The International Journal of Biostatistics

Volume 8, *Issue* 1 2012 *Article* 24

Instruments and Bounds for Causal Effects under the Monotonic Selection Assumption

Masataka Taguri, *Yokohama City University*
Yasutaka Chiba, *Kinki University School of Medicine*

Recommended Citation:
Taguri, Masataka and Chiba, Yasutaka (2012) "Instruments and Bounds for Causal Effects under the Monotonic Selection Assumption," *The International Journal of Biostatistics*: Vol. 8: Iss. 1, Article 24.
DOI: 10.1515/1557-4679.1386

Instruments and Bounds for Causal Effects under the Monotonic Selection Assumption

Masataka Taguri and Yasutaka Chiba

Abstract

Noncompliance with assigned treatment is an important problem of randomized clinical trials. In this situation, the structural mean model (SMM) approach focuses on the average treatment effect among patients actually treated (ATT). In contrast, the principal stratification (PS) approach addresses the effect on a certain subgroup defined by latent compliance behavior. While these approaches target different causal effects, the estimators have the same form as the classical instrumental variable estimator, under the assumption of no effect modification (NEM) and monotonic selection. In this article, we clarify the relation between SMM and PS under the monotonic selection assumption. Specifically, we translate the NEM assumption for the SMM estimator into the words of the PS approach. Then, we propose a new bound for the ATT by making a possibly more plausible assumption than the NEM assumption based on the PS approach. Furthermore, we extend these results to the average treatment effect for the entire population. The proposed bounds are illustrated with applications to a real clinical trial data. Although our assumption cannot be empirically verified, the proposed bounds can be considerably tighter than those previously proposed.

KEYWORDS: bounds, causal inference, noncompliance, principal stratification, structural mean model

Author Notes: The authors thank the reviewers for their constructive comments and suggestions. This work was supported partially by Grant-in-Aid for Scientific Research (No. 23700344, 24700278) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

1. INTRODUCTION

In randomized clinical trials, researchers are often interested in estimating the causal effect of a treatment on some outcome. However, patients often fail to adhere to their assigned treatment and select other trial treatments. Such noncompliance to assigned treatments is a common feature of clinical trials. Several approaches to estimate the causal treatment effects under the presence of noncompliance have been proposed in the causal inference literature (e.g., Sato, 2006; Bellamy et al., 2007; Pearl, 2009; Chiba, 2011). The average treatment effect is often discussed on the entire study population (average treatment effect for the entire population; ATE); researchers would also be interested in the average treatment effect on the patients actually treated (average treatment effect among the treated; ATT). These are estimated using the structural mean model (SMM) (Robins, 1989, 1994). The estimator of the ATT (i.e., the SMM estimator) has the same form as the classical instrumental variable (IV) estimator under the assumption of no effect modification (NEM). Moreover, the ATE has the same form as the IV estimator under somewhat stronger NEM assumptions than that for the SMM estimator (Robins, 1989).

Recently, Clarke and Windmeijer (2010) investigated the SMM estimator, in which the NEM assumption was highlighted. They showed that the NEM assumption depends crucially on the unknown causal model that generated the data by using the nonparametric structural equation model (Pearl, 2009). In this article, we discuss the NEM assumption in the framework of the principal stratification (PS) approach (Frangakis and Rubin, 2002; Rubin, 2004). Such discussions have not been conducted in Clarke and Windmeijer (2010). First, we translate the NEM assumption for the SMM estimator into the words of the PS approach. Second, we propose new bounds for the ATT by making a possibly more plausible assumption than the NEM assumption based on the PS approach. Finally, we extend these results to the ATE.

To achieve these objectives, this article is organized as follows. In Section 2, we present the framework used in this article. In Section 3, the NEM assumptions for the ATT and ATE are translated into the words of the PS approach. In addition, new bounds for the ATT and ATE are proposed with new assumptions based on the PS approach. Although our assumption cannot be empirically verified, the proposed bounds can be considerably tighter than those previously proposed. In Section 4, the proposed bounds are illustrated using a classic randomized trial. Section 5 concludes with a discussion.

2. FRAMEWORK

We present the notations and assumptions used through this article in Section 2.1 and review the PS approach in Section 2.2.

2.1. Notation and assumptions

We employed the potential outcomes or the counterfactual framework (Rubin, 1974, 1978, 1990). Let Z denote the randomization-assigned indicator, with $Z = 1$ and $Z = 0$ indicating the test treatment and the control treatment, respectively. Let X denote the corresponding indicator for the treatment actually received. Here, $X = 1$ if the test treatment was received, and $X = 0$ if the control treatment was received. Y denotes the observed outcome. We assume that observed data (Y_i, X_i, Z_i) $(i = 1, \ldots, n)$ are n independent and identically distributed random vectors.

In contrast to the observed outcome variable Y, we define $Y(x, z)$ to be the potential outcome if the treatment assigned and received (Z, X) had been set to the values (z, x). Similarly, let $X(z)$ denote the potential treatment if Z was set to z. We make the following four assumptions:

(i) The stable unit treatment value assumption (Rubin, 1990) or the no-interference assumption (Cole and Hernán, 2008) states that the potential outcome $Y(x, z)$ for an individual does not depend on the treatment assigned or the treatment actually received by any other patient.

(ii) Exclusion restriction $Y(x, z) = Y(x)$ constrains the effect of the treatment assignment to the study outcome only through its effect on the treatment choice.

(iii) Consistency assumption $Y(X) = Y$, i.e., the value of Y that would have been observed if X had been set to its actual value is equal to the actually observed value of Y. Therefore, the only potential outcome for an individual being observed is the potential outcome $Y(x)$, that is, the value of Y that would have been observed if X was set to its actual value. Similarly, $X(Z) = X$.

(iv) Independence assumption, which states that Z is independent of the potential treatment $X(z)$ and the potential outcome $Y(x)$ (Holland, 1986). This assures that expectations of the potential outcomes are constant across the sub-populations of subjects assigned to different treatment arms; $\mathrm{E}[Y(x) \mid Z = 1] = \mathrm{E}[Y(x) \mid Z = 0]$. Similarly, $\mathrm{E}[X(z) \mid Z = 1] = \mathrm{E}[X(z) \mid Z = 0]$.

In addition to these four assumptions that are made in the causal inference literature, we require the monotonic selection assumption, that is, $X(1) \geq X(0)$ for all individuals. Sometimes, this is called "monotonicity assumption."

2.2. Principal stratification

We applied the principal stratification approach (Frangakis and Rubin, 2002; Rubin, 2004). This approach considers four types of participants that define four principal strata.

- Always-takers: individuals who would receive the test treatment regardless of the assigned treatment arm, that is, $X(1) = X(0) = 1$.
- Never-takers: individuals who would receive the control treatment regardless of the assigned treatment arm, that is, $X(1) = X(0) = 0$.
- Compliers: individuals who would receive the test treatment if assigned to the test treatment arm, but would receive the control treatment if assigned to the control arm, that is, $X(1) = 1$ and $X(0) = 0$.
- Defiers: individuals who would receive the control treatment if assigned to the test treatment arm, but would receive the test treatment if assigned to the control arm, that is, $X(1) = 0$ and $X(0) = 1$.

