

Estimation of Intervention Effects With Noncompliance: Alternative Model Specifications

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Abstract

This study examines alternative ways of specifying models in the CACE (complier average causal effect) estimation method, where the major interest is in estimating causal effects of treatments for compliers. A fundamental difficulty involved in the CACE estimation method is in dealing with missing compliance information among study participants. Given that, the assumption of the exclusion restriction plays a critical role in separating the distributions of compliers and noncompliers. If no pre-treatment covariates are available, assuming the exclusion restriction is unavoidable to obtain unique ML estimates in CACE models, although the assumption can be often unrealistic. One disadvantage of assuming the exclusion restriction is that the CACE estimate can be biased if the assumption is violated. Another disadvantage is that the assumption limits the flexibility of CACE modeling in practice. However, if pre-treatment covariates are available, more modeling options other than strictly forcing the exclusion restriction can be considered to establish identifiability of CACE models. This study explores modeling possibilities of CACE estimation within an ML-EM framework in the presence of covariate information.

Keywords: noncompliance, CACE, assignment effects, exclusion restriction, pre-treatment covariates, missing data, ML-EM

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1 Introduction

Treatment noncompliance is a common problem in randomized intervention trials. Standard ITT (intent-to-treat) analysis has been widely used as a method to estimate treatment effects in the presence of noncompliance. This method provides an overall average treatment effect estimate by comparing outcomes based on assignment of the treatment, but ignoring receipt of the treatment. Since the ITT effect estimate does not represent treatment efficacy under noncompliance, researchers are often interested in estimating treatment effects only for compliers – individuals who would receive the treatment if offered.

To estimate treatment effects taking into account noncompliance, Bloom (1984) applied instrumental variable (IV) approach, where treatment effect estimates are adjusted by considering the noncompliance rate. More recently, a refined form of the IV approach with clear underlying assumptions has been proposed (Angrist, Imbens & Rubin, 1996; Imbens & Angrist, 1994). The estimation of CACE (complier average causal effect), originally based on the IV approach, made dramatic progress with the introduction of likelihood-based methods. Imbens and Rubin (1997) demonstrated CACE estimation through the maximum-likelihood (ML) estimation method using

the EM algorithm and with a Bayesian approach using the Data Augmentation algorithm. Little and Yau (1998) incorporated covariates in this framework and applied the ML-EM method.

The major difficulty involved in CACE estimation is in dealing with missing compliance information among study participants. In the absence of this information, the assumption of the exclusion restriction provides the basis for identifiability in CACE models. Under this assumption, the difference in the outcome between the treatment and the control condition is allowed for compliers, but is not allowed for never-takers – individuals who would not receive the treatment regardless of whether it is offered – or for always-takers – individuals who would receive the treatment regardless of whether it is offered. However, this assumption often limits realistic modeling of CACE in practice, as in two real data applications shown in this study.

In the Job Search Intervention Study for unemployed workers (Little & Yau, 1998, Vinokur, Price, & Schul, 1995; Vinokur & Schul, 1997), never-takers assigned to the treatment condition could be demoralized by failing to take the intervention opportunity. This negative psychological effect would not occur for never-takers assigned to the control condition, since the treatment is never offered. Therefore, the intervention effect for compliers can be understated if the effect of treatment assignment on never-takers is ignored.

In the Johns Hopkins School Prevention Study (Ialongo et al., 1999), there is a large variation in completed intervention activities (ranges 0 to 66), and over-reporting

of compliance level by parents is also expected. Therefore, the intervention may not show any desirable effects unless parents report a quite high level of compliance. In this case, categorizing individuals into low and high compliers will provide a more meaningful intervention effect estimate than categorizing them into never-takers and compliers (97% reported they completed at least one activity). The exclusion restriction cannot be assumed in this setting, because low compliers would partially receive the intervention if they were assigned to the treatment condition, while they would not receive the intervention at all if they are assigned to the control condition.

The assumption of the exclusion restriction can be often unrealistic in practice. However, testing the violation of the assumption is not straightforward, since the assumption is directly related to the identifiability of CACE models. Given this identifiability problem, previous studies demonstrated the possibility of testing the assumption using weakly identified models in the Bayesian framework (Hirano, Imbens, Rubin, & Zhou, 2000; Imbens & Rubin, 1997). Without the exclusion restriction, CACE models are considered as weakly identified, since they show proper posterior distributions, but they do not have unique ML estimates. In these weakly identified CACE models, relaxation of the exclusion restriction assumption relies on auxiliary information such as from proper priors and parametric form likelihood functions.

The current study explores a third option, where we build identifiability of CACE models relying on auxiliary information from observed pre-treatment covariates. In principle, the assumption of the exclusion restriction can be fully relaxed without

losing identifiability if the number of covariates increases in an appropriate way as sample size increases (Frangakis, 1999). This study, however, focuses on more common situations, where only a limited number of covariates are observed, and therefore some functional assumptions are needed to attain identifiability of CACE models. Identifying CACE models based on limited covariate information is not as straightforward as identifying CACE models based on the exclusion restriction. However, information from covariates is still valuable in the sense that it provides options in establishing identifiability of CACE models based on functional assumptions that are more reasonable in given situations.

2 Modeling Options in Estimating CACE

2.1 Common Setting

Assume the simplest experimental setting where there is only one outcome measure (Y), the treatment assignment (Z) is binary (1 = treatment, 0 = control), and the treatment received (D) has only two levels (1 = received, 0 = not received). Angrist et al. (1996) defined four behavior types based on treatment receipt status of individuals given treatment assignment status. Let $D_i(1)$ denote the potential treatment receipt status for individual i when assigned to the treatment condition, and $D_i(0)$ denote the potential treatment receipt status for individual i when assigned to the control condition. Compliers are subjects who do what they are assigned to do ($D_i(1) = 1$

and $D_i(0) = 0$). Never-takers are subjects who do not receive the treatment even if they are assigned to the treatment condition ($D_i(1) = 0$ and $D_i(0) = 0$). Defiers are the subjects who do the opposite of what they are assigned to do ($D_i(1) = 0$ and $D_i(0) = 1$). Always-takers are the subjects who always receive the treatment no matter which condition they are assigned to ($D_i(1) = 1$ and $D_i(0) = 1$).

Among these four behavior types, the possibility of having defiers is excluded based on the monotonicity assumption (Imbens & Angrist, 1994). Although defier is often regarded as the least likely behavior option, violation of monotonicity may cause substantial bias in causal effect estimates. The current study assumes monotonicity based on two real data examples shown in later sections.

Monotonicity: There are no defiers.

For simplicity, this study also assumes that there are no always-takers. In the two examples shown in this study, neither defier nor always-taker was a likely compliance option, since study participants were prohibited from receiving a different intervention condition than the one that they were assigned to. However, unlike monotonicity, the assumption of having no always-takers is not critical in estimating CACE, and can be relaxed depending on situations.

The possible compliance behavior types (C_i) can then be reduced to

$$C_i = \begin{cases} c \text{ (complier)} & \text{if } D_i(1) = 1, \text{ and } D_i(0) = 0 \\ n \text{ (never-taker)} & \text{if } D_i(1) = 0, \text{ and } D_i(0) = 0. \end{cases}$$

Let $C(t) = \{i \mid C_i = t\}$ for $t \in \{c, n\}$. The differential average causal effect of

treatment assignment based on compliance type can be defined as

$$ITT_t = \sum_{i \in C(t)} [Y_i(1, D_i(1)) - Y_i(0, D_i(0))] / N_t, \quad (1)$$

where $Y_i(1, D_i(1))$ denotes the potential outcome for individual i with treatment receipt status D_i when $Z_i = 1$, and $Y_i(0, D_i(0))$ denotes the potential outcome for individual i with treatment receipt status D_i when $Z_i = 0$. N_t is the number of individuals of compliance type t .

In line with Rubin's causal model approach, the effect of treatment assignment in equation (1) is defined at the individual level (Holland, 1986; Rubin, 1978, 1980). It is shown in equation (1) that the causal effect of treatment assignment cannot be estimated for individual i , since two potential outcomes $Y_i(1, D_i(1))$ and $Y_i(0, D_i(0))$ cannot be jointly observed. However, the causal effect of treatment assignment can be estimated at the average level assuming randomization and SUTVA (stable unit treatment value; Rubin, 1978, 1980, 1990).

Randomization: Treatment assignment is random.

SUTVA: Potential outcomes for each person are unrelated to the treatment status of other individuals.

The average causal effect of treatment assignment for compliers ($ITT_c = CACE$) can be defined as $\mu_{1c} - \mu_{0c}$, where μ_{1c} denotes population mean potential outcome for compliers if $Z = 1$, and μ_{0c} denotes population mean potential outcome for compliers if $Z = 0$. The average causal effect of treatment assignment for never-takers (ITT_n)

can be defined as $\mu_{1n} - \mu_{0n}$, where μ_{1n} denotes population mean potential outcome for never-takers if $Z = 1$, and μ_{0n} denotes population mean potential outcome for never-takers if $Z = 0$.

The current study employs a maximum likelihood estimation approach, which is known to be often more efficient than the traditional IV approach in the estimation of CACE (Imbens & Rubin, 1997; Little & Yau, 1998). If compliance type C_i can be completely observed, the complete-data likelihood function is

$$\begin{aligned} L(\theta \mid data) &\propto \prod_{i \in \{C(n), Z_i=1\}} \pi_n f(y_i \mid \mu_{1n}, \sigma_n^2) \times \prod_{i \in \{C(c), Z_i=1\}} \pi_c f(y_i \mid \mu_{1c}, \sigma_c^2) \\ &\times \prod_{i \in \{C(n), Z_i=0\}} \pi_n f(y_i \mid \mu_{0n}, \sigma_n^2) \times \prod_{i \in \{C(c), Z_i=0\}} \pi_c f(y_i \mid \mu_{0c}, \sigma_c^2), \end{aligned} \quad (2)$$

where $\theta = (\pi_n, \pi_c, \mu_{1n}, \mu_{1c}, \mu_{0n}, \mu_{0c}, \sigma_n^2, \sigma_c^2)$ is the set of parameters in the model, and $f(y_i \mid \mu, \sigma^2)$ denotes the probability density of a normal distribution with mean μ and variance σ^2 . However, note that the identification of CACE models discussed in this study does not depend on normality assumption. The proportion of never-takers in the population is π_n , and the proportion of compliers in the population is π_c . The variance for never-takers is σ_n^2 , and the variance for compliers is σ_c^2 . The likelihood function can be modified conditional on covariates.

