random variable \( \bar{A}(t) \). For each possible history \( \bar{a} \), we are assuming that a subject’s potential covariate/outcome process \( \{ \bar{L}_\pi \} \) is well defined, although generally unobserved. Each individual therefore has a corresponding set of counterfactual variables \( L_\mathcal{A} = \{ \bar{L}_\pi = \bar{L}_\pi(J) : \pi \in \mathcal{A} \} \) where \( \mathcal{A} \) is the support of \( \bar{A} \), and throughout, in accordance with reality, the future cannot cause the past, i.e., \( L_\pi(j) = L_{\pi(J-1)}(j), j = 1, \ldots, J-1 \).
3 Brief Review of MSM inference under sequential randomization

An MSM for \( \{ \overline{Y}_\pi : \pi \in A \} \) places restriction on the marginal distribution of the \( \overline{Y}_\pi \) possibly conditional on baseline variables \( V \in L(0) \). Robins (1998, 2000) describes a large number of MSMs reproduced below; however we note that this is certainly not exhaustive:

**Model 1.** in Models 1.1-1.3, suppose that \( Y(j) \equiv 0 \) for \( j < J \) and \( Y \equiv Y(J) \) at the end of follow-up \( J = K + 1 \) w.p.1. for a constant \( K \).

**Model 1.1: Non-linear least-squares:** \( E(Y_\pi | V) = g(\pi, V; \beta_0) \), where \( g(\cdot, \cdot; \cdot) \) is a known function.

**Model 1.2: Semiparametric Regression:** \( \eta(E(Y_\pi | V)) = g(\pi, V; \beta_0) + g^*(V) \), where \( \eta \) is a known monotone link function, \( g^* \) is an unknown unrestricted function, and \( g(\cdot, \cdot; \cdot) \) is a known function with \( g(0, \cdot; \cdot) = 0 \).

**Model 1.3. Stratified Transformation model:** \( \Pr(R(\pi, V; \beta_0) \leq r | V) = F_0(r | V) \), \( F_0 \) is an unknown distribution function, \( R(\pi, V; \beta_0) = r(Y_\pi, \pi, V; \beta) \) is a known increasing function of \( Y_\pi \) satisfying \( r(y, \pi, V; \beta) = y \) if \( \pi = 0 \) or \( \beta = 0 \).

**Model 1.4. Multivariate non-linear least squares:** Suppose that the outcome is observed longitudinally, so that the MSM restricts the marginal joint distribution

\[
\{ \overline{Y}_\pi(K + 1) : \pi \} = \{ Y_{\pi(0)}(1), Y_{\pi(1)}(2), ..., Y_{\pi(K)}(K + 1) : \pi \};
\]

the multivariate non-linear least squares MSM specifies

\[
E(Y_{\pi(m)} | V) = g_m(\pi(m-1), V; \beta_0), m = 1, ..., K + 1,
\]

where \( g_m \) are known functions.

**Model 2.** Suppose that \( J = \infty \), and \( Y_\pi \) is a failure time process which jumps from 0 to 1 at some particular time and stays at 1 thereafter. Define the failure time \( T_\pi \) by the equation \( Y_\pi(T_\pi) = 1 \) and \( Y_\pi(T_\pi^-) = 0 \). Let \( \lambda_W(t) \) denote the hazard function of \( W \).

**Model 2.1. Cox Proportional Hazards model**

\[
\lambda_{Y_\pi}(t | V) = \lambda_0(t) \exp\left( r(\pi(t^-), t, \beta_0, V) \right),
\]

where \( r(\cdot) \) is a known function which satisfies \( r(0, t, \beta, 0) = 0 \).
Model 2.2. Stratified Cox Proportional Hazards model

$$\lambda_{T \pi}(t|V) = \lambda_0(t|V) \exp \left( r(\overline{a}(t^-), t, \beta_0, V) \right),$$

where $r()$ is a known function which satisfies $r(\overline{0}, t, \beta, V) = 0$.

Model 2.3. Stratified time-dependent Accelerated Failure Time model.

$$\Pr(R(\overline{a}, V; \beta_0) \leq r|V) = F_0(r|V),$$

$F_0$ is an unknown distribution function, $R(\overline{a}, V; \beta_0) = r(T_{\pi}\overline{a}, V; \beta)$ is a known increasing function of $Y_{\pi}$ satisfying $r(y, \overline{a}, V; \beta) = y$ if $\overline{a} = 0$.

Other MSMs possibly of interest include quantile MSMs, additive hazards MSMs and restricted residual mean survival MSMs. While these and other possible MSMs are not discussed herein, our results readily extend to these MSMs. Having defined the underlying set of counterfactual variables and MSMs of interest, we now consider how they relate to the observed data. Three important assumptions are essential to the identification of the MSM parameter $\beta_0$ from the observed data. First, of the many counterfactual variables in $Y_A$, only one is ultimately observed in a given individual. In fact, we observe a realization of $Y_{\pi}$ only if the treatment history $\overline{a}$ is equal to a subject’s actual treatment history $\overline{A}$; that is $\overline{Y} = Y_{\pi}$ w.p.1. This identity constitutes the fundamental "consistency" assumption that links the counterfactual data $Y_{\pi}$ to the observed data $(Y, A)$. The next assumption is that there are no unmeasured confounders for the effect of $A(j)$ on $\overline{Y}$, that is, for all treatment histories $\overline{a}$,

$$Y_{\pi} \perp I(A(j)|A(j-1) = \overline{a}(j-1), \overline{L}(j), \ j = 1, \ldots, J. \quad (1)$$

This assumption generalizes Rosembaum and Rubin’s (1983) assumption of ignorable treatment assignment to longitudinal studies with time-varying treatments and confounders and is also referred to as the sequential randomization assumption (SRA) (Robins, 1998). It states that, conditional on treatment history and the history of all recorded covariates up to $j$, treatment at $j$ is independent of the counterfactual random variables $Y_{\pi}(j + 1), \ldots, Y_{\pi}(J)$. This will be true if, for example, all prognostic factors for $Y$ used by the physicians to determine whether treatment $A$ is given at $j$ are recorded in $(\overline{A}(j-1), \overline{L}(j))$. For example, physicians generally check HIV infected patients’ current CD4 count before deciding whether or not he or she needs to initiate HAART (highly active antiretroviral therapy) to delay death or progression.
to AIDS. Clearly, because CD4 count also correlates with the patient’s time of death or progression to AIDS, the assumption of no unmeasured confounders would be false if \( L(j) \) did not include patients’ current CD4 count.

In an observational study, the assumption of no unmeasured confounder cannot be guaranteed to hold, and it is not subject to empirical test. However it will hold to a reasonable approximation if good efforts are made to collect data on the crucial covariates. Investigating the sensitivity to violations of SRA through a formal sensitivity analysis is important but will not be discussed in this paper. Robins, Greenland, and Hu (1999), and Robins, Rotnitzky and Scharfstein (2000), have provided details on the theory of sensitivity analysis in causal models. Below, we will consider instrumental variable methods when SRA fails to hold.

We finally assume that the following positivity assumption holds. For all \( a(j) \) in the support of \( A(j) \)

\[
\text{if } f(L(j), A(j-1)) > 0 \text{ then } f(a(j)|L(j), A(j-1)) > 0.
\]

This assumption essentially states that if any set of subjects at time \( j \) have the opportunity of continuing on a treatment regime \( \pi \) under consideration, at least some will take that opportunity. Positivity is actually a sufficient but not a necessary condition to apply the methods described in this paper; see ref. (Robins 1998) for further details.

Consider the semiparametric model \( \mathcal{M}_{tp} \) where (i) the treatment process

\[
f (A(k) = 1|L(k), A(k-1)), \ k = 0, ..., J - 1, \text{is known},
\]

with (ii) observed data \( O = (\bar{A} = A(J - 1), L = L(J)) \); and (iii) an MSM with target parameter \( \beta_0 \). Also define \( \mathcal{M}^*_{tp} \) as \( \mathcal{M}_{tp} \) where in the data generating mechanism (ii), \( \mathcal{M} \) is replaced with user-specified density \( f^* (A(k) = 1|V, \bar{A}(k-1)) \), and the model is otherwise identical. As noted by Robins, under \( \mathcal{M}^*_{tp} \), MSMs 1-2 simplify to well-known statistical models, where “*” denotes expectation under the model.

