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A note about the identifiability of causal effect estimates in randomized trials with non-compliance

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Abstract

We show that assumptions that are sufficient for estimating an average treatment effect in randomized trials with non-compliance restrict the subgroup means for always takers, compliers, defiers and never takers to a two dimensional linear subspace of a four dimensional space. Implications and special cases are exemplified.

Keywords

Average treatment effect; Complier average treatment effect; Instrumental variables; Principal Stratification

1 Introduction

Making causal estimation for randomized clinical trials with noncompliance is important in practice but their validity relies on certain assumptions. Estimation of two causal parameters: the complier average casual effect (CACE) and the average causal effect (ACE) requires slightly different assumptions. Apart from common assumptions such as exclusion restriction, estimation of CACE requires a monotonicity assumption and the estimation of ACE requires a no-interaction assumption, which will be discussed in detail in Section 2. The two assumptions do not imply one another but their relationships are unclear. We discuss implications of the no-interaction assumption and connections to the estimation of CACE and ACE in Section 3. In Section 4, we show that under a plausible partial ranking between causal treatment effects among always takers, compliers and never takers, the hyperplane restriction implies that causal treatment effects among always takers, compliers, defiers and never takers are all equal. Therefore, CACE and ACE are the same and can be consistently estimated by an instrumental variable estimator.

2 Notations and assumptions

Let R be a binary treatment assignment indicator, where $R_i = 1$ when a subject is assigned to the treatment arm, and $R_i = 0$ when a subject is assigned to the control arm. Also, denote n_1 and n_0 be the sample sizes of the treatment and control arms respectively and $n = n_1 + n_0$. In the presence of noncompliance, the actual treatment received T may not be the same as the treatment assignment R . To define compliance classes among the subjects, we follow the potential outcome framework of [1]. Let $(T_i(1), T_i(0))$ be the potential treatment received if

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subject i was assigned to treatment and control respectively. Compliance classes are defined by cross classifying $T(1)$ and $T(0)$, as shown in Table 1.

For each subject, we can only observe $T_i = T_i(R_i)$, where R_i is the assigned treatment. Similarly, we can define potential outcomes $Y_i(R, T)$ to be the response from subject i given the treatment assignment R and actual treatment received T . We denote $Y_i = Y_i(R_i, T_i)$ be the observed outcome, $\mathbf{Y} = (Y_1, \dots, Y_n)^T$, $\mathbf{T} = (T_1, \dots, T_n)^T$ and $\mathbf{R} = (R_1, \dots, R_n)^T$.

To estimate the complier average causal effect (CACE), the following assumptions has been made in [1].

Assumption A Stable Unit Treatment Value Assumption: If $R_i = R'_i$, then $T_i(\mathbf{R}) = T_i(\mathbf{R}')$. If $T_i = T'_i$ and y, then $Y_i(\mathbf{R}, \mathbf{T}) = Y_i(\mathbf{R}', \mathbf{T}')$.

Assumption B Random Assignment: $P(\mathbf{R} = \mathbf{r}) = P(\mathbf{R} = \mathbf{r}')$ for all $\mathbf{r}$ and $\mathbf{r}'$ such that $\mathbf{e}^T \mathbf{r} = \mathbf{e}^T \mathbf{r}'$ where $\mathbf{e}$ is the n -dimensional column vector with all elements equal to one.

Assumption C Exclusion Restriction: $Y(\mathbf{R}, \mathbf{T}) = Y(\mathbf{R}', \mathbf{T})$ for all $\mathbf{R}, \mathbf{R}'$ and for all $\mathbf{T}$.

Assumption D Nonzero Average Causal Effect of R on T : $E(T(1) - T(0)) \neq 0$.

Assumption E Monotonicity: $T_i(1) \geq T_i(0)$ for all $i = 1, \dots, n$.

Assumption C guarantees that we can write $Y(T) = Y(R, T)$. Assumption E rules out defiers. [2] commented that Assumption E is very strong because it does not hold even when there is just one defier in the sample. Also, the subgroup of compliers are defined based on counterfactual outcomes and individual membership cannot be exactly identified from data. As a result, some researchers (see for example [3]) prefer estimation of the average causal effect (ACE) $\eta = m_A \pi_A + m_C \pi_C + m_D \pi_D + m_N \pi_N$, where m_A, m_C, m_D, m_N ($\pi_A, \pi_C, \pi_D, \pi_N$) are the expected values of $Y(1) - Y(0)$ (or population proportions) among always takers, compliers, defiers and never takers. Note that the definition of ACE involves the counterfactual effects of a treatment that is not taken. Whether it makes sense would depend on context.