Since compliance type C_i cannot be observed in the control condition, the observed-data likelihood function is

$$\begin{aligned} L(\theta \mid data) &\propto \prod_{i \in \{Z_i=1, D_i=0\}} \pi_n f(y_i \mid \mu_{1n}, \sigma_n^2) \times \prod_{i \in \{Z_i=1, D_i=1\}} \pi_c f(y_i \mid \mu_{1c}, \sigma_c^2) \\ &\times \prod_{i \in \{Z_i=0, D_i=0\}} [\pi_n f(y_i \mid \mu_{0n}, \sigma_n^2) + \pi_c f(y_i \mid \mu_{0c}, \sigma_c^2)]. \end{aligned} \quad (3)$$

By maximizing the likelihood in equation (3) with respect to the parameters of interest θ , ML estimates are obtained. The unknown compliance status (C) in the control condition is handled as missing data via the EM algorithm (Dempster, Laird, & Rubin, 1977; Little & Rubin, 1987; McLachlan & Krishnan, 1997; Tanner, 1996). π_c and $\pi_n (= 1 - \pi_c)$ are parameters that determine the distribution of C . The E step computes the expected values of the complete-data sufficient statistics given data y and current parameter estimates θ . The M step computes the complete-data ML estimates with complete-data sufficient statistics replaced by their estimates from the E step. This procedure continues until it reaches optimal status. ML-EM procedures for CACE estimation has been previously presented in Little and Yau (1998). For real data applications shown in this study, ML-EM estimation of CACE was carried out by the *Mplus* program (Muthén & Muthén, 1998-2001), which provides parametric standard errors computed from the information matrix of the ML estimator using both the first- and the second-order derivatives.

2.2 Modeling CACE Without Covariates

Based on the observed-data likelihood function in equation (3), three directly estimable population means can be expressed in terms of model parameters as

$$\mu_{1n} = \alpha_n + \gamma_n, \quad (4)$$

$$\mu_{1c} = \alpha_c + \gamma_c, \quad (5)$$

$$\mu_0 = \pi_n \alpha_n + \pi_c \alpha_c, \quad (6)$$

where α_n corresponds to μ_{0n} , α_c corresponds to μ_{0c} , and μ_0 is the overall population mean potential outcome if $Z = 0$. γ_n represents the average causal effect of treatment assignment for never-takers (ITT_n), and γ_c represents the average causal effect of treatment assignment for compliers ($ITT_c = CACE$).

From equation (4), α_n can be defined as

$$\alpha_n = \mu_{1n} - \gamma_n. \quad (7)$$

From equations (6) and (7), α_c can be defined as

$$\alpha_c = \frac{\mu_0 - \pi_n \mu_{1n}}{\pi_c} + \frac{\pi_n \gamma_n}{\pi_c}. \quad (8)$$

From equations (5) and (8), γ_c can then be defined as

$$\gamma_c = \frac{\mu_1 - \mu_0}{\pi_c} - \frac{\pi_n \gamma_n}{\pi_c}. \quad (9)$$

In equations (8) and (9), the possibility of zero denominator is excluded ($\pi_c > 0$). That is, treatment assignment Z has some effect on the average probability of treatment receipt D (Angrist et al., 1996).

Nonzero Average Causal Effect of Z on D : The average causal effect of Z on D is not equal to zero.

Equations (7), (8), and (9) show that suggested model parameters cannot be identified without additional information or restrictions. Here, the exclusion restriction plays a critical role in identifying CACE models by assuming no effect of treatment assignment on noncompliers. Under the assumption of the exclusion restriction, $\gamma_n = 0$

in equations (7), (8), and (9). Therefore, α_n , α_c , and γ_c can be identified based on directly estimable quantities in a straightforward way.

Exclusion Restriction: For never-takers and always-takers, the distributions of the potential outcomes are independent of the treatment assignment (Angrist et al., 1996). That is, $Y_i(0, D_i(0)) = Y_i(1, D_i(1))$ for units with $D_i(0) = D_i(1) = 0$ or $D_i(0) = D_i(1) = 1$.

However, if the assumption of the exclusion restriction does not hold (i.e., $\gamma_n \neq 0$), the estimator of CACE (γ_c) will be biased as much as $\pi_n \gamma_n / \pi_c$ as shown in equation (9). The bias in the CACE estimate increases, if the average causal effect of treatment assignment for never-takers (γ_n) increases and compliance rate (π_c) decreases (Angrist et al., 1996; Jo, in press). This implies that the CACE estimate not only can be understated, but also can be exaggerated depending on how the assignment of treatment affects noncompliers. The bias mechanism also shows that if compliance rate is very low, violation of the exclusion restriction can cause a substantial bias in the CACE estimate even when the effect of treatment assignment on never-takers is trivial. The assumption of the exclusion restriction can also be violated for always-takers, which further complicates the bias mechanism and interpretation of causal effect estimates (Hirano et al, 2000; Jo, in press). In clinical trials, where blind, double-blind, or placebo-control conditions are possible, the assumption of the exclusion restriction seems reasonable. In other situations such as social-behavioral intervention studies, whether the exclusion restriction holds is often questionable.

2.3 Modeling CACE With Covariates

The importance of covariate information in CACE estimation has been demonstrated in earlier studies. In the Bayesian estimation framework, it has been shown that covariate information plays a critical role in obtaining better posterior distributions especially in weakly identified models (Frangakis et al., 2002; Hirano et al., 2000). In the ML estimation method, it has been demonstrated that covariate information may increase statistical power (Jo, 2002) and reduce bias due to model misspecification (Jo, in press). The current study focuses on the role of covariate information in identifying CACE models.

If pre-treatment covariates are available in the study, the probability of being a complier for each individual (π_{ci}) varies depending on the influence of covariates. Let \mathbf{x} be a vector of pre-treatment covariates. The logistic regression of compliance on covariates is described as

$$\begin{aligned}
 P(i \in C(c) \mid \mathbf{x}_i) &= \pi_{ci}, \\
 P(i \in C(n) \mid \mathbf{x}_i) &= 1 - \pi_{ci}, \\
 \text{logit}(\pi_{ci}) &= \beta_0 + \boldsymbol{\beta}_1 \mathbf{x}_i,
 \end{aligned} \tag{10}$$

where β_0 represents a logit intercept, and $\boldsymbol{\beta}_1$ is a vector of logit coefficients. The level of association between compliance and covariates is represented by $\boldsymbol{\beta}_1$.

Pre-treatment covariates can also have direct influence on the outcome. Let $c_i = 0$ and $n_i = 1$ if $i \in C(n)$, and $c_i = 1$ and $n_i = 0$ if $i \in C(c)$. Consider an outcome

variable Y for individual i with compliance status c_i and n_i ,

$$\begin{aligned}
Y_i = & \alpha_n n_i + \alpha_c c_i + \gamma_n n_i Z_i + \gamma_c c_i Z_i + \gamma_{nx} n_i Z_i \mathbf{x}_i + \gamma_{cx} c_i Z_i \mathbf{x}_i + \\
& \boldsymbol{\lambda}_n n_i \mathbf{x}_i + \boldsymbol{\lambda}_c c_i \mathbf{x}_i + \epsilon_{in} n_i + \epsilon_{ic} c_i,
\end{aligned} \tag{11}$$

where α_n is the intercept for never-takers, and α_c is the intercept for compliers. $\boldsymbol{\lambda}_n$ denotes the main effect of covariates for never-takers, and $\boldsymbol{\lambda}_c$ denotes the main effect of covariates for compliers. γ_n denotes the main effect of treatment assignment for never-takers (ITT_n), and γ_c denotes the main effect of treatment assignment for compliers (ITT_c). γ_{nx} denotes the interaction effect of treatment assignment for never-takers, which varies across different levels of covariates (ITT_{nx}). γ_{cx} denotes the interaction effect of treatment assignment for compliers, which varies across different levels of covariates (ITT_{cx}). ϵ_{in} is a normally distributed residual if $i \in C(n)$ with zero mean and variance σ_n^2 , and ϵ_{ic} is a normally distributed residual if $i \in C(c)$ with zero mean and variance σ_c^2 .

In equation (11), the model parameters where functional assumptions can be considered are γ_n , γ_{nx} , γ_{cx} , $\boldsymbol{\lambda}_n$, and $\boldsymbol{\lambda}_c$. The assumption of the exclusion restriction can be imposed on γ_n and γ_{nx} . The assumption of additive effect of treatment assignment can be imposed on γ_{nx} and γ_{cx} . The assumption of the constant effect of covariate can be imposed on γ_{nx} , γ_{cx} , $\boldsymbol{\lambda}_n$, and $\boldsymbol{\lambda}_c$. Depending on which of these assumptions are imposed, CACE models are differently identified. The advantage of having covariate information is that one can choose functional assumptions that are more reasonable in given situations. The two key assumptions related to covariates

are defined as follows.

Additivity of Treatment Assignment Effect: The average causal effect of treatment assignment is constant regardless of varying values of covariates. That is, $\gamma_{nx} = 0$, and $\gamma_{cx} = 0$.

Constant Effects of Covariates: The effect of a covariate on the outcome does not depend on compliance type. That is, $\lambda_n = \lambda_c$, and $\gamma_{nx} = \gamma_{cx}$.

Assume that there is only one binary covariate X that predicts both compliance and outcome. The observed-data likelihood in equation (4) can be modified as

$$\begin{aligned}
L(\theta \mid data) \propto & \prod_{i \in \{Z_i=1, D_i=0, X_i=0\}} \pi_{n, X=0} f(y_i \mid \mu_{1n, X=0}, \sigma_n^2) \times \\
& \prod_{i \in \{Z_i=1, D_i=0, X_i=1\}} \pi_{n, X=1} f(y_i \mid \mu_{1n, X=1}, \sigma_n^2) \times \\
& \prod_{i \in \{Z_i=1, D_i=1, X_i=0\}} \pi_{c, X=0} f(y_i \mid \mu_{1c, X=0}, \sigma_c^2) \times \\
& \prod_{i \in \{Z_i=1, D_i=1, X_i=1\}} \pi_{c, X=1} f(y_i \mid \mu_{1c, X=1}, \sigma_c^2) \times \\
& \prod_{i \in \{Z_i=0, D_i=0, X_i=0\}} [\pi_{n, X=0} f(y_i \mid \mu_{0n, X=0}, \sigma_n^2) + \pi_{c, X=0} f(y_i \mid \mu_{0c, X=0}, \sigma_c^2)] \times \\
& \prod_{i \in \{Z_i=0, D_i=0, X_i=1\}} [\pi_{n, X=1} f(y_i \mid \mu_{0n, X=1}, \sigma_n^2) + \pi_{c, X=1} f(y_i \mid \mu_{0c, X=1}, \sigma_c^2)], \quad (12)
\end{aligned}$$

where the binary covariate X has two values ($X = 0$ or $X = 1$). The proportions of compliers and never-takers in the population vary across different values of X . The population mean potential outcomes for compliers and never-takers vary across different values of X .

