A Simple Weighted Approach for Instrumental Variable Estimation of Marginal Structural Mean Models

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Abstract

Robins [13] 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 rules out unmeasured confounding of treatment assignment over time. We consider sufficient conditions for identification of the parameters of a subclass, Marginal Structural Mean Models (MSMMs), when sequential randomization fails to hold due to unmeasured confounding, using instead a time-varying instrumental variable. Our identification conditions 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 [18]. We describe a simple weighted estimator and examine its finite-sample properties in a simulation study.

KEY WORDS: marginal structural models, time-varying endogeneity, instrumental variables
1 Introduction

Robins [13, 14, 15] introduced marginal structural models (MSMs), a class of counterfactual models that encode the joint causal effects of time-varying treatment in the presence of time-varying confounding. For identification, Robins relied on a sequential randomization assumption (SRA), which rules out unmeasured confounding of the time-varying treatment. MSMs have since become the standard analytic approach to evaluate causal effects in time-varying epidemiological studies [3, 4, 7, 10, 17]. However, SRA may be hard to justify in many such settings, and unmeasured confounding bias may invalidate causal claims inferred by the approach. In the case of a point treatment, a large literature in causal inference has developed over the years on the instrumental variable method aiming to address unmeasured confounding [2, 8, 12]. Instead of assuming that there is no unmeasured confounding, the IV approach relies on the key assumption that one has observed a pretreatment variable that can affect the outcome only through its effects on the treatment [6]. Many commonly used IVs, such as treatment compliance and tax rates, vary with time. Nevertheless, IV methods in longitudinal settings are far less developed. In this paper, we consider sufficient conditions for identification of the parameters of a Marginal Structural Mean Model (MSMM) with the aid of a time-varying instrumental variable when sequential randomization fails to hold due to unmeasured confounding. In doing so, we firmly establish the IV approach in the context of MSMMs for complex longitudinal settings, an extension previously believed out of reach [15]. Our identification conditions require longitudinal generalizations of standard IV assumptions, together with a key assumption that no unobserved confounder predicts compliance type for the time-varying treatment, a longitudinal generalization of the identification condition of [18]. Under these assumptions, we establish identification of the MSMM parameter and propose a simple estimation procedure analogous to inverse-probability weighted (IPW) estimation, the most common approach for estimating MSMs under SRA.

Prior to the current work, Robins [12] 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 mean model (SNMM). As described in [15], the parameters of an SNMM can under certain homogeneity conditions be interpreted as MSMM parameters, in
which case [12] provides alternative estimators to ours. In contrast, the proposed methodology is more general as it directly targets MSMM parameters irrespective of whether or not they can be interpreted as parameters of an equivalent SNMM.

The remainder of the paper is organized as follows. In Section 2 we provide context by describing identification and estimation of MSMM parameters under SRA. In Section 3 we present an alternative set of identification conditions to SRA, making use of a time-varying instrumental variable. In Section 5 we describe a simple weighted estimator for MSMM parameters using our instrumental variable approach. In Section 6 we present a simulation study to examine the finite-sample performance of our proposed estimator. We conclude in Section 7 with a brief discussion and description of future work.

2 Background

We consider i.i.d. discrete-time processes and adopt the “potential outcomes” framework. The data observed on a process consists of $T+2$ random vectors $\overline{L} = (L_0, \ldots, L_{T+1})$ and $T+1$ random variables $\overline{A} = (A_0, \ldots, A_T)$. The common state space of $A_t$, $t = 1, \ldots, T$, is denoted $\mathcal{A}$. Variables at time 0 are defined to be constant, e.g., $A_0 = 0$. The vectors $L_t$ and variables $A_t$ carry the interpretation of a subject’s time-varying covariates and a time-varying treatment, respectively. A variable $Y \in L_{T+1}$ is singled out as an outcome of interest. The number of time points $T$ is non-random. The statistical significance of these temporal relations are conditional independence relationships formalized in assumptions given below. We use script fonts to refer to state spaces, $f$ to refer to densities, and $\mu$ for measures relative to which densities are given, using subscripts to indicate the law. We use overbars to indicate the history of an RV, e.g., $\overline{L}_t = (L_0, \ldots, L_t)$. To simplify notation, we sometimes use a single overbar and single time index to indicate a history of random vectors, e.g., $\overline{AZL}_t = (A_t, Z_t, L_t) = (A_\tau, Z_\tau, L_\tau)_{\tau=0}^t$.

Besides the observed data, we assume the existence of $|\mathcal{A}|^T$ variables $Y_{\overline{Z}, \overline{a}} \in \mathcal{A}^T$. These “potential outcomes” or “counterfactuals” are not in general observed. They are related to the observed data by the “consistency” assumption,
**Assumption 1** (Consistency).

\[ Y = Y_{\pi} \quad \text{a.s.} \]

In case the treatments \( \overline{A} \) are discrete, the assumption may be written as \( Y = \sum_{\pi \in \mathcal{A}} Y_{\pi}\{ \overline{A} = \overline{a} \} \).

Thus \( \overline{a} \) may be interpreted as a particular treatment regime, and the potential outcome \( Y_{\pi} \) as the distribution of \( Y \) were everyone in the observed population to follow treatment regime \( \overline{a} \), i.e., if \( \{ \overline{A} = \overline{a} \} \equiv 1 \).

We focus on marginal structural mean models ("MSMMs"). An MSMM is a model on the marginal means of potential outcomes \[ [13] \]. For example, the effect of treatment may be modeled as linear in the cumulative treatment taken,

\[ E(Y_{\pi}) = \beta_0 + \beta_1 \sum_{t=0}^{T} a_t. \quad (1) \]

In this example, \( \beta \in \mathbb{R}^2 \) parameterizes the model and encodes the incremental effect of a unit of treatment. A link function can be introduced to accommodate binary or count outcome variables, e.g., for binary \( Y, \) \( E(Y_{\pi}) = (1 + \exp(\beta_0 + \beta_1 \sum_{t=0}^{T} a_t))^{-1} \). In general we write

\[ E(Y_{\pi}) = m_\beta(\overline{a}) \quad (2) \]

to describe an MSMM, where \( m_\beta : \mathcal{A}^T \to \mathbb{R} \) belongs to a family of functions parametrized by finite-dimensional \( \beta \). The model parameter \( \beta \) is the target of inference.

An MSMM is defined using the unobserved quantities \( Y_{\pi}, \overline{a} \neq \overline{A} \), and the model parameter is not in general identified by the observed data. Robins \[ [13] \] provides sufficient conditions for identification and estimation, the sequential randomization assumption and positivity:

\[ Y_{\pi} \perp \perp A_t \mid \overline{L}_t, \overline{A}_{t-1}, \quad 1 \leq t \leq T \quad \text{(SRA)} \]

\[ 0 < f_{A_t|\overline{A}_{t-1}, \overline{L}_t}(a_t \mid \overline{a}_{t-1}, \overline{l}_t) \quad \text{when} \quad f_{\overline{A}_{t-1}, \overline{L}_t}(\overline{a}_{t-1}, \overline{l}_t) > 0, \quad a_t \in \mathcal{A}, 1 \leq t \leq T, \quad \text{(positivity)} \]

using \( \perp \) to denote statistical independence. In the treatment setting, SRA will hold if the cumulative observed data at each time point captures all systematic associations between the treatment
and outcome of interest. Positivity will hold when, among all subpopulations defined by covariates \( L_t \) and a treatment regime \( A_{t-1}, t \leq T \), there are further subpopulations at each possible treatment level. These conditional independence relationships are implied by the directed acyclic graph given in Fig. 1 in which a node is independent of non-descendants conditional on its parent nodes; see [11] for details.

Robins [13] uses assumptions (3,4) to relate the law of a potential outcome \( Y_\pi \) to the law of the observed data \((Y, L, A)\). Specifically, given measurable \( g : (Y, A^T) \rightarrow \mathbb{R}^d \),

\[
\int_{A^T} \mathbb{E}(g(Y_\pi, \pi)) \mu_{A^T}(\pi) = \mathbb{E}\left(\frac{g(Y, A)}{W^{(SRA)}}\right),
\]

where the observation weights \(1/W^{(SRA)}\) are defined by

\[
W^{(SRA)}_t = f_{A_t|A_{t-1}, L_t}(A_t | A_{t-1}, L_t), \quad \overline{W}^{(SRA)}_t = \prod_{\tau=1}^t W^{(SRA)}_\tau, \quad t = 1, \ldots, T,
\]

\[
\overline{W}^{(SRA)} = \overline{W}^{(SRA)}_T = \prod_{\tau=1}^T W^{(SRA)}_\tau.
\]

This use of overbars to represent the running product of weights departs from our usual use of overbars to denote the history of a time-varying quantity collected in a vector. The case \( T = 1, g(y, a) = g_0(y) \times 1_a \), gives the inverse-probability-weighted estimator for \( g_0(Y_a) \) often used in propensity score analysis.

Besides identifying the parameter of an MSMM using fully observed data, relation (5) also suggests an estimator. Let \( g(y, \pi) = h(\pi)(y - m_\beta(\pi)) \), where \( h \) is a function on \( A^T \) of the same dimension as \( \beta \). Then the MSMM model (2) implies \( \mathbb{E}\left(\frac{h(A)}{W^{(SRA)}} (Y - \mu_\beta(A))\right) = \mathbb{E}(h(\pi) (Y_\pi - m_\beta(\pi))) = 0 \), giving rise to estimating equations for \( \beta \),

\[
0 = \mathbb{P}_n \left( h(A) \frac{Y - \mu_\beta(A)}{\overline{W}^{(SRA)}} \right),
\]

using \( \mathbb{P}_n \) to denote the empirical distribution on a sample of size \( n \). In practice, \( \overline{W}^{(SRA)} \) may not be known and an estimate is substituted. Assuming the usual conditions for M-estimation hold,
the empirical solution $\hat{\beta}$ is asymptotically normal as the number of observations $n$ grows, with a variance that can be approximated by its influence function.

Furthermore, a suitable choice of $h$ in (5) can in some situations provide a means to stabilize the weights (7), which may become unstable as $T$ increases. Stabilized weights are formed as the ratio of the weights (7) with an approximations depending only on $A$. A common choice for this approximation is $\prod_{t} f(A_t \mid A_{t-1})$, giving

$$W^{(SRA,\text{stabilized})} := \prod_{t=1}^{T} f(A_t \mid A_{t-1})/W^{(SRA)} = \prod_{t=1}^{T} f(A_t \mid A_{t-1})/f(A_t \mid A_{t-1}, L_t).$$

The quality of the approximation depends on the strength of the dependence of the density of $A_t$ and the covariates $L_t$ given $A_{t-1}$, i.e., to the extent that treatment is unconfounded. The qualitative result is that this estimation approach, similar to the one adopted below, requires for practical application that either $T$ not be too large or confounding not be too great.

We pursue parallel results using instrumental variables to relax SRA. We give an analogue of the identifying relation (5) in Section 3 and similar estimation techniques in Section 5.

Although we focus on marginal structural mean models, the marginal structural model ("MSM") theory of [13] is more general, allowing for models on many other functionals of the marginal distributions of the potential outcomes, as well as providing efficient estimators. See [16] for a more closely parallel development.

### 3 Identification of causal model parameters using IVs

We now allow for the possibility of unmeasured confounders in the form of an additional unobserved process associated with both the treatment and outcome. The sequential randomization assumption [3] is not warranted in this situation. We propose to use “instrumental variables”
Figure 2: Causal DAG describing confounding with unobserved confounders and IV, with $T = 2$ time points. Edges emerging from the IV $Z$ only end at the treatment $A$. The roles of $U$ and $L$ are symmetric except in respect of the IV, with which $L$ but not $U$ is dependent.

to identify an MSMM parameter in the absence of SRA. Informally, an IV is a random variable associated with the treatment of interest that only affects the outcome of interest through its effect on the treatment.

To this end, in addition to the data described in Section 2, let $\mathbf{U} = (U_1, \ldots, U_T)$ be an unobserved process, which may be associated with both $\mathbf{A}$ and $\mathbf{L}$, including $Y$. We assume that $\mathbf{U}$ captures all further confounding between $\mathbf{A}$ and $Y$ beyond $\mathbf{L}$, so that SRA would hold were $\mathbf{U}$ observed:

**Assumption 2** (Latent SRA). $Y_{\pi} \perp \!\!\!\!\!\perp A_t \mid \bar{A}_{t-1} = a_{t-1}, \bar{L}_t, \mathbf{U}_t \quad t = 1, \ldots, T, \quad \pi \in \mathcal{A}^T$

That is, there are no unobserved confounders at time $t$ other than $\mathbf{U}_t$. The assumptions given below impose restrictions on $\mathbf{U}$.

