Estimating Net Effects of Treatments in Treatment Sequence without the Assumption of Strongly Ignorable Treatment Assignment

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Abstract

In sequential causal inference, one estimates the causal net effect of treatment in treatment sequence on an outcome after last treatment in the presence of time-dependent covariates between treatments, improves the estimation by the untestable assumption of strongly ignorable treatment assignment, and obtains consistent but non-genuine likelihood-based estimate. In this article, we introduce the net effect of treatment as parameter for the conditional distribution of outcome given all treatments and time-dependent covariates and show that it is equal to the causal net effect of treatment under the assumption of strongly ignorable treatment assignment. As a result, we can estimate the net effect of treatment and evaluate its causal interpretation in two separate steps. The first step is focus of this article while the second step
can be accomplished by usual sensitivity analyses. We construct point parametrization for the conditional outcome distribution in which the parameters of interest are the point effects of single-point treatments. With point parametrization and without the untestable assumption, we estimate the net effect of treatment by maximum likelihood, improve the estimation by testable pattern of the net effect of treatment, and obtain unbiased consistent maximum-likelihood estimate for the net effect of treatment with finite-dimensional pattern.

Key words: Net effect of treatment; Pattern of net effects of treatments; Point effect of treatment; Constraint on point effects of treatments

1 Introduction

In many economic and medical practices, a sequence of treatments, i.e. economic interventions or medical treatments or exposures, are assigned to influence an outcome of interest that occurs after last treatment of the sequence. Between consecutive treatments, time-dependent covariates are present that may be posttreatment variables of the earlier treatments (Rosenbaum, 1984; Robins, 1989; Frangakis & Rubin, 2002) and confounders of the subsequent treatments. Under the assumption of strongly ignorable treatment assignment or called the assumption of no unmeasured confounders, Robins (1986, 1992, 1997, 1999, 2004, 2009) identified the causal net effect of each treatment in treatment sequence by standard parameters, which are usually the means of outcome given all treatments and time-dependent covariates. The causal net effect of treatment is also called the blip effect of treatment in the context of semi-parametric sequential causal inference.

Robins illustrated that any constraint imposing equalities among standard parameters leads to erroneous rejection of the null hypothesis of causal net
effects of treatments if the time-dependent covariates are simultaneously post-treatment variables of the earlier treatments and confounders of the subsequent treatments. As treatment sequence gets long, the number of standard parameters becomes huge, and with no constraint on these parameters, the maximum-likelihood (ML) estimates of causal net effects of treatments may not be consistent (Robins & Ritov, 1997; Robins, 1997).

To overcome this difficulty, two semi parametric approaches have been developed, the \( g \)-estimation model (Robins, 1992, 1997, 2004, 2009; Robins et al., 1999; Henderson et al., 2010) and the marginal structural model (Robins, 1999, 2009; Murphy et al., 2001). The \( g \)-estimation model uses the assumption of strongly ignorable treatment assignment and is based on the likelihood of treatments given previous time-dependent covariates and treatments. The marginal structural model also uses the assumption and is based on a weighted conditional likelihood of outcome given all treatments and time-dependent covariates. Both approaches yield consistent but non-genuine likelihood-based estimates of causal net effects of treatments. Both approaches are dependent on validity of the assumption, which is noticeably untestable with observed data.

In this article, we intend to estimate the causal net effect of treatment by maximum likelihood and improve the estimation by testable assumptions. To this end, we introduce the net effect of treatment as parameter for the conditional distribution of outcome given all treatments and time-dependent covariates and show that the parameter is equal to the causal net effect of treatment under the assumption of strongly ignorable treatment assignment. As a result, we can estimate the net effect of treatment and evaluate its causal interpretation in two separate steps. The first step is focus of this article whereas the second step can be accomplished by using subject knowledge in
combination of usual sensitivity analyses. We use testable pattern of the net effect of treatment to improve the estimation and obtain unbiased consistent ML estimate of the net effect of treatment if the pattern is of finite dimension.

In Section 2, we describe the relationship between the causal net effect of treatment and the net effect of treatment. In Section 3, we construct point parametrization for the conditional outcome distribution by using point effects of treatments or time-dependent covariates as point parameters and express pattern of net effects of treatments by constraint on point effects of treatments. In Section 4, we estimate net effects of treatments by maximum likelihood in the point parametrization and show that the ML estimates are both unbiased and consistent in many practical applications where the net effects of treatments have pattern of finite dimension. In Section 5, we study an example in which an employer rewards a sequence of bonuses to the employees in order to increase their productivity, but wonders if it is possible to reward bonuses less frequently while not reducing the productivity, and in Section 7, we continue the example to illustrate practical procedure of estimating net effects of treatments. In Section 7, we conclude the article with remarks.

2 Net Effects versus Causal Net Effects of Treatments in Treatment Sequence

2.1 Treatment sequence, time-dependent covariates and outcome

Let $z_t$ indicate the treatments at time $t$ ($t = 1, \ldots, T$). Assume that all $z_t$ are discrete variables and take the values $0, 1, \ldots$. We take $z_t = 0$ as control treatment and $z_t = 1, 2, \ldots$ as active treatments. Let $z_1^t = (z_1, \ldots, z_t)$. For no-
tational simplicity, we use one subpopulation defined by stationary covariates of the population as our population, and henceforth do not consider stationary covariates in the following development.

Between treatments \( z_t \) and \( z_{t+1} \) \((t = 1, \ldots, T-1)\), there is a time-dependent covariate vector \( x_t \), which can be confounders for subsequent treatments \( z_s \) \((s = t + 1, \ldots, T)\) and posttreatment variables of earlier treatment \( z_s \) \((s = 1, \ldots, t)\). Assume that \( x_t \) is a discrete vector with non-negative components. We take \( x_t = 0 \) as reference level. Let \( x_t^1 = \{x_1, x_2, \ldots, x_t\} \) be the time-dependent covariate array between treatments \( z_1 \) and \( z_{t+1} \). The outcome of interest after last treatment \( z_T \) is denoted by \( y \).

Instead of one set \((z_T^1, x_T^T, y)\) of the random variables, we consider \( N \) independent and identically distributed sets, \(\{z_{i1}^T, x_{i1}^{T-1}, y_i\}\), \(i = 1, \ldots, N\). In this article, we shall ignore the variability of \(\{z_{i1}^T, x_{i1}^{T-1}\}\) and focus on the conditional distribution of \(\{y_i\}_{i=1}^N\) given \(\{(z_{i1}^T, x_{i1}^{T-1})\}_{i=1}^N\), that is,

\[
\prod_{i=1}^N f(y_i \mid z_{i1}^T, x_{i1}^{T-1}).
\]  

(1)

Noticeably, standard parameters for (1) are the means \(\mu(z_T^1, x_T^{T-1}) = E(y \mid z_T^1, x_T^{T-1})\), where the expectation \(E(b \mid a)\) is with respect to the conditional distribution of \(b\) given \(a\).

Throughout the article, we adopt the following notational conventions. First, the notations \(z_u^v\) and \(x_u^v\) with \(u > v\) or \(u = v = 0\) or both \(u < 0\) and \(v < 0\) should be omitted from relevant expression. For instance, the notation \(x_0^0\) in \(\mu(z_T^1, x_1^{T-1})\) for \(T = 1\) should be omitted, so that we have \(\mu(z_1)\). Second, the sigma notation \(\sum_{i=u}^v a_i\) with \(v < u\) should be omitted from relevant expression. Third, the notations \(z_{u_i}^v, x_{u_i}^v\) and \(\sum_{i=u}^v a_i\) with \(u < 1\) and \(v \geq 1\) are treated as \(z_1^v\) and \(\sum_{i=1}^v a_i\) respectively. Fourth, the notation \((z_u^v, x_{u_i}^{v-1})\) is equal to \((z_{u-1}^v, x_{u-1}^{v-1}, z_v)\), and \((z_u^v, x_u^v)\) to \((z_u^v, x_{u-1}^{v-1}, x_v)\); we may use one or another notation in different contexts.
2.2 Net effects and causal net effects of treatments

Given \( N \) sets \( \{ z_{i1}^T, x_{i1}^{T-1} \} \) \( i = 1 \) to \( N \), a stratum is a set of those sets satisfying certain condition. For instance, stratum \( ( z_{11}^T, x_{11}^{T-1} ) \) is a set of those sets satisfying \( ( z_{11}^T, x_{11}^{T-1} ) = ( z_{11}^T, x_{11}^{T-1} ) \). Let \( \Pr(A) \) denote the proportion of stratum \( A \) in the \( N \) sets and \( \Pr(A \mid B) \) denote the conditional proportion of stratum \( A \) in stratum \( B \).