**Model 1.1:** \( E^* (Y|\pi, V) = g (\pi, V; \beta_0) \), where \( g (\cdot, \cdot, \cdot) \) is a known function.

**Model 1.2:** \( \eta (E^* (Y|\pi, V)) = g (\pi, V; \beta_0) + g^* (V) \).

**Model 1.3.** \( \Pr^* (R (\pi, V; \beta_0) \leq r|V) = F^*_0 (r|V), \ R (\pi, V; \beta_0) = r (Y, \pi, V; \beta) \).

**Model 1.4.** \( E^* (Y(m)|\pi, V) = g_m (\pi(m - 1), V; \beta_0), m = 1, ..., K + 1. \)

**Model 2.1.** \( \lambda^*_T (t|\pi (t), V) = \lambda_0 (t) \exp (r (\pi (t^-), t, \beta_0, V)) \).

**Model 2.2.** \( \lambda^*_T (t|\pi (t), V) = \lambda_0 (t|V) \exp (r (\pi (t^-), t, \beta_0, V)) \).
Model 2.3. Pr*(R(\(\bar{\pi}, V; \beta_0\)) ≤ r|V) = F_0^*(r|V), R(\(\bar{\pi}, V; \beta_0\)) = r(T, \(\bar{\pi}, V; \beta\))

Then, Robins established that all regular and asymptotically linear (RAL) estimators \(\hat{\beta}(h, \phi)\) in \(M_{tp}\) can be obtained by solving:

\[
op_t\left(n^{-1/2}\right) = \mathbb{P}_n \hat{D}(O; h, \phi, \beta)
\]

with \(\mathbb{P}_n \hat{D}(h, \phi, \beta) = \mathbb{P}_n \hat{D}_{sm}(h, \beta) / \mathcal{W} + D_{tp}(\phi),\)

\[
\mathcal{W} = \prod_{k=0}^{J-1} W_k = \prod_{k=0}^{J-1} \frac{f(A(k)|\mathcal{I}(k), \mathcal{A}(k-1))}{f^*(A(k)|V, \mathcal{A}(k-1))},
\]

\[
D_{tp}(\phi) = \sum_{k=0}^{J-1} \phi(k, \mathcal{A}(k), \mathcal{T}(k)) - E(\phi(k, \mathcal{A}(k), \mathcal{T}(k)) | \mathcal{A}(k-1), \mathcal{T}(k))
\]

and \(\mathbb{P}_n \hat{D}_{sm}(h, \beta) = \mathbb{P}_n V_{sm}^*(h, \beta) + o_p(1),\) where \(\{\hat{D}_{sm}(h, \beta) : h\}\) and \(\{V_{sm}^*(h, \beta) : h\}\) are the following familiar estimating functions of \(\beta\) of models 1-2 under \((2^*)\) and their associated influence functions.

Model 1.1: \(\hat{D}_{sm}(h, \beta) = V_{sm}^*(h, \beta)\) where \(V_{sm}^*(h, \beta) = h(\mathcal{A}, V) \varepsilon(\beta) ; \varepsilon(\beta) = Y - g(\mathcal{A}, V; \beta_0),\)

Model 1.2: For \(\eta(x) = x, \hat{D}_{sm}(h, \beta) = V_{sm}^*(h, \beta) = (\varepsilon(\beta) - h_1(\mathcal{A}, V)) (h_2(\mathcal{A}, V) - E^* \{h_2(\mathcal{A}, V) | V\}).\)

for any choice of \(h_1\) and \(h_2\) of same dimension as \(\beta.\) For \(\eta(x) = \log(x/(1-x)),\) let \(p(\beta) = \expit(g(\mathcal{A}, V; \beta_0) + g^*(V)),\)

\(\hat{p}(\beta) = \expit(g(\mathcal{A}, V; \beta_0) + \hat{g}^*(V))\) where \(\hat{g}^*(V)\) is a \(n^{1/4}\)- consistent estimatof of \(g^*(V).\)

\(\hat{D}_{sm}(h, \beta) = \hat{\varepsilon}(\beta) (h_2(\mathcal{A}, V) - E^* \{h_2(\mathcal{A}, V) \hat{p}(\beta)(1-\hat{p}(\beta)) | V\} / E^* \{\hat{p}(\beta)(1-\hat{p}(\beta)) | V\}), \hat{\varepsilon}(\beta) = Y - \hat{p}(\beta);\)

\(V_{sm}^*(h, \beta) = \varepsilon(\beta) (h_2(\mathcal{A}, V) - E^* \{h_2(\mathcal{A}, V) p(\beta)(1-p(\beta)) | V\} / E^* \{p(\beta)(1-p(\beta)) | V\})\)

Model 1.3. \(\hat{D}_{sm}(h, \beta) = V_{sm}^*(h, \beta) = h(R(\beta_0), \mathcal{A}, V) - h(R(\beta_0), \bar{\pi}, V) dF^*(\bar{\pi}|V)\) where \([??])\)

Model 1.4. \(\hat{D}_{sm}(h, \beta) = V_{sm}^*(h, \beta) = h(\mathcal{A}, V) \varepsilon(\beta)\) where \(\varepsilon(\beta) = (\varepsilon_1(\beta), \ldots, \varepsilon_{K+1}(\beta)), \varepsilon_m(\beta) = Y(m) - g_m(\bar{\pi}(m-1), V; \beta_0), m = 1, ..., K + 1,\) and \(h(\mathcal{A}, V)\) is of dimension \(\dim(\beta) \times (K + 1).\)

Model 2.1.

\[
\hat{D}_{sm}(h, \beta) = \int dN(t) \left\{ h(t, \mathcal{A}, V) - \frac{\mathbb{P}_n [h(t, \mathcal{A}, V) \exp (r(\mathcal{A}(t), t, \beta_0, V)) I(T \geq t)]}{\mathbb{P}_n [\exp (r(\mathcal{A}(t), t, \beta_0, V)) I(T \geq t)]} \right\}
\]

\[
U_{sm}(h, \beta) = \int dM_T(t) \left\{ h(t, \mathcal{A}, V) - \frac{E^* [h(t, \mathcal{A}, V) \exp (r(\mathcal{A}(t), t, \beta_0, V)) I(T \geq t)]}{E^* [\exp (r(\mathcal{A}(t), t, \beta_0, V)) I(T \geq t)]} \right\},
\]

where \(N_T(t) = I(T \leq t)\) and \(dM_T(t) = dN(t) - \lambda_T(t) \mathcal{A} V I(T \geq t) dt.\)
Model 2.2. \( \hat{D}_{sm}(h, \beta) \) and \( V_{sm}^*(h, \beta) \) are as above with \( \mathbb{P}^*_n[h(t, A, V) \exp (r(A(t), t, \beta_0, V)) I(T \geq t)] \) and \( \mathbb{P}^*_n[\exp (r(A(t), t, \beta_0, V)) I(T \geq t)] \) in \( \hat{D}_{sm}(h, \beta) \) replaced by an \( n^{-1/4} \) consistent estimator of \( \mathbb{E}^*[h(t, A, V) \exp (r(A(t), t, \beta_0, V)) I(T \geq t)|V] \) and \( \mathbb{E}^*[\exp (r(A(t), t, \beta_0, V)) I(T \geq t)|V] \).

Model 2.3.

\[
\hat{D}_{sm}(h, \beta) = \int_0^\infty dt I(R(\beta) \leq t) \{H_2(t, \beta) - \mathbb{E}^*[H_2(t, \beta) | V]\} \\
+ \int_0^\infty dN_{R(\beta)}(t) \{H_1(t, \beta) - \mathbb{E}^*[H_1(t, \beta) | V]\}
\]

and for \( j = 1, 2, H_j(t, \beta) = h_j(t, A(r^{-1}(t, A, V, \beta), V); V_{sm}^*(h, \beta) = D_{sm}(h, \beta) - \mathbb{E}^*[D_{sm}(h, \beta) | V]. \)

Note that in Model 2.1,

\[
\mathbb{E}^*[h(t, A, V) \exp (r(A(t), t, \beta, V)) I(T \geq t)] \\
= \mathbb{E} [\exp (r(A(t), t, \beta, V)) I(T \geq t)/W(int(t))] \\
\]

and

\[
\mathbb{E}^*[\exp (r(A(t), t, \beta, V)) I(T \geq t)] \\
= \mathbb{E} [\exp (r(A(t), t, \beta, V)) I(T \geq t)/W(int(t))] \\
\]

and likewise in Model 2.2

\[
\mathbb{E}^*[h(t, A, V) \exp (r(A(t), t, \beta, V)) I(T \geq t)|V] \\
= \mathbb{E} [\exp (r(A(t), t, \beta, V)) I(T \geq t)/W(int(t))]|V] \\
\]

and

\[
\mathbb{E}^*[\exp (r(A(t), t, \beta, V)) I(T \geq t)|V] \\
= \mathbb{E} [\exp (r(A(t), t, \beta, V)) I(T \geq t)/W(int(t))]|V]. \\
\]