Suppose further that a binary-valued process $\mathbf{Z} = (Z_1, \ldots, Z_T)$ is observed, satisfying the following IV assumptions: For all $1 \leq t \leq T$ and $\pi \in \mathcal{A}^T$, $\pi \in \{0, 1\}^T$,

**Assumption 3** (IV relevance). $\mathbb{E}(A_t \mid \bar{A}_{t-1}, \bar{L}_t, \mathbf{Z}_t) \neq \mathbb{E}(A_t \mid \bar{A}_{t-1}, \bar{L}_t, \mathbf{Z}_{t-1})$

**Assumption 4** (Exclusion restriction). $Y_{\pi\pi} = Y_{\pi}$

**Assumption 5** (IV–outcome independence). $Z_t \perp \!\!\!\!\!\perp (Y_{\pi\pi}, L_{t+1}, U_{t+1}) \mid \bar{A}_t = a_t, \bar{L}_t, \mathbf{U}_t$

**Assumption 6** (IV–unmeasured confounder independence). $Z_t \perp \!\!\!\!\!\perp \mathbf{U} \mid \bar{A}_{t-1}, \bar{L}_t, \mathbf{Z}_{t-1}$

**Assumption 7** (IV Positivity). $0 < \mathbb{P}(Z_t = 1 \mid \bar{A}_{t-1}, \bar{L}_t, \mathbf{Z}_{t-1}) < 1$ a.s.
Assumptions 3–7 are longitudinal generalizations of standard IV assumptions. As in the SRA case discussed in Section 2, the conditional independence relationships described by the key assumptions 2, 5, and 6 formalize the temporal relationships among the data $A_t, Y, L_t$, etc., that we use informally. A graph that provides a model of these assumptions is given in Fig. 2. The methods given in [11] may be used to establish that the graph in Fig. 2, properly interpreted, does in fact entail a model for the conditional independence relations given in Assumptions 2, 5, and 6. The DAG in Fig. 2 is illustrative and is not meant to preclude other models compatible with these assumptions, e.g., unmeasured confounding among the measured covariates $\{L_t\}$ or between $L_t$ and the outcome $Y$. As a shorthand we use the notation “an” to refer to an ancestor set in the DAG in Fig. 2, e.g., an($Z_t$) is an($A_{t-1}$) $\cup$ an($Z_{t-1}$) $\cup$ an($L_t$).

Finally, we make an additional orthogonality assumption. For $t = 1, \ldots, T$.

**Assumption 8** (Independent Compliance Type).

$$f (a_t|A_{t-1}, Z_{t-1}, Z_t = 1, L_t, U_t) - f (a_t|A_{t-1}, Z_{t-1}, Z_t = 0, L_t, U_t) \perp U_t | A_{t-1}, Z_{t-1}, L_t.$$  

Defining

$$\Delta_t(a_t, A_{t-1}, Z_{t-1}, L_t, U_t) = f (a_t|A_{t-1}, Z_{t-1}, Z_t = 1, L_t, U_t) - f (a_t|A_{t-1}, Z_{t-1}, Z_t = 0, L_t, U_t),$$

the assumption is that $\Delta_t(a_t, A_{t-1}, Z_{t-1}, L_t, U_t)$ does not depend on $U_t$, and so may be written as $\Delta_t(a_t, A_{t-1}, Z_{t-1}, L_t)$. The function $\Delta_t$ may be expressed using the observed data by the relation

$$\Delta_t(a_t, A_{t-1}, Z_{t-1}, L_t) = f (a_t|A_{t-1}, Z_{t-1}, Z_t = 1, L_t, U_t) - f (a_t|A_{t-1}, Z_{t-1}, Z_t = 0, L_t, U_t)
= f (a_t|A_{t-1}, Z_{t-1}, Z_t = 1, L_t) - f (a_t|A_{t-1}, Z_{t-1}, Z_t = 0, L_t).$$

The relation follows by integrating both sides of the first line with respect to the conditional density of $U_t$ given $(A_t, Z_{t-1}, Z_t = 1, L_t)$, which is the same as the density given $(A_t, Z_{t-1}, Z_t = 0, L_t)$, by Assumption 6.

Assumption 8 states that while $U_t$ may confound the causal effects of $A_t$, no component of $U_t$
interacts with \( Z_t \) in its additive effects on \( A_t \). This assumption is a longitudinal generalization of a similar assumption made by \[18\] in the point exposure setting.

Let \( f_{Z_t} \) denote the density of \( Z_t \) conditional on the prior observed history \((A_{t-1}, Z_{t-1}, L_t)\), which, by Assumption \[6\], has the same effect as conditioning on the full prior history \((A_{t-1}, Z_{t-1}, L_t, U_t)\).

We define subject-specific weights \( 1/W \) through:

\[
W = \prod_{t=1}^{T} W_t, \quad W_t = (-1)^{1-Z_t} f_{Z_t}(Z_t \mid L_t, A_{t-1}, Z_{t-1}) \Delta_t (L_t, A_{t-1}, Z_{t-1}).
\]

(8)

Assumptions \[3\] and \[7\] ensure that the weights are nonzero.

**Theorem 1.** Suppose that together with consistency \[1\], Assumptions \[2-8\] hold. For measurable \( g : (Y, A^T) \to \mathbb{R}^d \),

\[
\mathbb{E}(g(Y, A)/W) = \int_{A^T} g(Y, A) \mu_{A^T}(A),
\]

(9)

when the expectation exists.

Proofs are given in the appendix.

**Remark 2.** The conclusion of the theorem for the particular choice \( g(y, \bar{a}) = h(\bar{a})(y - m(A)) \), \( h \in L_1(\mathbb{A}) \), i.e.,

\[
\mathbb{E}(h(\bar{A})(Y - m(A))/W) = \int_{A^T} h(\bar{A})(Y, \bar{A}) \mu_{A^T}(A),
\]

(10)

may be established under weaker forms of Assumptions \[1\] and \[2\]. Assumption \[1\] may be replaced with

**Assumption \[1\].**

\[ \mathbb{E}(Y \mid A_t = \bar{a}_t, Z_t, L_t, U_t) = \mathbb{E}(Y_{\bar{a}} \mid A_t = \bar{a}_t, Z_t, L_t, U_t). \]

Assumption \[2\] may be replaced with

**Assumption \[2\].**

\[ \mathbb{E}(Y_{\bar{a}} \mid A_t = \bar{a}_t, Z_{t-1}, L_t, U_t) = \mathbb{E}(Y_{\bar{a}} \mid A_{t-1} = \bar{a}_{t-1}, Z_{t-1}, L_t, U_t) \quad t = 1, \ldots, T, \quad \bar{a} \in \mathbb{A}^T. \]
As the range of $W$ includes negative values, $1/W$ are not weights in the usual sense, a phenomenon that also occurs in other IV-weighted moment equations for point exposure [11, 18]. The weights in fact have mean zero, as follows by taking expectations on both sides of

$$E(W_T^{-1} \mid \text{an}(Z_T)) = W_{T-1}^{-1} \Delta_T^{-1} E \left( \frac{(-1)^{1-Z_T}}{f_{Z_T}(Z_T \mid AZ_{T-1}, T_T)} \right) \text{an}(Z_T) = W_{T-1}^{-1} \Delta_T^{-1} (1 - 1),$$

although, as mentioned previously, they are almost surely non-zero under the assumptions for identification.

**Example 3** (Binary treatment). Assumption 8 may, in some situations, be interpreted as a condition on the “compliance types” [2] of the population.

When the treatment is binary, $A_t \in \{0, 1\}, t = 1, \ldots, T$, so that $P(A_t = 0 \mid \text{an}(A_t)) = 1 - P(A_t = 1 \mid \text{an}(A_t))$, the differences $\Delta_t$ satisfy $\Delta_t(A_t = 1) = -\Delta_t(A_t = 0), t = 1, \ldots, T$. Consider an application in which $Z_t$ indicates whether a subject has been assigned to take an experimental or control treatment at time $t$ and $A_t$ indicates whether the assigned treatment was or was not in fact taken. Then $0 < \Delta(A_t = 1) = P(A_t = 1 \mid \text{an}(A_t), Z_t = 1) - P(A_t = 1 \mid \text{an}(A_t), Z = 0) = P(A_t = 0 \mid \text{an}(A_t), Z = 0) - P(A_t = 0 \mid \text{an}(A_t), Z = 1)$ has the interpretation that $A_t$ must concord with the IV $Z_t$, in the sense that individuals at stratum $\text{an}(A_t, Z_t)$ are more likely at time $t$ to take the treatment when assigned to do so than when assigned not to do so. Analogously, when $\Delta(A_t = 1) < 0$, individuals at stratum $\text{an}(A_t, Z_t)$ are more likely to do the opposite of their assignment.

An additional assumption leads to an interpretation in terms of a well-studied causal notion, the compliance type. As with the treatment-indexed potential outcomes $Y_a$ defined earlier, IV-indexed potential treatments may also be defined, which we denote as $A_{t,Z_t}$. These potential outcomes may be cross-classified by the four possible pairs of values of $A_{t,Z_t}$ and $Z_t$. Experimental subjects for whom $A_{t,Z_t=1} = 1$ and $A_{t,Z_t=0} = 0$ are termed “compliers,” as they comply with the assignment $Z_t$, and similarly for “defiers,” $A_{t,Z_t=1} - A_{t,Z_t=0} < 0$, “never-takers”, $A_{t,Z_t=0} = A_{t,Z_t=1} = 0$, and “always-takers,” $A_{t,Z_t=0} = A_{t,Z_t=1} = 1$. Suppose that, analogous to SRA, these potential outcomes
are conditionally independent of the IV,

\[ Z_t \perp A_{t,Z_t} \mid \mathbf{U}_t, \mathbf{L}_t, \mathbf{A}_{t-1}, \mathbf{Z}_{t-1}. \]

Then Assumption 8 asserts that, at each stratum \( \text{an}(A_t, Z_t) \), the compliance type is mean-independent of unknown confounders,

\[ \mathbb{E} \left( (A_{t,z_t=1} - A_{t,z_t=0}) \mid \mathbf{U}_t, \mathbf{L}_t, \mathbf{A}_{t-1}, \mathbf{Z}_{t-1}, \right) = \Delta_t \left( \mathbf{L}_t, \mathbf{A}_{t-1}, \mathbf{Z}_{t-1}, \right) , \ t = 0, ..., T - 1. \]

Under this interpretation, the inequalities \( \Delta(A_t = 1) > 0 \) or \( \Delta(A_t = 1) < 0 \) assert that a given stratum consists only of compliers or defiers. In any event, whether or not this interpretation is available, a population stratum cannot consist of never-takers or always-takers due to Assumption 3.

In this application, Assumption 8 is warranted when enough data on the patients are obtained to account for any systematic differences in compliance type. However, less is necessary. Assumption 8 requires only that compliance type be independent of unmeasured treatment-outcome confounders. Viewed this way, a benefit of Theorem 1 over the SRA theorem is to allow an MSMM parameter to be estimated upon collecting covariates that account for systematic differences both between treatment and outcome and also compliance types, rather than all treatment-outcome confounders.