The estimation of ACE requires slightly different assumptions. The Monotonicity Assumption E is replaced by the following collections of assumptions [3]

$$E(Y(0) | R=1) = E(Y(0) | R=0) \quad (1)$$

$$E(Y(1) | R=1) = E(Y(1) | R=0) \quad (2)$$

$$E(Y(1) - Y(0) | T=0, R=1) = E(Y(1) - Y(0) | T=0, R=0) \quad (3)$$

$$E(Y(1) - Y(0) | T=1, R=1) = E(Y(1) - Y(0) | T=1, R=0) \quad (4)$$

Conditions (1) and (2) are called mean independence assumptions and (3) and (4) are called no-interaction assumptions. The mean independence conditions are consequences of Assumptions A to C, and therefore the alternative assumption to monotonicity is the no-interaction assumptions. Let $\eta = E(Y(1) - Y(0))$ be the average causal effect (ACE). Under these assumptions, Theorem 1 in [3] showed that

$$\eta = \frac{E(Y|R=1) - E(Y|R=0)}{E(T|R=1) - E(T|R=0)}$$

and therefore the instrumental variable (IV) estimator of [5]

$$\hat{\eta}_{IV} = \frac{\bar{Y}_1 - \bar{Y}_0}{\bar{T}_1 - \bar{T}_0}$$

where $\bar{Y}_r$ and $\bar{T}_r$ are the sample averages of Y and T for $R = r$, $r = 0, 1$, is a consistent estimate of ACE. The conditions (1), (2), (3) and (4) are based on the observed subpopulations but these subpopulations are mixture of compliance classes. For instance, the subgroup $\{R = 1, T = 1\}$ is consists of a mixture of always takers and compliers; the subgroup $\{R = 1, T = 0\}$ is consists of a mixture of never takers and defiers; the subgroup $\{R = 0, T = 1\}$ is consists of a mixture of always takers and defiers; and the subgroup $\{R = 0, T = 0\}$ is consists of a mixture of never takers and compliers.

3 Induced hyperplane restrictions

Theorem 1a in [3] states that, under Assumptions D, (1) and (2), conditions (3) and (4) are equivalent to

$$E(Y(1) - Y(0) | T=1, R=1) = E(Y(1) - Y(0) | T=0, R=1), \quad (5)$$

$$E(Y(1) - Y(0) | T=1, R=0) = E(Y(1) - Y(0) | T=0, R=0). \quad (6)$$

Expressing (3), (4), (5) and (6) in terms of $(m_A, m_C, m_D, m_N, \pi_A, \pi_C, \pi_D, \pi_N)$, we have

$$\begin{aligned} \frac{m_D \pi_D}{\pi_D + \pi_A} + \frac{m_A \pi_A}{\pi_D + \pi_A} &= \frac{m_N \pi_N}{\pi_N + \pi_C} + \frac{m_C \pi_C}{\pi_N + \pi_C} \\ &= \frac{m_A \pi_A}{\pi_A + \pi_C} + \frac{m_C \pi_C}{\pi_A + \pi_C} \\ &= \frac{m_D \pi_D}{\pi_N + \pi_D} + \frac{m_N \pi_N}{\pi_N + \pi_D} \end{aligned} \quad (7)$$

Note that (7) is equivalent to the linear system $Am = 0$, where

$$A = \begin{pmatrix} \frac{\pi_A}{\pi_D + \pi_A} & -\frac{\pi_C}{\pi_N + \pi_C} & \frac{\pi_D}{\pi_D + \pi_A} & -\frac{\pi_N}{\pi_N + \pi_C} \\ \frac{\pi_A(\pi_C - \pi_D)}{(\pi_A + \pi_D)(\pi_A + \pi_C)} & -\frac{\pi_C}{\pi_A + \pi_C} & \frac{\pi_D}{\pi_D + \pi_A} & 0 \\ \frac{\pi_A}{\pi_D + \pi_A} & 0 & \frac{\pi_D(\pi_N - \pi_A)}{(\pi_D + \pi_A)(\pi_D + \pi_N)} & -\frac{\pi_N}{\pi_N + \pi_D} \end{pmatrix}$$

and $m = (m_A, m_C, m_D, m_N)^T$.