Robins (1998) also established that for fixed \( h \), the optimal choice of \( \phi \) in model \( \mathcal{M}_{tp} \) is given by \( \phi_{opt}(k, A(k), \bar{L}(k)) = -\mathbb{E}(D_{sm}(h, \beta)/W[A(k), \bar{L}(k)], \) in the sense that given \( h \), there is no estima-
tor with asymptotic variance smaller than $\tilde{\beta}(h, \phi_{opt})$. Let $C_J = \mathbb{E}(D_{sm}(h, \beta) | \bar{A}(J - 1), \bar{L}(J - 1))$, and define $C_j$ recursively as $C_j = \sum_{a(j)} \mathbb{E}(C_{j+1}(a_j) | \bar{A}(j - 1), \bar{L}(j - 1))$ for $j = J - 1, \ldots, 1$. As in practice neither $\hat{W}$ nor $\{\hat{C}_j : j\}$ are known and must be estimated using working models which are sufficiently parsimonious to resolve the curse of dimensionality, e.g. parametric working models, Robins (2000b) established that in models 1.1-1.4, $\hat{\beta}_{dr}$ is a doubly robust (dr) estimator in the sense that it is consistent and asymptotically normal if either $\hat{W}$ or $\{\hat{C}_j : j\}$ is consistent but not necessarily both, where $\hat{\beta}_{dr}$ solves:

$$0 = \mathbb{P}_n \hat{D}(h, \bar{A}, \bar{L}) = \mathbb{P}_n \hat{D}_{sm}(h, \beta) / \hat{W} + D_{tp}(\bar{A}),$$

with

$$D_{tp}(\bar{A}) = -\sum_{j=0}^{J-1} \hat{C}_{j+1}/\hat{W}(j) + \sum_{a(j)} \hat{C}_{j+1}/\hat{W}(j - 1),$$

and

$$\hat{W}(j) = \prod_{k=0}^{j} \hat{W}_k$$

Note that it is likewise possible to construct dr estimators in models 2.1-2.4, however, in Cox MSM 2.1, this requires construction of dr estimators of

$$\mathbb{E}^* \left[ h(t, \bar{A}, V) \exp \left( r(\bar{A}(t), t, \beta, V) \right) I(T \geq t) \right] = \mathbb{E} \left[ \exp \left( r(\bar{A}(t), t, \beta, V) \right) I(T \geq t) / \hat{W}(int(t)) \right],$$

and

$$\mathbb{E}^* \left[ \exp \left( r(\bar{A}(t), t, \beta, V) \right) I(T \geq t) \right] = \mathbb{E} \left[ \exp \left( r(\bar{A}(t), t, \beta, V) \right) I(T \geq t) / \hat{W}(int(t)) \right],$$

likewise for Model 2.2 which requires a dr estimator of versions of above quantities conditional on $V$ under $\mathbb{E}^*$; details are omitted, however see Tchetgen Tchetgen and Robins (2012) for an illustration in the case of point exposure. A similar approach applies to model 2.2.

4 MSM inference with time-varying instrumental variable.

4.1 New inverse-probability-of-instrumental-variable weighted estimators

In this section, we do not make the assumption of sequential randomization (\textbf{1}) and allow for unmeasured time-varying covariates $\bar{U} = (U(0), \ldots, U(J - 1))$, such that $U(j)$ is a common cause of $\bar{A}(j) =$
(A(j), ..., A(J − 1)) and Y(j + 1) = (Y(j + 1), ..., Y(J)). We assume that in addition to \((\overline{L}, \overline{A})\), a binary time-varying instrumental variable \(Z(j)\) is observed just prior to \(A(j), j = 0, ..., J − 1\); further, we assume that had \(U\) been observed, sequential ignorability would hold. Specifically, we make the following assumption of latent sequential randomization:

\[
\mathcal{I}_\pi \Pi A(j) | \overline{A}(j − 1) = \overline{a}(j − 1), \overline{L}(j), \overline{U}(j), \overline{Z}(j) \quad j = 1, ..., J − 1.
\]  

(3)

However, noting that \(\mathcal{I}_\pi \Pi A(j) | \overline{A}(j − 1) = \overline{a}(j − 1), \overline{L}(j), \overline{Z}(j)\), and given that \(U\) is unobserved, the MSM is not identified without an additional assumption. For the purpose of identification, we suppose that \(Z\) satisfies the following key time-varying IV conditions:

**Assumption (1): IV Relevance:**

\[
Z(j) \Pi A(j) | \overline{A}(j − 1), \overline{L}(j), \overline{Z}(j − 1) \quad j = 1, ..., J − 1
\]  

(4)

**Assumption (2): Exclusion Restriction:**

\[
(\mathcal{I}_{\pi_{\pi_2}}, \mathcal{U}_{\pi_2}) = (\mathcal{I}_{\pi_2}, \mathcal{U}_{\pi_2}) \quad \text{a.s.}
\]  

(5)

**Assumption (3): IV independence :**

\[
(\mathcal{U}_{\pi_2}, \mathcal{L}_{\pi_2}) \Pi Z(j) | \overline{A}(j − 1) = \overline{a}(j − 1), \overline{L}(j), \overline{Z}(j − 1) \quad j = 0, ..., J − 1
\]  

(6)

**Assumption (4): IV positivity:**

\[
0 < \Pr (Z(j) = 1 | \overline{A}(j − 1), \overline{L}(j), \overline{Z}(j − 1)) < 1 \quad \text{for} \quad j = 0, ..., J − 1
\]

In addition, we suppose the following holds.

**Assumption (5) Independent Compliance Type:**

\[
\mathbb{E} [A(j)|\overline{U}(j), \overline{L}(j), \overline{A}(j − 1), \overline{Z}(j − 1), Z(j) = 1] − \mathbb{E} [A(j)|\overline{U}(j), \overline{L}(j), \overline{A}(j − 1), \overline{Z}(j − 1), Z(j) = 0]
\]

\[
= \delta_j (\overline{L}(j), \overline{A}(j − 1), \overline{Z}(j − 1))
\]  

(7)
The assumption states that while $\mathbf{U}(j)$ may confound the causal effects of $\mathbf{A}(j)$, no component of $\mathbf{U}(j)$ interacts with $Z(j)$ in its additive effects on $A(j)$. A causal interpretation of the assumption is available if $Z(j) \perp A_z(j) | \mathbf{U}(j), \mathbf{L}(j), \mathbf{A}(j-1), Z(j-1)$ in which case (7) implies:

$$
\mathbb{E} \left[ A_{z(j)=1}(j) - A_{z(j)=0}(j) | \mathbf{U}(j), \mathbf{L}(j), \mathbf{A}(j-1), Z(j-1) \right] = \delta_j \left( \mathbf{L}(j), \mathbf{A}(j-1), Z(j-1) \right), \ j = 0, ..., J-1.
$$

that $\mathbf{U}(j)$ is conditionally independent of compliance type at time $j$, expressed in terms of a person’s potential treatment variables under hypothetical IV interventions $\{A_{z(j)=1}(j), A_{z(j)=0}(j)\}$. This assumption is a longitudinal generalization of a similar assumption made by Wang and Tchetgen Tchetgen (2018a) and Wang et al (2018b) in the case of point exposure and IV. Below, we will make use of the fact that under our assumptions, $\{\delta_j : j\}$ is empirically identified. Specifically,

**Lemma 1** Under assumptions (3) and (5), we have that

$$
\delta_j(\mathbf{L}(j), \mathbf{A}(j-1), Z(j-1)) = \mathbb{E} \left[ A(j) | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 1 \right] - \mathbb{E} \left[ A(j) | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 0 \right]
$$