Based on equations (11) and (12), six directly estimable population means can be

expressed in terms of unrestricted model parameters as

$$\mu_{1n,X=0} = \alpha_n + \gamma_n, \quad (13)$$

$$\mu_{1n,X=1} = \alpha_n + \gamma_n + \gamma_{nx} + \lambda_n, \quad (14)$$

$$\mu_{1c,X=0} = \alpha_c + \gamma_c, \quad (15)$$

$$\mu_{1c,X=1} = \alpha_c + \gamma_c + \gamma_{cx} + \lambda_c, \quad (16)$$

$$\mu_{0,X=0} = \pi_{n,X=0} \alpha_n + \pi_{c,X=0} \alpha_c, \quad (17)$$

$$\mu_{0,X=1} = \pi_{n,X=1} (\alpha_n + \lambda_n) + \pi_{c,X=1} (\alpha_c + \lambda_c), \quad (18)$$

where α_n corresponds to $\mu_{0n,X=0}$, and α_c corresponds to $\mu_{0c,X=0}$. $\mu_{0,X=0}$ is the population mean potential outcome if $Z = 0$ and $X = 0$, and $\mu_{0,X=1}$ is the population mean potential outcome if $Z = 0$ and $X = 1$. Equations (13) to (18) show that suggested model parameters cannot be identified without some functional assumptions. Three alternative ways of identifying CACE models are discussed in this study.

2.3.1 Model A: Exclusion Restriction

Model A represents conventional CACE models, where unique ML estimates are obtained relying on the exclusion restriction. In the presence of covariates, the exclusion restriction is imposed not only on a main effect (i.e., $\gamma_n = 0$), but also on interaction effects (i.e., $\gamma_{nx} = 0$). Assuming that there is only one binary covariate X , equations (19) to (24) describe Model A with zero degrees of freedom.

$$\mu_{1n,X=0} = \alpha_n, \quad (19)$$

$$\mu_{1n,X=1} = \alpha_n + \lambda_n, \quad (20)$$

$$\mu_{1c,X=0} = \alpha_c + \gamma_c, \quad (21)$$

$$\mu_{1c,X=1} = \alpha_c + \gamma_c + \gamma_{cx} + \lambda_c, \quad (22)$$

$$\mu_{0,X=0} = \pi_{n,X=0} \alpha_n + \pi_{c,X=0} \alpha_c, \quad (23)$$

$$\mu_{0,X=1} = \pi_{n,X=1} (\alpha_n + \lambda_n) + \pi_{c,X=1} (\alpha_c + \lambda_c). \quad (24)$$

From equation (19), the estimator of α_n is directly defined as

$$\hat{\alpha}_n = \hat{\mu}_{1n,X=0}. \quad (25)$$

where $\hat{\mu}_{1n,X=0}$ is an ML estimate of $\mu_{1n,X=0}$.

From equations (20) and (25), the estimator of λ_n can be defined as

$$\hat{\lambda}_n = \hat{\mu}_{1n,X=1} - \hat{\mu}_{1n,X=0}. \quad (26)$$

where $\hat{\mu}_{1n,X=1}$ is an ML estimate of $\mu_{1n,X=1}$.

From equations (23) and (25), the estimator of α_c can be defined as

$$\hat{\alpha}_c = \frac{\hat{\mu}_{0,X=0} - \hat{\pi}_{n,X=0} \hat{\alpha}_n}{\hat{\pi}_{c,X=0}}. \quad (27)$$

where $\hat{\mu}_{0,X=0}$, $\hat{\pi}_{n,X=0}$, and $\hat{\pi}_{c,X=0}$ are ML estimates of $\mu_{0,X=0}$, $\pi_{n,X=0}$, and $\pi_{c,X=0}$.

From equations (21) and (27), the estimator of γ_c can then be defined as

$$\hat{\gamma}_c = \hat{\mu}_{1c,X=0} - \hat{\alpha}_c. \quad (28)$$

where $\hat{\mu}_{1c,X=0}$ is an ML estimate of $\mu_{1c,X=0}$.

From equations (24), (25), (26), and (27), the estimator of λ_c is defined as

$$\hat{\lambda}_c = \frac{\hat{\mu}_{0,X=1} - \hat{\pi}_{n,X=1} \hat{\alpha}_n - \hat{\pi}_{n,X=1} \hat{\lambda}_n - \hat{\pi}_{c,X=1} \hat{\alpha}_c}{\hat{\pi}_{c,X=1}}. \quad (29)$$

where $\hat{\mu}_{0,X=1}$, $\hat{\pi}_{n,X=1}$, and $\hat{\pi}_{c,X=1}$ are ML estimates of $\mu_{0,X=1}$, $\pi_{n,X=1}$, and $\pi_{c,X=1}$.

Finally, the estimator of γ_{cx} can be defined from equations (22), (27), (28), and (29) as

$$\hat{\gamma}_{cx} = \hat{\mu}_{1c,X=1} - \hat{\alpha}_c - \hat{\gamma}_c - \hat{\lambda}_c. \quad (30)$$

where $\hat{\mu}_{1c,X=1}$ is an ML estimate of $\mu_{1c,X=1}$.

The advantage of Model A is that it provides both the main and the interaction effect estimates for compliers. However, ML estimates of parameters in Model A can be biased, if treatment assignment has any effect on never-takers. Treatment assignment can have not only a main effect (γ_n), but also an interaction effect (γ_{nx}) on never-takers depending on covariate values. The estimators of γ_c and γ_{cx} will be biased if $\gamma_n \neq 0$ and/or $\gamma_{nx} \neq 0$. The bias mechanism that involves both γ_n and γ_{nx} can be very complex, and it is hard to predict consistent patterns of bias (e.g., γ_n and γ_{nx} may have opposite effects).

2.3.2 Model B: Additive Effect of Treatment Assignment

Model B represents alternative CACE models, where unique ML estimates are obtained by assuming additive effect of treatment assignment across different values of covariates. Assuming additivity, Model B provides the main effect estimate of treat-

ment assignment for both compliers and noncompliers. Along with the additivity assumption, the identifiability of Model B relies on the association between compliance and covariate. In principle, Model B can be identified unless $\beta_1 = 0$ in equation (10).

Assuming that there is only one binary covariate X , equations (31) to (36) describe Model B.

$$\mu_{1n,X=0} = \alpha_n + \gamma_n, \quad (31)$$

$$\mu_{1n,X=1} = \alpha_n + \gamma_n + \lambda_n, \quad (32)$$

$$\mu_{1c,X=0} = \alpha_c + \gamma_c, \quad (33)$$

$$\mu_{1c,X=1} = \alpha_c + \gamma_c + \lambda_c, \quad (34)$$

$$\mu_{0,X=0} = \pi_{n,X=0} \alpha_n + \pi_{c,X=0} \alpha_c, \quad (35)$$

$$\mu_{0,X=1} = \pi_{n,X=1} (\alpha_n + \lambda_n) + \pi_{c,X=1} (\alpha_c + \lambda_c). \quad (36)$$

From equations (31) and (32), the estimator of λ_n can be defined as

$$\hat{\lambda}_n = \hat{\mu}_{1n,X=1} - \hat{\mu}_{1n,X=0}. \quad (37)$$

where $\hat{\mu}_{1n,X=1}$ and $\hat{\mu}_{1n,X=0}$ are ML estimates of $\mu_{1n,X=1}$ and $\mu_{1n,X=0}$.

From equations (33) and (34), the estimator of λ_c can be defined as

$$\hat{\lambda}_c = \hat{\mu}_{1c,X=1} - \hat{\mu}_{1c,X=0}. \quad (38)$$

where $\hat{\mu}_{1c,X=1}$ and $\hat{\mu}_{1c,X=0}$ are ML estimates of $\mu_{1c,X=1}$ and $\mu_{1c,X=0}$.

From equations (35), (36), and (37), the estimator of α_n can be defined as

$$\hat{\alpha}_n = \frac{\hat{\pi}_{c,X=0} \hat{\mu}_{0,X=1} - \hat{\pi}_{c,X=1} \hat{\mu}_{0,X=0} - \hat{\pi}_{c,X=0} \hat{\pi}_{n,X=1} \hat{\lambda}_n - \hat{\pi}_{c,X=0} \hat{\pi}_{c,X=1} \hat{\lambda}_c}{\hat{\pi}_{c,X=0} - \hat{\pi}_{c,X=1}}, \quad (39)$$

where $\hat{\mu}_{0,X=1}$, $\hat{\mu}_{0,X=0}$, $\hat{\pi}_{c,X=0}$, $\hat{\pi}_{c,X=1}$, and $\hat{\pi}_{n,X=1}$ are ML estimates of $\mu_{0,X=1}$, $\mu_{0,X=0}$, $\pi_{c,X=0}$, $\pi_{c,X=1}$, and $\pi_{n,X=1}$.

From equations (35) and (39), the estimator of α_c is defined as

$$\hat{\alpha}_c = \frac{\hat{\mu}_{0,X=0} - \hat{\pi}_{n,X=0} \hat{\alpha}_n}{\hat{\pi}_{c,X=0}}, \quad (40)$$

where $\hat{\pi}_{n,X=0}$ is an ML estimate of $\pi_{n,X=0}$.

From equations (31) and (39), the estimator of γ_n is defined as

$$\hat{\gamma}_n = \hat{\mu}_{1n,X=0} - \hat{\alpha}_n. \quad (41)$$

Finally, from equations (33) and (40), the estimator of γ_c is defined as

$$\hat{\gamma}_c = \hat{\mu}_{1c,X=0} - \hat{\alpha}_c. \quad (42)$$

Model B is an appropriate model if interaction between treatment assignment and covariates is unlikely. However, ML estimates in Model B can be biased if the additivity assumption does not hold (i.e., $\gamma_{nx} \neq 0$ and/or $\gamma_{cx} \neq 0$). The advantage of Model B is that the CACE estimate is not affected by violation of exclusion restriction. In Model B, the γ_c estimate is not sensitive to violation of $\gamma_{nx} = 0$. The γ_n estimate is not sensitive to violation of $\gamma_{cx} = 0$. For example, if true $\gamma_{nx} = 0$, and true $\gamma_{cx} \neq 0$, the λ_n estimate will not be biased (see equations (14) and (32)), but the λ_c estimate

will be biased (see equations (16) and (34)). Therefore, α_n can be estimated without bias from equations (35) and (36), but the α_c estimate will be biased. As a result, the γ_n estimate will not be biased, although the γ_c estimate is biased.