If we use the notation $\pi_{st} \equiv \Pr(X(1) = s, X(0) = t)$ (≥ 0), then

$$\sum_{s=0}^{1}\sum_{t=0}^{1}\pi_{st} = 1,$$

and the relationships between π_{st} and $p_z \equiv \Pr(X = 1 \mid Z = z)$ are

$$\pi_{10} + \pi_{11} = p_1,\ \pi_{00} + \pi_{01} = 1 - p_1,\ \pi_{11} + \pi_{01} = p_0, \text{ and } \pi_{10} + \pi_{00} = 1 - p_0,$$

respectively, because $\Pr(X(z) = x) = \Pr(X(z) = x \mid Z = z) = \Pr(X = x \mid Z = z)$.

$\mathrm{E}[Y(x) \mid X = 1, Z = 1]$ can be expressed by the weighted sum of $\mathrm{E}[Y(x) \mid X(1) = 1, X(0) = 0]$ and $\mathrm{E}[Y(x) \mid X(1) = X(0) = 1]$ because the subgroup with $Z = 1$ and $X = 1$ includes compliers and always-takers but does not include never-takers or defiers. Here, the weights are the proportions of compliers and always-takers in these two strata. Therefore, $\mathrm{E}[Y(x) \mid X = 1, Z = 1]$ can be expressed as

$$\mathrm{E}[Y(x) \mid X = 1, Z = 1] = \frac{\pi_{10}\mathrm{E}[Y(x) \mid X(1) = 1, X(0) = 0] + \pi_{11}\mathrm{E}[Y(x) \mid X(1) = X(0) = 1]}{\pi_{10} + \pi_{11}}.$$

Likewise, $\mathrm{E}[Y(x) \mid X = x, Z = z]$ can be expressed as the weighted sum of $\mathrm{E}[Y(x) \mid X(1) = s, X(0) = t]$ as follows:

$$\mathrm{E}[Y(x) \mid X = 1, Z = 0] = \frac{\pi_{01}\mathrm{E}[Y(x) \mid X(1) = 0, X(0) = 1] + \pi_{11}\mathrm{E}[Y(x) \mid X(1) = X(0) = 1]}{\pi_{01} + \pi_{11}},$$

$$\mathrm{E}[Y(x) \mid X=0, Z=1] = \frac{\pi_{00}\mathrm{E}[Y(x) \mid X(1)=X(0)=0] + \pi_{01}\mathrm{E}[Y(x) \mid X(1)=0, X(0)=1]}{\pi_{00}+\pi_{01}},$$

$$\mathrm{E}[Y(x) \mid X=0, Z=0] = \frac{\pi_{00}\mathrm{E}[Y(x) \mid X(1)=X(0)=0] + \pi_{10}\mathrm{E}[Y(x) \mid X(1)=1, X(0)=0]}{\pi_{00}+\pi_{10}}$$

Here, we apply the monotonic selection assumption that $X(1) \geq X(0)$ for all individuals. This assumption implies that no defier exists, that is, $\pi_{01} = 0$ because $X(1) = 0$ and $X(0) = 1$ cannot hold simultaneously under $X(1) \geq X(0)$. Therefore, $\pi_{00} = 1 - p_1$, $\pi_{11} = p_0$ and $\pi_{10} = p_1 - p_0$, and the above four equations can be re-written as follows:

$$\mathrm{E}[Y(x) \mid X=1, Z=1] = \left\{ \begin{matrix} (p_1 - p_0)\mathrm{E}[Y(x) \mid X(1)=1, X(0)=0] \\ + p_0 \mathrm{E}[Y(x) \mid X(1)=X(0)=1] \end{matrix} \right\} \Big/ p_1 , \tag{1}$$

$$\mathrm{E}[Y(x) \mid X=1, Z=0] = \mathrm{E}[Y(x) \mid X(1)=X(0)=1], \tag{2}$$

$$\mathrm{E}[Y(x) \mid X=0, Z=1] = \mathrm{E}[Y(x) \mid X(1)=X(0)=0], \tag{3}$$

$$\mathrm{E}[Y(x) \mid X=0, Z=0] = \left\{ \begin{matrix} (1-p_1)\mathrm{E}[Y(x) \mid X(1)=X(0)=0] \\ + (p_1 - p_0)\mathrm{E}[Y(x) \mid X(1)=1, X(0)=0] \end{matrix} \right\} \Big/ (1-p_0), \tag{4}$$

where it is assumed that $\pi_{10} = p_1 - p_0 > 0$, that is, at least a complier exists. Let us use E_{xz} to denote $\mathrm{E}[Y \mid X = x, Z = z]$, and $E_{\bullet z}$ to denote $\mathrm{E}[Y \mid Z = z]$. Equations (1) and (2) with $x = 1$ yield

$$\mathrm{E}[Y(1) \mid X(1) = X(0) = 1] = E_{10}, \tag{5}$$

$$\mathrm{E}[Y(1) \mid X(1) = 1, X(0) = 0] = (p_1 E_{11} - p_0 E_{10})/(p_1 - p_0), \tag{6}$$

and equations (3) and (4) with $x = 0$ yield

$$\mathrm{E}[Y(0) \mid X(1) = X(0) = 0] = E_{01}, \tag{7}$$

$$\mathrm{E}[Y(0) \mid X(1) = 1, X(0) = 0] = \{(1 - p_0)E_{00} - (1 - p_1)E_{01}\}/(p_1 - p_0). \tag{8}$$

Thus, the difference between equations (6) and (8) yields

$$\delta_{10} = (E_{\cdot 1} - E_{\cdot 0})/(p_1 - p_0),$$

where $\delta_{st} \equiv \mathrm{E}[Y(1) - Y(0) \mid X(1) = s, X(0) = t]$. This equation means that the average treatment effect for compliers (complier-specific average treatment effect; CATE) is identified and equal to the IV estimand under the monotonic selection assumption (Angrist, Imbens, and Rubin, 1996a). Similarly, the ratio of equation (6) to (8) yields the CATE on the multiplicative scale. However, the ATT and ATE are not generally identified even under the monotonic selection assumption.

3. AVERAGE CAUSAL EFFECTS UNDER THE PRINCIPAL STRATIFICATION APPROACH

We translate the ATT and ATE into the words of the PS approach, and propose new bounds for the ATT and ATE by making a possibly more plausible assumption based on the PS approach. In this section, we discuss the difference measures. These are extended to the ratio measures in Appendix 1. The ATT is discussed in Section 3.1, and the results are extended to the ATE in Section 3.2.

3.1. Average treatment effect among the treated

The ATT can be formalized using the following nonparametric (saturated) additive SMM:

$$\mathrm{E}[Y \mid X, Z] - \mathrm{E}[Y(0) \mid X, Z] = (\psi_0 + \psi_1 Z)X, \tag{9}$$

where ψ_0 and ψ_1 are unknown causal parameters. $\psi_0 = \mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = 0]$ and $\psi_0 + \psi_1 = \mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = 1]$ are the ATT with $Z = 0$ and $Z = 1$, respectively. It is clear that neither of the SMM parameters in (9) can be identified because we have only one moment restriction with two unknown parameters. However, ψ_0 is identified and equal to the IV estimand under the following NEM assumption (Hernán and Robins, 2006; Clarke and Windmeijer, 2010):

ASSUMPTION 1. $\mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = 0] = \mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = 1]$; that is, $\psi_1 = 0$.