**Proof.**

$$
P(A(j) = 1 | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 1) - P(A(j) = 1 | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 0)
$$

$$
= \int P(A(j) = 1 | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 1, \mathbf{A}(j)) dF(\mathbf{A}(j)) | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 1
$$

$$
- \int P \left( A(j) = 1 | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 0, \mathbf{A}(j) \right) dF(\mathbf{A}(j)) | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 0
$$

$$
= \int P(A(j) = 1 | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 1, \mathbf{A}(j)) dF(\mathbf{A}(j)) | \mathbf{L}(j), \mathbf{A}(j-1), Z(j-1)
$$

$$
- \int P \left( A(j) = 1 | \mathbf{L}(j), \mathbf{A}(j-1), Z(j) = 0, \mathbf{A}(j) \right) dF(\mathbf{A}(j)) | \mathbf{L}(j), \mathbf{A}(j-1), Z(j-1)
$$

$$
= \delta_j(\mathbf{L}(j), \mathbf{A}(j-1), Z(j-1)) dF(\mathbf{A}(j)) | \mathbf{L}(j), \mathbf{A}(j-1), Z(j-1)
$$

$$
= \delta_j(\mathbf{L}(j), \mathbf{A}(j-1), Z(j-1)).
$$


We define the following modified time varying weights:

\[
\mathcal{W}^\dagger (j) = \prod_{k=1}^{j} \mathcal{W}_{k,1}^\dagger \mathcal{W}_{k,2}^\dagger
\]

\[
\mathcal{W}^\dagger = \mathcal{W}^\dagger (J - 1)
\]

where

\[
\mathcal{W}_{k,1}^\dagger = \frac{f \left( Z(k) | \overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1) \right) \delta_k \left( \overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1) \right)}{(-1)^{1 - Z(k)}}
\]

and

\[
\mathcal{W}_{k,2}^\dagger = \frac{1}{(-1)^{1 - A(k)} f^* \left( A(k) | V, \overline{A}(k - 1) \right)}
\]

We give our main result.

**Lemma 2** Suppose that together with consistency, Assumptions (1)-(5) hold. For any measurable function \( G = g(\overline{A}, \overline{L}) \),

\[
\mathbb{E} \left( g(\overline{A}, \overline{L})|\mathcal{W}^\dagger |V \right) = \sum_{\pi} \mathbb{E} \left\{ g(\pi, \overline{\pi})|V \right\} \prod_{j=0}^{J-1} f^* (a(j)|V, \pi(j - 1))
\]

\[
= \mathbb{E}^* \left\{ G|V \right\}
\]

Note that the above Lemma continues to hold under the less stringent latent SRA \( Y_\pi \Pi A(j) | \overline{A}(j - 1) = \overline{a}(j - 1), \overline{L}(j), \overline{U}(j) \ j = 1, \ldots, J - 1 \), if \( g(\overline{A}, \overline{L}) \) only depends on \( \overline{L} \) through \( Y = Y(J) \). The Lemma motivates the following simple weighted estimating equation of \( \beta_0 \) in models 1 and 2. Suppose that one has obtained \( n^{1/2} \)-consistent estimators \( \hat{f} \left( Z(k) | \overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1) \right) \) and \( \hat{\delta}_k \left( \overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1) \right), \)

\( k = 0, \ldots, J - 1 \) and let \( \hat{\mathcal{W}}^\dagger \) denote the corresponding estimated weight. Then under the assumptions given in the lemma above, we have that \( \mathbb{E} \left\{ D_{sm} (h, \beta_0) | \mathcal{W}^\# \right\} = \mathbb{E}^* \left\{ D_{sm} (h, \beta_0) \right\} = 0 \) where \( \{ D_{sm} (h, \beta) : h \} \) is the set of unbiased estimating functions of \( \beta_0 \) corresponding to one of models 1-2 under (ii*). Then, assuming that \( \mathbb{E} \left\{ \nabla_\beta D_{sm} (h, \beta) | \beta_0, \mathcal{W}^\dagger \right\} \) is invertible, the above lemma motivates the following simple weighted estimating equation of the RAL estimator \( \hat{\beta}_{ipw} \):

\[
o_p \left( n^{-1/2} \right) = \mathbb{P}_n \hat{D}_{sm} (h, \hat{\beta}_{ipw}) / \hat{\mathcal{W}}^\dagger.
\]

The asymptotic distribution of \( \hat{\beta}_{ipw} \) follows from a standard Taylor expansion and is omitted, the non-parametric bootstrap may also be used for inference. Note that for estimating models 2.1-2.4 all unknown
expectations must be estimated with a corresponding weighted expectation as outlined in the previous Section, however now using the modified weights \( \hat{W} (\text{int}(t)) \).

### 4.2 New multiply robust estimators

Next, we describe multiply robust estimators of \( \beta_0 \) which is motivated by considering the set of influence functions associated with RAL estimators of \( \beta_0 \) in the semiparametric model \( M_{IV} \) defined only by the MSM, the consistency assumption and assumptions (1)-(5).

**Lemma 3** All RAL estimators \( \hat{\beta}_{np} = \hat{\beta}_{np} (h) \) of \( \beta_0 \) under \( M_{IV} \) are solutions to an estimating equation of the form

\[
op (n^{-1/2}) = \mathbb{P}_n \left[ D^\dagger (h, \hat{\beta}_{np} (h)) \right] \\
= \mathbb{P}_n \left[ \frac{D_{sm} (h, \hat{\beta}_{np} (h))}{\hat{W}^\dagger} \right] \\
- \mathbb{P}_n \left[ \sum_{j=0}^{J-1} \frac{1}{\hat{W}^\dagger (j-1)} \left\{ (-1)^{1-Z(j)} \Psi_j (\hat{\beta}_{np} (h)) - \bar{\Psi}_j \left( \hat{\beta}_{np} (h) \right) - \epsilon_j \overline{\Psi}_j \left( \hat{\beta}_{np} (h) \right) \right\} \right]
\]

where

\[
\Psi_{j-1} (\beta) = \mathbb{E} \left[ \frac{D_{sm} (h, \beta)}{\mathbb{W}_2^\dagger (J-1) \Delta_{j-1}} | \mathbb{A}(J-2), \mathbb{L}(J-1), \mathbb{Z}(J-1) \right],
\]

for \( j = J-2, \ldots, 0, \)

\[
\Psi_j (\beta) = \mathbb{E} \left[ \frac{\bar{\Psi}_{j+1} (\beta)}{\mathbb{W}^\dagger_2 (j) \Delta_j} | \mathbb{A}(j-1), \mathbb{L}(j), \mathbb{Z}(j) \right],
\]

for \( j = J-1, \ldots, 0, \)

\[
\bar{\Psi}_j (\beta) = \sum_{z(j)} (-1)^{1-z(j)} \Psi_j (z(j); \beta),
\]

\[
\Delta_j = \delta_j (\mathbb{A}(j-1), \mathbb{Z}(j-1), \mathbb{L}(j))
\]

\[
\epsilon_j = A(j) - \mathbb{E} (A(j)|\mathbb{A}(j-1), \mathbb{L}(j), \mathbb{Z}(j))
\]

The estimator \( \hat{\beta}_{np} (h) \) is not feasible in practice because it depends on the unknown quantities \( \Psi_j (\beta), \mathbb{E} (A(j)|\mathbb{A}(j-1), \mathbb{L}(j), \mathbb{Z}(j)) \) and \( f (Z(j)|\mathbb{L}(j), \mathbb{A}(j-1), \mathbb{Z}(j-1)) \). In practice, these unknown quantities can be estimated from the observed data under parametric working models. Let \( \Gamma_j^{(1)} (\beta) = \)
\( \tilde{\Psi}_j (\beta) ; \Gamma^0_j (\beta) = \Psi_j (Z (j) = 0 ; \beta) \) with corresponding estimators \( \hat{\Gamma}_j^{(1)} (\beta) \) and \( \hat{\Gamma}_j^{(0)} (\beta) \). Likewise, let

\[
\hat{E} (A(j)|\overline{A}(j-1), \overline{L}(j), \overline{Z}(j)) = \hat{\Delta}_j Z(j) + \hat{E} (A(j)|\overline{A}(j-1), \overline{L}(j), \overline{Z}(j-1), Z(j) = 0),
\]

\( \hat{f} (Z(j)|\overline{L}(j), \overline{A}(j-1), \overline{Z}(j-1)) \) and \( \hat{\Delta}_j \) also denote estimators of

\[
E (A(j)|\overline{A}(j-1), \overline{L}(j), \overline{Z}(j)) = \Delta_j Z(j) + E (A(j)|\overline{A}(j-1), \overline{L}(j), \overline{Z}(j-1), Z(j) = 0),
\]

\( f (Z(j)|\overline{L}(j), \overline{A}(j-1), \overline{Z}(j-1)) \) and \( \Delta_j \). We show in the appendix that the estimator \( \hat{\beta}_{mr} (h) \) that solves \( o_p (n^{-1/2}) = P_n \left[ \hat{D}^\top (h, \hat{\beta}_{mr} (h)) \right] \) where \( \hat{D}^\top \) replaces all unknown quantities with a corresponding estimator, is multiply robust in the sense that it is CAN if either one but not necessarily all three of the following conditions hold: (i) \( \hat{W}^\top \) is consistent for \( W^\top \), or (ii) \( \hat{f} (Z(j)|\overline{L}(j), \overline{A}(j-1), \overline{Z}(j-1)) \) is consistent and \( \hat{\Gamma}^1_j (\beta) \) is consistent for all \( j \leq J \); or (iii) \( \hat{\Gamma}^1_j (\beta), \hat{\Gamma}^0_j (\beta) \) and \( \hat{E} (A(j)|\overline{A}(j-1), \overline{L}(j), \overline{Z}(j)) \) are consistent. In Models 2.1-2.3, the result requires also replacing unknown expectations with corresponding multiply robust estimators analogous to the estimator given above, details are omitted. This result effectively generalizes that of Wang and Tchetgen Tchetgen (2017) to the time-varying setting.