We define the net effect of last treatment \( z_T > 0 \) on stratum \( ( z_{11}^T, x_{11}^{T-1} ) \) by

\[
\phi(z_{11}^T, x_{11}^{T-1}, z_T) = \mu(z_{11}^T, x_{11}^{T-1}, z_T) - \mu(z_{11}^T, x_{11}^{T-1}, z_T = 0).
\]

The mean of \( y \) in stratum \( ( z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1} ) \) is

\[
\mu(z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1}) = \sum_{x_{T-1}, z_T} \mu(z_{11}^T, x_{11}^{T-1}) \Pr(x_{T-1}, z_T \mid z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1}).
\]

With \( \phi(z_{11}^{T-1}, x_{11}^{T-1}, z_T) \), we calculate the mean of \( y \) in stratum \( ( z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1} ) \) under no active treatments at \( t = T \) by

\[
\nu(z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1}) = \\
\mu(z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1}) - \sum_{x_{T-1}, z_T > 0} \phi(z_{11}^{T-1}, x_{11}^{T-1}, z_T) \Pr(x_{T-1}, z_T \mid z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1}).
\]

With \( \nu(z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1}) \), we define the net effect of second last treatment \( z_{T-1} > 0 \) on stratum \( ( z_{11}^{T-2}, x_{11}^{T-2} ) \) by

\[
\phi(z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1}) = \nu(z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1}) - \nu(z_{11}^{T-2}, x_{11}^{T-2}, z_{T-1} = 0).
\]

Recursively, we define the net effect \( \phi(z_{11}^{t-1}, x_{11}^{t-1}, z_t) \) of treatment \( z_t > 0 \) on stratum \( ( z_{11}^{t-1}, x_{11}^{t-1} ) \) \( ( t = T - 2, \ldots, 1 ) \). In summary, we have, for \( t = T, \ldots, 1 \),

\[
\mu(z_{11}^{t-1}, x_{11}^{t-1}, z_t) = \sum_{z_{t+1}, x_{t+1}} \mu(z_{11}^T, x_{11}^{T-1}) \Pr(z_{t+1}^T, x_{t+1}^{T-1} \mid z_t, x_t^{t-1}),
\]

\[
\nu(z_{11}^{t-1}, x_{11}^{t-1}, z_t) = 
\]
\[ \mu(z_{1:t-1}, x_{1:t-1}, z_t) = \sum_{s=t+1}^{T} \sum_{z_{s:t+1}^{x_{s:t+1}} > 0} \phi(z_{s-1}^{x_{s-1}}, x_{s-1}^{x_{s-1}}, z_s) \Pr(z_{s:t+1}^{x_{s:t+1}}, x_{s:t+1}^{x_{s:t+1}} \mid z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}), \]

\[ \phi(z_{1:t-1}, x_{1:t-1}, z_t) = \nu(z_{1:t-1}, x_{1:t-1}, z_t) - \nu(z_{1:t-1}, x_{1:t-1}, z_t = 0). \] (2)

Noticeably, \( \nu(z_{1:T-1}^{x_{1:T-1}}, x_{1:T-1}^{x_{1:T-1}}, z_T) = \mu(z_{1:T-1}^{x_{1:T-1}}, x_{1:T-1}^{x_{1:T-1}}, z_T) \), according to the notational convention described in Section 2.1. Given \( \{z_{i1}^{T - 1}, x_{i1}^{T - 1}\}_{i = 1}^{N} \), the proportions of treatments and covariates can be treated as constants. Therefore the net effects are linear functions of the standard parameters \( \mu(z_{1:T-1}^{x_{1:T-1}}, x_{1:T-1}^{x_{1:T-1}}, z_T) \) and thus are parameters of the outcome distribution [1]. These parameters evaluate the association between treatment \( z_t \ (t = 1, \ldots, T) \) and the outcome \( y \).

Let \( z_{1:t}^{T} = (z_t, \ldots, z_T) \) be the treatment sequence given the variables \( (z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}) \).

Under \( z_{1:t}^{T} \) given \( (z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}) \), each unit could have a potential outcome \( y(z_{1:t}^{T}) \).

Let \( y(z_{1:t}^{T}) = y(z_{1:t}^{T}) \) for given \( (z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}) \). Under the assumption of strongly ignorable treatment assignment (Robins, 1986, 1989, 1992, 1997, 1999, 2004, 2009), we show, in Appendix A1,

\[ \nu(z_{1:t-1}^{x_{1:t-1}}, z_t) = \mathbb{E}\{y(z_t, z_{1:t+1}^{T} = 0) \mid z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}\}, \]

\[ \phi(z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}, z_t) = \]

\[ \mathbb{E}\{y(z_t, z_{1:t+1}^{T} = 0) \mid z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}\} - \mathbb{E}\{y(z_t = 0, z_{1:t+1}^{T} = 0) \mid z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}\} \] (3)

for \( t = 1, \ldots, T \), which is the causal net effect of treatment \( z_t > 0 \) on stratum \( (z_{1:t-1}^{x_{1:t-1}}, x_{1:t-1}^{x_{1:t-1}}) \) (Robins, 1986, 1989, 1992, 1997, 1999, 2004, 2009).

### 2.3 Difficulties in estimation of net effects of treatments in standard parametrization

If \( x_t \) are posttreatment variables of \( z_s \ (s \leq t) \), then the standard parameters \( \mu(z_{1:T}^{x_{1:T}}, x_{1:T}^{x_{1:T}}) \) essentially do not have any pattern (Rosenbaum, 1984; Robins, 1989; Frangakis & Rubin, 2002). If \( x_t \) are simultaneously confounders of
$z_s \ (s > t)$, then one needs to use all the standard parameters to identify the causal net effects of treatments (Robins, 1986, 1997, 1999, 2004, 2009; Robins & Ritov, 1997). As $T$ increases, the number of standard parameters increases exponentially and the ML estimates of the causal net effects may not be consistent (Robins & Ritov, 1997). In general, the difficulty applies to the net effects.

Although standard parameters do no have pattern, the net effects may have one, which is the focus of this article. Pattern of net effects implies constraint on standard parameters. Consider a simple case where $z_t = 0, 1 \ (t = 1, \ldots, T - 1)$ and $x_t = 0, 1 \ (t = 1, \ldots, T - 1)$. Then there are as many as $2^{2T-1}$ standard parameters. Suppose that the pattern of net effects is such that all the net effects are the same, denoted by $\varphi$. Then there exist as many as $(4^T - 1)/(4 - 1) - 1$ equalities among standard parameters. For $T = 10$, we may have to solve a system of 524288 likelihood equations under a constraint of 349524 equalities to estimate $\mu(z_1^T, x_1^{T-1})$ and then $\varphi$. As $T$ increases, the number of likelihood equations increases exponentially and so does the number of equalities among standard parameters, and it is practically impossible to solve such a huge system of likelihood equations under a constraint of so many equalities.
3 Point versus Net Effects of Treatments in Treatment Sequence

3.1 Point effects of treatments and point parametrization

The mean of $y$ in stratum $(z_{t-1}^i, x_{t-1}^i, z_t)$ is $\mu(z_{t-1}^i, x_{t-1}^i, z_t)$. We define the point effect of treatment $z_t > 0$ on stratum $(z_{t-1}^i, x_{t-1}^i)$ by

$$\theta(z_{t-1}^i, x_{t-1}^i, z_t) = \mu(z_{t-1}^i, x_{t-1}^i, z_t) - \mu(z_{t-1}^i, x_{t-1}^i, z_t = 0)$$

for $t = 1, \ldots, T$.

The mean of $y$ in stratum $(z_t^i, x_t^i)$ is

$$\mu(z_t^i, x_t^i) = \sum_{z_{t+1}^i, x_{t+1}^i} \mu(z_T^i, x_T^i) \Pr(z_{t+1}^i, x_{t+1}^i | z_t^i, x_t^i)$$

for $t = 1, \ldots, T-1$. We define the point effect of covariate $x_t > 0$ on stratum $(z_t^i, x_t^i)$ by

$$\gamma(z_t^i, x_t^i, x_t) = \mu(z_t^i, x_t^i, x_t) - \mu(z_t^i, x_t^i, x_t = 0).$$

We define the grand mean by

$$\mu = \sum_{z_T^i, x_T^i} \mu(z_T^i, x_T^i) \Pr(z_T^i, x_T^i).$$

Given $\{z_{t+1}^i, x_{t+1}^i\}_{i=1}^N$, the proportions of treatments and covariates can be treated as constants. Therefore the point effects of treatments, the point effects of covariates and the grand mean are linear functions of the standard parameters $\mu(z_T^i, x_T^i)$ and thus are parameters, called point parameters, of the outcome distribution ($\mu$).

From ($\mu$), we see that each point parameter can be expressed in terms of the standard parameters $\mu(z_T^i, x_T^i)$. Conversely, we show in Appendix A2...
that each standard parameter can be expressed in terms of the point parameters by

\[
\mu(z_1^T, x_1^{T-1}) = \sum_{t=1}^{T} \left[ \sum_{z_t} -\theta(z_1^{t-1}, x_1^{t-1}, z_t) \Pr(z_t^* | z_1^{t-1}, x_1^{t-1}) + \theta(z_1^{t-1}, x_1^{t-1}, z_t) \right] + \\
\sum_{t=1}^{T-1} \left[ \sum_{z_t} -\gamma(z_1^t, x_1^{t-1}, x_t^*) \Pr(x_t^* | z_1^t, x_1^{t-1}) + \gamma(z_1^t, x_1^{t-1}, x_t) \right] + \mu.
\]

Here we take \(\theta(z_1^{t-1}, x_1^{t-1}, z_t = 0) = 0\) and \(\gamma(z_1^t, x_1^{t-1}, x_t = 0) = 0\). Therefore the set of all point parameters, \(\Psi = \{\theta(z_1^{t-1}, x_1^{t-1}, z_t), t = 1, \ldots, T; \gamma(z_1^t, x_1^{t-1}, x_t), t = 1, \ldots, T-1; \mu\}\), forms a new parametrization, called point parametrization, for (1).

3.2 Pattern of net effects of treatments versus constraint on point effects of treatments

Combining (1) with (2), we obtain

\[
\theta(z_1^{t-1}, x_1^{t-1}, z_t) = \phi(z_1^{t-1}, x_1^{t-1}, z_t) + \\
\sum_{s=t+1}^{T} \sum_{z_{t+1}^{s-1}, x_{t+1}^{s-1}, z_s > 0} \phi(z_1^{s-1}, x_1^{s-1}, z_s) \Pr(z_{t+1}^{s-1}, x_{t+1}^{s-1}, z_s | z_1^t, x_1^{t-1}) - \\
\sum_{s=t+1}^{T} \sum_{z_{t+1}^{s-1}, x_{t+1}^{s-1}, z_s > 0} \phi(z_1^{s-1}, z_t = 0, x_1^{s-1}, x_1^{t-1}, z_s) \Pr(z_{t+1}^{s-1}, x_{t+1}^{s-1}, z_s | z_1^{t-1}, z_t = 0, x_1^{t-1})
\]

for \(t = 1, \ldots, T - 1\) and \(\theta(z_1^{T-1}, x_1^{T-1}, z_T) = \phi(z_1^{T-1}, x_1^{T-1}, z_T)\). The formula decomposes \(\theta(z_1^{t-1}, x_1^{t-1}, z_t)\) into the net effects of treatments \(z_s > 0\) at times \(s \geq t\) in strata \((z_1^{t-1}, x_1^{t-1}, z_t)\) versus \((z_1^{t-1}, x_1^{t-1}, z_t = 0)\).