If the γ_n estimate is biased in Model B, the bias is not due to violating $\gamma_{cx} = 0$, but due to violating $\gamma_{nx} = 0$. In other words, if $\gamma_n = 0$ and $\gamma_{nx} = 0$, the γ_n estimate should be zero. If $\gamma_n \neq 0$ and/or $\gamma_{nx} \neq 0$, the γ_n estimate will be different from zero, suggesting violation of the exclusion restriction. Having a zero γ_n estimate does not necessarily guarantee that the exclusion restriction holds, because it could result from nonzero γ_n and nonzero γ_{nx} . However, having a zero γ_n estimate does mean that the CACE estimate will be the same with and without assuming the exclusion restriction. In that sense, the exclusion restriction is not violated from the practical point of view. It is demonstrated in Tables 3.a and 3.b, using JOBS II, how γ_n and the γ_c estimates change when $\gamma_{cx} = 0$ and $\gamma_{nx} = 0$ are relaxed for different combinations of covariates.

2.3.3 Model C: Constant Effects of Covariates

Model C represents alternative CACE models, where unique ML estimates are obtained by assuming constant effects of covariates on the outcome across compliers and noncompliers. Assuming constant effects of covariates, Model C provides both the main and interaction effect estimates of treatment assignment. As in Model B, the identifiability in Model C relies on the association between compliance and covariate. This model also requires an additional restriction to maintain its identifiability.

That is, additive effect of treatment assignment needs to be imposed at least for one covariate. Therefore, the Model C framework can be useful when there are multiple covariates.

Equations (43) to (51) describe one example of building identifiability in the Model C framework assuming two binary covariates X_1 and X_2 .

$$\mu_{1n, X_1=0, X_2=0} = \alpha_n + \gamma_n, \quad (43)$$

$$\mu_{1n, X_1=1, X_2=0} = \alpha_n + \gamma_n + \lambda_{nX_1}, \quad (44)$$

$$\mu_{1n, X_1=0, X_2=1} = \alpha_n + \gamma_n + \gamma_{nX_2} + \lambda_{nX_2}, \quad (45)$$

$$\mu_{1c, X_1=0, X_2=0} = \alpha_c + \gamma_c, \quad (46)$$

$$\mu_{1c, X_1=1, X_2=0} = \alpha_c + \gamma_c + \lambda_{nX_1}, \quad (47)$$

$$\mu_{1c, X_1=0, X_2=1} = \alpha_c + \gamma_c + \gamma_{nX_2} + \lambda_{nX_2}, \quad (48)$$

$$\mu_{0, X_1=0, X_2=0} = \pi_{n, X_1=0, X_2=0} \alpha_n + \pi_{c, X_1=0, X_2=0} \alpha_c, \quad (49)$$

$$\mu_{0, X_1=1, X_2=0} = \pi_{n, X_1=1, X_2=0} (\alpha_n + \lambda_{nX_1}) + \pi_{c, X_1=1, X_2=0} (\alpha_c + \lambda_{nX_1}), \quad (50)$$

$$\mu_{0, X_1=0, X_2=1} = \pi_{n, X_1=0, X_2=1} (\alpha_n + \lambda_{nX_2}) + \pi_{c, X_1=0, X_2=1} (\alpha_c + \lambda_{nX_2}), \quad (51)$$

where nine population means in the left side of the equations are directly estimable based on sample statistics.

From equations (43) and (44), or from (46) and (47), the estimator of λ_{nX_1} can be defined as

$$\hat{\lambda}_{nX_1} = \hat{\mu}_{1n, X_1=1, X_2=0} - \hat{\mu}_{1n, X_1=0, X_2=0}, \quad (52)$$

where $\hat{\mu}_{1n, X_1=1, X_2=0}$ and $\hat{\mu}_{1n, X_1=0, X_2=0}$ are ML estimates of $\mu_{1n, X_1=1, X_2=0}$ and $\mu_{1n, X_1=0, X_2=0}$.

From equations (49), (50), and (52), the estimator of α_n can be defined as

$$\hat{\alpha}_n = \frac{\hat{\pi}_{c, X_1=0, X_2=0} \hat{\mu}_{0, X_1=1, X_2=0} - \hat{\pi}_{c, X_1=1, X_2=0} \hat{\mu}_{0, X_1=0, X_2=0} - \hat{\pi}_{c, X_1=0, X_2=0} \hat{\lambda}_{nX_1}}{\hat{\pi}_{c, X_1=0, X_2=0} - \hat{\pi}_{c, X_1=1, X_2=0}}, \quad (53)$$

where $\hat{\mu}_{0, X_1=1, X_2=0}$, $\hat{\mu}_{0, X_1=0, X_2=0}$, $\hat{\pi}_{c, X_1=0, X_2=0}$, and $\hat{\pi}_{c, X_1=1, X_2=0}$ are ML estimates of $\mu_{0, X_1=1, X_2=0}$, $\mu_{0, X_1=0, X_2=0}$, $\pi_{c, X_1=1, X_2=0}$, and $\pi_{c, X_1=1, X_2=0}$.

From equations (49) and (53), the estimator of α_c can be defined as

$$\hat{\alpha}_c = \frac{\hat{\mu}_{0, X_1=0, X_2=0} - \hat{\pi}_{n, X_1=0, X_2=0} \hat{\alpha}_n}{\hat{\pi}_{c, X_1=0, X_2=0}}, \quad (54)$$

where $\hat{\pi}_{n, X_1=0, X_2=0}$ is an ML estimate of $\pi_{n, X_1=0, X_2=0}$.

From equations (51), (53), and (54), the estimator of λ_{nX_2} can then be defined as

$$\hat{\lambda}_{nX_2} = \hat{\mu}_{0, X_1=0, X_2=1} - \hat{\pi}_{n, X_1=0, X_2=1} \hat{\alpha}_n - \hat{\pi}_{c, X_1=0, X_2=1} \hat{\alpha}_c, \quad (55)$$

where $\hat{\mu}_{0, X_1=0, X_2=1}$, $\hat{\pi}_{n, X_1=0, X_2=1}$, and $\hat{\pi}_{c, X_1=0, X_2=1}$ are ML estimates of $\mu_{0, X_1=0, X_2=1}$, $\pi_{n, X_1=0, X_2=1}$, and $\pi_{c, X_1=0, X_2=1}$.

Finally, from equations (43), (45), and (55), the estimator of γ_{nX_2} is defined as

$$\hat{\gamma}_{nX_2} = \hat{\mu}_{1n, X_1=0, X_2=1} - \hat{\mu}_{1n, X_1=0, X_2=0} - \hat{\lambda}_{nX_2}, \quad (56)$$

where $\hat{\mu}_{1n, X_1=0, X_2=1}$ is an ML estimate of $\mu_{1n, X_1=0, X_2=1}$.

The advantage of Model C is that it provides both the main and interaction effect estimates of treatment assignment. This model will be very useful if interaction effects are expected and covariates are unlikely to have different effects on outcomes

for compliers and noncompliers. However, ML estimates of parameters in Model C can be biased, if compliers and noncompliers are heterogeneous in terms of covariate effects on the outcome. Model C can be identified if two or more covariates are available. However, having multiple covariates provides more options in imposing additivity of treatment assignment effect.

3 Application to JOBS II Intervention Study

The Job Search Intervention Study (JOBS II: Vinokur et al., 1995; Vinokur & Schul, 1997) is a randomized field experiment intended to prevent poor mental health and to promote high-quality reemployment among unemployed workers. The experimental condition consisted of five half-day training sessions. Among study participants assigned to the intervention condition, 55% attended at least one session. Among attendees, 82% attended 4 or 5 sessions (mean = 4.3 sessions, median = 5 sessions). In the current study, individuals who completed at least one training session were categorized as compliers and the rest were categorized as never-takers. Based on that categorization, the compliance rate in JOBS II was 55%. The control condition consisted of a booklet briefly describing job-search methods and tips.

The present study focused on the high-risk status group based on previous studies (Price, van Ryn, & Vinokur, 1992; Vinokur et al., 1995), which indicated that the job search intervention had its primary impact on high-risk respondents. Risk score was

computed based on risk variables in the screening data (Price et al., 1992) predicting depressive symptoms at follow-up (depression, financial strain, and assertiveness) . A total sample size of 486 was analyzed in this study after listwise deletion of cases that had missingness in covariates and outcome variables. The response rate at follow-up six months after the intervention was 87%. In the CACE analyses shown in this section, the level of depression six months after the intervention (Dep6) is used as a continuous outcome. Depression was measured with a subscale of 11 items based on the Hopkins Symptom Checklist (Derogatis, Lipman, Rickles, Uhlenuth, & Covi, 1974). The variables used in the current study are described in Table 1.

[Table 1]

Table 2.a shows results from CACE models assuming additive effect of treatment assignment. Nine covariates are included in the CACE analyses shown in this section ($X_1 = \text{Dep0}$, $X_2 = \text{Mot}$, $X_3 = \text{Grade}$, $X_4 = \text{Econ}$, $X_5 = \text{NotM}$, $X_6 = \text{NonW}$, $X_7 = \text{Age}$, $X_8 = \text{Male}$, $X_9 = \text{Assert}$). In this table, the magnitude of main effect of treatment assignment on compliers (CACE) can be compared between models with and without assuming the exclusion restriction. Since the outcome measure is depression, negative coefficients indicate a desirable treatment effect (i.e., positive effect size). In the current study, the effect size of causal effect estimates is calculated in a conventional way by dividing the outcome difference in treatment and control condition means by the square root of the variance pooled across the control and treatment groups. This approach was chosen for easier comparison across different

models.

[Table 2.a]

The results from the model assuming the exclusion restriction show that the intervention assignment did not have a significant effect on the level of depression of compliers ($\widehat{ITT}_c = -0.361$, effect size = 0.498). The results from the model without assuming the exclusion restriction show that the intervention assignment had a significant effect on the level of depression of compliers ($\widehat{ITT}_c = -0.451$, effect size = 0.622). The level of depression is significantly lower for compliers in the intervention condition compared to that of control condition individuals who could have complied if they have had been assigned to the intervention condition. It is also shown in the model without the exclusion restriction that the intervention had a negative effect on never-takers ($\widehat{ITT}_n = 0.227$, effect size = -0.313). Although the ITT_n (γ_n) estimate should be interpreted carefully given possible confounding with γ_{nx} , it at least suggests that the CACE estimate will be affected if this parameter is fixed at zero. In Table 2.a, the CACE estimate with the exclusion restriction is affected by treatment assignment effect on never-takers, but the CACE estimate without assuming the exclusion restriction is not.