We can derive the following proposition by using the words of the PS approach:

PROPOSITION 1. *Suppose that the monotonic selection assumption holds. Then, Assumption 1 holds if and only if* $\delta_{10} = \delta_{11}$ *holds.*

PROOF. Substituting equations (2) and (1) into equation (9) yields

$$\psi_0 = \delta_{11},$$

$$\psi_0 + \psi_1 = \{(p_1 - p_0)\delta_{10} + p_0\delta_{11}\}/p_1.$$

Suppose that Assumption 1, that is, $\psi_1 = 0$, holds. Then, the difference between these two equations yields $(p_1 - p_0)(\delta_{10} - \delta_{11}) = 0$. Because $p_1 - p_0 > 0$ by assumption, $\delta_{10} = \delta_{11}$. Conversely, suppose that $\delta_{10} = \delta_{11} = \delta$. Then, the difference between these two equations yields $\psi_1 = \{(p_1 - p_0)\delta + p_0\delta\}/p_1 - \delta = 0$. □

Proposition 1 implies that, under the monotonic selection assumption, Assumption 1 is equivalent to common treatment effects for compliers and always-takers, and the additive SMM derives the IV estimator under $\delta_{10} = \delta_{11}$. This result was implied by Angrist, Imbens, and Rubin (1996b) in their reply to the comments of Heckman (1996). Conversely, if $\delta_{10} \neq \delta_{11}$, the IV estimator is a biased estimator of the ATTs with $Z = z$. We note that $\delta_{10} = \delta_{11} = \delta_{01} \Rightarrow \psi_1 = 0$ holds without the monotonic selection assumption; however, the converse does not hold.

It is obvious that the upper bounds on ψ_0 and $\psi_0 + \psi_1$ are δ_{10} if $\delta_{10} \geq \delta_{11}$ from the proof of Proposition 1. However, it would be difficult to speculate that δ_{10} is larger or smaller than δ_{11}. Thus, we propose an alternative assumption to derive new bounds for the ATT.

ASSUMPTION 2. *Either (a)* $\mathrm{E}[Y(x) \mid X(1) = X(0) = 1] \geq \mathrm{E}[Y(x) \mid X(1) = 1, X(0) = 0]$ *or (b)* $\mathrm{E}[Y(x) \mid X(1) = X(0) = 1] \leq \mathrm{E}[Y(x) \mid X(1) = 1, X(0) = 0]$ *holds for* $x = 0, 1$.

Under the monotonic selection assumption, $\mathrm{E}[Y(1) \mid X(1) = 1, X(0) = 0]$ and $\mathrm{E}[Y(1) \mid X(1) = X(0) = 1]$ can be estimated by equations (6) and (5), respectively. Thus, Assumption 2(a) or 2(b) with $x = 1$ can be evaluated from the observed data based on whether the value of $E_{10} - E_{11}$ is positive or negative because

$$\begin{aligned}&\mathrm{E}[Y(1) \mid X(1) = X(0) = 1] - \mathrm{E}[Y(1) \mid X(1) = 1, X(0) = 0] \\ &= E_{10} - (p_1E_{11} - p_0E_{10})/(p_1 - p_0) \\ &= p_1(E_{10} - E_{11})/(p_1 - p_0).\end{aligned}$$

PROPOSITION 2. *Suppose that the monotonic selection assumption holds. Then, under Assumption 2(a), the upper bounds for* $\psi_0 = \mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = 0]$ *and* $\psi_0 + \psi_1 = \mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = 1]$ *are*

$$\psi_0 \leq \psi_0^B,$$

$$\psi_0 + \psi_1 \leq (E_{\bullet 1} - E_{\bullet 0} + p_0\psi_0^B)/p_1,$$

where $\psi_0^B = \{p_1 E_{10} + (1-p_1)E_{01} - E_{\bullet 0}\}/(p_1 - p_0)$. *Moreover, the upper bound for ATT is*

$$\mathrm{E}[Y(1) - Y(0) \mid X = 1] \le \{(E_{\bullet 1} - E_{\bullet 0})\Pr(Z=1) + p_0 \psi_0^B\}/\Pr(X=1). \qquad (10)$$

Under Assumption 2(b), these results apply with the inequality signs reversed.

PROOF. As shown in the proof of Proposition 1, $\psi_0 = \delta_{11}$ under the monotonic selection assumption. Applying Assumption 2(a) to this equation yields

$$\begin{aligned}
&\psi_0 = \mathrm{E}[Y(1) \mid X(1) = X(0) = 1] - \mathrm{E}[Y(0) \mid X(1) = X(0) = 1] \\
&\le \mathrm{E}[Y(1) \mid X(1) = X(0) = 1] - \mathrm{E}[Y(0) \mid X(1) = 1, X(0) = 0] \\
&= E_{10} - \frac{(1-p_0)E_{00} - (1-p_1)E_{01}}{p_1 - p_0} \\
&= \frac{p_1 E_{10} + (1-p_1)E_{01} - E_{\bullet 0}}{p_1 - p_0}.
\end{aligned}$$

The inequality holds by Assumption 2(a), and the third equation holds from equations (5) and (8). Likewise, the upper bound of $\psi_0 + \psi_1 = \{(p_1 - p_0)\delta_{10} + p_0\delta_{11}\}/p_1$ becomes

$$\begin{aligned}
&\psi_0 + \psi_1 = \frac{1}{p_1}\left\{(p_1 - p_0)\frac{E_{\bullet 1} - E_{\bullet 0}}{p_1 - p_0} + p_0\psi_0\right\} \\
&\le \frac{E_{\bullet 1} - E_{\bullet 0} + p_0\psi_0^B}{p_1}
\end{aligned}.$$

Furthermore, from these results, the upper bound of $\mathrm{E}[Y(1) - Y(0) \mid X = 1]$ becomes

$$\begin{aligned}
&\mathrm{E}[Y(1) - Y(0) \mid X = 1] \\
&= \sum_{z=0}^{1} E[Y(1) - Y(0) \mid X = 1, Z = z]\Pr(Z = z \mid X = 1) \\
&= \psi_0 p_0 \frac{\Pr(Z=0)}{\Pr(X=1)} + (\psi_0 + \psi_1)p_1 \frac{\Pr(Z=1)}{\Pr(X=1)} \qquad (11) \\
&\le \frac{1}{\Pr(X=1)}\left\{\psi_0^B p_0 \Pr(Z=0) + \frac{E_{\bullet 1} - E_{\bullet 0} + p_0\psi_0^B}{p_1} p_1 \Pr(Z=1)\right\}
\end{aligned}$$

$$\leq \frac{(E_{\bullet 1} - E_{\bullet 0})\Pr(Z=1) + p_0\psi_0^B}{\Pr(X=1)}.$$

Under Assumption 2(b), these inequalities hold with the inequality signs reversed. □

We note that $\mathrm{E}[Y(1) - Y(0) \mid X = 1]$ is also equal to the IV estimand under Assumption 1. This is obvious because $\mathrm{E}[Y(1) - Y(0) \mid X = 1] = \psi_0$ when $\psi_1 = 0$ from equation (11).

3.2. Average treatment effect on the entire population

We extend Propositions 1 and 2 in Section 3.1 to the ATE. The ATE, $\mathrm{E}[Y(1) - Y(0)]$, is equal to the IV estimand under the following somewhat stronger assumption than Assumption 1 (Robins, 1994):

ASSUMPTION 3. $\mathrm{E}[Y(1) - Y(0) \mid X = x, Z = 0] = \mathrm{E}[Y(1) - Y(0) \mid X = x, Z = 1]$ *for* $x = 0, 1$.