Suppose that the data-generating mechanism is such that the net effects \(\phi(z_1^{t-1}, x_1^{t-1}, z_t)\) follow certain pattern. One example of such patterns is

\[
\phi(z_1^{t-1}, x_1^{t-1}, z_t) = \varphi_1 z_t + \varphi_2 z_{t-1} + \varphi_3 x_t^{t-1}
\]
for any \((z_{t-1}^1, x_{t-1}^1, z_t)\) at \(t = 1, \ldots, T\), where the parameter vector \(\varphi = (\varphi_1, \varphi_2, \varphi_3)\) indexes all the net effects. Generally, we consider a pattern of net effects described by a function

\[
\phi(z_{t-1}^1, x_{t-1}^1, z_t) = \phi(z_{t-1}^1, x_{t-1}^1, z_t; \varphi),
\]

where the \(k\)-dimensional parameter vector \(\varphi = (\varphi_1, \ldots, \varphi_k)\) indexes all the net effects. We call \(\varphi\) the net effect vector. Because the net effects describe the conditional distribution (1) of the observable outcome \(\{y_i\}_{i=1}^N\) given the observable variables \(\{(z_{t+1}^T, x_{t+1}^T)\}_{i=1}^N\), pattern (8) is testable with observed data.

With the pattern and the above decomposition, we obtain the constraint on point effects of treatments

\[
\theta(z_{t-1}^1, x_{t-1}^1, z_t) = \phi(z_{t-1}^1, x_{t-1}^1, z_t; \varphi) + \sum_{s=t+1}^{T} \sum_{z_{s-1}^1 > 0} \phi(z_{s-1}^1, x_{s-1}^1, z_s; \varphi) \text{pr}(z_{s+1}^1, x_{s+1}^1, z_s | z_1^1, x_1^1) - \]

\[
\sum_{s=t+1}^{T} \sum_{z_{s-1}^1 = 0, z_{s-1}^1 > 0} \phi(z_{s-1}^1, z_t = 0, z_{s-1}^1, z_s; \varphi) \text{pr}(z_{s+1}^1, x_{s+1}^1, z_s | z_1^1, z_t = 0, x_1^1)
\]

for \(t = 1, \ldots, T - 1\) and \(\theta(z_{T-1}^1, x_{T-1}^1, z_T) = \phi(z_{T-1}^1, x_{T-1}^1, z_T; \varphi)\).

If the function \(\phi(z_{t-1}^1, x_{t-1}^1, z_t; \varphi)\) in pattern (8) correctly describes the net effect \(\phi(z_{t-1}^1, x_{t-1}^1, z_t)\), then constraint (9) does not necessarily bias the estimate of \(\phi(z_{t-1}^1, x_{t-1}^1, z_t)\) (\(t = 1, \ldots, T\)). As a result, constraint (9) does not necessarily lead to automatic rejection of the null hypothesis of the net effects.

### 4 ML Estimation of Net Effects of Treatments through Point Effects of Treatments

The data set is independent observations \(\{z_{1i}^1, x_{1i}^1, y_i\}\) on units \(i = 1, \ldots, N\). Using the outcome distribution (1), we obtain the following likelihood of the
point parameters

\[ L\{\Psi; \{y_i\}_i^N, \{z_i^T, x_i^{T-1}\}_i^N\} = \prod_{i=1}^N f\{y_i \mid z_i^T, x_i^{T-1}; \mu(z_i^T, x_i^{T-1})\} \]

where \( \Psi \) is the set of point parameters constructed in Section 3.1 and \( \mu(z_i^T, x_i^{T-1}) = \mu(z_i^T = z_i^T, x_i^{T-1} = x_i^{T-1}) \) is expressed by \( \phi \) in terms of the point parameters in \( \Psi \). The outcome model is

\[ \mu_i = \mu(z_i^T, x_i^{T-1}) \]

where \( \mu_i = E(y_i \mid z_i^T, x_i^{T-1}) \) is the mean of \( y_i \) given \( (z_i^T, x_i^{T-1}) \). The constraint on the point parameters is \( \varphi \).

For common distributions, the net effects of treatments can be estimated according to the following procedure. First, we estimate \( \mu(z_i^{t-1}, x_i^{t-1}, z_t) \) \((t = 1, \ldots, T)\) by using likelihood \( \text{10} \) and model \( \text{11} \). The estimate \( \hat{\mu}(z_i^{t-1}, x_i^{t-1}, z_t) \) is the average of \( y \) in stratum \((z_i^{t-1}, x_i^{t-1}, z_t)\). Second, we use \( \hat{\mu}(z_i^{t-1}, x_i^{t-1}, z_t) \) to calculate the estimate of \( \hat{\theta}(z_i^{t-1}, x_i^{t-1}, z_t) \) according to \( \text{11} \). Third, we perform a regression of \( \hat{\theta}(z_i^{t-1}, x_i^{t-1}, z_t) \) on \( \text{pr}(z_i^{t+1}, x_i^{t+1}, z_s \mid z_i^{t}, x_i^{t-1}) \) and \( \text{pr}(z_i^{t+1}, x_i^{t+1}, z_s \mid z_i^{t-1}, x_i^{t-1}, z_t = 0, x_i^{t+1}) \) according to constraint \( \text{11} \) to estimate \( \varphi \). Finally, we replace \( \varphi \) by \( \hat{\varphi} \) in pattern \( \phi \) to obtain the estimate of \( \hat{\phi}(z_i^{t-1}, x_i^{t-1}, z_t) \), that is, \( \hat{\phi}(z_i^{t-1}, x_i^{t-1}, z_t) = \phi(z_i^{t-1}, x_i^{t-1}, z_t; \hat{\varphi}) \). The procedure will be further illustrated in the next section. Here we analyse unbiasedness and consistency of \( \hat{\phi}(z_i^{t-1}, x_i^{t-1}, z_t) \).

The estimate \( \hat{\mu}(z_i^{t-1}, x_i^{t-1}, z_t) \) is unbiased and so is \( \hat{\theta}(z_i^{t-1}, x_i^{t-1}, z_t) \). If \( \phi(z_i^{t-1}, x_i^{t-1}, z_t; \varphi) \) is a linear function of \( \varphi \), then the estimate \( \hat{\varphi} \) is unbiased according to \( \text{11} \) treated as a regression model, and so is \( \hat{\phi}(z_i^{t-1}, x_i^{t-1}, z_t) \). If \( \phi(z_i^{t-1}, x_i^{t-1}, z_t; \varphi) \) is not linear in \( \varphi \), then \( \hat{\varphi} \) may be biased, but \( \hat{\phi}(z_i^{t-1}, x_i^{t-1}, z_t) \) is usually unbiased.

Oftentimes, the dimension \( k \) of \( \varphi \) is finite, that is, the net effects \( \phi(z_i^{t-1}, x_i^{t-1}, z_t) \) have a pattern of finite dimension. From \( \text{11} \) treated as a regression model,
we see that \( \hat{\varphi} \) is consistent and so is \( \hat{\phi}(z_{t-1}^{t-1}, x_{t-1}^{t-1}, z_t) \) if there exist at least \( k \) different point effects \( \theta(z_{t-1}^{t-1}, x_{t-1}^{t-1}, z_t) \) of treatments which contain \( \varphi \) and whose estimates have zero covariance matrices as the sample size \( N \) tends to infinity. This condition can be satisfied in many practical applications, where the treatment variable \( z_t \) \( (t = 1, \ldots, T) \) and the covariate \( x_t \) \( (t = 1, \ldots, T - 1) \) take finite numbers of values.

5 Example: Net Effect of Bonus on Productivity of an Employee

5.1 Backgrounds and the setting

To improve productivity, an employer rewards bonuses to the employees each month. When bonus is rewarded, consideration is given to performance of an employee in the past month. The employer wishes to know how the bonus influences the productivity of an employee over a period of more than one month. If the bonus remained effective on productivity after one month, then the employer would reward bonuses less frequently.

In this context, bonuses form a treatment sequence. The productivity after a last bonus is the outcome of interest. The performance is a covariate between bonuses that is simultaneously posttreatment variable of the previous bonuses and confounder of the subsequent bonuses. The interest of the employer is the net effect of each treatment in treatment sequence on the outcome. Formally, the treatment variable \( z_t \) is binary: \( z_t = 1 \) if bonus is rewarded and \( z_t = 0 \) otherwise \( (t = 1, \ldots, T) \). The outcome \( y \) is the productivity after last treatment \( z_T \). The covariate \( x_t \) is also binary: \( x_t = 1 \) if the performance is good in the past month and \( x_t = 0 \) otherwise \( (t = 1, \ldots, T - 1) \).
Each treatment variable \( z_t \) has only one active treatment \( z_t = 1 \) and thus one net effect \( \phi(z_{t-1}^t, x_{t-1}^t, z_t = 1) \) of treatment and one point effect \( \theta(z_{t-1}^t, x_{t-1}^t, z_t = 1) \) of treatment on stratum \( (z_{t-1}^t, x_{t-1}^t) \). Denote \( \phi(z_{t-1}^t, x_{t-1}^t, z_t = 1) \) by \( \phi(z_{t-1}^t, x_{t-1}^t) \) and \( \theta(z_{t-1}^t, x_{t-1}^t, z_t = 1) \) by \( \theta(z_{t-1}^t, x_{t-1}^t) \) \((t = 1, \ldots, T)\). In particular, \( \phi(z_1 = 1) = \phi \) and \( \theta(z_1 = 1) = \theta \) at \( t = 1 \).

5.2 Pattern of net effects of treatments and constraint on point effects of treatments

First we consider the case of \( T = 2 \). The treatment \( z_1 \) has one net effect \( \phi \) denoted by \( \varphi_1 \). The treatment \( z_2 \) has four net effects \( \phi(z_1, x_1) \) for \((z_1, x_1) = (0, 0), (0, 1), (1, 0), (1, 1)\), and suppose that the four net effects are the same and denoted by \( \varphi_2 \). Then the pattern of these net effects is

\[
\begin{align*}
\phi &= \varphi_1, \\
\phi(z_1, x_1) &= \varphi_2
\end{align*}
\]

where \((z_1, x_1) = (0, 0), (0, 1), (1, 0), (1, 1)\).