Table 2.b shows the logistic regression part of the CACE model with the exclusion restriction. The CACE model without the exclusion restriction had very similar results. It is shown in Table 2.b that several covariates were significant predictors

of compliance. For example, the estimated odds of being a complier are 3.8 times higher for individuals who have a high level of motivation than for individuals who have a low level of motivation. Individuals also complied more if they were older, more educated, and less assertive.

[Table 2.b]

Table 3.a demonstrates how parameter estimates in Table 2.a change when γ_{cx} is freely estimated. In the first CACE analysis, γ_{cx} is fixed at zero for all nine covariates (see Tables 2.a and 2.b for full results). In the second analysis, γ_{cx} is relaxed for four covariates. In the third analysis, γ_{cx} is relaxed for eight covariates, which is the maximum number of interaction effects that can be relaxed in this example without losing identifiability. It is assumed that the effect of intervention assignment on depression is the same for compliers regardless of their ethnicity ($\gamma_{cX_6} = 0$). In all three analyses, γ_{nx} is fixed at zero for all nine covariates. In Tables 3.a and 3.b, only parameters that are related to treatment assignment are listed.

[Table 3.a]

The results in Table 3.a show that the γ_c estimate is sensitive to violation of $\gamma_{cx} = 0$. However, the γ_n estimate remains stable when $\gamma_{cx} = 0$ is relaxed for any combinations of the eight covariates. Therefore, the γ_n estimate might be biased in Model B, but the bias is not due to violating $\gamma_{cx} = 0$, but to violating $\gamma_{nx} = 0$. Also, the γ_c estimate might be biased in Model B, but the bias is not due to violating

$\gamma_{nx} = 0$, but to violating $\gamma_{cx} = 0$. Assuming that $\gamma_{cX_6} = 0$, the main and interaction effect estimates shown in the third analysis (8 relaxed) can be considered as unbiased for compliers. The main effect of intervention has a large effect size, but is not significant. Intervention assignment showed some significant interaction effects on compliers. The intervention assignment had a positive impact on compliers if they were highly motivated and married. However, high motivation and being married had a negative impact on individuals who would have complied with the intervention if offered, but were assigned to the control condition.

Table 3.b demonstrates how parameter estimates in Table 2.a change when γ_{nx} is freely estimated. In the first CACE analysis, γ_{nx} is fixed at zero for all nine covariates (see Tables 2.a and 2.b for full results). In the second analysis, γ_{nx} is relaxed for four covariates. In the third analysis, γ_{nx} is relaxed for eight covariates. It is assumed that the effect of intervention assignment on depression is the same for never-takers regardless of their motivation level ($\gamma_{nX_2} = 0$). In all three analyses, γ_{cx} is fixed at zero for all nine covariates.

[Table 3.b]

The results in Table 3.b show that the γ_n estimate is sensitive to violation of $\gamma_{nx} = 0$. However, the γ_c estimate remains stable when $\gamma_{nx} = 0$ is relaxed for any combinations of the eight covariates. Assuming that $\gamma_{nX_2} = 0$, the main and interaction effect estimates shown in the third analysis (8 relaxed) can be considered

as unbiased for never-takers. The main effect of intervention is not significant for never-takers. Although insignificant, intervention assignment showed some interaction effects on never-takers. The intervention assignment had a positive impact on never-takers if they were single and less assertive. However, being single and less assertive had a negative impact on individuals who would have complied with the intervention if offered, but were assigned to the control condition.

Table 4 shows results from CACE estimation assuming constant effects of covariates. For all nine covariates, it is assumed that $\lambda_n = \lambda_c$, and $\gamma_{nx} = \gamma_{cx}$. Additionally, it is assumed that being assigned to the intervention condition will have the same effect on depression regardless of participants' ethnicity (i.e., $\gamma_{nX_6} = \gamma_{cX_6} = 0$), which is necessary to maintain identifiability of the CACE model. It is shown in Table 4 that the main effect of intervention assignment was not significant either for compliers ($\widehat{ITT}_c = -0.687$, effect size = 0.948) or for never-takers ($\widehat{ITT}_n = -0.064$, effect size = 0.088). The intervention had a positive but insignificant (p -value = 0.086) effect on depression if study participants were highly motivated ($\hat{\gamma}_{nX_2} = \hat{\gamma}_{cX_2} = -0.288$, effect size = 0.397). Study participants showed a higher level of depression if they had economic hardship at the beginning of the study. The results of the logistic regression of compliance on covariates (not shown here) are similar to those in Table 2.b. Individuals complied more if they were older, more motivated, more educated, and less assertive.

[Table 4]

4 Application to JHU PIRC Intervention Study

The Johns Hopkins Public School Preventive Intervention Study was conducted by the Johns Hopkins University Preventive Intervention Research Center (JHU PIRC) in 1993-1994 (Ialongo et al., 1999). The study was designed to improve academic achievement and to reduce early behavioral problems of school children. Teachers and first-grade children were randomly assigned to intervention conditions. The control condition and the Family-School Partnership Intervention condition are compared in this example. In the intervention condition, parents were asked to implement 66 take-home activities related to literacy and mathematics over a six-month period.

A total sample size of 284 was analyzed after listwise deletion of cases that had missingness in covariates and outcome variables. One of the major outcome measures in the JHU PIRC preventive trial was the TOCA-R score (Teacher Observation of Classroom Adaptation-Revised; Werthamer-Larsson, Kellam, & Wheeler, 1991). The TOCA-R is designed to assess children's adequacy of performance on the core tasks in the classroom as rated by the teacher. Among various TOCA-R measures, shy behavior assessed in the spring of the second grade (18 months after the pre-intervention assessment) is used as a continuous outcome in the CACE analyses shown in this section. The shy behavior is a composite variable that consists of TOCA-R items such as friendly to classmates, interact with classmates, play with classmates, and initiate interactions with classmates. Table 5 describes the variables used in this example.

[Table 5]

For CACE models reported in this section, individuals are categorized into low and high compliers based on the level of completeness in 66 home learning activities. Parents who completed at least 45 activities are categorized as high compliers (upper 50% of parents) and the rest (lower 50% of parents) are categorized as low compliers. To be consistent with previous sections, the same notations will be used in this section. That is, $i \in C(c)$, if individual i is a high complier, and $i \in C(n)$, if individual i is a low complier.

Table 6.a shows results from CACE models assuming an additive effect of treatment assignment. Eight covariates are included in CACE analyses shown in this section ($X_1 = \text{Shy0}$, $X_2 = \text{Agg0}$, $X_3 = \text{Male}$, $X_4 = \text{Lunch}$, $X_5 = \text{Phealth}$, $X_6 = \text{Page}$, $X_7 = \text{Pmale}$, $X_8 = \text{NonW}$). In this table, the magnitude of main effect of treatment assignment on compliers (CACE) can be compared between models with and without assuming the exclusion restriction. Since the outcome is shy behavior, negative coefficients indicate a desirable treatment effect (i.e., positive effect size).

[Table 6.a]

Table 6.a shows that the results from models with and without the exclusion restriction are almost identical, given that the γ_n estimate is actually close to zero. In other words, the CACE estimate is unaffected by treatment assignment effect on never-takers in both models with and without the exclusion restriction. The

intervention assignment had a positive impact on children's shy behavior when their parents were highly involved in the intervention activities ($\widehat{ITT}_c = -0.652$, effect size = 0.643). Among several covariates, baseline shy behavior and parent's gender were found to be significant predictors of the level of shy behavior, if parents were not actively involved in the intervention activities. Children had a higher level of shy behavior in spring of the second grade if their baseline shy behavior was higher and if fathers were their major caregivers.

Table 6.b shows the logistic regression part of the CACE model. It is shown that parent's ethnic background was a significant predictor of compliance. The estimated odds of being a high complier are about three times higher for parents with White ethnic background than for parents with non-White ethnic background. Parent's gender had a pretty high, but not significant association with compliance. The estimated odds of being a high complier are about 2.5 times higher for mothers than for fathers.

[Table 6.b]

Table 7 shows results from CACE estimation assuming constant effects of covariates. For all eight covariates, it is assumed that $\lambda_n = \lambda_c$, and $\gamma_{nx} = \gamma_{cx}$. Additionally, it is assumed that intervention assignment will have the same effect on a child's shy behavior regardless of the parent's ethnicity (i.e., $\gamma_{nX_8} = \gamma_{cX_8} = 0$), which is necessary to maintain identifiability of the CACE model. It is shown in Table 7 that the main effect of intervention assignment was not significant either for compliers

($\widehat{ITT}_c = -0.382$, effect size = 0.377) or for never-takers ($\widehat{ITT}_n = 0.240$, effect size = 0.237). The intervention had a positive but insignificant (p -value = 0.080) effect on children's shy behavior if they were initially more aggressive ($\hat{\gamma}_{nX_2} = \hat{\gamma}_{cX_2} = -0.358$, effect size = 0.353). Children showed a higher level of shy behavior if their baseline shy behavior was higher, and if their baseline aggression level was higher. No covariates were found to be significant predictors of compliance in the logistic regression of compliance on covariates (not shown here). Although insignificant, some covariates were highly associated with compliance. Parents complied more if they were younger, if they were female, and if they were from White ethnic background.

[Table 7]

5 Conclusion

The current study demonstrated alternative ways of modeling CACE in the presence of pre-treatment covariates. The three models discussed in the study showed that the identifiability of CACE models can be built based on functional assumptions that are more reasonable given specific situations. Model A relies on the exclusion restriction, Model B relies on additivity of treatment assignment, and Model C relies on the constant effect of covariates in establishing identifiability of CACE models. Further study is needed to provide more modeling options, and to provide practical guidelines that will help intervention researchers to better select CACE estimation models given

alternative assumptions.

It was demonstrated in the study that Model B-type analysis is a practical way to test violation of the exclusion restriction within the ML-EM framework. The limitation of Model B is that it does not separate the main and interaction effects of treatment assignment simultaneously for compliers and never-takers. However, it is still useful to separate bias in the CACE estimate due to violation of the exclusion restriction, which was considered impossible in the ML-EM framework. The limitation leaves room for future study to explore other alternative ways of dealing with lack of identifiability in CACE models.

This study demonstrated the relaxation of the exclusion restriction for never-takers assuming that there are no always-takers. Relaxing the exclusion restriction for both never-takers and always-takers may complicate CACE estimation, since several sub-populations need to be distinguishable from each other in a multinomial distribution based on auxiliary information. A reasonable strategy would be to focus only on a plausible violation for a specific study. For example, the assumption is more likely to be violated for never-takers (or low compliers); or it is more likely to be violated for always-takers (e.g., Hirano et al., 2000); or the violation of the assumption is unlikely to be violated for both never-takers and always-takers (e.g., Imbens & Rubin, 1997). Further investigation is needed to clarify how suggested models can be applied in more general situations, where several sub-populations are studied.