For $x = 1$, Assumption 3 is a restatement of Assumption 1. We note that although Heckman (1997) used the alternative assumption $\mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = z] = \mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = z]$ for $z = 0, 1$ instead of Assumption 3, this assumption is equivalent to Assumption 3 (Hernán and Robins, 2006). We can derive the following proposition as an extension of Proposition 1.

PROPOSITION 3. *Suppose that the monotonic selection assumption holds. Then, Assumption 3 holds if and only if* $\delta_{10} = \delta_{11} = \delta_{00}$ *holds.*

PROOF. The proof of $\mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = 0] = \mathrm{E}[Y(1) - Y(0) \mid X = 1, Z = 1] \Leftrightarrow \delta_{10} = \delta_{11}$ follows the proof of Proposition 1. The proof of $\mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = 0] = \mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = 1] \Leftrightarrow \delta_{10} = \delta_{00}$ is also similar to that of Proposition 1. From equations (3) and (4), we have

$$\mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = 1] = \delta_{00},$$

$$\mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = 0] = \{(1 - p_1)\delta_{00} + (p_1 - p_0)\delta_{10}\}/(1 - p_0).$$

Assume that $\mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = 0] = \mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = 1]$ holds. Then, the difference between the above two equations yields $(p_1 - p_0)(\delta_{10} - \delta_{00}) = 0$. Because $p_1 - p_0 > 0$ by assumption, $\delta_{10} = \delta_{00}$. Conversely, assume that $\delta_{10} = \delta_{00} = \delta$. Then, the difference between the two abovementioned equations yields

$$\mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = 1] - \mathrm{E}[Y(1) - Y(0) \mid X = 0, Z = 0]$$

$$= \{(1 - p_1)\delta + (p_1 - p_0)\delta\}/(1 - p_0) - \delta$$
$$= 0.$$

Because Assumption 3 is that $\mathrm{E}[Y(1) - Y(0) \mid X = x, Z = 0] = \mathrm{E}[Y(1) - Y(0) \mid X = x, Z = 1]$ holds for both $x = 0$ and 1, the proof of Proposition 1 and the information given above complete the proof of Proposition 3. □

We note that, similar to Proposition 1, $\delta_{10} = \delta_{11} = \delta_{00} = \delta_{01}$ implies that Assumption 3 holds without the monotonic selection assumption; however, the converse does not hold.

In order to derive the new bound for the ATE, we extend Assumption 2 as follows:

ASSUMPTION 4. *Either (a)* $\mathrm{E}[Y(x) \mid X(1) = X(0) = 1] \geq \mathrm{E}[Y(x) \mid X(1) = 1, X(0) = 0] \geq \mathrm{E}[Y(x) \mid X(1) = X(0) = 0]$ *or (b)* $\mathrm{E}[Y(x) \mid X(1) = X(0) = 1] \leq \mathrm{E}[Y(x) \mid X(1) = 1, X(0) = 0] \leq \mathrm{E}[Y(x) \mid X(1) = X(0) = 0]$ *holds for* $x = 0, 1$.

As mentioned in Section 3.1, whether $\mathrm{E}[Y(1) \mid X(1) = X(0) = 1] - \mathrm{E}[Y(1) \mid X(1) = 1, X(0) = 0]$ is positive or negative can be evaluated from the observed data according to whether the value of $E_{10} - E_{11}$ is positive or negative. Likewise, whether $\mathrm{E}[Y(0) \mid X(1) = 1, X(0) = 0] - \mathrm{E}[Y(0) \mid X(1) = X(0) = 0]$ is positive or negative can be evaluated from the observed data according to whether the value of $E_{00} - E_{01}$ is positive or negative because from equations (7) and (8), we obtain

$$\mathrm{E}[Y(0) \mid X(1) = 1, X(0) = 0] - \mathrm{E}[Y(0) \mid X(1) = X(0) = 0]$$
$$= \{(1 - p_0)E_{00} - (1 - p_1)E_{01}\}/(p_1 - p_0) - E_{01}$$
$$= (1 - p_0)(E_{00} - E_{01})/(p_1 - p_0).$$

Thus, we can partly evaluate Assumption 4(a) or 4(b) with $x = 0$, 1 from the observed data. If both $E_{10} - E_{11}$ and $E_{00} - E_{01}$ take positive values, then Assumption 4(a) could be assumed. If both $E_{10} - E_{11}$ and $E_{00} - E_{01}$ take negative values, then Assumption 4(b) could be assumed. If one of them takes a positive value and the other is a negative value, Assumption 4 cannot be assumed.

PROPOSITION 4. *Suppose that the monotonic selection assumption holds. Then, under Assumption 4(a), the upper bound for the ATE is*

$$\mathrm{E}[Y(1) - Y(0)] \leq \{(1 - p_0)p_1(E_{11} - E_{00}) - p_0(1 - p_1)(E_{10} - E_{01})\}/(p_1 - p_0). \quad (12)$$

Under Assumption 4(b), the result applies with the inequality sign reversed.

PROOF. Because $\pi_{01} = 0$ under the monotonic selection assumption, we have

$$\mathrm{E}[Y(1) - Y(0)] = \pi_{00}\delta_{00} + \pi_{10}\delta_{10} + \pi_{11}\delta_{11}.$$

Applying Assumption 4(a) to this equation yields

$$\begin{aligned}
&\mathrm{E}[Y(1) - Y(0)] \\
&\leq (1 - p_1)\{\mathrm{E}[Y(1) \mid X(1) = 1, X(0) = 0] - \mathrm{E}[Y(0) \mid X(1) = X(0) = 0]\} \\
&\quad + (p_1 - p_0)\mathrm{E}[Y(1) - Y(0) \mid X(1) = 1, X(0) = 0] \\
&\quad + p_0\{\mathrm{E}[Y(1) \mid X(1) = X(0) = 1] - \mathrm{E}[Y(0) \mid X(1) = 1, X(0) = 0]\} \\
&= (1 - p_0)\mathrm{E}[Y(1) \mid X(1) = 1, X(0) = 0] + p_0\mathrm{E}[Y(1) \mid X(1) = X(0) = 1] \\
&\quad - p_1\mathrm{E}[Y(0) \mid X(1) = 1, X(0) = 0] - (1 - p_1)\mathrm{E}[Y(0) \mid X(1) = X(0) = 0].
\end{aligned}$$

After substituting equations (5)–(8) into this inequality, some algebra yields inequality (12). The lower bound under Assumption 4(b) holds with the inequality signs reversed. □

In practice, if one is willing to use our proposed bounds (Proposition 2 or 4), one should first consider the plausibility of the monotonic selection assumption and Assumption 2 or 4 based on the subject matter grounds. As noted above, we can partly evaluate Assumption 2 or 4 from the observed data by assessing the sign of $E_{10} - E_{11}$ and $E_{00} - E_{01}$. Then, our bounds would be used in conjunction with those proposed before (e.g., the monotone treatment response (MTR) assumption presented in the next section) to obtain narrower bounds.

4. ILLUSTRATION

For illustration, bounds proposed in Section 3 are applied to data from the Multiple Risk Factor Intervention Trial (MRFIT) (MRFIT Research Group, 1982). The MRFIT was a large field trial to test the effect of a multifactorial intervention program on mortality from coronary heart disease (CHD) in middle-aged men with sufficiently high risk-levels resulting from cigarette smoking, high serum cholesterol, and high blood pressure. Intervention consisted of hypertension medication, smoking cessation counseling, and dietary advice on ways of reducing blood cholesterol. All subjects were randomly assigned to the intervention program or the control group.