**Example 4** (Continuous treatment). We consider the implications of Assumption 8 for continuous treatment densities. First, because \( f_{A_t | \mathbf{X}_{t-1}, \mathbf{LUZ}_t}(a_t, Z_t = 1) \) and \( f_{A_t | \mathbf{X}_{t-1}, \mathbf{LUZ}_t}(a_t, Z_t = 0) \) both integrate to 1 with respect to \( \mu_{A_t} \), their difference \( \Delta_t(a_t) \) must integrate to 0. As the densities vanish at infinity, so must \( \Delta_t \). As discussed in Section 5, MSMM estimators are typically unstable when the magnitude of \( \Delta_t \) is small, and therefore the tails must decay quickly for good performance. Second, \( \Delta_t \) must be nonzero almost surely with respect to \( \mu_{A_t} \), by Assumption 7. Third, the nonnegativity of \( f_{A_t | \mathbf{X}_{t-1}, \mathbf{LUZ}_t}(a_t, Z_t = 1) \) requires, for all \( U_t \), that \( |\Delta_t(a_t)| \leq f_{A_t | \mathbf{X}_{t-1}, \mathbf{LUZ}_t}(a_t, Z_t = 0) \) for \( a \) such that \( \Delta_t(a_t) < 0 \). The first two requirements hold for the difference of any two densities that are unequal a.s. \(-\mu_{A_t} \), but the last is not as easily satisfied. It requires that for a range of densities obtained by varying \( U_t \), adding \( \Delta_t \) doesn’t lead to a function that has negative values.
An example is a location-scale parametrization for the treatment density. Let the baseline density $f_{A_t | A_{t-1}, LUZ_t}(A_t = a, L_t = (l_1, l_2), U_t = u, Z_t = 0)$ be normal $\phi((a - l_1)/u)/u$. The first component of the observed confounder $L_t$ controls the location and the unobserved confounder $U_t$ controls the spread. Let $\Delta_t(a | L_t = (l_1, l_2))$ be a difference between normal densities that does not depend on $U_t$, say, $\phi(a) - \phi(a/l_2)/l_2$. If the spread $u$ of the baseline density lies within a certain range, then $f_{A_t | A_{t-1}, LUZ_t}(A_t = a, L_t = (l_1, l_2), U_t = u, Z_t = 0) + \Delta_t(a)$ is a valid density for $A_t$. In particular, given $L_t = (l_1, l_2)$ with $l_2 \in (0, 1)$, suppose $l_2 < u < \min(1, l_2/(1 - l_2))$ for the standard deviation $u$ of the baseline. Let $l_1 = 0$ since the location is irrelevant to the argument. Then

$$f_{A_t | A_{t-1}, LUZ_t}(A_t = a, L_t = (l_1, l_2), U_t = u, Z_t = 1) = f_{A_t | A_{t-1}, LUZ_t}(A_t = a, L_t = (l_1, l_2), U_t = u, Z_t = 0) + \Delta_t(a) = \phi(a/u)/u + \phi(a) - \phi(a/l_2)/l_2$$

$$= \phi(a) \left\{ 1 + \exp(a^2(1 - 1/u^2)/2)/u - \exp(a^2(1 - 1/l_2^2)/2)/l_2 \right\}$$

$$= \phi(a) \frac{\exp(a^2(1 - 1/l_2^2)/2)/l_2 \left\{ l_2 \exp(a^2(1/l_2^2 - 1)/2) + (l_2/u) \exp(a^2(1/l_2^2 - 1/u^2)/2) - 1 \right\}}{l_2 + l_2/u - 1}$$

$$\geq \phi(a) \exp(a^2(1 - 1/l_2^2)/2)/l_2 \{ l_2 + l_2/u - 1 \}$$

$$> 0.$$
4 Partial converse

Let data \((A_1, Z_1, L_1, U_1), (A_2, Z_2, L_2, U_2), \ldots\), be given. Suppose there exists a process \(\omega_1, \omega_2, \ldots\) adapted to the observed data such that for any \(T, h, m,\) and \(Y\) compatible with \(m,\)

\[
E(h(\overline{A})\omega_T(\overline{ALZ}_T))(Y - m(A)) = 0.
\]

For example, under the assumptions of Theorem 1, \(\omega_t = 1/W_t\), with \(W_t\) given in (8), is an example of such a process. In this section, we consider whether there are other processes in the class \(\omega_1, \omega_2, \ldots\) that require less than Assumption 8. We relax the assumption that the time-varying instrument process \(\{Z_t\}\) is binary. We do restrict the treatment process \(\{A_t\}\) and the instrument process \(\{Z_t\}\) to be discrete-valued.

Given an MSMM \(m(\overline{A})\), the residual \(Y - m(\overline{A})\) may be decomposed as the sum of two noise terms \(\epsilon\) and \(\eta,\)

\[
\epsilon + \eta = Y - E(Y \mid \overline{A}, \overline{Z}, \overline{L}, \overline{U}) + E(Y \mid \overline{A}, \overline{Z}, \overline{L}, \overline{U}) - m(\overline{A}).
\]

The first difference, \(\epsilon\), is orthogonal to the vectors \((\overline{A}, \overline{Z}, \overline{L}, \overline{U})\), whereas the second, \(\eta\), need not be.

Under Assumptions 2, 5, and an MSMM \(E(Y_\pi) = m(\overline{\pi})\), \(\eta\) may be written as a sum of martingales restricted to the treatment levels \(\overline{\pi} \in \mathcal{A}^T,\)

\[
\eta = E(Y \mid \overline{AZL}) - m(\overline{A}) =
\sum_{\overline{\pi} \in \mathcal{A}^T} \{\overline{A} = \overline{\pi}\} \left( E(Y_\pi \mid \overline{aZL}) - m(\overline{a}) \right)
= \sum_{\overline{\pi} \in \mathcal{A}^T} \{\overline{A} = \overline{\pi}\} \left( \sum_{t=1}^{T} \left( E(Y_\pi \mid \overline{aZLU}_t) - E(Y_\pi \mid \overline{aZLU}_{t-1}) + E(Y_\pi) - m(\overline{a}) \right) \right)
= \sum_{\overline{\pi} \in \mathcal{A}^T} \{\overline{A} = \overline{\pi}\} \sum_{t=1}^{T} \left( E(Y_\pi \mid \overline{aZ}_{t-1}, \overline{LU}_t) - E(E(Y_\pi \mid \overline{aZ}_{t-1}, \overline{LU}_t) \mid \overline{aZLU}_{t-1}) \right).
\]

For \(1 \leq t \leq T, \overline{a} \in \mathcal{A}^T\), let \(\eta_t(\overline{a}, \overline{a}_t, \overline{z}_t, \overline{l}_t, \overline{u}_t) = E(Y_\pi \mid \overline{aZ}_{t-1}, \overline{LU}_t) - E(E(Y_\pi \mid \overline{aZ}_{t-1}, \overline{LU}_t) \mid \overline{aZLU}_{t-1}) \mid \)
Then for any \( \bar{a} \in \mathcal{A}^T \),

\[
\mathbb{E}(Y \mid \bar{a}ZLU) - m(\bar{a}) = \sum_{t=1}^{T} \eta_t(\bar{a}, \bar{a}_t, \bar{Z}_t, \bar{L}_t, \bar{U}_t)
\]

and \( \mathbb{E}(\eta(\bar{a}, \bar{a}_t, \bar{Z}_t, \bar{L}_t, \bar{U}_t) \mid \bar{a}ZLU) = 0 \) for all \( t \).

Conversely,

Lemma 5. Let \( \eta_t(\bar{a}, \bar{a}_t, \bar{Z}_t, \bar{L}_t, \bar{U}_t), 1 \leq t \leq T \), be measurable functions \( \mathcal{A}^T \times \mathcal{A}^{t-1} \times \mathcal{Z}^{t-1} \times \mathcal{L}^t \times \mathcal{U}^t \rightarrow \mathbb{R} \) such that for all \( \bar{a} \in \mathcal{A}^T \), \( \eta_t(\bar{a}, \bar{a}_t, \bar{Z}_t, \bar{L}_t, \bar{U}_t) \) is integrable and

\[
\mathbb{E}(\eta(\bar{a}, \bar{a}_t, \bar{Z}_t, \bar{L}_t, \bar{U}_t) \mid \bar{a}ZLU) = 0.
\]

Suppose for all \( \bar{a} \in \mathcal{A}^T \), variables \( Y_{\bar{a}} \) satisfy

\[
\mathbb{E}(Y_{\bar{a}} \mid \bar{a}zLU) - m(\bar{a}) = \eta = \sum_{t=1}^{T} \eta_t(\bar{a}, \bar{a}_t, \bar{Z}_t, \bar{L}_t, \bar{U}_t) \tag{11}
\]

and a variable \( Y \) satisfies

\[
\mathbb{E}(Y \mid \bar{a}zLU) = \mathbb{E}(Y_{\bar{a}} \mid \bar{a}zLU), \tag{12}
\]

with \( \mathbb{E}(Y_{\bar{a}} \mid \bar{a}zLU) \) as in (11). Then the data \( (Y, \bar{A}, \bar{O}lZ, \bar{L}, \bar{U}) \) satisfy the MSMM \( \mathbb{E}(Y_{\bar{a}}) = m(\bar{a}) \) and Assumptions [1] [2] and [3].

Lemma 5 gives a class of distributions for outcomes \( Y \) compatible with the previously described identification results. That is, if the remaining data \( (\bar{A}, \bar{Z}, \bar{L}, \bar{U}) \) satisfy Assumptions [6] and [8] then (10) holds. This class of distributions for outcomes \( Y \) are described by the endogenous noise \( \eta \) in (11). As an example, \( \eta_t(\bar{a}, \bar{a}_t, \bar{Z}_t, \bar{L}_t, \bar{U}_t) = \zeta(\bar{a}_t, \bar{Z}_t, \bar{L}_t, \bar{U}_t) \) for some \( 1 \leq t \leq T \) and \( \eta_{t'}(\bar{a}, \bar{a}_{t'}, \bar{Z}_{t'-1}, \bar{L}_{t'}, \bar{U}_{t'}) = 0 \) for \( t' \neq t \), satisfies the requirements for (11) whenever \( \zeta \in L_1(\bar{A}Z_{t-1}, \bar{L}U_t) \) and \( \mathbb{E}(\zeta \mid \bar{A}ZLU_{t-1}) = 0 \).

Theorem 6. Let data \( A, Z, L, U, \ldots \) be given. Suppose there exists a process \( \omega_t \) adapted to the
observed data such that for any $T, h, m$,

$$\mathbb{E}(h(\bar{A}_T)\omega_T(\bar{A}LZ_T)(Y - m(\bar{A}_T))) = 0 \quad (13)$$

whenever the data satisfy Assumptions $2^\prime$ and $5$ and the MSMM $\mathbb{E}(Y_\bar{\pi}) = m(\bar{\pi}), \bar{\pi} \in \mathcal{A}_T$, holds. Then for any $t, a_t \in \mathcal{A}$,

$$\sum_{z_t \in Z} f_{A_t|A_{t-1},Z_t,L_t,U_t}(a_t \mid \bar{A}_{t-1}, \bar{Z}_{t-1}, z_t, \bar{L}U_t)\omega'_t(\bar{A}_{t-1}, a_t, \bar{Z}_{t-1}, z_t, \bar{L}_t) \quad (14)$$

does not depend on $(L_t, U_t)$, where the process $\omega'_t$ also satisfies $13$.

The condition on the data imposed by Theorem $6$ is similar to Assumption $8$ insofar as it requires a linear combination of the levels of the treatment density given by the IV to be mean-independent of $U_t$ for each $t$. Assumption $8$ corresponds to the particular linear combination given by the difference of the two levels of the IV, assumed binary. Assumption $8$ is, however, stronger than the necessary condition $14$ since it requires mean-independence of the entire vector $\mathcal{U}$, not just $U_t$. Condition $14$ requires additionally mean-independence of $L_t$, but that too is implied by Assumption $8$ by the choice of the weights $\omega$. For example, if $\alpha = \sum_{z_t \in Z} f_{A_t|A_{t-1},Z_t,L_t,U_t}(a_t \mid \bar{A}_{t-1}, \bar{Z}_{t-1}, z_t, \bar{L}U_t)\omega_t(\bar{A}_{t-1}, a_t, \bar{Z}_{t-1}, z_t, \bar{L}_t)$ does not depend on $\mathcal{U}_t$ one may take $\omega'_t = \omega_t/\alpha$. The difficulty in meeting the condition is mean-independence of $U_t$, since the weights $\omega$ can only depend on the observed data.

On the other hand, Theorem $6$ allows the data $(A_1, Z_1, L_1, U_1), (A_2, Z_2, L_2, U_2), \ldots$, to be given a priori, i.e., $14$ is a necessary condition even if the weights are chosen based on the data process so long as the weights satisfy $13$. Theorem $6$ therefore makes weaker assumptions about the weights than Theorem $1$ where the same weights must hold for any data that satisfy Assumptions $2 \& 8$.