The rows of A , however, are linearly dependent. The solution of (m_A, m_C, m_D, m_N) be found by the solving the reduced system $\tilde{A}m=0$ where

$$\tilde{A} = \begin{pmatrix} \frac{\pi_A(\pi_C - \pi_D)}{(\pi_A + \pi_D)(\pi_A + \pi_C)} & -\frac{\pi_C}{\pi_A + \pi_C} & \frac{\pi_D}{\pi_D + \pi_A} & 0 \\ \frac{\pi_A}{\pi_D + \pi_A} & 0 & \frac{\pi_D(\pi_N - \pi_A)}{(\pi_D + \pi_A)(\pi_D + \pi_N)} & -\frac{\pi_N}{\pi_N + \pi_D} \end{pmatrix}$$

The range space of $\tilde{A}$ has dimension 2, and the null space of $\tilde{A}$ also has dimension 2. The solution set for (m_A, m_C, m_D, m_N) is

$$\left\{ s, t \in \mathbb{R} : \left(\frac{\pi_N(\pi_A + \pi_C)t - \pi_C(\pi_N - \pi_A)s}{\pi_A(\pi_C + \pi_N)}, s, \frac{\pi_C(\pi_D + \pi_N)s - \pi_N(\pi_C - \pi_D)t}{\pi_D(\pi_C + \pi_N)}, t \right) \right\} \quad (8)$$

Since the proportion of always takers, compliers, defiers and never takers are fixed in a population, the no-interaction assumption is satisfied only in a two-dimensional linear subspace for (m_A, m_C, m_D, m_N) . From (8), (m_A, m_C, m_D, m_N) are restricted in a way that depends on $(\pi_A, \pi_C, \pi_D, \pi_N)$, which does not admit a natural interpretation. Special cases will be explored in the next section.

4 Implications

It is often natural to impose additional order restrictions on m_A, m_C, m_D and m_N . For instance, one can assume that self-selection is intrinsically beneficial, so that the treatment effect among always takers are greater than that for never takers, *i.e.* $m_A \geq m_N$. From (8), we have

$$\frac{\pi_N(\pi_A + \pi_C)t}{\pi_A(\pi_C + \pi_N)} - \frac{\pi_C(\pi_N - \pi_A)s}{\pi_A(\pi_C + \pi_N)} \geq t$$

which is equivalent to $t \geq s$. Therefore, we can conclude that $m_D \geq m_A \geq m_N \geq m_C$. However, the conclusion that treatment effect is highest among defiers and lowest among compliers does not admit a natural interpretation.

Suppose we assume that $m_A = m_N$, we can then conclude from (8) that $m_A = m_N = m_C = m_D = \eta$. In this case, CACE and ACE are equivalent, and the IV estimator consistently estimates both quantities. Note that when Assumptions A-D are satisfied, the IV estimate is consistently estimating a linear combination of m_C and m_D [1]. When Assumption E is replaced by $m_C = m_D$, the IV estimate is still a consistent estimator of CACE. However, this set of assumptions, which is weaker than the no-interaction assumption under this case, is not sufficient for identifying ACE, because there is no further restriction on m_A and m_N .

When baseline covariates X are present, one may estimate $\text{CACE}(x)$ and $\text{ACE}(x)$ for each value x of X . The marginal averaged CACE and ACE can then be estimated by averaging over the distribution of X among compliers and in the whole population. The average CACE and ACE can differ even when $\text{CACE}(x) = \text{ACE}(x)$ for all x , since the distribution of X for compliers can be different from the distribution X for the whole population. This point is noted in [4].

Acknowledgments

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Table 1

Compliance classes defined by cross classifying $T(1)$ and $T(0)$.

	$T(1) = 1$	$T(1) = 0$
$T(0) = 1$	Always taker (A)	Defiers (D)
$T(0) = 0$	Compliers (C)	Never taker (N)