For this illustration, attention is restricted to the effects of cessation of cigarette smoking. This restriction followed Mark and Robins (1993) and was applied because of the paucity of differences achieved for the other risk factors. Table 1 summarizes the incidence of subject mortality due to CHD during the 7-year follow-up period based on the assigned treatment and the actual subject smoking status one year after the study entry. Z represents the assigned group (Z = 1 for the test group and Z = 0 for the control group); X is the actual smoking status one year after entry (X = 1 for smoking cessation and X = 0 for continued

smoking); and Y is the incidence of CHD deaths ($Y = 1$ for dead and $Y = 0$ for alive). The usual IV analysis yielded a risk difference of -0.82×10^{-2} (95% confidence interval [CI]: -4.59×10^{-2}, 2.95×10^{-2}) and a risk ratio of 0.58 (95% CI: 0.07, 4.82). The variance formulas are found in Greenland (2000) and Chiba (2010).

Table 1. The status of cigarette smoking and the incidence of mortality due to CHD in the MRFIT during a 7-year follow-up period.

Group	No. of Subjects	CHD deaths	Smoking status at 1 year	No. of subjects	CHD deaths
Test	3833	69	Quit	991	11
			Not quit	2842	58
Control	3830	74	Quit	374	4
			Not quit	3456	70
Totals	7663	143			

However, the IV estimate would be biased because no one can assure that $\delta_{11} = \delta_{10}$, that is, the average treatment effects for always-takers (who would quit smoking regardless of the assigned group) is equal to that for the compliers (who would quit smoking if assigned to the test group and would continue smoking if assigned to the control group). Therefore, we yielded bounds on the ATT and ATE under Assumption 4 (or under Assumption 2 for the ATT). Here, we note that in this trial, defiers are participants who would continue smoking if assigned to the test group and would quit smoking if assigned to the control group; such participants would not exist, although this cannot be confirmed from the observed data. Never-takers are participants who would continue smoking regardless of the assigned group. We further note that whether Assumption 4 (or 2) holds cannot also be confirmed from the observed data. Thus, it is important to discuss its plausibility. It seems likely that the mortality proportion for always-takers tended to be lower than that for never-takers and compliers because always-takers would be health-conscious individuals in comparison with never-takers and compliers. Conversely, the mortality proportion for never-takers would tend to be higher than that for always-takers and compliers. This observation shows that Assumption 4(b) is reasonable. The data yielded $E_{10} - E_{11} = -0.04 \times 10^{-2} < 0$ and $E_{00} - E_{01} = -0.02 \times 10^{-2} < 0$.

In order to assess the extent to which the bounds are narrowed by posing the assumptions, we compare the proposed bounds with those presented in the past literature. We here consider 3 types of bounds. First, when the outcome Y has finite range ([0,1] in this example), we can draw bounds without any assumptions other than the basic assumptions (i)-(iv) in Section 2.1. For the ATT, bounds are derived by substitution of 0 or 1 for $\mathrm{E}[Y(0) \mid X = 1]$. Because observed data contains no information about $\mathrm{E}[Y(0) \mid X = 1]$, the width of bounds for $\mathrm{E}[Y(1) -$

$Y(0) \mid X = 1]$ is always 1. For the ATE, we can use bounds proposed by Balke and Pearl (1997) and those by Robins (1989) and Manski (1990). In Appendix 2, we show that the proposed bounds improve the Robins-Manski bounds under the monotonic selection assumption. Although the Balke-Pearl bounds can be narrower than the Robins-Manski bounds in some situations, they gave the same results in our application.

Second, with bounded outcome, we could improve nonparametric bounds described above by posing the monotonic selection assumption. For binary outcomes, the bounds for the ATT are as follows:

$$\begin{aligned}
&\mathrm{E}[Y \mid X = 1] - \frac{\{(1-p_0)E_{00} - (1-p_1)E_{01}\}\Pr(Z=1) + p_0}{\Pr(X=1)} \\
&\le \mathrm{E}[Y(1) - Y(0) \mid X = 1] \\
&\le \mathrm{E}[Y \mid X = 1] - \frac{\{(1-p_0)E_{00} - (1-p_1)E_{01}\}\Pr(Z=1)}{\Pr(X=1)}.
\end{aligned} \tag{13}$$

The derivation is given in Appendix 3. For the ATE, the monotonic selection assumption does not improve the Balke-Pearl bounds, as noted by Robins and Greenland (1996) and Angrist, Imbens, and Rubin (1996b).

Third, we could assume further unverifiable assumptions based on the subject-matter considerations. We yielded the bounds under the assumptions of (a) the monotone treatment response (MTR), $Y(1) \le Y(0)$ for all participants and (b) the monotone treatment selection (MTS), $\mathrm{E}[Y(x) \mid X = 1] \le \mathrm{E}[Y(x) \mid X = 0]$ and $\mathrm{E}[Y(x) \mid X = 1, Z = z] \le \mathrm{E}[Y(x) \mid X = 0, Z = z]$ for $x = 0, 1$ and $z = 0, 1$ (Manski, 1997; Manski and Pepper, 2000; Chiba, 2011). See Chiba (2011) for the discussion of the plausibility of these assumptions on the MRFIT data. Under these assumptions, bounds for the ATT and ATE are as follows without the monotonic selection assumption:

$$\begin{aligned}
&\mathrm{E}[Y \mid X = 1] - \mathrm{E}[Y \mid X = 0] \le \mathrm{E}[Y(1) - Y(0) \mid X = 1] \le 0, \\
&\max\{E_{11}, E_{10}\} - \min\{E_{01}, E_{00}\} \\
&\le \mathrm{E}[Y(1) - Y(0)] \le \min\{E_{\cdot 1} - E_{\cdot 0}, E_{\cdot 0} - E_{\cdot 1}\},
\end{aligned}$$

where the lower bounds are derived under the MTS and the upper bounds are derived under the MTR (Chiba, 2011). With the monotonic selection assumption, the MTR improves the upper bound for the ATT as follows:

$$\mathrm{E}[Y(1) - Y(0) \mid X = 1] \le \mathrm{E}[Y \mid X = 1] - \frac{\{(1-p_0)E_{00} - (1-p_1)E_{01}\}\Pr(Z=1) + p_0 E_{10}}{\Pr(X=1)}, \tag{14}$$

while it may not improve the upper bound for the ATE. The derivation of inequality (14) is given in Appendix 4. The upper bound given in (14) is smaller than that given in (13) without MTS.

The results for bounds under various assumptions are summarized in Table 2 for the difference and in Table 3 for the ratio measures, with bootstrap 95% confidence intervals (CIs). The bound formulas for ratio measures are given in Appendix 1. Tables 2 and 3 showed that bounds under the basic assumptions with or without monotonicity had very broad widths, and thus they did not provide enough information on the ATT and ATE. However, MTS + MTR gave considerably narrower bounds for both the ATT and ATE. The proposed bounds further improved the lower bounds under the MTS, though their 95% CIs were broader than those by MTS + MTR. In addition, the MTR with monotonic selection considerably improved the upper bounds for the ATT. Moreover, we note that unlike our Assumptions 2 and 4, MTS is not even partially identifiable from the observed data. We further note that the bootstrap CIs would not retain the nominal coverage because bounds are not smooth functionals of the empirical cumulative distribution function (Hall, 1992).