**Example 7** (Point exposure, binary treatment and IV). When $T = 1, A \in \{0, 1\}$, and $Z \in \{0, 1\}$,
the conclusion of Theorem 6 is that
\[
\omega(0,0,L)P(A = 0 \mid Z = 0, LU) + \omega(0,1,L)P(A = 0 \mid Z = 1, LU) = c_0
\]
\[
\omega(1,0,L)P(A = 1 \mid Z = 0, LU) + \omega(1,1,L)P(A = 1 \mid Z = 1, LU) = c_1
\]
for constants \(c_0, c_1 \in \mathbb{R}\). Since \(P(A = 1 \mid AZL) = 1 - P(A = 0 \mid AZL)\), (15) is
\[
\omega(0,0,L)P(A = 0 \mid Z = 0, LU) + \omega(0,1,L)P(A = 0 \mid Z = 1, LU) = c_0
\]
\[
\omega(1,0,L)P(A = 0 \mid Z = 0, LU) + \omega(1,1,L)P(A = 0 \mid Z = 1, LU) = \omega(1,0,L) + \omega(0,1,L) - c_1.
\]

Fixing \(L\) and letting \(U\) vary leads to an overdetermined system of linear equations, implying
\[
\omega(0,1,L)/\omega(0,0,L) = \omega(1,1,L)/\omega(1,0,L)
\]
\[
\omega(1,0,L)/\omega(0,0,L) = \omega(1,1,L) + \omega(1,0,L) - 1.
\]
The latter must hold for any \(L\) such that \(P(A = 1 \mid ZLU)\) is not constant with respect to \(U\).

Conversely, let the data \(A, Z, L, U\), and \(P(A = 0 \mid Z = 0, L, U) < 1, \omega(0,0,L), \omega(0,1,L)\) be given. Then (16) determine \(P(A = 0 \mid Z = 1, L, U), \omega(1,0,L), \omega(1,1,L)\).

Suppose the common value of the ratios in the first line of (16) is -1. Then for \(a \in \{0,1\}\)
\[
c_a = \omega(a,0,L)P(A = a \mid Z = 0, L, U) + \omega(a,1,L)P(A = a \mid Z = 1, L, U)
\]
\[
= \omega(a,0,L)P(A = a \mid Z = 0, L, U) - \omega(a,0,L)P(A = a \mid Z = 1, L, U)
\]
or,
\[
P(A = a \mid Z = 0, L, U) - P(A = a \mid Z = 1, L, U)
\]
is a function of \(L\) for \(a \in \{0,1\}\). In [18] the authors establish that this condition is, in fact, sufficient
to identify the MSMM parameter in the binary IV, binary exposure, \(T = 1\), setting considered
here, when that parameter is the ATE (defined in Example 9).
5 Estimation and Inference

Let \( E(Y_\pi) = m_\beta(\pi) \) be an MSMM, and suppose that the assumptions of Theorem 1 hold. Then
\[
E \left( h(\overline{A}) (Y - m_\beta(\overline{A})) / W \right) = 0,
\]
and
\[
s_\beta = \mathbb{P}_n \left( h(\overline{A}) (Y - m_\beta(\overline{A})) / W \right)
\]
may serve as estimating equations for \( \beta \). When the MSMM is linear, \( m_\beta(\overline{A}) = \beta^T \overline{A} \), the solution to \( s_\beta = 0 \) is a weighted least squares estimator,
\[
\hat{\beta} = (\mathbb{P}_n (h(\overline{A}) \overline{A}^T / W))^{-1} \mathbb{P}_n h(\overline{A}) Y / W.
\]

In practice, \( W \) may not be known, and a \( \sqrt{n} \)-consistent estimate, say \( \hat{W} \), may be substituted,
\[
\hat{\beta} = (\mathbb{P}_n (h(\overline{A}) \overline{A}^T / \hat{W}))^{-1} \mathbb{P}_n h(\overline{A}) Y / \hat{W}.
\]

To describe the practical behavior of the estimator \( \hat{\beta} \) given by (19), suppose nuisance parameters include \( \alpha \), parameterizing \( \Delta_t \); \( \gamma \), parameterizing \( f_{Z_t}, t = 1, \ldots, T \); and \( \nu \), containing any additional nuisance parameters. In the parametrization described in Section 6 below, for example, \( \nu \) parametrizes the “baseline” probability \( \mathbb{P}(A_t = 1 \mid \overline{A}_{t-1}, \overline{L}_t, \overline{Z}_{t-1}, Z_t = 0) \). Besides \( s_\beta \), let \( s_\alpha, s_\gamma \), and \( s_\nu \) be estimating equations for \( \alpha_t, \gamma_t \), and \( \nu_t \), collected as \( s = (s_\beta, s_\alpha, s_\gamma, s_\nu) \). That is, they are functions of the observed data \( \overline{O} = (\overline{A}, \overline{L}, \overline{Z}) \) and parameters \( (\beta, \alpha, \gamma, \nu) \) such that, if the data is generated under parametrization \( (\beta_0, \alpha_0, \gamma_0, \nu_0) \), then
\[
E(s_\beta(O; \beta_0)) = E(s_\alpha(O; \alpha_0)) = E(s_\gamma(O; \gamma_0)) = E(s_\nu(O; \nu_0)) = 0.
\]
In the parametrization described in Section 6 below, for example, we use maximum likelihood to estimate \( \alpha, \gamma, \) and \( \nu \), and the estimating equations are scores for the model. By a standard expansion, the influence function for the estimator \( (\hat{\beta}, \hat{\alpha}, \hat{\gamma}, \hat{\nu}) \) is
\[
- \left( E \left( \frac{\partial s}{\partial \beta, \alpha, \gamma, \nu} \right) \right)^{-1} s.
\]
Provided the usual regularity conditions for M-estimation hold, the solution \( \hat{\beta} \) to (20) is asymptotically normal with influence function given by the first \( p \) components of (20), where \( p \) is the dimension of \( \beta \). Inference may be carried out with the nonparametric bootstrap or the “sandwich” asymptotic variance estimator; we compare both in Section 6.

If many observations \( n \) are available relative to \( T \), separate models may be imposed and estimated at different time points; if \( T \) is small relative to \( n \), the data may be pooled to estimate a single model common to all time points. In the latter case,

\[
\frac{\partial s_{\beta}}{\partial \beta, \alpha, \gamma, \nu} = h(A) \left( -\widehat{W}^{-1} \frac{\partial}{\partial \beta} m_{\beta}, Y - m_{\beta} \sum_t \frac{\partial}{\partial \Delta_t} \Delta_t(\alpha), Y - m_{\beta} \sum_t \frac{\partial}{\partial f} f_{Z_t}(\gamma), 0 \right) .
\] (21)

The form of the remaining components of the matrix \( \frac{\partial s_{\beta}}{\partial \beta, \alpha, \gamma, \nu} \) will depend on the parametrization chosen; see Section 6 for an example.

**Example 8** (Linear omitted variables model, comparing biases). Given a linear MSMM, suppose an estimator is obtained as the root of weighted estimating equations

\[
\mathbb{P}_n \left( \omega h(A) \left( Y - \beta^T \tilde{A} \right) \right) = 0.
\]

where the weight \( \omega \) is an integrable function of the observed data \((A, Z, L)\). This root is a weighted least squares estimator

\[
\hat{\beta} = \left( \mathbb{P}_n(\omega h(A) \tilde{A}^T) \right)^{-1} \mathbb{P}_n(\omega h(A) Y) .
\] (22)

Suppose the data satisfy the assumptions of Theorem 1 and the observed outcome is

\[
Y = \sum_t \left( \beta_{L_t} g_{L_t}(L_t) + \beta_{U_t} g_{U_t}(U_t) \right) + \beta^T \tilde{A} + \epsilon,
\]

with \( \epsilon \) exogenous, \( \beta_{L_t}, \beta_{U_t} \in \mathbb{R}^p \), and \( \mathbb{E}(g_{L_t}(L_t) \mid \tilde{L}_{t-1}, \tilde{A}_{t-1}) = \mathbb{E}(g_{U_t}(U_t) \mid \tilde{U}_{t-1}, \tilde{A}_{t-1}) = 0 \). As
discussed in the passage following Lemma 5, this outcome model is consistent with the MSMM

$$\mathbb{E}(Y_\pi) = \beta^T \tilde{a}.$$ 

The estimator (22) is

$$\hat{\beta} = \left( \mathbb{P}_n \left( h(\overline{A}) \overline{A}^T / \omega \right) \right)^{-1} \mathbb{P}_n \left( \omega^{-1} h(\overline{A}) \left( \sum_t (\beta_{L_t} g_{L_t}(L_t) + \beta_{U_t} g_{U_t}(U_t) + \epsilon) \right) \right) + \beta.$$ 

We consider the asymptotic bias of this estimator,

$$\text{plim} \hat{\beta} - \beta = \left( \mathbb{P}_n \left( h(\overline{A}) \overline{A}^T / \omega \right) \right)^{-1} \mathbb{P}_n \left( \omega^{-1} h(\overline{A}) \left( \sum_t (\beta_{L_t} g_{L_t}(L_t) + \beta_{U_t} g_{U_t}(U_t)) \right) \right),$$

for various choices of weights $\omega$.

When $\omega = 1$, the resulting estimator $\hat{\beta}$, known as the “associational” or “crude” estimator, ignores all confounding. The implied model is misspecified by omitting covariates $L_t, U_t$. The bias is

$$\left( \mathbb{E} \left( h(\overline{A}) \overline{A}^T \right) \right)^{-1} \mathbb{E} \left( h(\overline{A}) \left( \sum_t g_{L_t}(L_t) + g_{U_t}(U_t) \right) \right).$$

This bias is related to the strength of the dependency between the treatments and all confounders, known and unknown. When $g_{L_t}, g_{U_t},$ and $h$ are linear, for example, the bias is linear in the covariance between the treatments and the sum of the confounders.

The SRA estimator, given by the choice $\omega = 1/\overline{W}^{(SRA)} = 1/ \prod_t f(A_t \mid L_t, \overline{A}_{t-1})$, has bias

$$\left( \mathbb{E} \left( h(\overline{A}) \overline{A}^T / \prod_t f(A_t \mid L_t, A_{t-1}) \right) \right)^{-1} \mathbb{E} \left( h(\overline{A}) \frac{\sum_t (\beta_{L_t} g_{L_t}(L_t) + \beta_{U_t} g_{U_t}(U_t))}{\prod_t f(A_t \mid L_t, A_{t-1})} \right).$$ (23)
Since it is assumed \( \mathbb{E}(g_{LT}(L_T) \mid A_{T-1}, L_{T-1}) = 0, \)

\[
\mathbb{E} \left( \frac{h(A) g_{LT}(L_T)}{\prod_{t=1}^{T} f(A_t \mid L_t, A_{t-1})} \right) = \mathbb{E} \left( \mathbb{E} \left( \frac{h(A) g_{LT}(L_T)}{\prod_{t=1}^{T} f(A_t \mid L_t, A_{t-1})} \mid L_T, A_{T-1} \right) \right) 
\]

\[
= \mathbb{E} \left( \int_{A} \frac{h(A_{T-1}, a_T) g_{LT}(L_T)}{\prod_{t=1}^{T-1} f(A_t \mid L_t, A_{t-1})} \mu_{A_T}(a_T) \right) 
\]

\[
= \mathbb{E} \left( \int_{A} h(A_{T-1}, a_T) \mu_{A_T}(a_T) \times \mathbb{E}(g_{LT}(L_T) \mid A_{T-1}, L_{T-1}) \right) = 0,
\]

and similarly for \( t < T \). The inverted factor in (23) is, by (5), \( \int_{A} h(a) \mu_{A}(a) \). The resulting expression

\[
\left( \int_{A} h(a) \mu_{A}(a) \right)^{-1} \mathbb{E} \left( h(A) \left( \sum_{t} g_{U_t}(U_t) \right) / W^{(SRA)} \right),
\]

shows that the bias is a quantity related to the dependence between the treatment and unknown confounders, as expected due to the violation of SRA. In comparison with the bias of the associational estimator, the term corresponding to treatment and known confounder dependency is eliminated. As \( \sum_{t} g_{U_t}(U_t) \) and \( h(A) / W^{(SRA)} \) are generally correlated when \( U_t \) are in fact confounders, the bias is nonzero.

When \( \omega \) are the IV weights (8), the asymptotic bias is zero since we have assumed the conditions of Theorem 1 which entails

\[
\mathbb{E} \left( W^{-1} h(A) \sum_{t} (\beta_{L_t} g_{L_t}(L_t) + \beta_{U_t} g_{U_t}(U_t)) \right) = \mathbb{E} \left( W^{-1} h(A) (Y - m_{\beta}(A)) \right) - \mathbb{E} \left( W^{-1} h \cdot \epsilon \right) = 0.
\]

A Monte Carlo simulation comparing these three estimators is described in Section 6.