Decomposing the point effect of \( z_1 = 1 \) into the net effects of \( z_1 = 1 \) and \( z_2 = 1 \) in strata \( z_1 = 1 \) versus \( z_1 = 0 \) and using the pattern above, we obtain the following constraint on \( \theta \)

\[
\theta = \varphi_1 + \varphi_2 \{ \text{pr}(z_2 = 1 \mid z_1 = 1) - \text{pr}(z_2 = 1 \mid z_1 = 0) \},
\]

where \( \text{pr}(z_2 = 1 \mid z_1) \) is the proportion of \( z_2 = 1 \) in stratum \( z_1 \). We can also obtain the formula by inserting the pattern into constraint (11) for \( t = 1 \) and using the equality \( \sum_{x_2} \text{pr}(x_2, z_2 = 1 \mid z_1) = \text{pr}(z_2 = 1 \mid z_1) \). Noticing \( \theta(z_1, x_1) = \phi(z_1, x_1) \) at \( t = T = 2 \) and using the pattern above, we obtain the following constraint on \( \theta(z_1, x_1) \)

\[
\theta(z_1, x_1) = \varphi_2,
\]
where \((z_1, x_1) = (0, 0), (0, 1), (1, 0), (1, 1)\).

For an arbitrary \(T\), suppose that the pattern of the net effects is

\[
\begin{cases}
\phi(z_1^{t-1}, x_1^{t-1}) = \varphi_1, & t \leq T - 2 \\
\phi(z_1^{T-2}, x_1^{T-2}) = \varphi_2, \\
\phi(z_1^{T-1}, x_1^{T-1}) = \varphi_3.
\end{cases}
\]

Decomposing \(\theta(z_1^{t-1}, x_1^{t-1})\) into net effects of \(z_s (s \geq t)\) in strata \((z_1^{t-1}, x_1^{t-1}, z_t)\) versus \((z_1^{t-1}, x_1^{t-1}, z_t = 0)\) and using the pattern above, we obtain the following constraint on \(\theta(z_1^{t-1}, x_1^{t-1}) (t = 1, \ldots, T)\)

\[
\theta(z_1^{t-1}, x_1^{t-1}) = \varphi_1 c^{(1)}(z_1^{t-1}, x_1^{t-1}) + \varphi_2 c^{(2)}(z_1^{t-1}, x_1^{t-1}) + \varphi_3 c^{(3)}(z_1^{t-1}, x_1^{t-1}), \tag{14}
\]

where

\[
c^{(1)}(z_1^{t-1}, x_1^{t-1}) = \\
\sum_{s=t}^{T-2} \{\text{pr}(z_s = 1 \mid z_1^{t-1}, x_1^{t-1}, z_t = 1) - \text{pr}(z_s = 1 \mid z_1^{t-1}, x_1^{t-1}, z_t = 0)\},
\]

which is difference between the sums of proportions of the employees receiving the treatments \(z_s = 1\) at \(s = t, \ldots, T - 2\) in stratum \((z_1^{t-1}, x_1^{t-1}, z_t = 1)\) versus in stratum \((z_1^{t-1}, x_1^{t-1}, z_t = 0)\), and

\[
c^{(2)}(z_1^{t-1}, x_1^{t-1}) = \\
\text{pr}(z_{T-1} = 1 \mid z_1^{t-1}, x_1^{t-1}, z_t = 1) - \text{pr}(z_{T-1} = 1 \mid z_1^{t-1}, x_1^{t-1}, z_t = 0),
\]

which is difference between the proportions of the employees receiving the second last treatment \(z_{T-1} = 1\) in stratum \((z_1^{t-1}, x_1^{t-1}, z_t = 1)\) versus in stratum \((z_1^{t-1}, x_1^{t-1}, z_t = 0)\), and

\[
c^{(3)}(z_1^{t-1}, x_1^{t-1}) = \\
\text{pr}(z_T = 1 \mid z_1^{t-1}, x_1^{t-1}, z_t = 1) - \text{pr}(z_T = 1 \mid z_1^{t-1}, x_1^{t-1}, z_t = 0),
\]

which is difference between the proportions of the employees receiving the last treatment \(z_T = 1\) in stratum \((z_1^{t-1}, x_1^{t-1}, z_t = 1)\) versus in stratum \((z_1^{t-1}, x_1^{t-1}, z_t = 0)\).
0). The constraint can also be obtained by inserting the above pattern into (9) and using the equality

\[ \sum_{z_{i+1}^s, x_{i+1}^s} \text{pr}(z_{i+1}^s, x_{i+1}^s, z_s = 1 | z_i^s, x_i^t) = \text{pr}(z_s = 1 | z_i^s, x_i^t). \]

5.3 ML estimates of point effects of treatments

Suppose that \( y \) is normally distributed. For simplicity, further suppose that the variance is known and equal to one for any given \( (z_i^T, x_i^T) \). Given the data set \( \{z_{i1}^T, x_{i1}^T, y_i\}_{i=1}^N \), likelihood (10) becomes

\[
\prod_{i=1}^N \frac{1}{\sqrt{2\pi}} \exp \left[ -\frac{1}{2} \{y_i - \mu(z_i^T, x_i^T)\}^2 \right]
\]

where \( \mu(z_i^T, x_i^T) \) is expressed in terms of point parameters by (7). The outcome model we use is (11), i.e.

\[ \mu_i = \mu(z_{i1}^T, x_{i1}^T). \]

Let \( s(A) \) be the set of units in stratum \( A \) and \( n(A) \) be the number of units in stratum \( A \). Using the likelihood and the outcome model above, we obtain

\[ \hat{\mu}(z_{i1}^T, x_{i1}^T, z_t) = \frac{\sum_{i \in s(z_{i1}^T, x_{i1}^T, z_t)} y_i}{n(z_{i1}^T, x_{i1}^T, z_t)}, \]

\[ \text{var}\{\hat{\mu}(z_{i1}^T, x_{i1}^T, z_t)\} = \frac{1}{n(z_{i1}^T, x_{i1}^T, z_t)}. \]

Using (11), we obtain

\[ \hat{\theta}(z_{i1}^T, x_{i1}^T) = \hat{\mu}(z_{i1}^T, x_{i1}^T, z_t = 1) - \hat{\mu}(z_{i1}^T, x_{i1}^T, z_t = 0) \]

(15)

for \( t = 1, \ldots, T \); in particular, for \( t = 1 \),

\[ \hat{\theta} = \frac{\sum_{i \in s(z_1 = 1)} y_i}{n(z_1 = 1)} - \frac{\sum_{i \in s(z_1 = 0)} y_i}{n(z_1 = 0)}. \]
We also obtain
\[
\begin{align*}
\text{var}\{\hat{\theta}(z_t^{-1}, x_t^{-1})\} &= \text{var}\{\hat{\mu}(z_t^{-1}, x_t^{-1}, z_t = 1)\} + \text{var}\{\hat{\mu}(z_t^{-1}, x_t^{-1}, z_t = 0)\} \\
&= \frac{1}{n(z_t^{-1}, x_t^{-1}, z_t = 1)} + \frac{1}{n(z_t^{-1}, x_t^{-1}, z_t = 0)}
\end{align*}
\]
for \(t = 1, \ldots, T\); in particular, for \(t = 1\),
\[
\text{var}(\hat{\theta}) = \frac{1}{n(z_1 = 1)} + \frac{1}{n(z_1 = 0)}.
\]

In Appendix A3, we prove

**Proposition 1** Suppose that the outcome \(y\) is normal and has the same known variance for all given \((z_T^T, x_T^{-1})\). Then the score function \(U_{\theta(x_t^{-1}, x_t^{-1})}\) depends only on \(\theta(x_t^{-1}, x_t^{-1})\). Therefore \(\hat{\theta}(z_t^{-1}, x_t^{-1})\) is independent of the estimates of all other point parameters.

### 5.4 ML estimates of net effects of treatments

Following the procedure described in Section 4, we estimate the net effects of treatments by a regression of the obtained estimates of the point effects of treatments on the proportions of treatments. To have insight into the regression, we consider the case of \(T = 2\). The constraint (13) on \(\theta(z_1, x_1)\) implies
\[
\varphi_2 = \frac{\sum_{(z_1, x_1)} \hat{\theta}(z_1, x_1)/\text{var}\{\hat{\theta}(z_1, x_1)\}}{\sum_{(z_1, x_1)} 1/\text{var}\{\hat{\theta}(z_1, x_1)\}}
\]
with the variance
\[
\text{var}(\varphi_2) = \frac{1}{\sum_{(z_1, x_1)} 1/\text{var}\{\hat{\theta}(z_1, x_1)\}},
\]
where \(\hat{\theta}(z_1, x_1)\) is given by (13) for \(t = 2\) and \(\text{var}\{\hat{\theta}(z_1, x_1)\}\) by (16) for \(t = 2\).

The constraint (12) on \(\theta\) implies
\[
\varphi_1 = \hat{\theta} - \varphi_2\{\text{pr}(z_2 = 1 \mid z_1 = 1) - \text{pr}(z_2 = 1 \mid z_1 = 0)\}
\]
where $\hat{\theta}$ is given by (15) for \( t = 1 \).