References

- Angrist, J. D., Imbens, G. W., & Rubin, D. B. (1996). Identification of causal effects using instrumental variables. *Journal of the American Statistical Association*, *91*, 444-455.
- Bloom, H. S. (1984). Accounting for no-shows in experimental evaluation designs. *Evaluation Review*, *8*, 225-246.
- Dempster, A., Laird, N., & Rubin, D. B. (1977). Maximum likelihood from incomplete data via the EM algorithm. *Journal of the Royal Statistical Society, Series B*, *39*, 1-38.
- Derogatis, L. R., Lipman, R. S., Rickles, K., Uhlenuth, E. H., & Covi, L. (1974). The Hopkins Symptom Checklist (HSCL). In *Psychological measurements in psychopharmacology: Modern problems in pharmacopsychiatry* (ed. P. Pichot), *7*, 79-110. New York: Karger, Basel.
- Frangakis, C. E. (1999). Coexistent complications with noncompliance with study-protocols, and implications for statistical analysis. Unpublished doctoral dissertation. Harvard University.
- Frangakis, C. E., Rubin, D. B., & Zhou, X. H. (2002). Clustered encouragement design with individual noncompliance: Bayesian inference and application to advance directive forms. *Biostatistics*, *3*, 147-164.
- Hirano, K., Imbens, G. W., Rubin, D. B. & Zhou, X. H. (2000). Assessing the effect of an influenza vaccine in an encouragement design. *Biostatistics*, *1*, 69-88.
- Holland, P. W. (1986). Statistics and causal inference. *Journal of the American Statistical Association*, *81*, 945-970

- Holland, P. W. (1988). Causal inference, path analysis, and recursive structural equation models. *Sociological methodology* 18, 449-484. Washington, DC: American Statistical Association.
- Ialongo, N. S., Werthamer, L., Kellam, S. G., Brown, C. H., Wang, S., & Lin, Y. (1999). Proximal impact of two first-grade preventive interventions on the early risk behaviors for later substance abuse, depression and antisocial behavior. *American Journal of Community Psychology*, 27, 599-642.
- Imbens, G. W., & Angrist, J. (1994). Identification and estimation of local average treatment effects. *Econometrica*, 62, 467-476.
- Imbens, G. W., & Rubin, D. B. (1997). Bayesian inference for causal effects in randomized experiments with non-compliance. *The Annals of Statistics*, 25, 305-327.
- Jo, B. (in press). Model misspecification sensitivity analysis in estimating causal effects of interventions with noncompliance. *Statistics in Medicine*.
- Jo, B. (2002). Statistical power in randomized intervention studies with noncompliance. *Psychological Methods*, 7, 178-193.
- Little, R. J. A., & Rubin, D. B. (1987). *Statistical analysis with missing data*. New York: John Wiley & Sons
- Little, R. J. A., & Yau, L. H. Y. (1998). Statistical techniques for analyzing data from prevention trials: Treatment of no-shows using Rubin's causal model. *Psychological Methods*, 3, 147-159.
- McLachlan, G. J., & Krishnan, T. (1997). *The EM algorithm and extensions*. New York: Wiley Series.

- Muthén, L. K. & Muthén, B. O. (1998-2001). *Mplus user's guide*. Los Angeles: Muthén & Muthén.
- Price, R.H., van Ryn, M., & Vinokur, A.D. (1992). Impact of a preventive job search intervention on the likelihood of depression among the unemployed. *Journal of Health and Social Behavior*, *33*, 158-167.
- Rubin, D. B. (1978). Bayesian inference for causal effects: the role of randomization. *Annals of Statistics*, *6*, 34-58.
- Rubin, D. B. (1980). Discussion of "Randomization analysis of experimental data in the Fisher randomization test" by D. Basu. *Journal of the American Statistical Association*, *75*, 591-593.
- Rubin, D. B. (1990). Comment on "Neyman (1923) and causal inference in experiments and observational studies." *Statistical Science*, *5*, 472-480.
- Tanner, M. (1996). *Tools for statistical inference: Methods for the exploration of posterior distributions and likelihood functions*. New York: Springer.
- Vinokur, A. D., Price, R. H., & Schul, Y. (1995). Impact of the JOBS intervention on unemployed workers varying in risk for depression. *American Journal of Community Psychology*, *23*, 39-74.
- Vinokur, A. D., & Schul, Y. (1997). Mastery and inoculation against setbacks as active ingredients in intervention for the unemployed. *Journal of Consulting and Clinical Psychology*, *65*, 867-877.
- Werthamer-Larsson, L., Kellam, S. G., & Wheeler, L. (1991). Effect of first-grade classroom environment on child shy behavior, aggressive behavior, and concentration problems. *American Journal of Community Psychology*, *19*, 585-602.

Table 1. JOBS II: Sample Statistics (N = 486)

| Variable | Mean | <i>SD</i> | Description |
|----------|-------|-----------|---|
| <i>Z</i> | 0.67 | 0.47 | Intervention assignment (0=control, 1=intervention) |
| <i>c</i> | 0.55 | 0.50 | Compliance (0=never-taker, 1=complier) |
| Dep6 | 2.01 | 0.73 | Depression level 6 months after the treatment |
| Dep0 | 2.45 | 0.30 | Depression level before the treatment |
| Mot | 0.32 | 0.47 | Motivation level before the treatment (0=low, 1=high) |
| Grade | 13.37 | 2.01 | School grade completed |
| Econ | 3.60 | 0.87 | Economic hardship before the treatment |
| NotM | 0.62 | 0.49 | Marital status (0=married, 1=not married) |
| NonW | 0.19 | 0.39 | Race (0=White, 1=non-White) |
| Age | 36.61 | 10.04 | Age in years |
| Male | 0.42 | 0.49 | Gender (0=female, 1=male) |
| Assert | 3.07 | 0.91 | Assertiveness before the treatment |

Table 2.a. JOBS II: CACE Estimation Assuming Additive Effect of Intervention Assignment

| Exclusion Restriction Parameter | <u>With</u> | | <u>Without</u> | |
|------------------------------------|-------------|-----------|----------------|-----------|
| | Estimate | <i>SE</i> | Estimate | <i>SE</i> |
| ITT_c (CACE) | -0.361 | 0.191 | -0.451 | 0.131 |
| ITT_n | 0.000 | . | 0.227 | 0.094 |
| λ_{cX_1} (Dep0) | 0.249 | 0.177 | 0.231 | 0.163 |
| λ_{cX_2} (Mot) | -0.037 | 0.102 | -0.043 | 0.099 |
| λ_{cX_3} (Grade) | -0.039 | 0.024 | -0.041 | 0.023 |
| λ_{cX_4} (Econ) | 0.178 | 0.078 | 0.194 | 0.061 |
| λ_{cX_5} (NotM) | -0.124 | 0.149 | -0.153 | 0.119 |
| λ_{cX_6} (NonW) | -0.106 | 0.170 | -0.077 | 0.158 |
| λ_{cX_7} (Age) | -0.004 | 0.006 | -0.006 | 0.005 |
| λ_{cX_8} (Male) | -0.127 | 0.110 | -0.134 | 0.106 |
| λ_{cX_9} (Assert) | -0.067 | 0.058 | -0.061 | 0.054 |
| λ_{nX_1} (Dep0) | -0.077 | 0.166 | -0.033 | 0.152 |
| λ_{nX_2} (Mot) | 0.047 | 0.182 | -0.009 | 0.130 |
| λ_{nX_3} (Grade) | -0.023 | 0.031 | -0.026 | 0.026 |
| λ_{nX_4} (Econ) | 0.114 | 0.064 | 0.098 | 0.054 |
| λ_{nX_5} (NotM) | -0.121 | 0.133 | -0.113 | 0.105 |
| λ_{nX_6} (NonW) | 0.173 | 0.137 | 0.165 | 0.125 |
| λ_{nX_7} (Age) | 0.002 | 0.006 | 0.001 | 0.005 |
| λ_{nX_8} (Male) | -0.088 | 0.106 | -0.078 | 0.101 |
| λ_{nX_9} (Assert) | -0.009 | 0.062 | -0.018 | 0.056 |
| α_c | 2.103 | 0.654 | 2.260 | 0.599 |
| α_n | 2.091 | 0.605 | 1.936 | 0.561 |
| σ_c^2 | 0.516 | 0.068 | 0.512 | 0.052 |
| σ_n^2 | 0.440 | 0.080 | 0.406 | 0.049 |

Table 2.b. JOBS II: Logistic Regression of Compliance on Covariates
(compliers vs. never-takers)

| Parameter | Estimate | <i>SE</i> |
|-----------------------|----------|-----------|
| β_0 (Intercept) | -4.657 | 1.635 |
| β_{11} (Dep0) | -0.459 | 0.432 |
| β_{12} (Mot) | 1.335 | 0.302 |
| β_{13} (Grade) | 0.309 | 0.071 |
| β_{14} (Econ) | -0.209 | 0.163 |
| β_{15} (NotM) | 0.507 | 0.297 |
| β_{16} (NonW) | -0.382 | 0.333 |
| β_{17} (Age) | 0.078 | 0.016 |
| β_{18} (Male) | 0.369 | 0.260 |
| β_{19} (Assert) | -0.334 | 0.150 |

Table 3.a. JOBS II: Relaxing Additivity of Treatment Effect for Compliers
 ($\gamma_{nx} = 0$ for all covariates)

| γ_{cx} Parameter | <u>0 relaxed</u> | | <u>4 relaxed</u> | | <u>8 relaxed</u> | |
|----------------------------|------------------|-----------|------------------|-----------|------------------|-----------|
| | Estimate | <i>SE</i> | Estimate | <i>SE</i> | Estimate | <i>SE</i> |
| ITT_c (CACE) | -0.451 | 0.131 | 0.544 | 0.434 | -1.440 | 1.670 |
| ITT_n | 0.227 | 0.094 | 0.233 | 0.092 | 0.231 | 0.090 |
| γ_{cX_1} (Dep0) | 0.000 | . | 0.000 | . | 0.231 | 0.385 |
| γ_{cX_2} (Mot) | 0.000 | . | -0.503 | 0.230 | -0.607 | 0.234 |
| γ_{cX_3} (Grade) | 0.000 | . | 0.000 | . | 0.048 | 0.064 |
| γ_{cX_4} (Econ) | 0.000 | . | -0.241 | 0.148 | -0.267 | 0.138 |
| γ_{cX_5} (NotM) | 0.000 | . | 0.000 | . | 0.586 | 0.240 |
| γ_{cX_6} (NonW) | 0.000 | . | -0.080 | 0.531 | 0.000 | . |
| γ_{cX_7} (Age) | 0.000 | . | 0.000 | . | 0.013 | 0.012 |
| γ_{cX_8} (Male) | 0.000 | . | 0.073 | 0.238 | 0.178 | 0.243 |
| γ_{cX_9} (Assert) | 0.000 | . | 0.000 | . | -0.012 | 0.144 |