5 Semiparametric Efficiency

The semiparametric efficiency bound in a semiparametric model is the inverse of the variance of the efficient score \( S_{eff, \beta_0} \) for the model. By Theorem 5.3 of Newey and McFadden (1993), the efficient score \( S_{eff, \beta_0} = D^\top (h_{eff}, \beta_0) \) in model \( \mathcal{M}_{IV} \) is uniquely characterized by the requirement that for all \( D^\top (h, \beta_0) : \)

\[
E \left\{ D^\top (h, \beta_0) D^\top (h_{eff}, \beta_0)^T \right\} = -E \left\{ \nabla_{\beta}^T D^\top (h, \beta) |_{\beta_0} \right\}
\]

In order to illustrate the result, consider MSM 1.1. Note that because \( \overline{A} \) is discrete valued with finite support, let \( \Xi = \varepsilon (\beta_0) \times \{ 1 (\overline{A} = \overline{a}_1), \ldots, 1 (\overline{A} = \overline{a}_c) \}^T \) where \{\overline{a}_c : c\} are the \( 2^J \) possible values of \( \overline{a} \), also let \( H = h (V) \) denote a \( p \times 2^J \) function of \( V \). The set of influence functions of \( \beta_0 \) under \( \mathcal{M}_{IV} \), can be
written \( \{ D^\dagger(h) : h \} \) where \( D^\dagger(h) = H\tilde{\Xi} \), and

\[
\tilde{\Xi} = \frac{\Xi}{W_1} - \sum_{j=0}^{J-1} \frac{1}{W_1(j-1)} \left\{ (-1)^{1-Z(j)} \mathbb{E} \left[ \frac{\Xi}{W_2(J-1)\Delta_{j-1}} | A(j-1), \bar{L}(j), Z(j) \right] \right.

\]

\[
- \sum_{z(j)} \mathbb{E} \left[ \frac{\Xi}{W_2(J-1)\Delta_{j-1}} | A(j-1), \bar{L}(j), Z(j) - 1, z(j) \right]

\]

\[
\left. \frac{\epsilon_j \sum_{z(j)} \mathbb{E} \left[ \frac{\Xi}{W_2(J-1)\Delta_{j-1}} | A(j-1), \bar{L}(j), Z(j) - 1, z(j) \right]}{W_1(j)} \right\}

A straightforward application of equation (9) gives the efficient influence function: \( D^\dagger_{eff}(h) = H_{eff}\tilde{\Xi} \) where \( H_{eff} = \mathbb{E} \left\{ \nabla_{\beta^T} \tilde{\Xi}(\beta_0) | V \right\} \mathbb{E} \left\{ \tilde{\Xi}\tilde{\Xi}^T | V \right\}^{-1} \). The efficient influence function for other MSMs considered in this paper can likewise be obtained by straightforward application of equation (9) although details are omitted.

6 Final Remarks

This technical report provides identification conditions for MSMs using a time-varying instrumental variable in the case of time-varying endogenous binary treatment, a long-standing problem in the causal inference literature. The case of polytomous or continuous treatments will be discussed elsewhere. The paper also provides weighted estimating equations that are easy to implement, as well as multiply robust estimating equations which are substantially more computationally intensive. Evaluation of final sample performance and application of these methods is currently underway and will be published elsewhere.

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APPENDIX

Proof of Lemma 1.

The proof is by induction backwards on the time index \( j \). That is, supposing for some \( j, 1 \leq j \leq J - 1 \), we have established

\[
E \left( \frac{g(A, L)}{W^\dagger} \right) = E \left\{ (W^\dagger)^{-1} \sum_{a_{j+1}} E[g(A(j+1) = a_{j+1}, L_{A(j+1)} = a_{j+1}(j + 2), A(j), L(j + 1) | L(j + 1), A(j))] \right. \\
\times \prod_{k = j+1}^{J-1} f^*(a_k | A(j), A_{j+1} = a_{j+1}, \ldots, A_{k-1} = a_{k-1}) \left. \right\},
\]

we establish the same with \( j \) replaced by \( j - 1 \) throughout. In the preceding display, the notation \( A_{j+1} = a_{j+1}, \ldots, A_{k-1} = a_{k-1} \) is to be read as an empty list when \( j + 1 > k - 1 \); the product \( \prod_{k = j+1}^{J-1} \) is 1 for \( j + 1 > J - 1 \); and similarly \( L_{a}(j) = L_{a}(J) \) for \( j > J \). The summation \( \sum_{a_{j+1}} \) ranges over all treatment regimes \( a_{j+1}, a_{j+2}, \ldots, a_{J-1} \) \( \in A^{J-j-1} \); for \( j + 1 > J - 1 \), the sum \( \sum_{a_{j+1}} E[g(A(j + 1) = a_{j+1}, L_{A(j+1)} = a_{j+1}(j + 2), A(j), L(j + 1) | L(U(j + 1), A(Z)(j))] \) is just \( E[g(A(j-1), L(j) | L(U(j), A(Z)(j-1))] \).

Conditioning on \( V \) is assumed throughout, though suppressed. With these notation conventions, the \( j = J - 1 \) case holds trivially. Conditioning with respect to \( L(U)(j), A(Z)(j-1) \), the rhs is

\[
= E \left\{ (W_{j-1}^\dagger)^{-1} \sum_{a_{j+1}} E \left\{ (W_j^\dagger)^{-1} E[g(\ldots | \ldots)] \prod f^*(\ldots) | L(U)(j), A(Z)(j-1) \right\} \right\}.
\]
Considering a single term of the sum,

\[
\mathbb{E}\left\{ (W_j^\dagger)^{-1}\mathbb{E}\left[g(A(j + 1) = a_{j+1}, L_{A(j+1)=a_{j+1}}(j + 2), \overline{A}(j), \overline{L}(j + 1) | \overline{LU}(j + 1), \overline{AZ}(j) \right] \times \prod_{k=j+1}^{J-1} f^*(a_k | A(j), A_{j+1} = a_{j+1}, \ldots, A_{k-1} = a_{k-1}) \bigg| \overline{LU}(j), \overline{AZ}(j - 1) \right\} 
\]

\[
= \mathbb{E}\left\{ (W_j^\dagger)^{-1}\mathbb{E}\left[g(A(j + 1) = a_{j+1}, L_{A(j+1)=a_{j+1}}(j + 2), \overline{A}(j), \overline{L}(j + 1) | \overline{LUAZ}(j) \right] \times \prod_{k=j+1}^{J-1} f^*(a_k | A(j), A_{j+1} = a_{j+1}, \ldots, A_{k-1} = a_{k-1}) \bigg| \overline{LU}(j), \overline{AZ}(j - 1) \right\} 
\]

\[
= \mathbb{E}\left\{ (W_j^\dagger)^{-1}(-1)^{1 - A(j)}\mathbb{E}\left[g(A(j + 1) = a_{j+1}, L_{A(j+1)=a_{j+1}}(j + 2), \overline{A}(j), \overline{L}(j + 1) | \overline{LUAZ}(j) \right] \times f^*(A(j) | \overline{A}(j - 1)) \prod_{k=j}^{J-1} f^*(a_k | A(j), A_{j+1} = a_{j+1}, \ldots, A_{k-1} = a_{k-1}) \bigg| \overline{LU}(j), \overline{AZ}(j - 1) \right\} 
\]

\[
= \mathbb{E}\left\{ \sum_{a_j \in \{0,1\}} \frac{\mathbb{I}\{A(j) = a_j\}(-1)^{1-a_j}}{W_j^\dagger} \mathbb{E}\left[g(A(j) = a_j, L_{A(j)=a_j}(j + 1), \overline{A}(j - 1), \overline{L}(j) | \overline{LUZ}(j), \overline{A}(j - 1), A(j) = a_j \right] \times \prod_{k=j}^{J-1} f^*(a_k | A(j - 1), A_j = a_j, \ldots, A_{k-1} = a_{k-1}) \bigg| \overline{LU}(j), \overline{AZ}(j - 1) \right\}. 
\]