**Example 9** (Wald Estimator). Suppose \( T = 1, \Delta_1(a_1, L_1) = \Delta_1(a_1), \) and \( f_{Z_t \mid L_t, U_t}(z_1, L_1, U_1) = 1/2 \). For purposes of estimation, both \( f_{Z_t} \) and \( \Delta_1 \) terms in the IV weights (8) may be canceled by taking \( h \) in the estimating equations (17) to be

\[
h(a_1) = h_1(a_1) \Delta_1(a_1)/2,
\]

with \( h_1(a_1) \) available to be specified. The remaining weight term is just \((-1)^{1-Z_1}\). Consider the
regression model

\[ \mathbb{E}(Y_a) = \beta a. \]

Taking \( h_1(a_1) = 1 \), the solution to the estimating equation (17) is then

\[ \hat{\beta} = \left( \mathbb{P}_n A(-1)^{1-Z} \mathbb{P}_n(-1)^{1-Z} Y \right)^{-1} \mathbb{P}_n Y \{ Z = 1 \} - \mathbb{P}_n Y \{ Z = 0 \} \]

\[ = \mathbb{P}_n Y \{ Z = 1 \} - \mathbb{P}_n Y \{ Z = 0 \}. \] (24)

This estimator is known as the Wald estimator. If \( Z \) is an IV and the consistency assumption (1) is satisfied, the Wald estimator is consistent for the “average treatment effect,” the average difference in the potential outcome \( Y_a \) across the two groups defined by \( a \). In [18], the authors directly establish identification of the ATE using IVs and provide further results on estimation.

The finite sample mean of this estimator may be infinite; see, e.g., [9]. The variance estimator obtained from the influence function, suggested in Section [5] is asymptotic. For example, suppose \( A \) is discrete, and multiply the numerator and denominator of the ratio in (24) by \( n \). The denominator, viewed as a process indexed by \( n \), is a random walk on the integers that goes up with probability \( \mathbb{P}(A = 1, Z = 1) \), down with probability \( \mathbb{P}(A = 1, Z = 0) \), and does not move otherwise. The probability the denominator is 0 is then the probability the walk is at 0, which decreases as \( 1/\sqrt{n} \).

**Example 10** (Two-state markov chain). We examine the relationship between confounding and the variance of the estimator obtained from the estimating equation (17), using a simple model to compare expressions in the SRA and IV contexts.

SRA weights include probability densities at each time point, and IV weights include a difference of densities. As the number of time points \( T \) grows and these weights are multiplied, an estimator may quickly become unstable. Let \( \hat{\beta} \) be obtained as the solution to (17). Assuming standard regularity conditions, the asymptotic variance of \( \hat{\beta} \) is the variance of the influence function,

\[ \text{Var}(\sqrt{n}(\hat{\beta} - \beta_0)) \rightarrow \left( \mathbb{E} \frac{\partial}{\partial \beta} (h m_{\beta}/W) \right)^{-2} \mathbb{E} \left( (h(A)(Y - m_{\beta})/W)^2 \right). \] (25)

In this display, the weights \( W \) refer generically to either SRA weights (7) or IV weights (8). The
term $h(\bar{A})m_\beta(\bar{A})$ is a function of the treatments, so by (3), in the case $W$ are SRA weights, or by Theorem II in the case of IV weights,

$$E \frac{\partial}{\partial \beta} \left( hm_\beta/W \right) |_{\beta=\beta_0} = \int \frac{\partial}{\partial \beta} hm_\beta d\mu_{\bar{A}}$$

does not depend on the weights. A first order approximation to the asymptotic variance is

$$\left( \int \frac{\partial}{\partial \beta} hm_\beta d\mu_{\bar{A}} \right)^{-2} E \left( (h(\bar{A})(Y - m_\beta))^2 \right) E \left( 1/\Pi_t W_t^2 \right). \quad (26)$$

This expression appears to grow exponentially in the number of time points. In the SRA framework, various techniques have been proposed to stabilize the weights. These involve using a function of the treatments to cancel out the weights, functions of both treatment and confounders. The stability of the weights therefore depends on the strength of the dependence between treatment and confounder, a relationship that can be quantified in simple models. We consider analogous stabilization for the IV estimator.

**SRA weights.** Suppose treatment and covariates are binary, and

$$P(L_t \mid an(L_t)) = P(L_t \mid L_{t-1}) = p_{LA},$$

$$P(A_t \mid an(A_t)) = P(A_t \mid L_{t-1}) = p_{AL},$$

$$P(L_1 = 0) = P(L_1 = 1) = 1/2. \quad (27)$$

The data is a two-state markov chain with alternating doubly stochastic transition matrices,

$$\begin{pmatrix} p_{LA} & 1 - p_{LA} \\ 1 - p_{LA} & p_{LA} \end{pmatrix}, \begin{pmatrix} p_{AL} & 1 - p_{AL} \\ 1 - p_{AL} & p_{AL} \end{pmatrix}. $$

The parameter $p_{LA}$ is the probability that the state of $A_{t+1}$ is the same as $L_t$. It may be interpreted as the strength of the dependence of $A$ on $L$, a type of confounding, with the strongest confounding occurring as $p_{LA}$ nears the border of $[0, 1]$, and the weakest at $p_{LA} = .5$. The situation is analogous for $p_{AL}$. The marginal distributions of both $L_t$ and $A_t, t = 1, \ldots, T$, are bernoulli with
success probability 1/2.

The SRA weights are $\prod_t f(A_t \mid L_{t-1}) = \prod_t p_{LA}^{A_t=L_{t-1}} (1-p_{LA})^{A_t \neq L_{t-1}} = (1-p_{LA})^T \prod_t (p_{LA}/(1-p_{LA}))^{(A_t=L_{t-1})}$. Because $\mathbb{E}\{(A_t = L_{t-1}) \mid A_{t-1} = p_{LA}\}$ and the states are binary, the factors that make up the weights are independent and identically distributed, and

$$\mathbb{E}(1/W^2) = (\mathbb{E}(1/W_1^2))^T = (p_{LA}(1-p_{LA}))^{-T}. \quad (28)$$

The variance is polynomial in the inverse of $p_{LA}(1-p_{LA})$, a measure of treatment–covariate dependence, with order given by the number of time points $T$. The parameter $p_{AL}$ determining $A_{t-1} \rightarrow L_t$ transitions does not play a role, although it plays the main role in weight stabilization discussed below. The dependence on $p_{LA}$ is through $p_{LA}(1-p_{LA}) = 1/4 - (p_{LA} - 1/2)^2$, so that (28) is minimized over $p_{LA}$ at 1/2, when treatment and covariate are independent, and increases without bound as $|p_{LA} - 1/2| \rightarrow 1/2$.

Although the focus on this example is the behavior of the weights, an estimate of the variance of the full estimator is straightforward once an outcome model is specified. Suppose the observed outcome $Y$ satisfies

$$\mathbb{E}(Y \mid \bar{A}, \bar{Z}, \bar{L}, \bar{U}) = \lambda \sum_t (L_t - \mathbb{E}(L_t \mid L_{t-1}, \bar{A}_{t-1})) + \beta \sum_t A_t + \epsilon,$$

where $\epsilon$ has mean zero and variance $\sigma^2$. While parameter $p_{LA}$ describes one part of confounding, the dependence of treatment on the confounding covariate, the parameter $\lambda$ describes the other part of confounding, the dependence of the outcome on the covariate. By Lemma 5 this model...
Figure 4: The variance of the unstabilized SRA estimator $\hat{\beta}$ in the two-state markov model. The solid line is the first-order approximation (29) and the plotted characters come from a Monte Carlo simulation. For the simulation the number of time points $T$ is 7 and sample size is 500.

for $Y$ is consistent with the MSMM

$$\mathbb{E}(Y_{\pi}) = \beta \sum_t a_t.$$ 

It follows that the first order approximation (26) is

$$\frac{\lambda^2 (1 + \sigma^2 / (Tp_{LA}(1 - p_{LA})))}{(T + 1)(4p_{LA}(1 - p_{LA}))^{T-1}}$$

(29)

The principal difference from the second moment of the weights (28) is that the exponent is $T - 1$ rather than $T$, and quadratic dependence on $\lambda$. A plot of the dependence on $p_{LA}$, along with the empirical variance from a small simulation to indicate the quality of the approximation, is given in Fig. 4.

Modified weights are often used to mitigate the instability of the SRA estimator. A factor $h'$ in the function $h(\overline{A})$ is chosen to approximate $f(A_t | \overline{L}_t, \overline{A}_{t-1})$, with a view to minimizing the mean square of the influence function (25). In the trivial case that $L$ is not in fact a confounder, $h'$ may be taken to be $f(A_t | \overline{L}_t, \overline{A}_{t-1}) = f(A_t | \overline{A}_{t-1})$. The weights are cancelled out and the estimator is no
Figure 5: Variance of stabilized SRA weights in the two-state markov model. The variance blows up as \( p_{LA} \) approaches 0 or 1, as in the unstabilized case, but remains bounded if \( p_{AL} \) approaches 0 or 1 with at least the same rate.

longer exponential in \( T \). In general, the quality of an approximation of \( f(A|L) \) using a function of \( A \) depends on how well \( A \) predicts \( L \), controlled in this example by \( p_{AL} \). The variance of the influence function (25) does not change on multiplying \( h \) by a constant, so the minimization is well-posed, and there is no loss of generality to assume \( \int h' = 1 \).

A common choice of stabilized weights, which we consider, uses the density \( f(A_t|\bar{A}_{t-1}) \) as the approximation to \( f(A_t|\bar{L}_t, \bar{A}_{t-1}) \), that is, \( h \) contains as a factor the joint density of \( \bar{A} \). For the two-state markov model, the markov property gives as stabilized weights,

\[
W = \prod_t \frac{f(A_t|L_t)}{f(A_t|A_{t-1})}.
\]

The factors are again i.i.d., and the second moment of the inverted weights is computed to be

\[
\mathbb{E}(1/W^2) = \left( \mathbb{E}\left( \frac{f(A_2|A_1)}{f(A_2|L_1)} \right) \right)^T = \left( 1 + 4\frac{p_{AL}(1-p_{AL})}{p_{LA}(1-p_{LA})}(p_{LA} - 1/2)^2 \right)^T.
\]

Holding \( T \) fixed, consider the behavior of the variance as the parameters \( p_{LA}, p_{AL} \) vary. When \( p_{LA} = p_{AL} = p \), this expression is \((1 + 4(p - 1/2))^T\), and the blowup at the boundary points present
in the case of unstabilized weights is eliminated (Fig. 5). For \( p \in [0, 1] \) let \( \rho(p) = p(1-p) = 1/4 - (p - 1/2)^2 \), a measure of the distance of \( p \) to the boundary of \([0, 1] \). With this notation,

\[
\mathbb{E}(1/W^2) = \left(1 + 4 \frac{\rho(p_{LA})}{\rho(p_{LA})}(p_{LA} - 1/2)^2\right)^T \leq \left(1 + \frac{\rho(p_{AL})}{\rho(p_{LA})}\right)^T. \tag{30}
\]

The behavior of stabilized weights as \( p_{LA} \) nears the boundary of \([0, 1] \) is governed not by \( 1/\rho(p_{LA}) \), as in the unstabilized case, but the ratio \( \rho(p_{AL})/\rho(p_{LA}) \), and will be bounded when \( \rho(p_{AL}) = O(\rho(p_{LA})) \). Qualitatively, this situation occurs when the degree of treatment-covariate confounding does not grow faster than the treatment’s predictiveness of the covariate.

Next, let \( T \) grow. It follows from (30) that the variance can be stabilized by controlling the decay of \( \rho(p_{AL})/\rho(p_{LA}) \). By comparison with \( t \mapsto (1 + 1/t)^t \) it follows \( \rho(p_{AL})/\rho(p_{LA}) = O(1/T) \) is sufficient. This possibility is not available with unstabilized weights. Since \( p_{AL}(1-p_{AL}) \leq 1/4 \), the unstabilized weight moment (28) \((p_{AL}(1-p_{AL}))^{-T} \geq 4^T \) always diverges with \( T \).