Now we calculate the variance $\text{var}(\hat{\phi}_1)$ and the correlation $\text{cov}(\hat{\phi}_1, \hat{\phi}_2)$. The variance $\text{var}(\hat{\theta})$ is given by (16) for \( t = 1 \). Because $\hat{\theta}(z_1, x_1)$ are independent of $\hat{\theta}$ according to Proposition 1, we see that $\hat{\phi}_2$ is independent of $\hat{\theta}$. Thus we obtain

\[
\text{var}(\hat{\phi}_1) = \text{var}(\hat{\theta}) + \text{var}(\hat{\phi}_2) \{\text{pr}(z_2 = 1 \mid z_1 = 1) - \text{pr}(z_2 = 1 \mid z_1 = 0)\}^2
\]

and

\[
\text{cov}(\hat{\phi}_1, \hat{\phi}_2) = \text{var}(\hat{\phi}_2) \{\text{pr}(z_2 = 1 \mid z_1 = 1) - \text{pr}(z_2 = 1 \mid z_1 = 0)\}
\]

For an arbitrary \( T \), we treat constraint (14) as a linear regression with unequal variances $\text{var}\{\hat{\theta}(z_{t-1}^T, x_{t-1}^T)\}$. Using the standard techniques of a linear regression, we regress $\hat{\theta}(z_{t-1}^T, x_{t-1}^T)$ on $c^{(1)}(z_{t-1}^T, x_{t-1}^T)$ and $c^{(2)}(z_{t-1}^T, x_{t-1}^T)$ and $c^{(3)}(z_{t-1}^T, x_{t-1}^T)$ to estimate $\varphi_1$ and $\varphi_2$ and $\varphi_3$.

In this regression, we need $\text{var}\{\hat{\theta}(z_{t-1}^{t-1}, x_{t-1}^{t-1})\}$, which has been calculated by using a known variance of \( y \) given \((z_{1}^{T}, x_{1}^{T-1})\), as described in Section 5.3. If the variance of \( y \) given \((z_{1}^{T}, x_{1}^{T-1})\) is unknown, we estimate it, which is possible for short treatment sequence. Even for treatment sequence of median length, however, it may not be possible to estimate this variance. In this case, we use the model

\[\mu_i = \mu(z_{i1}^{t-1}, x_{i1}^{t-1}),\]
where $\mu_i = E(y_i \mid z_{i1}^t, x_{i1}^{t-1})$ and $\mu(z_{i1}^t, x_{i1}^{t-1}) = \mu(z_1^t = z_{i1}^t, x_1^{t-1} = x_{i1}^{t-1})$, to estimate $\text{var}\{\hat{\mu}(z_1^t, x_1^{t-1})\}$. The estimate is
\[
\text{var}\{\hat{\mu}(z_1^t, x_1^{t-1})\} = \frac{\sum_{i \in S(z_1^t, x_1^{t-1})} \{y_i - \hat{\mu}(z_1^t, x_1^{t-1})\}^2}{n(z_1^t, x_1^{t-1})(n(z_1^t, x_1^{t-1}) - 1)}.
\]

With $\text{var}\{\hat{\mu}(z_1^t, x_1^{t-1})\}$, we calculate the estimate of $\text{var}\{\hat{\theta}(z_1^{t-1}, x_1^{t-1})\}$ according to (3) and obtain
\[
\text{var}\{\hat{\theta}(z_1^{t-1}, x_1^{t-1})\} = \text{var}\{\hat{\mu}(z_1^{t-1}, x_1^{t-1}, z_t = 1)\} + \text{var}\{\hat{\mu}(z_1^{t-1}, x_1^{t-1}, z_t = 0)\}.
\]

5.5 ML estimates of net effects of treatments in long treatment sequence

For long treatment sequences, the number of possible strata $(z_1^{t-1}, x_1^{t-1})$ becomes huge at large $t$. With a finite sample, most of these strata do not have both active and control treatments of the variable $z_t$, and so the point effect $\theta(z_1^{t-1}, x_1^{t-1}, z_t)$ of treatment is not estimable on them. However, the treatment assignment often satisfies certain condition, which can be used to reduce the number of point parameters in estimation of net effects of treatments in long treatment sequence.

For illustration, we consider a Markov process, in which the assignment of $z_t$ $(t = 1, \ldots, T)$ depends only on the latest covariate and treatment $(z_{t-1}, x_{t-1})$, so that,
\[
\text{pr}(z_1^{t-2}, x_1^{t-2} \mid z_{t-1}, x_{t-1}, z_t) = \text{pr}(z_1^{t-2}, x_1^{t-2} \mid z_{t-1}, x_{t-1}).
\]

Consider the following mean of $y$ in stratum $(z_{t-1}, x_{t-1}, z_t)$
\[
\mu(z_{t-1}, x_{t-1}, z_t) = \sum_{z_1^{t-2}, x_1^{t-2}} \mu(z_1^t, x_1^{t-1})\text{prop}(z_1^{t-2}, x_1^{t-2} \mid z_{t-1}, x_{t-1}, z_t)
\]
\[
= \sum_{z_1^{t-2}, x_1^{t-2}} \mu(z_1^t, x_1^{t-1})\text{prop}(z_1^{t-2}, x_1^{t-2} \mid z_{t-1}, x_{t-1}).
\]
Taking average on both sides of (4) with respect to \( \text{prop}(z_{t-1}, x_{t-1}) \) and then using the equality above, we obtain the following point effect of treatment \( z_t = 1 \) on stratum \((z_{t-1}, x_{t-1})\)

\[
\theta(z_{t-1}, x_{t-1}) = \sum_{z_{t-2}, x_{t-2}} \theta(z_{t-1}, x_{t-1}) \text{prop}(z_{t-1}, x_{t-1} | z_{t-1}, x_{t-1}) \\
= \mu(z_{t-1}, x_{t-1}, z_t = 1) - \mu(z_{t-1}, x_{t-1}, z_t = 0).
\]

Stratum \((z_{t-1}, x_{t-1})\) is much larger than stratum \((z_{t-1}^{t-1}, x_{t-1}^{t-1})\) for large \( t \) and thus has a large probability of having both active and control values of \( z_t \). Therefore \( \theta(z_{t-1}, x_{t-1}) \) is estimable.

Taking average on both sides of constraint (14) with respect to \( \text{pr}(z_{t-2}, x_{t-2} | z_{t-1}, x_{t-1}) \), we obtain the constraint on \( \theta(z_{t-1}, x_{t-1}) \)

\[
\theta(z_{t-1}, x_{t-1}) = \varphi_1 c^{(1)}(z_{t-1}, x_{t-1}) + \varphi_2 c^{(2)}(z_{t-1}, x_{t-1}) + \varphi_3 c^{(3)}(z_{t-1}, x_{t-1}), \quad (17)
\]

with

\[
c^{(1)}(z_{t-1}, x_{t-1}) = \sum_{s=t}^{T-2} \{\text{pr}(z_s = 1 | z_{t-1}, x_{t-1}, z_t = 1) - \text{pr}(z_s = 1 | z_{t-1}, x_{t-1}, z_t = 0)\},
\]

\[
c^{(2)}(z_{t-1}, x_{t-1}) = \text{pr}(z_{T-1} = 1 | z_{t-1}, x_{t-1}, z_t = 1) - \text{pr}(z_{T-1} = 1 | z_{t-1}, x_{t-1}, z_t = 0),
\]

\[
c^{(3)}(z_{t-1}, x_{t-1}) = \text{pr}(z_T = 1 | z_{t-1}, x_{t-1}, z_t = 1) - \text{pr}(z_T = 1 | z_{t-1}, x_{t-1}, z_t = 0).
\]

The constant \( c^{(1)}(z_{t-1}, x_{t-1}) \) describes difference between sums of proportions of the employees receiving the treatments \( z_s = 1 \) \((s = t, \ldots, T - 2)\) in stratum \((z_{t-1}, x_{t-1}, z_t = 1)\) versus in stratum \((z_{t-1}^{t-1}, x_{t-1}, z_t = 0)\), and similarly for \( c^{(2)}(z_{t-1}, x_{t-1}) \) and \( c^{(3)}(z_{t-1}, x_{t-1}) \).

The estimate \( \hat{\mu}(z_{t-1}, x_{t-1}, z_t) \) is the average of \( y \) in stratum \((z_{t-1}, x_{t-1}, z_t)\). Then \( \hat{\theta}(z_{t-1}, x_{t-1}) = \hat{\mu}(z_{t-1}, x_{t-1}, z_t = 1) - \hat{\mu}(z_{t-1}, x_{t-1}, z_t = 0) \). Applying Proposition 1 to \( \hat{\theta}(z_{t-1}, x_{t-1}) \) expressed in terms of \( \hat{\theta}(z_{t-1}^{t-1}, x_{t-1}^{t-1}) \), we see that
\( \hat{\theta}(z_{t-1}, x_{t-1}) \) is independent of the estimates of point parameters at the other times, in particular,
\[
\text{cov}\{\hat{\theta}(z_{t-1}, x_{t-1}); \hat{\theta}(z_{s-1}, x_{s-1})\} = 0, \quad t \neq s.
\]
To obtain the variance \( \text{var}\{\hat{\theta}(z_{t-1}, x_{t-1})\} \), we can use the model
\[
\mu_i = \mu(z_{i(t-1)}, x_{i(t-1)}, z_{it}),
\]
where \( \mu_i = E(y_i \mid z_{i(t-1)}, x_{i(t-1)}, z_{it}) \) and \( \mu(z_{i(t-1)}, x_{i(t-1)}, z_{it}) = \mu(z_{t-1} = z_{i(t-1)}, x_{t-1} = x_{i(t-1)}, z_t = z_{it}) \), to estimate \( \text{var}\{\hat{\mu}(z_{t-1}, x_{t-1}, z_t)\} \) and then \( \text{var}\{\hat{\theta}(z_{t-1}, x_{t-1})\} \). With \( \hat{\theta}(z_{t-1}, x_{t-1}) \) and \( \text{var}\{\hat{\theta}(z_{t-1}, x_{t-1})\} \), we use (17) as regression model to estimate the net effects \( \varphi_1, \varphi_2 \) and \( \varphi_3 \).

### 5.6 Outcomes of other distributions

For some outcome distributions such as binomial one, \( \hat{\theta}(z_{t-1}^{l-1}, x_{t-1}^{l-1}) \) at time \( t \) may be correlated with estimates of point parameters at the other times. On the other hand, \( \hat{\mu}(z_{t-1}^{l-1}, x_{t-1}^{l-1}, z_t) \) and thus \( \hat{\theta}(z_{t-1}^{l-1}, x_{t-1}^{l-1}) \) are highly robust to point parameters at time \( s > t \), so that \( \hat{\theta}(z_{t-1}^{l-1}, x_{t-1}^{l-1}) \) at time \( t \) is weakly correlated with estimates of the point parameters at the other times and the correlation may be omitted. Therefore we may use the method described in Section 5.4 to estimate \( \varphi_1, \varphi_2 \) and \( \varphi_3 \). The situation for \( \hat{\mu}(z_{t-1}, x_{t-1}, z_t) \) and \( \hat{\theta}(z_{t-1}, x_{t-1}) \) is similar, and we may use the method described in Section 5.5 to estimate \( \varphi_1, \varphi_2 \) and \( \varphi_3 \) for long treatment sequence.