Table 3.b. JOBS II: Relaxing Additivity of Treatment Effect for Never-takers
 ($\gamma_{cx} = 0$ for all covariates)

| γ_{nx} Parameter | <u>0 relaxed</u> | | <u>4 relaxed</u> | | <u>8 relaxed</u> | |
|----------------------------|------------------|-----------|------------------|-----------|------------------|-----------|
| | Estimate | <i>SE</i> | Estimate | <i>SE</i> | Estimate | <i>SE</i> |
| ITT_c (CACE) | -0.451 | 0.131 | -0.457 | 0.129 | -0.432 | 0.137 |
| ITT_n | 0.227 | 0.094 | -0.044 | 0.380 | 0.343 | 1.103 |
| γ_{nX_1} (Dep0) | 0.000 | . | 0.000 | . | -0.045 | 0.290 |
| γ_{nX_2} (Mot) | 0.000 | . | -0.004 | 0.283 | 0.000 | . |
| γ_{nX_3} (Grade) | 0.000 | . | 0.000 | . | -0.018 | 0.054 |
| γ_{nX_4} (Econ) | 0.000 | . | 0.088 | 0.102 | 0.058 | 0.105 |
| γ_{nX_5} (NotM) | 0.000 | . | 0.000 | . | -0.328 | 0.201 |
| γ_{nX_6} (NonW) | 0.000 | . | 0.100 | 0.288 | -0.016 | 0.302 |
| γ_{nX_7} (Age) | 0.000 | . | 0.000 | . | -0.009 | 0.011 |
| γ_{nX_8} (Male) | 0.000 | . | -0.154 | 0.183 | -0.272 | 0.215 |
| γ_{nX_9} (Assert) | 0.000 | . | 0.000 | . | 0.199 | 0.116 |

Table 4. JOBS II: CACE Estimation Assuming Constant Effects of Covariates

| Parameter | Estimate | <i>SE</i> |
|--|----------|-----------|
| ITT_c (CACE) | -0.687 | 0.933 |
| ITT_n | -0.064 | 0.893 |
| $\lambda_{cX_1} = \lambda_{nX_1}$ (Dep0) | 0.029 | 0.209 |
| $\lambda_{cX_2} = \lambda_{nX_2}$ (Mot) | 0.191 | 0.145 |
| $\lambda_{cX_3} = \lambda_{nX_3}$ (Grade) | -0.045 | 0.032 |
| $\lambda_{cX_4} = \lambda_{nX_4}$ (Econ) | 0.195 | 0.075 |
| $\lambda_{cX_5} = \lambda_{nX_5}$ (NotM) | -0.170 | 0.132 |
| $\lambda_{cX_6} = \lambda_{nX_6}$ (NonW) | 0.074 | 0.092 |
| $\lambda_{cX_7} = \lambda_{nX_7}$ (Age) | -0.004 | 0.007 |
| $\lambda_{cX_8} = \lambda_{nX_8}$ (Male) | -0.073 | 0.124 |
| $\lambda_{cX_9} = \lambda_{nX_9}$ (Assert) | -0.075 | 0.079 |
| $\gamma_{cX_1} = \gamma_{nX_1}$ (Dep0) | 0.053 | 0.242 |
| $\gamma_{cX_2} = \gamma_{nX_2}$ (Mot) | -0.288 | 0.168 |
| $\gamma_{cX_3} = \gamma_{nX_3}$ (Grade) | 0.015 | 0.038 |
| $\gamma_{cX_4} = \gamma_{nX_4}$ (Econ) | -0.066 | 0.089 |
| $\gamma_{cX_5} = \gamma_{nX_5}$ (NotM) | 0.058 | 0.160 |
| $\gamma_{cX_6} = \gamma_{nX_6}$ (NonW) | 0.000 | . |
| $\gamma_{cX_7} = \gamma_{nX_7}$ (Age) | 0.003 | 0.008 |
| $\gamma_{cX_8} = \gamma_{nX_8}$ (Male) | -0.029 | 0.149 |
| $\gamma_{cX_9} = \gamma_{nX_9}$ (Assert) | 0.041 | 0.090 |
| α_c | 2.634 | 0.801 |
| α_n | 2.065 | 0.767 |
| σ_c^2 | 0.506 | 0.051 |
| σ_n^2 | 0.425 | 0.053 |

Table 5. Johns Hopkins PIRC: Sample Statistics ($N = 284$)

| Variable | Mean | <i>SD</i> | Description |
|----------|------|-----------|--|
| <i>Z</i> | 0.50 | 0.50 | Intervention assignment (0=control, 1=treatment) |
| <i>c</i> | 0.50 | 0.50 | High compliance (0=low complier, 1=high complier) |
| Shy18 | 2.31 | 1.02 | TOCA-R mean shy behavior 18 months after the baseline assessment |
| Shy0 | 2.22 | 1.06 | TOCA-R mean shy behavior at the baseline assessment |
| Agg0 | 1.45 | 0.69 | TOCA-R mean aggression at the baseline assessment |
| Male | 0.49 | 0.50 | Student's gender (0=female, 1=male) |
| Lunch | 0.62 | 0.49 | Free lunch program (0=no, 1=yes) |
| Phealth | 0.09 | 0.29 | Parent limited by health problem(0=no, 1=yes) |
| Page | 3.02 | 1.44 | Parent's age in 5 year brackets |
| Pmale | 0.07 | 0.26 | Parent's gender (0=female, 1=male) |
| NonW | 0.87 | 0.33 | Parent's ethnicity (0=White, 1=non-White) |

Table 6.a. Johns Hopkins PIRC: CACE Estimation Assuming Additive Effect of Intervention Assignment

| Exclusion Restriction Parameter | <u>With</u> | | <u>Without</u> | |
|------------------------------------|-------------|-----------|----------------|-----------|
| | Estimate | <i>SE</i> | Estimate | <i>SE</i> |
| ITT_c (CACE) | -0.652 | 0.221 | -0.652 | 0.225 |
| ITT_n | 0.000 | . | -0.001 | 0.148 |
| λ_{cX_1} (Shy0) | 0.231 | 0.136 | 0.231 | 0.136 |
| λ_{cX_2} (Agg0) | 0.205 | 0.162 | 0.205 | 0.163 |
| λ_{cX_3} (Male) | 0.001 | 0.228 | 0.001 | 0.228 |
| λ_{cX_4} (Lunch) | 0.197 | 0.206 | 0.197 | 0.206 |
| λ_{cX_5} (Phealth) | 0.164 | 0.368 | 0.164 | 0.369 |
| λ_{cX_6} (Page) | 0.015 | 0.017 | 0.015 | 0.017 |
| λ_{cX_7} (Pmale) | -0.058 | 0.456 | -0.058 | 0.455 |
| λ_{cX_8} (NonW) | 0.155 | 0.219 | 0.155 | 0.221 |
| λ_{nX_1} (Shy0) | 0.202 | 0.076 | 0.202 | 0.076 |
| λ_{nX_2} (Agg0) | -0.037 | 0.159 | -0.036 | 0.164 |
| λ_{nX_3} (Male) | 0.243 | 0.187 | 0.243 | 0.187 |
| λ_{nX_4} (Lunch) | 0.205 | 0.169 | 0.205 | 0.171 |
| λ_{nX_5} (Phealth) | 0.186 | 0.310 | 0.186 | 0.310 |
| λ_{nX_6} (Page) | 0.009 | 0.008 | 0.009 | 0.008 |
| λ_{nX_7} (Pmale) | 0.679 | 0.291 | 0.679 | 0.291 |
| λ_{nX_8} (NonW) | 0.181 | 0.245 | 0.181 | 0.250 |
| α_c | 1.401 | 0.687 | 1.400 | 0.692 |
| α_n | 0.815 | 0.426 | 0.816 | 0.444 |
| σ_c^2 | 0.929 | 0.111 | 0.929 | 0.111 |
| σ_n^2 | 0.628 | 0.108 | 0.628 | 0.111 |

Table 6.b. Johns Hopkins PIRC: Logistic Regression of Compliance on Covariates (high compliers vs. low compliers)

| Parameter | Estimate | <i>SE</i> |
|------------------------|----------|-----------|
| β_0 (Intercept) | 2.140 | 1.071 |
| β_{11} (Shy0) | -0.204 | 0.234 |
| β_{12} (Agg0) | 0.239 | 0.266 |
| β_{13} (Male) | 0.207 | 0.369 |
| β_{14} (Lunch) | 0.100 | 0.362 |
| β_{15} (Phealth) | -0.603 | 0.629 |
| β_{16} (Page) | -0.035 | 0.022 |
| β_{17} (Pmale) | -0.937 | 0.670 |
| β_{18} (NonW) | -1.091 | 0.541 |

Table 7. Johns Hopkins PIRC: CACE Estimation Assuming Constant Effects of Covariates

| Parameter | Estimate | SE |
|---|----------|-------|
| ITT_c (CACE) | -0.382 | 0.579 |
| ITT_n | 0.240 | 0.614 |
| $\lambda_{cX_1} = \lambda_{nX_1}$ (Shy0) | 0.219 | 0.085 |
| $\lambda_{cX_2} = \lambda_{nX_2}$ (Agg0) | 0.323 | 0.151 |
| $\lambda_{cX_3} = \lambda_{nX_3}$ (Male) | -0.004 | 0.202 |
| $\lambda_{cX_4} = \lambda_{nX_4}$ (Lunch) | 0.043 | 0.182 |
| $\lambda_{cX_5} = \lambda_{nX_5}$ (Phealth) | 0.375 | 0.295 |
| $\lambda_{cX_6} = \lambda_{nX_6}$ (Page) | 0.010 | 0.011 |
| $\lambda_{cX_7} = \lambda_{nX_7}$ (Pmale) | 0.521 | 0.311 |
| $\lambda_{cX_8} = \lambda_{nX_8}$ (NonW) | 0.200 | 0.170 |
| $\gamma_{cX_1} = \gamma_{nX_1}$ (Shy0) | 0.027 | 0.119 |
| $\gamma_{cX_2} = \gamma_{nX_2}$ (Agg0) | -0.358 | 0.204 |
| $\gamma_{cX_3} = \gamma_{nX_3}$ (Male) | 0.245 | 0.255 |
| $\gamma_{cX_4} = \gamma_{nX_4}$ (Lunch) | 0.207 | 0.238 |
| $\gamma_{cX_5} = \gamma_{nX_5}$ (Phealth) | -0.262 | 0.426 |
| $\gamma_{cX_6} = \gamma_{nX_6}$ (Page) | -0.001 | 0.014 |
| $\gamma_{cX_7} = \gamma_{nX_7}$ (Pmale) | -0.045 | 0.424 |
| $\gamma_{cX_8} = \gamma_{nX_8}$ (NonW) | 0.000 | . |
| α_c | 1.417 | 0.424 |
| α_n | 0.448 | 0.508 |
| σ_c^2 | 0.931 | 0.116 |
| σ_n^2 | 0.642 | 0.121 |

Discussion of “Estimation of intervention effects with noncompliance: Alternative model specifications” by Booil Jo

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We thank the editors for the opportunity to offer our comments on this very readable paper on recent work on noncompliance. Since Angrist, Imbens, and Rubin (1996), there has been an explosion of interest and activities in noncompliance related methods and applications, which include the bridging of work in different fields such as statistics, economics, epidemiology, sociology, and education. This paper contributes nicely to this expanding literature by explicating various assumptions involving covariates that can be used to uniquely identify maximum likelihood estimates in place of exclusion restrictions.