**IV weights.**

We next consider an extension of the two-state markov model (27) in order to examine the behavior of the IV weights in relation to confounding. The states \( L_t \) are augmented with additional binary variables \( U_t \) and \( Z_t \), giving rise to a process \( \ldots (L_{t-1}, U_{t-1}, Z_{t-1}) \rightarrow A_{t-1} \rightarrow (L_t, U_t, Z_t) \rightarrow A_t \ldots \). For \( q, p_L, p_U \in (0, 1) \) and \( \delta_0, \delta_1 \) satisfying \(|\delta_i| < 1/2 - \max(|p_{01} - 1/2|, |p_{10} - 1/2|), l \in \{0, 1\} \), define transition probabilities through

\[
\mathbb{P}(A_t = a \mid an(A_t)) = \mathbb{P}(A_t = a \mid L_t = l, U_t = u, Z_t = z)
\]

\[
= \mathbb{P}(A_t = a \mid L_t = l, U_t = u) + (-1)^{1-z}(-1)^{1-a}\delta_i/2
\]

\[
\mathbb{P}(A_t = a \mid L_t = l, U_t = u) = (1 - q)p_{L}^{l=a}(1 - p_{L})^{l\neq a} + q_{l}^{u=a}(1 - p_{U})^{u\neq a}
\]

\[
\mathbb{P}(L_{t+1} = l, U_{t+1} = u, Z_{t+1} = z \mid an(L_{t+1}, U_{t+1}, Z_{t+1})) = \mathbb{P}(Z_{t+1} = z)\mathbb{P}(L_{t+1} = l, U_{t+1} = u \mid A_t = a)
\]

\[
= (1/4)\mathbb{P}(A_t = a \mid L_t = l, U_t = u)
\]

\[
\mathbb{P}(Z_t = z) = 1/2.
\tag{31}
\]

The initial state \((L_1, U_1, Z_1)\) is distributed as three i.i.d. symmetric bernoulli variables. It follows
Figure 6: DAG for the two-state markov model with unknown confounding and IV, with 2 time points.

Figure 7: The distribution of the two-state markov model with unknown confounding (31) may be obtained by combining two chains with no unknown confounders (See Fig. 3). Corresponding covariate states $L_t$ and $U_t$ are concatenated along with an exogenous IV to give the new covariate state $(L_t, U_t, Z_t)$. The new treatment states are obtained by mixing with probability $q$, $A_t := B_t A_t^L + (1 - B_t) A_t^U$, with $B_t$ i.i.d. bernoulli with parameter $q$.

that the marginal distribution of each of $L_t, U_t, A_t$, $t = 1, \ldots$, is bernoulli with success probability 1/2, as with $Z_t$. A DAG is given in Fig. 6. The model for the conditional density of $A_t$ given $(L_t, U_t, Z_t)$ has parameters, $p_{lu} \in [0, 1]$ and $\delta_l$ for $l, u \in \{0, 1\}$; see Table 1. Requiring $|\delta_l| < 1/2 - \max(|p_{l0} - 1/2|, |p_{l1} - 1/2|)$ ensures $P(a_t \mid l_t, u_t, z_t) > 0$. Summing horizontally in Table 1 shows $\sum_a P(a_t \mid l_t, u_t, z_t) = 1$. Therefore $P(a_t \mid l_t, u_t, z_t)$ is a valid density. Moreover,
Assumption 8 is satisfied since

$$\Delta_t(\tilde{a}_t, \tilde{z}_{t-1}, \tilde{l}_t, \tilde{u}_t) \equiv \sum_{z_t \in \{0,1\}} (-1)^{1-z_t} \mathbb{P}(A_t = a_t \mid L_t = l_t, U_t = u_t, Z_{t-1} = \tilde{z}_{t-1}, Z_t = z, \tilde{A}_{t-1} = \tilde{a}_{t-1})$$

$$= \sum_{z_t \in \{0,1\}} (-1)^{1-z_t} \mathbb{P}(A_t = a_t \mid L_t = l_t, U_t = u_t, Z_t = z_t)$$

$$= (-1)^{1-a_t} \delta_t$$

does not depend on $\tilde{u}_t$. The magnitude of $\delta_0$ and $\delta_1$ are interpretable as IV strength. Their difference $|\delta_1 - \delta_0|$ gives the dependence of $\delta$ on $L_t$, which has an analogous role in weight stabilization to the treatment-confounder dependence $p_{LA}$ parameter in the SRA setting. That is, to the extent that this dependence may be approximated by a standardized function of $A$, an analogue of stabilized weights may be used to decrease the variance of the estimator.

The parameters $q, p_L, p_U$ used to describe the model (31) are not identified by the data $(A_t, Z_t, L_t, U_t)$, nor are the observed parameters $q, p_L$ identified by the observed data $(A_t, Z_t, L_t)$. We use them because they are easy to compare with the SRA case. For purposes of estimation (e.g., Appendix 7), an identifying condition like $p_B = 1/2$ or $p_L = p_U$ is needed, or reparameterization.

The distribution of the resulting markov chain can also be obtained by mixing two independent chains of the type described in the ([ref sra section above]), say, $\ldots \rightarrow L_{t-1} \rightarrow A^L_{t-1} \rightarrow L_t \rightarrow \ldots$ with parameters $p_{AL}, p_{LA}$, and $\ldots \rightarrow U_{t-1} \rightarrow A^U_{t-1} \rightarrow U_t \rightarrow \ldots$ with parameters $p_{AU}, p_{UA}$. See Fig. 7. Corresponding covariate states $L_t$ and $U_t$ are concatenated along with an exogenous IV to give the new covariate state $(L_t, U_t, Z_t)$. The new treatment states are obtained by mixing with probability $q$, $A_t = B_t A^L_t + (1 - B_t) A^U_t$, with $B_t$ i.i.d. bernoulli with parameter $q$. The mixing parameter $q$ controls the relative dependence of the treatment on known confounding as compared with unknown confounding. The IVs are then added as independent, exogenous perturbations of the new treatment states $A_t$ in such a way that the Assumption 8 is satisfied. The parameters $p_{LA}, p_{AL}, p_{UA}$, and $p_{AU}$ have similar interpretations as before.

The conditional density of $Z_t$ is a constant in $(0,1)$ and may be canceled by the choice of $h$, so
Table 1: The conditional treatment densities \( P(A = a \mid L = l, U = u, Z = z) \) for the two-state markov model with IVs. The densities are the same at all times. There are 6 parameters, \( p_{lu} \in [0, 1] \) and \( \delta_l \) for \( l, u \in \{0, 1\} \). The magnitude of \( \delta_0 \) and \( \delta_1 \) are interpretable as IV strength. Their difference \( |\delta_1 - \delta_0| \) gives the dependence of \( \delta \) on \( L_t \), which has an analogous role in weight stabilization to the treatment-confounder dependence parameter \( p_{LA} \) in the SRA setting.

| \( U = 1 \) | \( Z = 1 \) | \( p_{01} \pm \delta_0 \) | \( p_{01} \pm \delta_0 \) | \( p_{11} \pm \delta_1 \) | \( p_{11} \pm \delta_1 \) |
| \( Z = 0 \) | \( p_{01} \) | \( p_{01} \pm \delta_0 \) | \( p_{01} \pm \delta_0 \) | \( p_{11} \) | \( p_{11} \) |
| \( U = 0 \) | \( Z = 1 \) | \( p_{00} \pm \delta_0 \) | \( p_{00} \pm \delta_0 \) | \( p_{01} \pm \delta_1 \) | \( p_{01} \pm \delta_1 \) |
| \( Z = 0 \) | \( p_{00} \) | \( p_{00} \) | \( p_{00} \) | \( p_{01} \) | \( p_{01} \) |

\( L = 0 \) \( A = 0 \) \( A = 1 \) \( A = 0 \) \( A = 1 \)
\( L = 1 \)

the square of the inverse of the IV weights \( [8] \) is

\[
W^{-2} = \prod_{t=1}^{T} \delta_{Lt}^{-2}.
\]

For \( t = 2, \ldots, T \), and \( l_{t-1} \in \{0, 1\} \) define \( \phi_t(l_{t-1}) = \mathbb{E}(\prod_{t'=t}^{T} \delta_{L_t'}^{-2} \mid L_{t-1} = l_{t-1}) \) and \( \phi_t = (\phi_t(0), \phi_t(1)) \). With this notation, \( \mathbb{E}(W^{-2}) = \sum_{l_t \in \{0, 1\}} \mathbb{E}(W^{-2} \mid L_1 = l_1) \mathbb{P}(L_1 = l_1) = \delta_0^{-2} \phi_2(0)/2 + \delta_1^{-2} \phi_2(1)/2 \). Let \( p = \mathbb{P}(L_{t-1} = 1 \mid L_t = 1) = \mathbb{P}(L_{t-1} = 0 \mid L_t = 0) \), which does not in fact depend on \( t \) as the chain has been assumed to be started in its stationary distribution. Then \( \phi_t \) satisfies the recurrence

\[
\phi_{t-1} = \begin{pmatrix}
p/\delta_0^2 & (1-p)/\delta_1^2 \\
(1-p)/\delta_0^2 & p/\delta_1^2
\end{pmatrix} \phi_t
\]  

with boundary condition \( \phi_{T+1} = (1, 1) \). The growth of \( \mathbb{E}(W^{-2}) \) is determined by the largest eigenvalue of the matrix in \( [32] \),

\[
\lambda_1 = p/2(1/\delta_0^2 + 1/\delta_1^2) + \sqrt{p^2/4(1/\delta_0^2 + 1/\delta_1^2)^2 - (2p - 1)/(\delta_0 \delta_1)^2} 
\]  

(33)
The eigenvalue is real for \( p \in (0, 1) \). To reinterpret this expression, let

\[
\omega := 1/(\delta_0 \delta_1) \\
\kappa := 1/\delta_0^2 - 1/\delta_1^2
\]

The product \( \omega \) is a measure of IV weakness, and the difference \( \kappa \) is a measure of confounding between the IV and \( L \). After some algebra, it follows that \( 1/\delta_0^2 + 1/\delta_1^2 = \pm \sqrt{\kappa^2 + 4 \omega^2} \), and the principal eigenvalue \((33)\) is

\[
\lambda_1 = p/2\sqrt{\kappa^2 + 4 \omega^2} \left( 1 + \sqrt{1 - \frac{\omega^2(2p - 1)}{\kappa^2 + 4 \omega^2}} \right). 
\]

The term in parentheses is at most 2, so \( \lambda_1 \leq p\sqrt{\kappa^2 + 4 \omega^2} \), with equality occurring when the transition probability \( p \) is 1/2. Therefore, \( \lambda_1 \), which determines the exponential growth of the second moment of the weights, is approximately linear in the weakness of the IV and the degree of IV confounding. In comparison to the case of SRA weights, the transition probabilities \( p \) have a relatively small effect; see Fig. 8.

As with SRA weights, the function \( h(\overline{A}) \) in Theorem 1 may be chosen to partially stabilize IV weights. A function of \( \overline{A} \) approximating \( \Delta_t \) may be used to cancel out the magnitude of the weights and minimize the second moment of the weights. As in the SRA case, the influence function \((20)\) does not change when \( h \) is multiplied by a constant scalar, so the minimization is well-posed. Analogously to SRA weights, we consider stabilizing a weight term \( \delta_{L_t} \) by an arbitrary term depending on the treatment previous to \( L_t \), say, \( \gamma_{A_{t-1}} \), with values \( \gamma_0, \gamma_1 \). For example, analogous to the term \( f(A_t \mid \overline{A}_{t-1}) = \mathbb{E}(f(A_t \mid L_t, \overline{A}_{t-1}) \mid \overline{A}_{t-1}) \) commonly used to stabilize SRA weights, we may take

\[
\gamma_{A_{t-1}} = \mathbb{E}(\delta_{L_t} \mid \overline{A}_{t-1}) = \mathbb{E}(\delta_{L_t} \mid A_{t-1}) = p_L \delta_{A_{t-1}} + (1 - p_L) \delta_{1-A_{t-1}}, \quad t > 1, \\
\gamma_{A_0} = \mathbb{E}(\delta_{L_1} \mid A_0) = \mathbb{E}(\delta_{L_1}).
\]
Figure 8: The second moment of the unstabilized IV weights in the two-state markov model. The effect of the known confounding, as measured by $\rho$, is small relative to the effect of the IV weakness, as measured by $1/(\delta_0 \delta_1)$. Another factor, the degree of known confounding of the IV, is fixed in this figure. The lines are the theoretical values and the plotted characters come from a Monte Carlo simulation. For the simulation the number of time points $T$ is 5 and the sample size $n$ is 50.