(10)

By SRA, \( L_{A(j)=a_j} \perp A(j) | \overline{A}(j - 1), Z_{LU}(j) \),

\[
\mathbb{E}\left[g(A(j) = a_j, L_{A(j)=a_j}(j + 1), \overline{A}(j - 1), \overline{L}(j) | \overline{LUZ}(j), \overline{A}(j - 1), A(j) = a_j \right]
\]

\[
= \mathbb{E}\left[g(A(j) = a_j, L_{A(j)=a_j}(j + 1), \overline{A}(j - 1), \overline{L}(j) | \overline{LUZ}(j), \overline{A}(j - 1), A(j - 1) \right]
\]

and by IV independence, \( L_{A(j)=a_j} \perp Z(j) | \overline{AZ}(j - 1), \overline{LU}(j) \),

\[
\mathbb{E}\left[g(A(j) = a_j, L_{A(j)=a_j}(j + 1), \overline{A}(j - 1), \overline{L}(j) | \overline{LUZ}(j), \overline{A}(j - 1) \right]
\]

\[
= \mathbb{E}\left[g(A(j) = a_j, L_{A(j)=a_j}(j + 1), \overline{A}(j - 1), \overline{L}(j) | \overline{LU}(j), \overline{AZ}(j - 1) \right].
\]
so that (11) is

\[
\sum_{a_j \in \{0, 1\}} (-1)^{1-a_j} \mathbb{E}[g(A(j) = a_j, L_A(j) = a_j(j + 1), \overline{A}(j - 1), \overline{L}(j) \mid \overline{LU}(j), \overline{AZ}(j - 1)] \\
\times \prod_{k=j}^{J-1} f^*(a_k \mid \overline{A}(j - 1), A_j = a_j, \ldots, A_{k-1} = a_{k-1}) \mathbb{E} \left\{ (W_{1,j}^\dagger)^{-1} \mathbbm{1}\{A(j) = a_j\} \mid \overline{LU}(j), \overline{AZ}(j - 1) \right\}
\]

= \sum_{a_j \in \{0, 1\}} (-1)^{1-a_j} \mathbb{E}[g(A(j) = a_j, L_A(j) = a_j(j + 1), \overline{A}(j - 1), \overline{L}(j) \mid \overline{LU}(j), \overline{AZ}(j - 1)] \\
\times \prod_{k=j}^{J-1} f^*(a_k \mid \overline{A}(j - 1), A_j = a_j, \ldots, A_{k-1} = a_{k-1}) \delta_j(\overline{L}(j), \overline{AZ}(j - 1)) \mathbb{E} \left\{ \frac{(-1)^{1-Z(j)} \mathbbm{1}\{A(j) = a_j\}}{f(Z(j) \mid \overline{L}(j), \overline{AZ}(j - 1))} \mid \overline{LU}(j), \overline{AZ}(j - 1) \right\}.
\]

(11)

By another application of IV independence,

\[
\mathbb{E} \left\{ \frac{(-1)^{1-Z(j)} \mathbbm{1}\{A(j) = a_j\}}{f(Z(j) \mid \overline{L}(j), \overline{AZ}(j - 1))} \mid \overline{LU}(j), \overline{AZ}(j - 1) \right\}
\]

= \mathbb{E} \left\{ \mathbbm{1}\{A(j) = a_j\} \sum_{z_j \in \{0, 1\}} (-1)^{1-z_j} \mathbbm{1}\{Z(j) = z_j\} \frac{1}{f(z_j \mid \overline{L}(j), \overline{AZ}(j - 1))} \mid \overline{LU}(j), \overline{AZ}(j - 1) \right\}
\]

= \mathbb{E} \left\{ P[A(j) = a_j \mid \overline{LUZ}(j), \overline{A}(j - 1)] \sum_{z_j \in \{0, 1\}} (-1)^{1-z_j} \mathbbm{1}\{Z(j) = z_j\} \frac{1}{f(z_j \mid \overline{L}(j), \overline{AZ}(j - 1))} \mid \overline{LU}(j), \overline{AZ}(j - 1) \right\}
\]

= \sum_{z_j \in \{0, 1\}} (-1)^{1-z_j} P[A(j) = a_j \mid \overline{LU}(j), \overline{AZ}(j - 1), Z(j) = z_j] \frac{P[Z(j) = z_j \mid \overline{LU}(j), \overline{AZ}(j - 1)]}{f(z_j \mid \overline{L}(j), \overline{AZ}(j - 1))}
\]

= \sum_{z_j \in \{0, 1\}} (-1)^{1-z_j} P[A(j) = a_j \mid \overline{LU}(j), \overline{AZ}(j - 1), Z(j) = z_j]
\]

= (-1)^{1-a_j} \delta_j(\overline{L}(j), \overline{AZ}(j - 1)).

Therefore, (11) is

\[
\sum_{a_j \in \{0, 1\}} \mathbb{E}[g(A(j) = a_j, L_A(j) = a_j(j + 1), \overline{A}(j - 1), \overline{L}(j) \mid \overline{LU}(j), \overline{AZ}(j - 1)] \\
\times \prod_{k=j}^{J-1} f^*(a_k \mid \overline{A}(j - 1), A_j = a_j, \ldots, A_{k-1} = a_{k-1})
\]

as required. ■
Proof of Lemma 2. Consider the MSM indexed by $\beta$ that solves

$$\mathbb{E} \left\{ \frac{D_{sm}(h, \beta_0)}{W_t^\dagger} \right\} = 0$$

at $\beta = \beta_0 = \beta_0(h)$ for all $h \in H$, functions of $(A, V)$ such that $D_{sm}(h, \beta_0) / W_t^\dagger$ is in the Hilbert space $L_2$ of functions with finite variance. Let $\{F_t(A, L) : t \in (-\epsilon, \epsilon)\}$ denote a regular parametric submodel for a unit’s observed data distribution indexed by a scalar parameter $t$ such that $F_{t=0}(A, L) = F(A, L)$ generated the observed data. We have that

$$\mathbb{E}_t \left\{ \frac{D_{sm}(h, \beta(F_t))}{W_t^\dagger} \right\} = 0 \text{ for all } t \in (-\epsilon, \epsilon),$$

and therefore

$$0 = \nabla_t \mathbb{E}_t \left\{ \frac{D_{sm}(h, \beta(F_t))}{W_t^\dagger} \right\}$$

$$= \mathbb{E} \left\{ \frac{D_{sm}(h, \beta(F_t))}{W_t^\dagger} \right\} S + \mathbb{E}_t \left\{ \frac{D_{sm}(h, \beta(F_t))}{W_t^\dagger} \nabla_t W_t^\dagger \right\}$$

$$+ \mathbb{E} \left\{ \nabla_\beta D_{sm}(h, \beta) \right\} \nabla_t \beta(F_t)$$