Table 2. Bounds and their 95% confidence limits (in parentheses) for the ATT and ATE on the difference scale under basic assumptions only (the Balke-Pearl bounds for the ATE), monotonicity assumption, MTR + MTS without monotonicity, and MTR + Assumption 4(b) with monotonicity.

	Bounds		
Assumptions	**Lower**	**Upper**	**Width**
ATT ($\times 10^{-2}$)			
Basic assumptions	–98.90 (–99.41, –98.34)	1.10 (0.58, 1.66)	100.00
Monotonicity	–54.60 (–59.05, –50.04)	0.22 (–1.31, 1.69)	54.82
MTR + MTS	–0.93 (–1.54, –0.21)	0.00 (0.00, 0.00)	0.93
MTR + A4(b)	–0.84 (–4.51, 2.51)	–0.51 (–1.91, 1.25)	0.33
ATE ($\times 10^{-2}$)			
Basic assumptions	–11.31 (–12.36, –10.33)	72.60 (71.51, 74.30)	83.91
Monotonicity	–11.31 (–12.36, –10.33)	72.60 (71.51, 74.30)	83.91
MTR + MTS	–0.93 (–1.31, –0.46)	–0.13 (–0.73, 0.46)	0.80
MTR + A4(b)	–0.89 (–2.15, 0.54)	–0.13 (–0.73, 0.46)	0.76

Table 3. Bounds and their 95% confidence limits (in parentheses) for the ATT and ATE on the ratio scale under basic assumptions only, monotonicity assumption, MTR + MTS without monotonicity, and MTR + Assumption 4(b) with monotonicity.

	Bounds		
Assumptions	**Lower**	**Upper**	**Width**
ATT			
Basic assumptions	0.01 (0.01, 0.02)	∞	∞
Monotonicity	0.02 (0.01, 0.03)	1.24 (0.00, 5.53)	1.22
MTR + MTS	0.54 (0.37, 1.26)	1.00 (1.00, 1.00)	0.46
MTR + A4(b)	0.57 (0.00, 2.46)	0.69 (0.00, 3.28)	0.12
ATE			
Basic assumptions	0.01 (0.01, 0.04)	49.43 (35.98, 63.04)	49.42
Monotonicity	0.01 (0.01, 0.04)	49.43 (35.98, 63.04)	49.42
MTR + MTS	0.55 (0.37, 1.26)	0.93 (0.66, 0.99)	0.38
MTR + A4(b)	0.56 (0.06, 1.34)	0.93 (0.66, 0.99)	0.37

5. DISCUSSION

In this article, we first showed the meaning of NEM assumptions in SMMs from the PS framework under the assumption of monotonic selection. Clarke and Windmeijer (2010) have stated that NEM assumptions "depend crucially on the unknown causal model that generated the data; therefore, it is difficult to justify." Indeed, NEM assumptions are equivalent to common treatment effects for compliers and always-takers, which we can never assure with certainty. A more realistic approach is to assume NEM *conditional on* baseline covariates because effect modification in these two subgroups can (at least partly) be attributed to measured baseline covariates. However, if we model causal effects conditional on many covariates, we must cope with model selection problems, as in classical regression confounding adjustment settings. In addition, even if we can use many baseline covariates, we cannot confirm whether the NEM assumption holds from the observed data due to the identification problems. If the NEM assumption does not hold, then neither the ATT nor ATE is identified.

We derived the bounds for the ATT and ATE. Our proposed bounds could be useful if we can reasonably suppose further assumptions, which include the monotonic selection, in addition to the usual IV assumptions. Our illustration showed that proposed bounds can be dramatically tighter than the nonparametric bounds. This tendency would be clearer if the range of the outcome Y is broader.

Indeed, when Y is not bounded (i.e., has infinite range), nonparametric bounds are no longer obtained. Of course the tightening of bounds comes at the price of making a stronger assumption. Our results are limited insofar as the added assumptions are not identified from the data, and hence must be derived from contextual considerations. Although assumptions are not themselves identifiable, they are nonetheless reasonable in some situations. For example, when patients with a worse condition tend to prefer to receive the new treatment, it should be anticipated that the incidence proportion of a bad event ($Y = 1$) (e.g., death) will be highest for never-takers, followed in order by compliers, and always-takers.

Unlike former studies, our proposed bounds explicitly use the monotonic selection assumption. Under this assumption, CATE is identifiable. Thus, we could expect that if most individuals in the target population were compliers, then p_1 would be much larger than p_0; thus, the proposed bounds could give much narrower bounds than the existing bounds, as inferred from the inequalities (10) and (12). In our illustration, the MRFIT was a preventive study, and thus the compliance of the intervention was not good. Indeed, estimates of π_{00}, π_{11}, and π_{10} were 0.741, 0.098, and 0.161, respectively. These indicated that most of the study populations were never-takers, and the proportion of compliers was small. However, in many clinical trials, in order to evaluate the effect of a drug, the proportion of compliers would be much higher than the proportions of individuals in the other principal strata. Thus, our proposed bounds have the possibility of providing bounds with a very narrow width when the monotonic selection assumption holds.

APPENDIX 1. Ratio measures

In this appendix, we extend the propositions in Section 3 to ratio measures. The proofs of propositions derived in this appendix are similar to those in Section 3. Therefore, we give only the results below.

Let us use the notation $\exp(\varphi_{st}) \equiv \mathrm{E}[Y(1) \mid X(1) = s, X(0) = t] / \mathrm{E}[Y(0) \mid X(1) = s, X(0) = t]$. Then, the ratio between equations (6) and (8), that is, the ratio version of the IV estimator, is given by

$$\exp(\varphi_{10}) = (p_1 E_{11} - p_0 E_{10}) / \{(1 - p_0) E_{00} - (1 - p_1) E_{01}\}, \tag{15}$$

where it is assumed that $(1 - p_0)E_{00} - (1 - p_1)E_{01} > 0$ (Angrist, 2001).

Similar to the additive SMM (9), the ATT can be formalized using the following nonparametric (saturated) multiplicative SMM:

$$\mathrm{E}[Y \mid X, Z] / \mathrm{E}[Y(0) \mid X, Z] = \exp\{(\theta_0 + \theta_1 Z)X\},$$

where $\exp(\theta_0)$ and $\exp(\theta_0 + \theta_1)$ are unknown causal parameters. The ATTs are $\exp(\theta_0) = \mathrm{E}[Y(1) \mid X = 1, Z = 0] / \mathrm{E}[Y(0) \mid X = 1, Z = 0]$ with $Z = 0$, and $\exp(\theta_0 + \theta_1) = \mathrm{E}[Y(1) \mid X = 1, Z = 1] / \mathrm{E}[Y(0) \mid X = 1, Z = 1]$ with $Z = 1$. The parameter θ_0 is identified and is equal to equation (15) under the following NEM assumption for the multiplicative treatment effect (Hernán and Robins, 2006; Clarke and Windmeijer, 2010):

ASSUMPTION 5. $\mathrm{E}[Y(1) \mid X = 1, Z = 0] / \mathrm{E}[Y(0) \mid X = 1, Z = 0] = \mathrm{E}[Y(1) \mid X = 1, Z = 1] / \mathrm{E}[Y(0) \mid X = 1, Z = 1]$; that is, $\theta_1 = 0$.