The squared inverse of the weights is

$$1/W^2 = \prod_t \gamma_{A_{t-1}}^2/\delta_{L_t}^2.$$  

Proceeding as before, let

$$\phi_t(l_{t-1}) := \mathbb{E} \left( \prod_{t' = t}^T \gamma_{A_{t'-1}}^2/\delta_{L_{t'}}^2 \mid L_{t-1} = l_{t-1} \right), \quad l_{t-1} \in \{0, 1\},$$

$$\phi_t := (\phi_t(0), \phi_t(1)).$$

Then $\mathbb{E}(1/W^2) = \gamma_0^2(\phi_2(0)/2 + \phi_2(1)/2)$, $\phi$ satisfies the recurrence

$$\phi_{t-1} = \left( \begin{array}{c}
\quad p_{LA}p_{AL}\gamma_0^2/\delta_0^2 + (1 - p_{LA})(1 - p_{AL})\gamma_0^2/\delta_0^2 & p_{LA}(1 - p_{AL})\gamma_0^2/\delta_1^2 + p_{AL}(1 - p_{LA})\gamma_1^2/\delta_1^2 \\
(1 - p_{LA})\gamma_1^2/\delta_0^2 + p_{AL}(1 - p_{LA})\gamma_0^2/\delta_0^2 & p_{LA}p_{AL}\gamma_1^2/\delta_0^2 + (1 - p_{LA})(1 - p_{AL})\gamma_0^2/\delta_1^2
\end{array} \right) \phi_t,$$

(35)
and the growth of $\mathbb{E}(1/W^2)$ is determined by the eigenvalues of the matrix $P$ in (35),

$$\text{tr}(P)/2 \pm \sqrt{\text{tr}(P)^2/4 - \det(P)}$$

where

$$\text{tr}(P) = p_L p_A L (\gamma_0^2/\delta_0^2 + \gamma_1^2/\delta_1^2) + (1 - p_L)(1 - p_A)(\gamma_0^2/\delta_0^2 + \gamma_1^2/\delta_1^2)$$

$$\det(P) = (2p_L - 1)(2p_A - 1)\frac{\gamma_0^2\gamma_1^2}{\delta_0^2\delta_1^2}.$$

In terms of the IV weakness and confounding terms (34), the principal eigenvalue may be rewritten as

$$\lambda_1 = \frac{1}{4} \left( \sqrt{\kappa^2 + 4\omega^2(\gamma_0 + \gamma_1)(p_L p_A L + (1 - p_L)(1 - p_A)) + \kappa(\gamma_0 - \gamma_1)(1 - p_L - p_A)} \right) \times \left( 1 + \sqrt{1 - 4\det(P)/\text{tr}(P)^2} \right).$$

The last factor in parentheses has magnitude at most 2. As mentioned previously, it may be assumed without loss of generality that $\prod_j \gamma_{A_j}$ has expectation 1 for any law under which $\prod_j \gamma_{A_j}$ has finite expectation. For the variance of the influence function (20) does not change on multiplying $h(A) = h_1(A) \prod_j \gamma_{A_j}$ by a constant, so that any choice of $\prod_j \gamma_{A_j}$ may be replaced by another with mean 1, i.e., $\prod_j \gamma_{A_j}/\int \prod_j \gamma_{A_j} d\mu$. Letting $\mu$ be counting measure, the assumption becomes

$$1 = \int \prod_j \gamma_{A_j} d\mu = \sum_{j=0}^{T} \binom{T}{j} \gamma_0^{j+1}\gamma_1^{T-j} = (\gamma_0 + \gamma_1)^T.$$

Therefore $\gamma_0 + \gamma_1 = 1$ and the principal eigenvalue is

$$\lambda_1 = \frac{1}{4} \left\{ \sqrt{\kappa^2 + 4\omega^2(p_L p_A L + (1 - p_L)(1 - p_A)) + \kappa(\gamma_0 - \gamma_1)(1 - p_L - p_A)} \right\} \left( 1 + \sqrt{1 - 4\det(P)/\text{tr}(P)^2} \right).$$

Therefore, the effect of IV confounding $\kappa$ on the variance may be reduced by choosing $\gamma_0 - \gamma_1$ close to 0, but no choice of $(\gamma_0, \gamma_1)$ will have an effect on the weakness of the IV, $\omega$, due to the term
Figure 9: The variance of the IV estimator depends on the weakness of the IV and the dependence of the IV on the covariates. An approximation to the variance is plotted against IV weakness and IV confounding using unstabilized and stabilized weights. The effect of IV confounding is mitigated by stabilization, but the effect of a weak IV remains.

√κ² + 4ω². See Fig. 9 for a simulation.

Given below is a summary of the discussion of the asymptotic variance of the estimator in the four situations considered in this example.

1. SRA weights, unstabilized: The variance is exponential in \( T \), and for fixed \( T \) the variance blows up at a quadratic rate as the confounding \( p_{LA} = \mathbb{P}(A \mid L) \) approaches 0 or 1.

2. SRA weights, stabilized: The variance is bounded as long as the confounding \( p_{LA} = \mathbb{P}(A \mid L) \) is of the same order as the “predictiveness” \( p_{AL} = \mathbb{P}(L \mid A) \).

3. IV weights, unstabilized: The variance of the weight terms is exponential in \( T \), and for fixed \( T \) is linear in a terms relating to the weakness of the IV and the degree of dependency between the IV and covariates.

4. IV weights, stabilized: The variance due to dependency between the IV and covariates may be reduced, but the variance due to the weakness of the IV remains.
The difference between the SRA and IV cases seems to be the following. In both cases the stabilization terms may be assumed to integrate to 1, due to the scale invariance property of the variance of the influence function mentioned earlier. In the case of SRA weights, the weights themselves also satisfy this type of property, being densities. Specifically, the terms $\prod_t f(a_t | l_{t-1})$ cannot be uniformly small across all choices $a_t, l_{t-1}, t = 1, \ldots, T$. One may therefore hope to choose the stabilizing terms to match the magnitude of the corresponding weight terms. The IV weights do not satisfy this type of property, i.e., $\delta_0$ and $\delta_1$ may both be arbitrarily small at the same time, and no choice of $(\gamma_0, \gamma_1)$, which cannot both be small at the same time due to the scale invariance, will control the weights.

6 Simulation

We examine the finite-sample behavior of the simple weighted estimator described in Section 5 under a data-generation process in which SRA does not hold but the assumptions of Theorem 1, allowing for IV weights, do hold. We consider the following linear MSMM:

$$E(Y_{\pi}) = \beta_0 + \beta_1 \sum_t a_t.$$ 

An additional simulation using a different data-generation process is given in ((markov example in appendix)).

6.1 Data generation

Lemma 5 gives appropriate conditions on the endogenous noise term $\eta$ for sampling outcomes $Y = m(\bar{A}) + \eta + \epsilon$ consistent with a MSMM model and the assumptions of Theorem 1. For example, we may sample outcomes as

$$E(Y | \bar{A}, Z, L, U) = \sum_t (f_t(L_t, U_t) - E(f_t(L_t, U_t) | A_{t-1}, L_{t-1}, U_{t-1})) + m_\beta(\bar{A}),$$

$$(L_t, U_t) \perp Z_t | A_t U_{t-1}$$
for arbitrary functions $f_t$, once we have chosen a sampling scheme for $(A, Z, L, U)$ satisfying the stated conditional independence assumption. We choose linear functions, so that outcome variables $Y$ are sampled as

$$Y = \sum_{t=0}^{T} \left( \tau_t(L_t - \mathbb{E}(L_t | ALU_{t-1})) + \rho_t(U_t - \mathbb{E}(U_t | ALU_{t-1})) \right) + m_\beta(A) + \epsilon$$

with $\rho_t, \tau_t \in \mathbb{R}$ and $\epsilon$ standard normal. We set $\rho_t = \tau_t = 1$ in our simulation.

For $1 \leq t \leq T$, $U_t$ is sampled as standard normal and $Z_t$ is bernoulli with success probability $1/2$, all mutually independent, ensuring the IV assumptions. The treatments $A_t$ and covariates $L_t$ are sampled recursively as:

$$L_{t+1} = \lambda_0 + \lambda_1 A_t + \epsilon_t$$

$$\Phi^{-1}(\Delta_{t+1}) = \Phi^{-1}\left( \mathbb{P}(A_{t+1} = 1 | L_{t+1}, U_{t+1}, A_t, Z_t, Z_{t+1} = 1) - \mathbb{P}(A_{t+1} = 1 | L_{t+1}, U_{t+1}, A_t, Z_t, Z_{t+1} = 0) \right)$$

$$= \alpha_0 + \alpha_1 L_{t+1}$$

$$\mathbb{P}(A_{t+1} = 1 | A_t, Z_{t+1}, L_{t+1}, U_{t+1}) = \Phi(\nu_0 + \nu_1 L_{t+1} + \nu_2 U_{t+1}) \times (1 - \Delta_{t+1}) + Z_{t+1} \times \Delta_{t+1}.$$  

Here, $\Phi$ denotes the standard normal CDF and $\epsilon_t$ are mutually independent standard normal variables. The models chosen for $A_t$ and $\Delta_t$ ensure that Assumption (S) holds. The parameters $\lambda_0, \lambda_1 \in \mathbb{R}$ control the extent to which the treatment confounds subsequent covariates, whereas $\nu_1, \nu_2 \in \mathbb{R}$ control the extent to which observed and unobserved confounders confound treatment, respectively, confound treatment. The reciprocal arrangement ensures that the confounding is truly longitudinal, so that, e.g., a series of propensity score analyses would not likely estimate the MSMM parameter accurately. The dependence between treatment and a confounder unavailable for estimation, provided $\nu_2 \neq 0$, violates SRA. The parameters $\alpha_0, \alpha_1$, bear on the strength of the IV. We set $\lambda_0 = \lambda_1 = .5, \alpha_0 = \alpha_1 = .3, \nu_0 = -.2, \nu_1 = \nu_2 = .2$ in the simulation described below.
6.2 Estimation

As $f_{Z_t}$ is known under our data generation method (36), only $\beta, \alpha,$ and $\nu$ require estimation. We use (17) as an estimating equation for $\beta$ and obtain $\frac{\partial s_{\beta}}{\partial \beta, \alpha}$ from (21) by substituting

$$\frac{\partial}{\partial \beta} \mu(\beta) = \frac{\partial}{\partial \beta} \left( \beta_0 + \beta_1 \sum A_t \right) = (1, \sum A_t)$$

and

$$\frac{\partial}{\partial \alpha} \Delta_t(\alpha) = \frac{\partial}{\partial \alpha} \Phi(\alpha^T L_t) = \phi(\alpha^T L_t) L_t.$$

We use maximum likelihood to estimate $\alpha$ and $\nu$, pooling over the time points. After integrating out $U_t$, model (36) implies the observed-data model

$$\pi_t(\alpha, \nu) = \mathbb{P}(A_t = 1 \mid \overline{A}_{t-1}, L_t, Z_t) = \Phi(\nu^T L_t)(1 - \Phi(\alpha^T L_t)) + Z_t \Phi(\alpha^T L_t),$$

so that the conditional density of $A_t$ given the observed data is $\pi_t(\alpha, \nu)^{A_t}(1 - \pi_t(\alpha, \nu))^{1-A_t}$, the scores for $\alpha$ and $\nu$ are

$$s(\alpha, \nu) = \left( \frac{A_t}{\pi_t(\alpha, \nu)} - \frac{1 - A_t}{1 - \pi_t(\alpha, \nu)} \right) \frac{\partial \pi_t(\alpha, \nu)}{\partial \alpha, \nu},$$

and the information is

$$\frac{\partial s(\alpha, \nu)}{\partial \alpha, \nu} = \left(- \frac{A_t}{\pi_t(\alpha, \nu)^2} - \frac{1 - A_t}{(1 - \pi_t(\alpha, \nu))^2} \right) \frac{\partial \pi_t(\alpha, \nu)}{\partial \alpha, \nu} \left( \frac{\partial \pi_t(\alpha, \nu)}{\partial \alpha, \nu} \right)^T + \left( \frac{A_t}{\pi_t(\alpha, \nu)} - \frac{1 - A_t}{1 - \pi_t(\alpha, \nu)} \right) \frac{\partial^2 \pi_t(\alpha, \nu)}{\partial (\alpha, \nu)^2}$$

with

$$\frac{\partial \pi_t(\alpha, \nu)}{\partial \alpha, \nu} = \left((Z_t - \Phi(\nu^T L_t))\phi(\alpha^T L_t)L_t, (1 - \Phi(\alpha^T L_t))\phi(\nu^T L_t)L_t \right)$$

and

$$\frac{\partial^2 \pi_t(\alpha, \nu)}{\partial (\alpha, \nu)^2} = \begin{pmatrix} -(Z_t - \Phi(\nu^T L_t))\phi(\alpha^T L_t)(\alpha^T L_t) L_t^T & -\phi(\nu^T L_t)\phi(\alpha^T L_t)L_t L_t^T \\ -\phi(\alpha^T L_t)\phi(\nu^T L_t)L_t L_t^T & -(1 - \Phi(\alpha^T L_t))\phi(\nu^T L_t)(\nu^T L_t)L_t L_t^T \end{pmatrix}.$$
6.3 Results

Besides our inverse-weighted estimator, also computed for comparison were an “oracle” estimator, an SRA estimator, and the associational or “crude” estimator. The oracle estimator uses inverse probability weighting with the true propensity score \( P(A_t = 1 \mid \bar{A}_{t-1}, \bar{L}_t, \bar{Z}_t, \bar{U}_t) \), i.e., treating \( \bar{U} \) as known and taking into account all confounders. The SRA estimator uses inverse probability weighting with the propensity score taking into account only observed confounders, \( P(A_t = 1 \mid \bar{A}_{t-1}, \bar{L}_t, \bar{Z}_t) \). The associational estimator uses no weights, ignoring all confounding.