### 6 Practical Procedure of Estimating Net Effects of Treatments: a Hypothetical Study

We consider the same economic example of Section 5. For illustrative clarity, we consider the case of \( T = 2 \), but the same procedure can be used for treat-
ment sequences with \( T > 2 \). For \( T = 2 \), there are two treatment variables \( z_1 = 0,1 \) and \( z_2 = 0,1 \), one covariate \( x_1 = 0,1 \) and a normal outcome \( y \). The data is presented in Table 1 whereas the economic background is described in Section 5.1.

The hypothetical economic study is extension of a well-known hypothetical medical study (Robins, 2009). In the original study, the variability of all the variables is suppressed in order to illustrate the various aspects of sequential causal inference including causal directed acyclic graph, problems with the standard parametrization, the \( G \)-computation algorithm formula and estimation methods such as the marginal structural model and the \( g \)-estimation model. In our hypothetical study, we allow variability of the outcome \( y \) and estimate net effects of treatments by maximum likelihood.

The point effect of \( z_1 = 1 \) on the sample is
\[
\theta = \mu(z_1 = 1) - \mu(z_1 = 0)
\]
and the point effect of treatment \( z_2 = 1 \) on stratum \( (z_1, x_1) = (0,0), (0,1), (1,0), (1,1) \) is
\[
\theta(z_1, x_1) = \mu(z_1, x_1, z_2 = 1) - \mu(z_1, x_1, z_2 = 0).
\]
We estimate \( \theta \) and \( \theta(z_1, x_1) \) by the direct calculation described in Section 5.3 and present the estimates in Table 1. The estimates \( \hat{\theta}(z_1, x_1) \) are independent of \( \hat{\theta} \) according to Proposition 1. Clearly, they are also independent of one another because they are based on different strata \( (z_1, x_1) \).

We first suppose that there is no pattern among net effects of treatments, i.e. every net effect of treatment is different from another. So we have five net effects, \( \phi = \phi(z_1 = 1) \) and \( \phi(z_1, x_1) = \phi(z_1, x_1, z_2 = 1) \) with \( (z_1, x_1) = (0,0), (0,1), (1,0), (1,1) \). Decomposing the point effects of treatments into the net effects of treatments, we express the point effects of treatments in terms
of the net effects of treatments by
\[
\theta(z_1, x_1) = \phi(z_1, x_1), \quad \text{for } (z_1, x_1) = (0, 0), (0, 1), (1, 0), (1, 1),
\]
\[
\theta = \phi + \phi(z_1 = 1, x_1 = 0) \Pr(x_1 = 0, z_2 = 1 \mid z_1 = 1)
\]
\[
+ \phi(z_1 = 1, x_1 = 1) \Pr(x_1 = 1, z_2 = 1 \mid z_1 = 1)
\]
\[
- \phi(z_1 = 0, x_1 = 0) \Pr(x_1 = 0, z_2 = 1 \mid z_1 = 0)
\]
\[
- \phi(z_1 = 0, x_1 = 1) \Pr(x_1 = 1, z_2 = 1 \mid z_1 = 0).
\]

The proportions in the formula are given in Table 1. By linear regression of \( \hat{\theta} \) and \( \hat{\theta}(z_1, x_1) \) on the proportions, we obtain the estimates \( \hat{\phi} = 30, \hat{\phi}(z_1 = 1, x_1 = 1) = -20 \), and \( \hat{\phi}(z_1 = 0, x_1 = 0) = \hat{\phi}(z_1 = 1, x_1 = 0) = \hat{\phi}(z_1 = 0, x_1 = 1) = 20 \), together with their covariance matrix (not shown here).

Now we find pattern of the net effects in the framework of statistical modeling. By the usual significance test, we see that \( \hat{\phi} \) is different from the other net effects at a significance level of, say, 5%, and so is \( \hat{\phi}(z_1 = 1, x_1 = 1) \). Because \( \hat{\phi}(z_1 = 0, x_1 = 0) = \hat{\phi}(z_1 = 0, x_1 = 1) = \hat{\phi}(z_1 = 1, x_1 = 0) \), we hypothesize the following pattern of the net effects

\[
\begin{cases}
\phi = \varphi_1, \\
\phi(z_1 = 0, x_1 = 0) = \phi(z_1 = 0, x_1 = 1) = \phi(z_1 = 1, x_1 = 0) = \varphi_2, \\
\phi(z_1 = 1, x_1 = 1) = \varphi_3.
\end{cases}
\]

Hence the constraint on \( \theta \) and \( \theta(z_1, x_1) \) is
\[
\theta(z_1, x_1) = \varphi_2, \quad \text{for } (z_1, x_1) = (0, 0), (0, 1), (1, 0),
\]
\[
\theta(z_1 = 1, x_1 = 1) = \varphi_3,
\]
\[
\theta = \varphi_1 + \varphi_3 \Pr(x_1 = 1, z_2 = 1 \mid z_1 = 1)
\]
\[
+ \varphi_2 \{ \Pr(x_1 = 0, z_2 = 1 \mid z_1 = 1) - \Pr(x_1 = 0, z_2 = 1 \mid z_1 = 0) \}.
\]
\[-\Pr(x_1 = 1, z_2 = 1 \mid z_1 = 0)\].

By the linear regression of \(\hat{\theta}\) and \(\hat{\theta}(z_1, x_1)\) on the proportions, we obtain estimates of \(\varphi_1\), \(\varphi_2\) and \(\varphi_3\) and their covariance matrix, which are presented in Table 2. From the table, we see (1) \(\hat{\varphi}_1 = 30\) with \(\text{var}(\hat{\varphi}_1) = 3.17\), indicating a strong association between \(z_1\) and \(y\), and (2) \(\hat{\varphi}_3 = -20\) with \(\text{var}(\hat{\varphi}_3) = 4.4\), indicating a strong negative association between \(z_2\) and \(y\) given \((z_1 = 1, x_1 = 1)\).

Furthermore, if no unmeasured confounders exist as can be assessed by subject knowledge in combination of sensitivity analysis, these net effects of treatments are the causal net effects of treatments. Then the point (1) above implies that the bonus at \(t = 1\) remains effective on the productivity after \(T = 2\) and the employer perhaps should reward bonuses once in two months. Interestingly, the point (2) implies that the second bonus has not improved productivity if the first one has. In this case the employees perhaps have outperformed their capability for productivity.

7 Concluding Remarks

In this article, we have introduced the net effect of treatment in treatment sequence as parameter for the conditional distribution of outcome given all treatments and covariates and shown that the net effect of treatment is the causal net effect of treatment under the assumption of strongly ignorable treatment assignment. As a result, we can estimate the net effect of treatment and evaluate its causal interpretation in two separately steps. We have studied estimation of the net effect of treatment whereas the causal identification can be carried out by using subject knowledge in combination of usual sensitivity analyses. With point parametrization and without the treatment assignment assumption, we are able to estimate the net effect of treatment by maximum
likelihood in a straightforward way.

In our approach, we express pattern of net effects of treatments by constraint on point effects of treatments. Point effects of treatments are the effects of single-point treatments, so we can estimate them by standard methods. With estimates of point effects of treatments, we estimate net effects of treatments by treating constraint on point effects of treatments as a regression model.

Given data, model and the likelihood, our estimates of net effects of treatments are most efficient due to the nature of maximum likelihood estimation. They are also unbiased. Furthermore, they are consistent in many practical situations, where net effects of treatments have pattern of finite dimension. The consistency is true even when treatment sequence gets long and the number of point parameters increases exponentially. It is interesting to compare this consistency with the inconsistency of the ML estimate of the effect of a single-point treatment in adjustment of a confounder of infinite dimension (Robins & Ritov, 1997). In the latter case, the ML estimate of the treatment effect is highly correlated with that of the confounder of infinite dimension.

The major limitation of our approach to estimation of net effects of treatments is that the variability of treatments and covariates has been ignored. In much of the current literature on estimation of causal net effects of treatments, this variability has also been ignored. No matter if the net effect of treatment is causal or not, however, it is important to incorporate this variability into the estimation. On the other hand, our method is based on the conditional likelihood of a final outcome given all treatments and covariates, which implies that the variability of treatments and covariates can be considered separately and based on the likelihood of treatments and covariates.

Due to the scope of this article, we have only considered a relative simple
setting: treatments are assigned at fixed times, treatments and covariates are
discrete, there is no missing data, the outcome model is linear and the point
and net effects of treatments are measured by differences. However, methods
are available to estimate the effect of a single-point treatment in more complex
settings. We believe that analogous methods can be developed to estimate net
effects of treatments in treatment sequence in more complex setting.

Appendix

A1: Deriving formula (3)

Like \( z_t \), let \( z_t^* \) also indicate the treatments at time \( t \). The assumption of
strongly ignorable assignment of treatment \( z_t^* \) (\( t = 1, \ldots, T \)) is

\[
\begin{align*}
& x_i^{T-1}(z_i^{T-1}), y(z_i^T) \perp z_i^*, z_i^{T-1}, x_i^{T-1} \\
& 0 < \text{pr}(z_i^* \mid z_i^{T-1}, x_i^{T-1}) < 1
\end{align*}
\]

(18)

for any treatment sequence \( z_i^{T} \) given the variables \( (z_i^{T-1}, x_i^{T-1}) \). Here \( A \perp B \mid C \)
means that \( A \) is conditionally independent of \( B \) given \( C \). The variable \( z_i^* \)
indicates the treatments to be randomly assigned at \( t \) whereas \( z_i \) in \( z_i^{T} \) indicates
the treatments at \( t \) in the treatment sequence. Under assumption (18), we are
going to derive (3) from (2) by mathematical induction.