PROPOSITION 5. *Suppose that the monotonic selection assumption holds. Then, Assumption 5 holds if and only if* $\varphi_{10} = \varphi_{11}$ *holds.*

PROPOSITION 6. *Suppose that the monotonic selection assumption holds. Then, under Assumption 2(a), the upper bounds for* $\exp(\theta_0) = \mathrm{E}[Y(1) \mid X = 1, Z = 0] / \mathrm{E}[Y(0) \mid X = 1, Z = 0]$ *and* $\exp(\theta_0 + \theta_1) = \mathrm{E}[Y(1) \mid X = 1, Z = 1] / \mathrm{E}[Y(0) \mid X = 1, Z = 1]$ *are*

$$\exp(\theta_0) \le \frac{(p_1 - p_0)E_{10}}{(1 - p_0)E_{00} - (1 - p_1)E_{01}},$$

$$\exp(\theta_0 + \theta_1) \le \frac{(p_1 - p_0)E_{11}}{(1 - p_0)E_{00} - (1 - p_1)E_{01}}.$$

Moreover, the upper bound for the multiplicative ATT is

$$\frac{\mathrm{E}[Y(1) \mid X = 1]}{\mathrm{E}[Y(0) \mid X = 1]} \le \frac{(p_1 - p_0)\{p_0 \Pr(Z = 0)E_{10} + p_1 \Pr(Z = 1)E_{11}\}}{\{(1 - p_0)E_{00} - (1 - p_1)E_{01}\} \Pr(X = 1)}.$$

Under Assumption 2(b), these results apply with the inequality signs reversed.

The ATE, $\mathrm{E}[Y(1)] / \mathrm{E}[Y(0)]$, is equal to equation (15) under Assumption 6 (Hernán and Robins, 2006) given below.

ASSUMPTION 6. $\{\mathrm{E}[Y(1) \mid X = x, Z = 0] / \mathrm{E}[Y(0) \mid X = x, Z = 0]\} = \{\mathrm{E}[Y(1) \mid X = x, Z = 1] / \mathrm{E}[Y(0) \mid X = x, Z = 1]\}$ *for* $x = 0, 1$.

PROPOSITION 7. *Suppose that the monotonic selection assumption holds. Then, Assumption 6 holds if and only if* $\varphi_{10} = \varphi_{11} = \varphi_{00}$ *holds.*

PROPOSITION 8. *Suppose that the monotonic selection assumption holds. Then, under Assumption 4(a), the upper bound for the multiplicative ATE is given by*

$$\frac{\mathrm{E}[Y(1)]}{\mathrm{E}[Y(0)]} \leq \frac{(1-p_0)p_1E_{11} - p_0(1-p_1)E_{10}}{(1-p_0)p_1E_{00} - p_0(1-p_1)E_{01}}.$$

Under Assumption 4(b), the result applies with the inequality sign reversed.

APPENDIX 2. Proof that the proposed bounds improve the Robins-Manski bounds under the monotonic selection assumption

Two of the four terms of the Balke-Pearl bounds for E[$Y(x)$] (x = 0, 1), which were proposed by Robins (1989) and Manski (1990), are given as follows:

$$\max\begin{Bmatrix} p_1E_{11} \\ p_0E_{10} \end{Bmatrix} \leq \mathrm{E}[Y(1)] \leq \min\begin{Bmatrix} p_1E_{11} + (1-p_1) \\ p_0E_{10} + (1-p_0) \end{Bmatrix},$$

$$\max\begin{Bmatrix} (1-p_1)E_{01} \\ (1-p_0)E_{00} \end{Bmatrix} \leq \mathrm{E}[Y(0)] \leq \min\begin{Bmatrix} (1-p_1)E_{01} + p_1 \\ (1-p_0)E_{00} + p_0 \end{Bmatrix}.$$

We show that the new upper bound of the ATE under Assumption 4(b) is not larger than those of the Robins-Manski bounds under the monotonic selection assumption. By randomization,

$$\begin{aligned} \mathrm{E}[Y(1)] &= \mathrm{E}[Y(1) \mid Z = z] \\ &= \mathrm{E}[Y(1) \mid X = 0, Z = z]\Pr(X = 0 \mid Z = 1) \\ &\quad + \mathrm{E}[Y(1) \mid X = 1, Z = z]\Pr(X = 1 \mid Z = z) \end{aligned} \tag{16}$$

for z = 0, 1. The upper bounds on E[Y(1)] of the Robins-Manski bounds are obtained by substituting 1 into E[Y(1) | X = 0, Z = z] in equation (16). The new upper bound can be derived by substituting E[Y(1) | X (1) = 1, X (0) = 0] given in equation (6) into E[Y(1) | X = 0, Z = 0] in equation (16) with z = 0 by using equation (4). The new upper bound can also be derived by substituting E[Y(1) | X (1) = 1, X (0) = 0] into E[Y(1) | X = 0, Z = 1] in equation (16) with z = 1 by using equation (3). Under the monotonic selection assumption, equation (6) must be the same or smaller than 1. Thus, the new upper bound of E[Y(1)] is the same or smaller than the Robins-Manski bounds. Similarly, by randomization,

$$\begin{aligned} \mathrm{E}[Y(0)] &= \mathrm{E}[Y(0) \mid Z = z] \\ &= \mathrm{E}[Y(0) \mid X = 0, Z = z]\Pr(X = 0 \mid Z = 1) \\ &\quad + \mathrm{E}[Y(0) \mid X = 1, Z = z]\Pr(X = 1 \mid Z = z) \end{aligned} \tag{17}$$

for z = 0, 1. The lower bounds on E[Y(0)] of the Robins-Manski bounds are obtained by substituting 0 into E[Y(0) | X = 1, Z = z] in equation (17). The new lower bound can be derived by substituting E[Y(0) | X (1) = 1, X (0) = 0] given in

equation (8) into E[$Y(0) \mid X = 1, Z = 0$] in equation (17) with $z = 0$ by using equation (2). The new upper bound can also be derived by substituting E[$Y(0) \mid X(1) = 1, X(0) = 0$] into E[$Y(0) \mid X = 1, Z = 1$] in equation (17) with $z = 1$ by using equation (1). Under the monotonic selection assumption, equation (8) must be the same or larger than 0. Thus, the new lower bound of E[$Y(0)$] is the same or larger than the Robins-Manski bounds. These facts complete the proof because the upper bound of the ATE is given by $\max\{\mathrm{E}[Y(1)]\} - \min\{\mathrm{E}[Y(0)]\}$.

By the same way, we can show that the new lower bound of the ATE under Assumption 4(a) is not smaller than those of the Robins-Manski bounds. We note that our proposed bounds can be used in conjunction with the remaining two terms of the Balke-Pearl bounds.