For few time points, \( 2 \leq T \leq 4 \), the bias of the proposed estimator falls off at a comparable rate to that of the oracle estimator. As expected, the SRA and associational estimators are biased. See Figure 10 for plots of the mean bias versus sample size. The estimator is relatively noisy, however, with standard deviations on the order of 1/10 when the bias is on the order of 1/1000. See Table 2 for measures of scale. A semiparametric efficient estimator mitigates the noisiness; see [16] for details.

For inference, we use the sandwich estimator and nonparametric bootstrap. Using each, we examine the empirical coverage of a nominal 95% CI, varying the sample size \( n \) and total number of time points \( T \), with the observed standard deviation of the estimators reported for comparison. The coverage is close to the nominal level for smaller \( T \) and larger \( n \), and overconservative for larger \( T \) and smaller \( n \). The sample size needed for tight coverages grows about exponentially with the number of time points \( T \), consistent with the discussion in Example 10. Table 2 presents the detailed results.

The code used to carry out the simulations described above is available at https://github.com/haben-michael/iv-mmsm. Also provided is an R package to estimate the parameters of an MSMM under the models described in Section 6.1 and Example 10.

7 Discussion

We have shown how IVs may be used to identify causal parameters in marginal structural mean models. Our assumptions are mainly variations of standard IV or MSM assumptions, the exception
Figure 10: Mean bias versus sample size of the proposed weighted estimator, for T=2, 3, and 4, time points, compared with oracle (weights including observed and unobserved confounders), SRA (weights including observed confounders), and associational (no weighting) estimators.

|   | n   | bias | $\sigma_{mc}$ | $\sigma_{sw}$ | $\sigma_{bs}$ | coverage (sw) | coverage (bs) |
|---|-----|------|---------------|---------------|---------------|---------------|---------------|
| 1 | 2.00| 1000.00 | 0.03 | 1.40 | 1.55 | 7.96 | 0.99 | 1.00 |
| 2 | 2.00| 2000.00 | -0.06 | 0.72 | 0.71 | 1.31 | 0.99 | 0.99 |
| 3 | 2.00| 3000.00 | 0.10 | 0.57 | 0.54 | 0.59 | 0.95 | 0.96 |
| 4 | 2.00| 4000.00 | 0.02 | 0.44 | 0.46 | 0.48 | 0.96 | 0.97 |
| 5 | 2.00| 5000.00 | 0.04 | 0.40 | 0.41 | 0.43 | 0.95 | 0.96 |
| 6 | 3.00| 10000.00 | -0.02 | 1.79 | 1.74 | 12.59 | 0.98 | 1.00 |
| 7 | 3.00| 20000.00 | 0.09 | 0.95 | 0.97 | 1.33 | 0.96 | 0.99 |
| 8 | 3.00| 30000.00 | -0.02 | 0.75 | 0.75 | 0.81 | 0.96 | 0.97 |
| 9 | 3.00| 40000.00 | 0.01 | 0.63 | 0.64 | 0.67 | 0.95 | 0.97 |
| 10| 3.00| 50000.00 | -0.00 | 0.56 | 0.57 | 0.59 | 0.95 | 0.95 |
| 11| 4.00| 100000.00 | -0.05 | 1.79 | 1.88 | 12.03 | 0.98 | 1.00 |
| 12| 4.00| 200000.00 | -0.16 | 1.10 | 1.11 | 1.24 | 0.96 | 0.99 |
| 13| 4.00| 300000.00 | 0.17 | 0.92 | 0.92 | 0.97 | 0.97 | 0.99 |
| 14| 4.00| 400000.00 | -0.01 | 0.79 | 0.80 | 0.83 | 0.95 | 0.95 |
| 15| 4.00| 500000.00 | 0.03 | 0.72 | 0.70 | 0.71 | 0.94 | 0.95 |

Table 2: Empirical bias, Monte Carlo standard deviation, sandwich sd, bootstrap sd, and the coverage of nominal 95% sandwich and bootstrap CIs. The sandwich variance estimator appears more efficient than the bootstrap.
being Assumption 8. This assumption requires that unknown confounders not interact with the IV in its additive effect on the treatment. We further showed that the conclusion of our identification theorem requires an assumption of a form similar to Assumption 8.

Several extensions to these results suggest themselves. First, the method of proof of our identification may be generalized to apply to other MSMs besides mean models. In [5], a Cox MSM for right-censored survival data is considered, and [16] treats MSMs in generality.

Second, we have required that the instrumental variable be binary. Continuous IVs are often encountered, the difference in distances. Dichotomizing such IVs to fit our framework entails a loss of efficiency and may introduce other difficulties into the estimation procedure. Therefore, it would be useful to extend our identification and estimation results to allow for ordinal or continuous IVs. The resulting estimator would generalized two-stage least squares to the longitudinal setting in the way that the estimator proposed here generalizes the Wald estimator (Example 9).

Third, the estimator proposed here, the solution to the estimating equation (17), while convenient, does not make efficient use of all the available data. We expect improved performance from a robust, semiparametric efficient estimator.

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Appendix: Markov model estimation

The data and model are described in Example 10. The treatment model given in (31),

\[
P(A_t = a \mid L_t = l, U_t = u, Z_t = z) =
\]

\[
(1 - q)p_L^{\{l=a\}}(1 - p_L)^{\{l\neq a\}} + qp_U^{\{u=a\}}(1 - p_U)^{\{u\neq a\}} + (-1)^{1-z}(-1)^{1-a} \delta t/2,
\]

implies the observed-data model

\[
P(A_t = a \mid L_t = l, Z_t = z) = q/2 + (1 - q)p_L^{\{l=a\}}(1 - p_L)^{\{l\neq a\}}.
\]

In order to identify the model we assume the mixing probability \( q \) is known. For all \( t \), the differences
\( \Delta_t \) are parametrized by \((\delta_0, \delta_1)\), and the remaining parameter for the treatment model is \( p_L \). The MSMM model is

\[
E(Y_\bar{a}) = m_\beta(\bar{a}) = \beta \sum_t a_t.
\]

As discussed in Section 6.1, outcomes consistent with this MSMM may be generated as

\[
Y = \eta + \epsilon
\]

\[
\eta = \sum_{t=1}^T \tau_t(L_t - (1 - q)p_L^{A_t-1}(1 - p_L)^{1 - A_t-1} - q/2) + \sum_{t=1}^T \rho_t(U_t - q\rho_{U_t}^{A_t-1}(1 - p_U)^{1 - A_t-1} - (1 - q)/2) + E(Y_\bar{a}),
\]

where \( \epsilon \) is standard normal and exogenous, and \( \tau_t = \rho_t = 1, t = 1, \ldots, T \).

Using the notation in Section 5, the parameters are the MSMM parameter \( \beta, \alpha = (\delta_0, \delta_1) \) and \( \nu = p_L \). Theorem 1 is used to estimate \( \beta \) and \( \alpha \) and \( \nu \) are estimated by maximum likelihood. That is, the weighted residuals \( P_n(\sum_t A_t)(Y - m_\beta(\bar{A})) / W \) serve as an estimating equation for \( \beta \) and the scores as estimating equations for \( \alpha \) and \( \nu \). Formulas for these scores and the information for all the parameters are obtained as in Section 6.2 by substituting

\[
\pi_{\alpha, \nu}(A, L, Z) = q/2 + (1 - q)p_L^L(1 - p_L)^{1 - L}
\]

\[
\partial \pi_{\alpha, \nu}/\partial \alpha, \nu(A, L, Z) = ((-1)^{1-Z}(1 - L)(\delta_1/\delta_0)^L, (-1)^{1-Z}(\delta_0/\delta_1)^{1-L},
\]

\[
(1 - q)L(1/p_L - 1)^{1 - L} - (1 - q)(1 - L)(1/p_L - 1)^{-L}.
\]

The second derivative \( \partial^2 \pi_{\alpha, \nu}/\partial (\alpha, \nu)^2 \) is 0.

The results of a simulation are given in Table 3. In contrast to the model described in Section 6, the sandwich-derived CI appears more conservative than the bootstrap CI.

Appendix: Continuous treatment density A small simulation using a continuous treatment density for a single time point is presented below. Following Example 4, \( L \) and \( U \) are sampled from a uniform distribution on the unit interval, \( Z \) is a standard bernoulli, and the treatment
Table 3: Empirical bias, Monte Carlo standard deviation, sandwich sd, bootstrap sd, and the coverage of nominal 95% sandwich and bootstrap CIs, using the simple markov model discussed in Example 10.

| T     | n    | bias | $\sigma_{mc}$ | $\sigma_{sw}$ | $\sigma_{bs}$ | coverage (sw) | coverage (bs) |
|-------|------|------|--------------|---------------|--------------|---------------|---------------|
| 1     | 2.00 | 0.02 | 26.92        | 279.40        | 38.27        | 0.99          | 0.97          |
| 2     | 2.00 | 0.02 | 6.77         | 11.57         | 11.71        | 0.98          | 0.97          |
| 3     | 2.00 | 0.02 | 0.64         | 0.64          | 1.67         | 0.98          | 0.97          |
| 4     | 2.00 | 0.02 | 0.55         | 0.54          | 1.49         | 0.97          | 0.96          |
| 5     | 2.00 | 0.02 | 0.45         | 0.47          | 1.17         | 0.96          | 0.96          |
| 6     | 3.00 | 0.07 | 11.43        | 48.03         | 17.29        | 0.99          | 0.96          |
| 7     | 3.00 | 0.03 | 0.70         | 0.68          | 2.77         | 0.98          | 0.98          |
| 8     | 3.00 | 0.02 | 0.59         | 0.54          | 2.32         | 0.98          | 0.97          |
| 9     | 3.00 | 0.04 | 0.47         | 0.43          | 0.53         | 0.96          | 0.96          |
| 10    | 3.00 | 0.01 | 0.39         | 0.38          | 0.42         | 0.96          | 0.95          |
| 11    | 4.00 | 0.01 | 4.57         | 7.81          | 15.80        | 0.98          | 0.97          |
| 12    | 4.00 | 0.02 | 0.55         | 0.54          | 4.71         | 0.97          | 0.95          |
| 13    | 4.00 | 0.01 | 0.44         | 0.43          | 0.59         | 0.96          | 0.96          |
| 14    | 4.00 | 0.01 | 0.39         | 0.35          | 0.38         | 0.95          | 0.95          |
| 15    | 4.00 | 0.01 | 0.31         | 0.31          | 0.34         | 0.96          | 0.96          |

density is defined as

$$\Delta(a \mid L) = \phi(a) - \phi(a/l)/l$$

$$f_{A \mid Z,L,U}(A = a, L = l, U = u) = \phi(a/u)/u + Z\Delta(a \mid L = l),$$

using $\phi$ to denote the standard normal density. The outcome is sampled as $Y = (L - \mathbb{E}(L)) + (U - \mathbb{E}(U)) + \beta A + \epsilon$, with $\beta = 2$. The sample size is 1000. The observed bias and standard deviation of the estimates are -.195 and 0.64, and the median absolute error is .249. Figure 11 gives a histogram of the observed biases, as well as histograms of the weights and the plot of the conditional treatment density $f_{A \mid Z=1,L,U}$ for one choice of $L, U$. 

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Figure 11: (Continuous treatment density.) The left panel is a histogram of the observed bias of the estimated coefficient in a simulation of size 1000. The middle panel is a histogram of the weights in one simulated data set. The right panel is a plot of the density $f_{A|Z=1,L,U}$, i.e., the sum of the baseline treatment density, which is normal, and the function $\Delta(a,l,u)$ for sample values of $l$ and $u$. 