From assumption (18) at \( t = T \), i.e.

\[
\begin{align*}
& y(z_T) \perp z_T^* \mid z_1^{T-1}, x_1^{T-1} \\
& 0 < \text{pr}(z_T^* \mid z_1^{T-1}, x_1^{T-1}) < 1
\end{align*}
\]

we obtain

\[
\mu(z_1^{T-1}, x_1^{T-1}, z_T) = E(y(z_T) \mid z_1^{T-1}, x_1^{T-1}, z_T) = E\{y(z_T) \mid z_1^{T-1}, x_1^{T-1}\}. \tag{19}
\]

Combining (19) with (2) at \( t = T \), we obtain

\[
\nu(z_1^{T-1}, x_1^{T-1}, z_T) = \mu(z_1^{T-1}, x_1^{T-1}, z_T) = E\{y(z_T) \mid z_1^{T-1}, x_1^{T-1}\},
\]

26
\[ \phi(z_1^{T-1}, x_1^{T-1}, z_T) = E\{y(z_T) \mid z_1^{T-1}, x_1^{T-1}\} - E\{y(z_T = 0) \mid z_1^{T-1}, x_1^{T-1}\} \]

which is (3) at \( t = T \).

Assuming that (3) is also true at times \( T - 1, \ldots, t + 1 \), we are going to derive (3) at \( t \). Using (19), we have

\[
\mu(z_1^t, x_1^{t-1}) = \sum_{z_1^{T}, x_1^{T-1}} \mu(z_1^{T}, x_1^{T-1}) \Pr(z_1^{T}, x_1^{T-1} \mid z_1^t, x_1^{t-1})
\]

\[
= \sum_{z_1^{T}, x_1^{T-1}} E\{y(z_T) \mid z_1^{T-1}, x_1^{T-1}\} \Pr(z_1^{T}, x_1^{T-1} \mid z_1^t, x_1^{t-1})
\]

Let

\[
A(s) = \sum_{z_1^s, x_1^{s-1}} E\{y(z_s, z_1^{T}, x_1^{T-1} = 0) \mid z_1^s, x_1^{s-1}\} \Pr(z_1^{s}, x_1^{s-1} \mid z_1^t, x_1^{t-1})
\]

for \( s = T, \ldots, t + 1 \), and \( A(t) = E\{y(z_t, z_1^{T}, x_1^{T-1} = 0) \mid z_1^t, x_1^{t-1}\} \). Noticeably, \( A(T) = \mu(z_1^t, x_1^{t-1}) \).

We rewrite \( A(T) \) by

\[
A(T) = \sum_{z_1^{T}, x_1^{T-1}} [E\{y(z_T) \mid z_1^{T-1}, x_1^{T-1}\} - E\{y(z_T = 0) \mid z_1^{T-1}, x_1^{T-1}\}] \Pr(z_1^{T}, x_1^{T-1} \mid z_1^t, x_1^{t-1})
\]

\[
+ \sum_{z_1^{T}, x_1^{T-1}} E\{y(z_T = 0) \mid z_1^{T-1}, x_1^{T-1}\} \Pr(z_1^{T}, x_1^{T-1} \mid z_1^t, x_1^{t-1}) \]

\[
= \sum_{z_1^{T-1}, x_1^{T-2}} \sum_{z_T > 0} \phi(z_1^{T-1}, x_1^{T-1}, z_T) \Pr(z_1^{T-1}, x_1^{T-1}, z_T \mid z_1^t, x_1^{t-1})
\]

\[
+ \sum_{z_1^{T-1}, x_1^{T-2}} E\{y(z_T = 0) \mid z_1^{T-1}, x_1^{T-2}\} \Pr(z_1^{T-1}, x_1^{T-2} \mid z_1^t, x_1^{t-1})
\]

(20)

Here the first summation term in (20) is equal to the first summation term in (21) according to (3) at \( t = T \); the second summation term in (20), after being summed up over \( z_T \) and then \( x_{T-1} \), is equal to the second summation term in (21).
Assumption (18) at $t = T - 1$ implies

$$y(z_{T-1}, z_T) \perp z_{T-1}^* \mid z_1^{T-2}, x_1^{T-2}$$

which implies

$$E\{y(z_{T-1}, z_T = 0) \mid z_1^{T-2}, x_1^{T-2}\} = E\{y(z_{T-1}, z_T = 0) \mid z_1^{T-2}, x_1^{T-2}, z_{T-1}\}$$

$$= E\{y(z_T = 0) \mid z_1^{T-2}, x_1^{T-2}, z_{T-1}\}.$$ 

Hence the second summation term in (21) is equal to

$$\sum_{z_{t+1}^{T-1}, x_{t+1}^{T-2}} E\{y(z_{T-1}, z_T = 0) \mid z_1^{T-2}, x_1^{T-2}\} \text{pr}(z_{t+1}^{T-1}, x_{t+1}^{T-2} \mid z_t^t, x_t^0)$$

which is $A(T - 1)$.

Therefore we obtain

$$A(T) =$$

$$\sum_{z_{t+1}^{T-1}, x_{t+1}^{T-2}} \sum_{z_T > 0} \phi(z_1^{T-1}, x_1^{T-1}, z_T) \text{pr}(z_{t+1}^{T-1}, x_{t+1}^{T-2}, z_T \mid z_t^t, x_t^0) + A(T - 1).$$

We continue with the same procedure to rewrite $A(T - 1), \ldots, A(t + 1)$ consecutively and obtain

$$\mu(z_1^t, x_1^{t-1}) = \sum_{s=t+1}^T \sum_{z_{t+1}^{s-1}, x_{t+1}^{s-1}} \sum_{z_s > 0} \phi(z_1^{s-1}, x_1^{s-1}, z_s) \text{pr}(z_{t+1}^{s-1}, x_{t+1}^{s-1}, z_s \mid z_t^t, x_t^0) \mu(z_1^t, x_1^{t-1}) + E\{y(z_t, z_{t+1}^T = 0) \mid z_1^{t-1}, x_1^{t-1}\}.$$ 

Combining this with (2) at $t$, we obtain (3) at $t$.

**A2: Deriving formula (7)**

Using (4) at $t = T$, we obtain

$$\mu(z_1^T, x_1^{T-1}) = \mu(z_1^{T-1}, x_1^{T-1}, z_T = 0) + \theta(z_1^{T-1}, x_1^{T-1}, z_T),$$

(23)
where we take \( \theta(z_1^{T-1}, x_1^{T-1}, z_T = 0) = 0 \). Taking average on both sides of (23) with respect to \( \text{pr}(z_T | z_1^{T-1}, x_1^{T-1}) \), we obtain

\[
\mu(z_1^{T-1}, x_1^{T-1}) = \mu(z_1^{T-1}, x_1^{T-1}, z_T = 0) + \sum_{z_T} \theta(z_1^{T-1}, x_1^{T-1}, z_T^*) \text{pr}(z_T^* | z_1^{T-1}, x_1^{T-1})
\]

which implies

\[
\mu(z_1^{T-1}, x_1^{T-1}, z_T = 0) = -\sum_{z_T} \theta(z_1^{T-1}, x_1^{T-1}, z_T^*) \text{pr}(z_T^* | z_1^{T-1}, x_1^{T-1}) + \mu(z_1^{T-1}, x_1^{T-1}).
\]

Inserting this into (23), we obtain

\[
\mu(z_1^T, x_1^{T-1}) = \sum_{z_T} -\theta(z_1^{T-1}, x_1^{T-1}, z_T^*) \text{pr}(z_T^* | z_1^{T-1}, x_1^{T-1}) + \theta(z_1^{T-1}, x_1^{T-1}, z_T) + \mu(z_1^{T-1}, x_1^{T-1}).
\]  

Using (5) at \( t = T - 1 \) and then following the above procedure, we obtain

\[
\mu(z_1^{T-1}, x_1^{T-1}) = \sum_{x_{T-1}} -\gamma(z_1^{T-1}, x_1^{T-2}, x_{T-1}^*) \text{pr}(x_{T-1}^* | z_1^{T-1}, x_1^{T-2}) + \gamma(z_1^{T-1}, x_1^{T-2}, x_{T-1}) + \mu(z_1^{T-1}, x_1^{T-2}).
\]

Inserting (25) into (24), we obtain

\[
\mu(z_1^T, x_1^{T-1}) = \sum_{z_T} -\theta(z_1^{T-1}, x_1^{T-1}, z_T^*) \text{pr}(z_T^* | z_1^{T-1}, x_1^{T-1}) + \theta(z_1^{T-1}, x_1^{T-1}, z_T) + \sum_{x_{T-1}} -\gamma(z_1^{T-1}, x_1^{T-2}, x_{T-1}^*) \text{pr}(x_{T-1}^* | z_1^{T-1}, x_1^{T-2}) + \gamma(z_1^{T-1}, x_1^{T-2}, x_{T-1}) + \mu(z_1^{T-1}, x_1^{T-2}).
\]

We go on with the same procedure for \( \mu(z_1^{T-1}, x_1^{T-2}), \ldots, \mu(z_1) \) consecutively and finally obtain (7).

Formula (24) is true for any \( T \). Taking \( T = t \), we obtain

\[
\mu(z_1^t, x_1^{t-1}) = \sum_{z_{t}^* > 0} -\theta(z_1^{t-1}, x_1^{t-1}, z_{t}^*) \text{pr}(z_{t}^* | z_1^{t-1}, x_1^{t-1}) + \theta(z_1^{t-1}, x_1^{t-1}, z_t) + \mu(z_1^{t-1}, x_1^{t-1})
\]

which will be used in Appendix A3.
A3: Proving Proposition\[1\]

In the example of Section 6, treatment \( z_t \) takes either one or zero and \( \theta(z_{1t}^{-1}, x_{1t}^{-1}, z_t = 1) \) is denoted by \( \theta(z_{1t}^{-1}, x_{1t}^{-1}) \). According to the chain rule, the score function for \( \theta(z_{1t}^{-1}, x_{1t}^{-1}) \) is equal to

\[
U_{\theta(z_{1t}^{-1}, x_{1t}^{-1})} = \sum_{z_{1t}^{*T}, x_{1t}^{*(T-1)}} U_{\mu(z_{1t}^{*T}, x_{1t}^{*(T-1)}, \theta_{1})} \frac{\partial \mu(z_{1t}^{*T}, x_{1t}^{*(T-1)}, \theta_{1})}{\partial \theta(z_{1t}^{-1}, x_{1t}^{-1})}.
\]

(27)

Let \( I_a(x) \) be an indicator function taking one if \( x = a \) and zero otherwise.