APPENDIX 3. Deviation of inequality (13)

Under the monotonic selection assumption, we can represent E[$Y(0) \mid X = 1$] as follows:

$$
\begin{aligned}
&\mathrm{E}[Y(0) \mid X = 1] \\
&= \sum_{z=0}^{1} \mathrm{E}[Y(0) \mid X = 1, Z = z] \Pr(Z = z \mid X = 1) \\
&= \mathrm{E}[Y(0) \mid X = 1, Z = 0] p_0 \frac{\Pr(Z = 0)}{\Pr(X = 1)} + \mathrm{E}[Y(0) \mid X = 1, Z = 1] p_1 \frac{\Pr(Z = 1)}{\Pr(X = 1)} \\
&= \mathrm{E}[Y(0) \mid X(1) = X(0) = 1] p_0 \frac{\Pr(Z = 0)}{\Pr(X = 1)} \\
&+ \frac{(p_1 - p_0)\mathrm{E}[Y(0) \mid X(1) = X(0) = 0] + p_0 \mathrm{E}[Y(0) \mid X(1) = X(0) = 1]}{p_1} p_1 \frac{\Pr(Z = 1)}{\Pr(X = 1)} \\
&= \frac{(p_1 - p_0)\mathrm{E}[Y(0) \mid X(1) = 1, X(0) = 0] \Pr(Z = 1) + p_0 \mathrm{E}[Y(0) \mid X(1) = X(0) = 1]}{\Pr(X = 1)} \\
&= \frac{\{(1 - p_0)E_{00} - (1 - p_1)E_{01}\} \Pr(Z = 1) + p_0 \mathrm{E}[Y(0) \mid X(1) = X(0) = 1]}{\Pr(X = 1)}, \quad (18)
\end{aligned}
$$

where the third equality follows from equations (1) and (2) with $x = 0$, and the last equality follows from equation (8). Then, by substitution of 0 or 1 for E[$Y(0) \mid X(1) = X(0) = 1$] in equation (18), we obtain the upper and lower bounds of E[$Y(0) \mid X = 1$]. Because E[$Y(1) \mid X = 1$] = E[$Y \mid X = 1$], the difference between them derives inequality (13).

APPENDIX 4. Deviation of inequality (14)

Using the assumptions of monotonic selection and MTR, we have

$$
\begin{aligned}
&\mathrm{E}[Y(0) \mid X = 1] \\
&= \frac{\{(1-p_0)E_{00} - (1-p_1)E_{01}\}\Pr(Z=1) + p_0\mathrm{E}[Y(0) \mid X(1) = X(0) = 1]}{\Pr(X=1)} \\
&\geq \frac{\{(1-p_0)E_{00} - (1-p_1)E_{01}\}\Pr(Z=1) + p_0\mathrm{E}[Y(1) \mid X(1) = X(0) = 1]}{\Pr(X=1)} \\
&= \frac{\{(1-p_0)E_{00} - (1-p_1)E_{01}\}\Pr(Z=1) + p_0E_{10}}{\Pr(X=1)}. \qquad (19)
\end{aligned}
$$

The first equality follows from (18), the inequality holds by the MTR, and the last equality is derived from equation (5). The difference between $\mathrm{E}[Y \mid X = 1]$ and equation (19) derives inequality (14). We note that, even when similar calculations are made for $\mathrm{E}[Y(1)]$ and $\mathrm{E}[Y(0)]$, these upper bounds cannot be improved.

REFERENCES

Angrist, J. D. (2001). Estimation of limited dependent variable models with dummy endogenous regressors: simple strategies for empirical practice. *Journal of Business and Economic Statistics* 19, 2–16.

Angrist, J. D., Imbens, G. W. and Rubin, D. B. (1996a). Identification of causal effects using instrumental variables. *Journal of the American Statistical Association* 91, 444–455.

Angrist, J. D., Imbens, G. W. and Rubin, D. B. (1996b). Rejoinder: Identification of causal effects using instrumental variables. *Journal of the American Statistical Association* 91, 468–472.

Balke, A. and Pearl., J. (1997). Bounds on treatment effects from studies with imperfect compliance. *Journal of the American Statistical Association* 92, 1171–1177.

Bellamya, S. L., Jinb, J. Y. and Ten Have, T. R. (2007). An introduction to causal modeling in clinical trials. *Clinical Trials* 4, 58–73.

Chiba, Y. (2010). An approach for estimating causal effects in randomized trials with noncompliance. *Communications in Statistics – Theory and Methods* 39, 2146–2156.

Chiba, Y. (2011). Causal inference in randomized trials with noncompliance. In: *Health Management – Different Approaches and Solutions*, K. Śmigórski (ed). Rijeka: Intech, 315–336.

Clarke, P. S. and Windmeijer, J. (2010). Identification of causal effects on binary outcomes using structural mean models. *Biostatistics* 11, 756–770.

Cole, S. R. and Hernán, M. A. (2008). Constructing inverse probability weights for marginal structural models. *American Journal of Epidemiology* 168, 656–664.

Frangakis, C. E. and Rubin, D. B. (2002). Principal stratification in causal inference. *Biometrics* 58, 21–29.

Greenland, S. (2000). An introduction to instrumental variables for epidemiologists. *International Journal of Epidemiology* 29, 722–729.

Hall, P. (1992). *Bootstrap and Edgeworth Expansion*. New York: Springer.

Heckman, J. (1996). Comment: Identification of causal effects using instrumental variables. *Journal of the American Statistical Association* 91, 459–461.

Heckman, J. (1997). Instrumental variables: A study of implicit behavioral assumptions used in making program evaluations. *Journal of Human Resources* 32, 441–462.

Hernán, M. A. and Robins, J. M. (2006). Instruments for causal inference: An epidemiologist's dream? *Epidemiology* 17, 360–372.

Holland, P. W. (1986). Statistics and causal inference (with discussion). *Journal of the American Statistical Association* 81, 945–960.

Manski, C. F. (1990). Nonparametric bounds on treatment effects. *American Economic Review* 80, 319–323.

Manski, C. F. (1997). Monotone treatment response. *Econometrica* 65, 1311–1334.

Manski, C. F. and Pepper, J. V. (2000). Monotone instrumental variables: With an application to the returns to schooling. *Econometrica* 68, 997–1010.

Mark, S. D. and J. M. Robins (1993). A method for the analysis of randomized trials with noncompliance information: An application to the multiple risk factor intervention trial. *Controlled Clinical Trials* 14, 79–97.

Multiple Risk Factor Intervention Trial Research Group (1982). Multiple risk factor intervention trial: Risk factor changes and mortality results. *Journal of the American Medical Association* 248, 1465–1477.

Pearl, J. (2009). *Causality: Models, Reasoning and Inference*. 2nd edition. Cambridge: Cambridge University Press.

Robins, J. M. (1989). The analysis of randomized and non-randomized AIDS treatment trials using a new approach to causal inference in longitudinal studies. In: L. Sechrest, H. Freeman, and A. Mulley (editors), *Health Service Research Methodology: A Focus on AIDS*, Washington, DC: US Public Health Service, National Center for Health Services Research, 113–159.

Robins, J. M. (1994). Correcting for noncompliance in randomized trials using structural nested mean models. *Communications in Statistics – Theory and Methods* 23, 2379–2412.

Robins, J. M. and Greenland, S. (1996). Comment: Identification of causal effects using instrumental variables. *Journal of the American Statistical Association* 91, 456–458.

Rubin, D. B. (1974). Estimating causal effects of treatments in randomized and nonrandomized studies. *Journal of Educational Psychology* 66, 688–701.

Rubin, D. B. (1978). Bayesian inference for causal effects: The role of randomization. *Annals of Statistics* 6, 34–58.

Rubin, D. B. (1990). Formal models of statistical inference for causal effects. *Journal of Statistical Planning and Inference* 25, 279–292.

Rubin, D. B. (2004). Direct and indirect causal effects via potential outcomes. *Scandinavian Journal of Statistics* 31:161–170.

Sato, T. (2006). Randomization-based analysis of causal effects. In: *Handbook of Clinical Trials: Design and Analysis*, T. Tango and H. Uesaka (eds). Tokyo: Asakura Publishing, 535–556 (in Japanese).