Consider term

$$\mathbb{E} \left\{ \frac{D_{sm}(h, \beta(F))}{W_t^\dagger} \nabla_t W_t^\dagger \right\}$$

$$= \mathbb{E} \left\{ \sum_{k=0}^{J-1} \frac{D_{sm}(h, \beta(F))}{W_t^\dagger} \left( \prod_{j \neq k} W_t^\dagger(j) \right) \nabla_i W_t^\dagger(k) \right\}$$

$$= \mathbb{E} \left\{ \sum_{k=0}^{J-1} \frac{D_{sm}(h, \beta(F))}{W_t^\dagger} \nabla_i W_t^\dagger(k) \left( \prod_{j \neq k} W_t^\dagger(j) \right) W_t^\dagger(k)^2 \right\}$$
Next consider term

\[
\frac{\nabla_t W^\dagger_t(k)}{W^\dagger_t(k)^2} = \frac{\nabla_t W^\dagger_{t,1}(k) W^\dagger_{t,2}(k)}{W^\dagger_t(k)^2 W^\dagger_t(k)^2} = \frac{S(Z(k))}{W^\dagger_t(k)} + \frac{\nabla_t \delta_{k,t}(\overline{L}(k), \overline{A}(k - 1), Z(k - 1))}{W^\dagger_t(k) \delta_k (\overline{L}(k), \overline{A}(k - 1), Z(k - 1))}
\]

where \( S(Z(k)) \) is the score function of \( f_t(Z(k)|\overline{L}(k), \overline{A}(k - 1), Z(k - 1)) \) and \( S(A(k)) \) is the score function of \( f_t(A(k)|\overline{L}(k), \overline{A}(k - 1), Z(k)) \). Further noting that

\[
\nabla_t \delta_{k,t}(\overline{A}(k - 1), Z(k - 1), \overline{L}(k)) = \mathbb{E} \left\{ S(A(k)) \frac{(-1)^{-Z(k)}}{-\mathbb{E} (A(k)|\overline{A}(k - 1), Z(k - 1), \overline{L}(k))} \right\} \frac{f(Z(k)|\overline{L}(k), \overline{A}(k - 1), Z(k - 1))}{\overline{A}(k - 1), Z(k - 1), \overline{L}(k)}
\]
we have

\[
\mathbb{E} \left\{ \frac{D_{sm}(h, \beta(F))}{W^2} \nabla_t W_1^t \right\} = \mathbb{E} \left\{ \sum_{k=0}^{J-1} \frac{1}{\prod_{j<k} W^t(j)} \frac{(-1)^{1-Z(k)} S(Z(k))}{f(Z(k)|Z(k), A(k-1), Z(k-1))} \right\} \\
+ \mathbb{E} \left\{ D_{sm}(h, \beta(F)) \frac{\delta_k(Z(k-1), Z(k-1)) W^t_2(k)}{f(Z(k)|Z(k), A(k-1), Z(k-1))} \prod_{j<k} W^t(j) \right\} \\
+ \mathbb{E} \left\{ \sum_{k=0}^{J-1} \frac{S(A(k))}{\prod_{j<k} W^t(j)} \frac{(-1)^{1-Z(k)} (A(k)-E(A(k)|\overline{A}(k-1), Z(k-1), Z(k)))}{f(Z(k)|Z(k), A(k-1), Z(k-1))} \right\} \\
+ \mathbb{E} \left\{ D_{sm}(h, \beta(F)) \frac{\delta_k(Z(k-1), Z(k-1)) W^t_2(k)}{f(Z(k)|Z(k), A(k-1), Z(k-1))} \prod_{j<k} W^t(j) \right\} \\
+ \mathbb{E} \left\{ \sum_{k=0}^{J-1} \frac{S(A(k))}{\prod_{j<k} W^t(j)} \frac{(-1)^{1-Z(k)} (A(k)-E(A(k)|\overline{A}(k-1), Z(k-1), Z(k)))}{f(Z(k)|Z(k), A(k-1), Z(k-1))} \right\} \\
= \mathbb{E} \left\{ S(O) \sum_{k=0}^{J-1} \frac{1}{W^t(k-1)} \left\{ \frac{(-1)^{1-Z(k)} \Psi_k \left( \tilde{\beta}_{np}(h) \right)}{f(Z(k)|Z(k), A(k-1), Z(k-1))} - \Psi_k \left( \tilde{\beta}_{np}(h) \right) \right\} \right\} \\
+ \mathbb{E} \left\{ S(O) \sum_{k=0}^{J-1} \frac{\epsilon_k \Psi_k \left( \tilde{\beta}_{np}(h) \right)}{W^t(k-1) W^t_1(k)} \right\}
\]
Therefore, we conclude that

\begin{align*}
0 &= \nabla \mathbb{E}_t \left\{ \frac{D_{sm} (h, \beta (F_i))}{W_i^t} \right\} \\
&= \mathbb{E} \left\{ \frac{D_{sm} (h, \beta (F))}{W_i} S \right\} - \mathbb{E} \left\{ \frac{D_{sm} (h, \beta (F))}{W_i^2} \nabla \mathbb{E}_t \left\{ \frac{D_{sm} (h, \beta (F))}{W_i^t} \right\} \right\} \\
&+ \mathbb{E} \left\{ \frac{\nabla_\beta D_{sm} (h, \beta)}{W_i} \right\} \nabla \mathbb{E}_t \left\{ \frac{D_{sm} (h, \beta (F))}{W_i^t} \right\}
\end{align*}

proving the result. ■

**Proof of triple robustness of \( \hat{\beta}_{mr} \).** It suffices to show that

\begin{align*}
\mathbb{E} \left[ \frac{D_{sm} (h, \beta_0)}{W_i^{t*}} - \sum_{k=0}^{J-1} \frac{1}{W_i^{t*} (k-1)} \left\{ \frac{(-1)^{1-Z(k)} \Psi^*_k (\beta_0)}{f^*(Z(k)|L(k), \overline{A}(k-1), Z(k-1))} - \tilde{\Psi}_k (\beta_0) \right\} \right] = 0
\end{align*}

provided that either

(i) \( W_i^{t*} = W_i^t \), i.e. \( f^* (Z(j)|\overline{L}(j), \overline{A}(j-1), Z(j-1)) = f (Z(j)|\overline{L}(j), \overline{A}(j-1), Z(j-1)) \) and \( \delta_j^* (\overline{L}(j), \overline{A}(j-1), Z(j-1)) = \delta_j (\overline{L}(j), \overline{A}(j-1), Z(j-1)) \) for all \( j \); or

(ii) \( f^* (Z(j)|\overline{L}(j), \overline{A}(j-1), Z(j-1)) = f (Z(j)|\overline{L}(j), \overline{A}(j-1), Z(j-1)) \) and \( \Gamma_j^1 (\beta_0) = \Gamma_j^1 (\beta_0) \) for all \( j \); or

(iii) \( \Gamma_j^1 (\beta_0) = \Gamma_j^0 (\beta_0), \Gamma_j^0 (\beta_0) = \Gamma_j^0 (\beta_0) \), and \( E^* (A(j)|\overline{A}(j-1), \overline{L}(j), Z(j)) = E (A(j)|\overline{A}(j-1), \overline{L}(j), Z(j)) \).

The result for (i) holds because \( \mathbb{E} \left\{ \frac{D_{sm} (h, \beta_0)}{W_i^t} \right\} = 0 \),

\begin{align*}
\mathbb{E} \left[ \sum_{k=0}^{J-1} \frac{(-1)^{1-Z(k)} \Psi^*_k (\beta_0)}{f (Z(k)|L(k), \overline{A}(k-1), Z(k-1))} \right] = 0,
\end{align*}

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and $E \left\{ \epsilon_k^*/\mathcal{W}_1^*(k) | \overline{A} (k - 1), \overline{L} (k), \overline{Z} (k - 1) \right\} = 0$, because

$$
E \left\{ \frac{(-1)^{1-Z(k)} \epsilon_k^*}{f (Z(k)|L(k), \overline{A}(k - 1), \overline{Z}(k - 1))} \delta_k^* (\overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1)) \overline{A}(k - 1), \overline{L} (k), \overline{Z} (k - 1) \right\}
$$

$$
= E \left\{ \left( \frac{(-1)^{1-Z(k)} (A(k) - \delta_k (\overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1)) Z(k))}{f (Z(k)|L(k), \overline{A}(k - 1), \overline{Z}(k - 1))} \delta_k (\overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1)) \right) \overline{A}(k - 1), \overline{L} (k), \overline{Z} (k - 1) \right\}
$$

$$
= \frac{-\delta_k (\overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1)) - \delta_k (\overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1))}{\delta_k (\overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1))}
$$

$$
+ \sum_{z(k)} (-1)^{1-z(k)} \frac{-E^* (A(k)|\overline{A}(k - 1), \overline{L}(k), \overline{Z}(k - 1), Z(k) = 0)}{\delta_k (\overline{L}(k), \overline{A}(k - 1), \overline{Z} (k - 1))}
$$

$$
= 0
$$

Next, suppose that

(ii) $f^* (Z(j)|\overline{L}(j), \overline{A}(j - 1), \overline{Z}(j - 1)) = f (Z(j)|\overline{L}(j), \overline{A}(j - 1), \overline{Z}(j - 1))$ and $\Gamma_j^{(1)*} (\beta_0) = \Gamma_j^{(1)} (\beta_0) = \tilde{\Psi}_j (\beta_0)$ for all $j$. Then