Using formula (7), which has been proved in Appendix A2, we obtain

\[
\mu(z_{1t}^{*T}, x_{1t}^{*(T-1)}) = \sum_{t=1}^{T} \left\{ -\theta(z_{1t}^{*(t-1)}, x_{1t}^{*(t-1)}) \text{pr}(z_{it}^{**} = 1 | z_{1i}^{*}, x_{1i}^{*(t-1)}) \right. \\
+ \theta(z_{1t}^{*(t-1)}, x_{1t}^{*(t-1)})I_{1}(z_{1t}^{*}) \left. \right\} + A
\]

where \( A \) is some function of the terms that do not depend on \( \theta(z_{1t}^{*(t-1)}, x_{1t}^{*(t-1)}) \) \((t = 1, \ldots, T)\). Hence we obtain

\[
\frac{\partial \mu(z_{1t}^{*T}, x_{1t}^{*(T-1)})}{\partial \theta(z_{1t}^{-1}, x_{1t}^{-1})} = \frac{\partial \mu(z_{1t}^{*T}, x_{1t}^{*(T-1)})}{\partial \theta(z_{1t}^{-1}, x_{1t}^{-1})} = (28)
\]

\[I_{(z_{1t}^{-1}, x_{1t}^{-1})}(z_{1t}^{*}) = \text{pr}(z_{1t}^{**} = 1 | z_{1t}^{*}) \}
\]

Furthermore, the score function \( U_{\mu(z_{1t}^{*T}, x_{1t}^{*(T-1)})} \) for \( \mu(z_{1t}^{*T}, x_{1t}^{*(T-1)}) \) is

\[
U_{\mu(z_{1t}^{*T}, x_{1t}^{*(T-1)})} = \sum_{i \in s(z_{1t}^{*T}, x_{1t}^{*(T-1)})} \{ y_i - \mu(z_{1t}^{*T}, x_{1t}^{*(T-1)}) \}
\]

(29)

because \( y \) is normal, where the variance of \( y \) given \( (z_{1t}^{*T}, x_{1t}^{*(T-1)}) \) is assumed to be one for notational simplicity.

Inserting (28) and (29) into (27) and then summing the expression over \( (x_{1t}^{*(T-1)}, z_{1t}^{*T}) \), we obtain

\[
U_{\theta(z_{1t}^{-1}, x_{1t}^{-1})} = \sum_{z_{1t} = 0, 1} \left\{ I_{1}(z_{1t}^{*}) - \text{pr}(z_{1t}^{**} = 1 | z_{1t}^{*}, x_{1t}^{*(T-1)}) \right\} \sum_{i \in s(z_{1t}^{*T}, x_{1t}^{*(T-1)})} \{ y_i - \mu(z_{1t}^{*T}, x_{1t}^{*(T-1)}, z_{1t}^{*}) \} = 30
From this formula, we see that \( U \) proving the proposition.

Replacing \( z_t \) by \( z_t^* \) and \( z_t^* \) by \( z_t^{**} \) in formula (26) and noticing that \( z_t^* \) and \( z_t^{**} \) take either one or zero, we obtain

\[
\mu(z_t^{l-1}, x_t^{l-1}, z_t^*) = \theta(z_t^{l-1}, x_t^{l-1}) \left\{ I_1(z_t^*) - \text{pr}(z_t^{**} = 1 | z_t^{l-1}, x_t^{l-1}) \right\} + \mu(z_t^{l-1}, x_t^{l-1}).
\]

Hence we obtain

\[
U_{\theta(z_t^{l-1}, x_t^{l-1})} = \sum_{z_t^{*} = 0, 1} \left\{ I_1(z_t^*) - \text{pr}(z_t^{**} = 1 | z_t^{l-1}, x_t^{l-1}) \right\} \left\{ \sum_{i \in s(z_t^{l-1}, x_t^{l-1}, z_t^*)} y_i - n(z_t^{l-1}, x_t^{l-1}, z_t^*) \right\} \theta(z_t^{l-1}, x_t^{l-1}) \left\{ I_1(z_t^*) - \text{pr}(z_t^{**} = 1 | z_t^{l-1}, x_t^{l-1}) \right\} - n(z_t^{l-1}, x_t^{l-1}, z_t^*) \mu(z_t^{l-1}, x_t^{l-1}).
\]

Furthermore, we have

\[
\sum_{z_t^{*} = 0, 1} \left\{ I_1(z_t^*) - \text{pr}(z_t^{**} = 1 | z_t^{l-1}, x_t^{l-1}) \right\} n(z_t^{l-1}, x_t^{l-1}, z_t^*) \mu(z_t^{l-1}, x_t^{l-1}) = \{ n(z_t^{l-1}, x_t^{l-1}, z_t^*) = 1 \} - \text{pr}(z_t^{**} = 1 | z_t^{l-1}, x_t^{l-1}) n(z_t^{l-1}, x_t^{l-1}) \} \mu(z_t^{l-1}, x_t^{l-1}) = \{ n(z_t^{l-1}, x_t^{l-1}, z_t^*) = 1 \} - n(z_t^{l-1}, x_t^{l-1}, z_t^{**} = 1) \} \mu(z_t^{l-1}, x_t^{l-1}) = 0.
\]

Therefore we obtain

\[
U_{\theta(z_t^{l-1}, x_t^{l-1})} = \sum_{z_t^{*} = 0, 1} \left\{ I_1(z_t^*) - \text{pr}(z_t^{**} = 1 | z_t^{l-1}, x_t^{l-1}) \right\} \left\{ \sum_{i \in s(z_t^{l-1}, x_t^{l-1}, z_t^*)} y_i - n(z_t^{l-1}, x_t^{l-1}, z_t^*) \right\} \theta(z_t^{l-1}, x_t^{l-1}) \left\{ I_1(z_t^*) - \text{pr}(z_t^{**} = 1 | z_t^{l-1}, x_t^{l-1}) \right\}.
\]

From this formula, we see that \( U_{\theta(z_t^{l-1}, x_t^{l-1})} \) depends only on \( \theta(z_t^{l-1}, x_t^{l-1}) \), thus proving the proposition.
References

Frangakis, C. E. & Rubin, D. B. (2002), ”Principal stratification in Causal Inference,” *Biometrics*, 58, 21–29.

Henderson, R., Ansell, P. & Alshibani, D. (2010), ”Regret-Regression for Optimal Dynamic Treatment Regimes”, *Biometrics*, 66, 1192-1201.

Murphy, S. A., Van Der Laan, J., Robins, J. M. & CPPRG (2001), ”Marginal Mean Model for Dynamic Regimes”, *Journal of American Statistical Association*, 96, 1410-1423.

Murphy, S. A. (2003), ”Optimal dynamic treatment regions”, *Journal of the Royal Statistical Society: Series B*, 62, 331–354.

Robins, J. M. (1986), ”A new approach to causal inference in mortality studies with saturated exposure periods - application to control of the healthy worker survival effect”, *Mathematical Modeling*, 7, 1393–1512.

Robins, J. M. (1989), ”The control of confounding by intermediate variables”, *Statistics in Medicine*, 8, 679–701.

Robins, J. M. (1992), ”Estimation of the time-dependent accelerated failure time model in the presence of confounding factors”, *Biometrika*, 79, 321–334.

Robins, J. M. (1997), ”Causal inference from complex longitudinal data”, In *Latent variable modeling and applications to causality, Lecture notes in Statistics 120*, ed. by Berkane, M., pp. 69–117, New York: Springer-Verlag.

Robins, J. M. (1999), ”Association, causation and marginal structural models”, *Synthese*, 121, 151–179.

Robins, J. M. (2004), ”Optimal structural nested models for optimal sequential decisions”, In *Lecture notes in Statistics 179*, ed. by Berkane, M., pp. 189–326, New York: Springer-Verlag.

Robins, J. M. (2009), ”Longitudinal Data Analysis”, In *Handbooks of*
Modern Statistical Methods, ed. by Fitzmaurice, G., pp. 553–599, Chapman and Hall / CRC

Robins, J. M., Rotnitzky, A. & Scharfstein, D. (1999), ”Sensitivity Analysis for Selection Bias and Unmeasured Confounding in Missing Data and Causal Inference Models”, In Statistical Models in Epidemiology: The Environment and Clinical Trials, ed. by Halloran, M. E. & Berry, D., IMA Volume 116, pp. 1–92, NY: Springer-Verlag.

Robins, J. M. & Wasserman, L. (1997), ”Estimation of effects of Sequential Treatments by Reparameterizing Directed Acyclic Graph”, In Proceedings of the Thirteenth Conference on Uncertainty in Artificial intelligence, Providence Rhode Island, August 1-3, 1997, ed. by Gerger, D. & Shenoy, P., pp. 409–420, San Francisco: Morgan Kaufmann.

Robins, J. M. & Ritov, Y. (1997), ”Towards a curse of dimensionality asymptotic theory for semi-parametric models”, Statistics in Medicine, 16, 285–319.

Rosenbaum, P. R. (1984), ”The consequence of adjustment for a concomitant variable that has been affected by the treatment”, Journal of the Royal Statistical Society: Series A, 147, 656–666.

Rosenbaum, P. R. & Rubin, D. B. (1983), ”The central role of the propensity score in observational studies for causal effects”, Biometrika, 70, 41-55.

Rosenbaum, P. R. (1995), ”Observational studies”, New York, NY: Springer Rubin, D. B. (2005), ”Causal inference using potential outcomes: design, modeling, decisions”, Journal of the American Statistical Association, 100, 322-331.