$$
E \left[ \sum_{k=0}^{J-1} \frac{1}{\mathcal{W}^*(k - 1)} \left\{ \frac{(-1)^{1-Z(k)} \Psi_k^* (\beta_0)}{f (Z(k)|\overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1))} - \tilde{\Psi}_k (\beta_0) \right\} \right]
$$

$$
= E \left[ \sum_{k=0}^{J-1} \frac{1}{\mathcal{W}^*(k - 1)} E \left\{ \left( \frac{(-1)^{1-Z(k)} \Psi_k^* (\beta_0)}{f (Z(k)|\overline{L}(k), \overline{A}(k - 1), \overline{Z}(k - 1))} - \tilde{\Psi}_k (\beta_0) \right) \right\} \right]
$$

$$
= 0
$$
Furthermore,

\[
\mathbb{E} \left[ \frac{\epsilon_{j-1}^* \tilde{\Psi}_{j-1} (\beta_0)}{W_j^* (j-2) W_j^* (j-1)} \right] = \mathbb{E} \left[ (-1)^{1-Z(j-1)} \frac{(A(J - 1) - \delta_{j-1}^* (L(J - 1), A(J - 2), Z(J - 2)) Z(J - 1)}{-E^* (A(J - 1)|A(J - 2), L(J - 1), Z(J - 2), Z(J - 1) = 0)} \tilde{\Psi}_{j-1} (\beta_0) \right] \\
= \mathbb{E} \left[ (-1)^{1-Z(j-1)} \frac{(A(J - 1) - \delta_{j-1}^* (L(J - 1), A(J - 2), Z(J - 2)) Z(J - 1)}{-E^* (A(J - 1)|A(J - 2), L(J - 1), Z(J - 2), Z(J - 1) = 0)} \tilde{\Psi}_{j-1} (\beta_0) \right] \\
= \mathbb{E} \left[ \frac{\delta_{j-1} (L(J - 1), A(J - 2), Z(J - 2)) \Gamma_{j-1}^{(1)} (\beta_0)}{W_j^* (j-2) \delta_{j-1}^* (L(J - 1), A(J - 2), Z(J - 2))} \right] - \mathbb{E} \left[ \frac{\delta_{j-1} (L(J - 1), A(J - 2), Z(J - 2)) \Gamma_{j-1}^{(1)} (\beta_0)}{W_j^* (j-2) \delta_{j-1}^* (L(J - 1), A(J - 2), Z(J - 2))} \right] \\
= \mathbb{E} \left[ \frac{\Delta_{j-1} \Gamma_{j-1}^{(1)} (\beta_0)}{W_j^* (j-2) \Delta_{j-1}^*} \right] - \mathbb{E} \left[ \frac{\Gamma_{j-1}^{(1)} (\beta_0)}{W_j^* (j-2)} \right]
\]

Likewise for all \( 1 \leq j < J - 1 \)

\[
\mathbb{E} \left[ \frac{\epsilon_j^* \tilde{\Psi}_j (\beta_0)}{W_j^* (j-1) W_j^* (j)} \right] = \mathbb{E} \left[ \frac{\Delta_j \Gamma_j^{(1)} (\beta_0)}{W_j^* (j-1) \Delta_j^*} \right] - \mathbb{E} \left[ \frac{\Gamma_j^{(1)} (\beta_0)}{W_j^* (j-1)} \right]
\]

and

\[
\mathbb{E} \left[ \tilde{\Psi}_j (\beta_0) \right] = \mathbb{E} \left[ \frac{1}{W_j^* (j-2) f(Z(j-1)|L(j-1), A(j-2), Z(j-2))} \tilde{\Psi}_j (\beta_0) \right] \times \mathbb{E} \left[ \frac{(-1)^{1-Z(j-1)} \tilde{\Psi}_j (\beta_0)}{W_j^* (j-1) \Delta_j^*} \right] \\
= \mathbb{E} \left[ \frac{1}{W_j^* (j-2) f(Z(j-1)|L(j-1), A(j-2), Z(j-2))} \tilde{\Psi}_j (\beta_0) \right] \times \mathbb{E} \left[ \frac{(-1)^{1-Z(j-1)} \tilde{\Psi}_j (\beta_0)}{W_j^* (j-1) \Delta_j^*} \right] \\
= \mathbb{E} \left[ \frac{\tilde{\Psi}_{j-1} \Delta_{j-1}}{W_j^* (j-2) \Delta_{j-1}^*} \right]
\]
Therefore

\[
E \left[ \sum_{k=0}^{J-1} \frac{1}{W^*_{(k-1)}} \left\{ f^* \left( Z(k) \mid \bar{W}(k), \bar{Z}(k-1) \right) \right\} \Psi_k (\beta_0) \right] - \sum_{k=0}^{J-1} \frac{\epsilon_k^* \Psi_k (\beta_0)}{W^*_{(k-1)} W^*_{1} (k)}
\]

\[
= E \left[ \frac{D_{sm}(h, \beta_0)}{W^*} \right] - E \left[ \frac{\epsilon_k^* \Psi_k (\beta_0)}{W^*_{1} (k-1)} \right]
\]

\[
= E \left[ \frac{D_{sm}(h, \beta_0)}{W^*} \right] - \sum_{k=0}^{J-1} \frac{\epsilon_k^* \Psi_k (\beta_0)}{W^*_{1} (k-1)}
\]

\[
= E \left[ \frac{\Delta_{J-1} \Gamma_{J-1} (\beta_0)}{W^*_{1} (J-2) \Delta_{J-1}^*} \right] - \sum_{k=0}^{J-1} \frac{\Delta_k \Gamma_k (\beta_0)}{W^*_{1} (k-1) \Delta_k^*} - \frac{\Gamma_k (\beta_0)}{W^*_{1} (k-1)}
\]

\[
= E \left[ \frac{\Delta_{J-1} \Gamma_{J-1} (\beta_0)}{W^*_{1} (J-2) \Delta_{J-1}^*} \right] - \sum_{k=0}^{J-1} \frac{\Delta_k \Gamma_k (\beta_0)}{W^*_{1} (k-1) \Delta_k^*} + \sum_{k=0}^{J-1} \frac{\Delta_k \Gamma_k (\beta_0)}{W^*_{1} (k-1) \Delta_k^*}
\]

\[
= E \left[ \frac{\Gamma_0 (\beta_0)}{W^*_{1} (J-2) \Delta_{J-1}^*} \right] = 0
\]

where \( \Delta_{-1} \equiv 0 \). \( W^*_{1} (-2) = W^*_{1} (-1) = 1, \Delta_{-1}^* = 1 \). Finally, suppose that (iii) \( \Gamma_1^* (\beta_0) = \Gamma_1 (\beta_0) \), \( \Gamma_0^* (\beta_0) = \Gamma_1 (\beta_0) \) and \( E^* (A(j) \mid \bar{W}(j-1), \bar{Z}(j)) = E (A(j) \mid \bar{W}(j-1), \bar{Z}(j)) \), then note that

\[
E \left\{ \sum_{k=0}^{J-1} \frac{\epsilon_k^* \Psi_k (\beta_0)}{W^*_{1} (k-1) \Delta_k^*} \right\}
\]

\[
= E \left\{ \sum_{k=0}^{J-1} \frac{\epsilon_k^* \Psi_k (\beta_0)}{W^*_{1} (k-1) \Delta_k^*} \right\}
\]

\[
= E \left\{ \sum_{k=0}^{J-1} \frac{\epsilon_k^* \Psi_k (\beta_0)}{W^*_{1} (k-1) \Delta_k^*} \right\}
\]

\[
= 0
\]
Therefore

\[
\mathbb{E} \left[ \frac{D_{sm}(h, \beta_0)}{W^*} - \sum_{k=0}^{J-1} \frac{1}{W^{*}(k-1)} \left\{ \frac{(-1)^{1-Z(k)} \Psi_k'(\beta_0)}{f^*(Z(k)|\mathcal{L}(k), A(k-1), Z(k-1))} - \widetilde{\Psi}_k(\beta_0) \right\} \right]
\]

\[
= \mathbb{E} \left[ \frac{D_{sm}(h, \beta_0) - \Psi_{J-1}(\beta_0) \Delta_{J-1} W^{*}_2(J-1)}{W^{*}} + \sum_{k=0}^{J-1} \frac{\Psi_k(\beta_0) - \Psi_{k-1}(\beta_0) \Delta_{k-1} W^{*}_2(k-1)}{W^{*}(k-1)} \right]
\]

\[
= \mathbb{E} \left[ \Gamma_0^{(1)}(\beta_0) \right] = 0,
\]

proving the result.

\[\blacksquare\]