Although we like the paper very much, as discussants we focus on points designed to stimulate further discussion. Thus the casual reader may get the mistaken impression that we are more critical than we really are. The four topics we address are: 1) summarizing results by “significant” versus “not significant”; 2) handling missing data by listwise deletion; 3) describing subpopulation differences as “impacts” or “effects”; 4) discussing the scientific plausibility of competing models.

1. Sensitivity of significant/not significant results

The author’s main interest is sensitivity analysis, which we support, but the focus seems to be on sensitivity of “significant” and “not significant” results. For instance:

“The results from the model assuming the exclusion restriction show that the intervention assignment did not have a significant effect on the level of depression of compliers ($\hat{ITT}_c = -0.361$, effect size = 0.498). The results from the model without assuming the exclusion restriction show that the intervention assignment had a significant effect on the level of depression of compliers ($\hat{ITT}_c = -0.451$, effect size = 0.622).”

Even if the -0.451 estimate were known without any sampling variability, the difference between it and the ITT_c estimate under the exclusion restriction (0.080) would be only 0.4 standard error away from zero (see Table 2.a). This insensitivity of \hat{ITT}_c holds despite the apparent superiority of the “without exclusion” model ($\hat{ITT}_n = 0.227$, s.e. = 0.094), suggesting

the need for this extra parameter. There are more sophisticated ways to assess the different implications of such models; for example, our preference would be to employ the Bayesian paradigm, possibly using posterior predictive checks of the ability of the more parsimonious models to predict important aspects of the observed data (Rubin, 1984; Gelman, Meng, and Stern, 1996).

2. Dealing with missing data by listwise deletion

We were somewhat disappointed by Jo's general handling of missing data in the datasets, because the author was so careful when dealing with noncompliance, a special kind of missing data. The method known as "listwise deletion" is quite generally inferior to other methods (e.g., see Little and Rubin, 1987, chapter 3). There has been a tremendous amount of development in missing data methodology in the past quarter century (e.g., since Rubin, 1976; Dempster, Laird, and Rubin, 1977), and recent work has addressed the simultaneous complications of noncompliance and missing data (Frangakis and Rubin, 1999; Baker, 2000). A highly relevant publication in the context of a randomized educational intervention is Barnard et al. (2002). In these publications, the assumption of latent ignorability of missing data plays a key role: for groups of subjects with the same true compliance status, the missing data are ignorable. Because the software needed to implement fully principled analyses of data with both missing values (in covariates and outcome measures) and noncompliance is not readily available (e.g., Barnard et al., 2002), we are sympathetic to restricting the analysis to people with covariates fully observed, because this limits the inference to subpopulations of people with complete covariates. However, also restricting the analysis to those with complete outcomes is in principle incorrect for any subpopulation, because this implies the comparison of outcomes under treatment for those units who would produce outcome data if treated, with outcomes under control for those units who would produce outcome data if control; this is not

generally a comparison leading to causal effects because these two subpopulations are not the same (see Frangakis and Rubin, 2002).

3. Language that tends to confuse subpopulation differences and treatment effects

Our third point concerns language that can often be easily read to imply causal effects for variables that cannot be manipulated. We feel that it is especially important to avoid such language in the context of social sciences, where it has too often been misused. As Jo explains clearly, the basic idea underlying the proper analysis of data with noncompliance is to distinguish between (a) subpopulations defined by the true compliance status and (b) the effect of treatments on outcomes within those subpopulations. An example of a potentially deceptive statement is:

“The intervention assignment had a positive impact on compliers if they were highly motivated and married. However, high motivation and being married had a negative impact on individuals who would have complied with the intervention if offered, but were assigned to the control condition.”

What we believe is actually meant by these two sentences can be explained by the example in following table where, in order to simplify the presentation, depression is assumed to have only two levels, high and low.

Table 1: Depression level of true compliers by treatment assignment and subpopulation

| True compliers subpopulation | Intervention | |
|------------------------------|-----------------|----------------|
| | Control | Treatment |
| NM ² | Low depression | Low depression |
| M ² | High depression | Low depression |

NM² = not married or not highly motivated; M² – married and highly motivated

The meaning of the first sentence is that for the subpopulation of people who are true compliers and highly motivated and married, the intervention reduces depression: this is indeed an impact (causal effect) that can be observed by comparing the two cells in the M^2 row of Table 1. What is meant by the second sentence instead is that, if all members of the subpopulation of true compliers are assigned control, those who are highly motivated and married will have a depression level that is higher than the subpopulation of true compliers who are not highly motivated and married. This is not an “impact” of an intervention but a description of a difference between two subpopulations under the same treatment condition, which can be observed by comparing the two cells in the Control column of Table 1. Similar confusing language appears later and in other places, where a difference between subpopulations under the same treatment condition is described as an “impact” or “effect”.

4. Scientific rationale for various specifications

Although we applaud the specification of different identifying models, we wished that the resulting comparisons of estimates across the models had included more discussion of the scientific plausibility of the models, and thereby of the resulting estimates. Also, Jo's analysis of alternative assumptions involving covariates is restricted to the case where, in addition to monotonicity (i.e., there are no defiers), there are no always-takers. Always-takers are likely to be present in many observational studies and randomized trials - for example in randomized encouragement designs (Hirano et al., 2000), where people in the control arm are not encouraged to take the treatment (flu shot), but it is nevertheless accessible. It is thus interesting to see how Jo's results generalize to that case.

For example, consider the common setting introduced in section 2.1 and allow always-takers, i.e.,

$$C_i = \begin{cases} c(\text{complier}) & \text{if } D_i(1) = 1 \text{ and } D_i(0) = 0 \\ n(\text{never-taker}) & \text{if } D_i(1) = 0 \text{ and } D_i(0) = 0 \\ a(\text{always-taker}) & \text{if } D_i(1) = 1 \text{ and } D_i(0) = 1 \end{cases}$$

Also, assume there is only one binary covariate X , and, in addition to the notation introduced in section 2.3, let π_{ai} be the probability that the i -th individual with covariate x_i is an always-taker, and let $a_i = 1$ if $i \in C(a)$ and $a_i = 0$ if $i \in \{C(c) \cup C(n)\}$. Equation 11 can be modified to represent the outcome variable for an individual with compliance status c_i , n_i , and a_i :

$$Y_i = \alpha_n n_i + \alpha_c c_i + \alpha_a a_i + \gamma_n n_i Z_i + \gamma_c c_i Z_i + \gamma_a a_i Z_i + \gamma_{nx} n_i Z_i x_i + \gamma_{cx} c_i Z_i x_i + \gamma_{ax} a_i Z_i x_i + \lambda_n n_i x_i + \lambda_c c_i x_i + \lambda_a a_i x_i + \varepsilon_{in} n_i + \varepsilon_{ic} c_i + \varepsilon_{ia} a_i \quad (11a)$$

where the additional parameters and residual have the same interpretation for always-takers as the already introduced parameters and residuals have for compliers and never-takers.

Based on equation (11a), eight directly estimable population means can be expressed in terms of unrestricted model parameters as:

$$\begin{aligned} \mu_{1n,X=0} &= \alpha_n + \gamma_n \\ \mu_{1n,X=1} &= \alpha_n + \gamma_n + \gamma_{nx} + \lambda_n \\ \mu_{0a,X=0} &= \alpha_a \\ \mu_{0a,X=1} &= \alpha_a + \lambda_a \\ \mu_{00,X=0} &= \pi_{n,X=0} \alpha_n + \pi_{c,X=0} \alpha_c \\ \mu_{00,X=1} &= \pi_{n,X=1} (\alpha_n + \lambda_n) + \pi_{c,X=1} (\alpha_c + \lambda_c) \\ \mu_{11,X=0} &= \pi_{a,X=0} (\alpha_a + \gamma_a) + \pi_{c,X=0} (\alpha_c + \gamma_c) \\ \mu_{11,X=1} &= \pi_{a,X=1} (\alpha_a + \gamma_a + \gamma_{ax} + \lambda_a) + \pi_{c,X=1} (\alpha_c + \gamma_c + \gamma_{cx} + \lambda_c), \end{aligned}$$

where $\mu_{jh,X=k}$ is the population mean potential outcome if $Z = j$, $D(j) = h$ and $X = k$. Because the probabilities of being of a certain compliance status are directly estimable at both values of X , these equations show that the twelve model parameters $\{\alpha_n, \gamma_n, \gamma_{nx}, \lambda_n, \alpha_c, \gamma_c, \gamma_{cx}, \lambda_c, \alpha_a, \gamma_a, \gamma_{ax}, \lambda_a\}$ cannot be identified without some assumptions.

The exclusion restriction for always-takers and never-takers (i.e. $\gamma_a = \gamma_{ax} = \gamma_n = \gamma_{nx} = 0$) reduces the number of parameters to eight and allows the identification of CACE. The same is true for the assumption of constant effects of covariates (i.e. $\lambda_a = \lambda_n = \lambda_c$, and $\gamma_{ax} = \gamma_{nx} = \gamma_{cx}$),

whereas the assumption of additivity of treatment assignment effect (i.e. $\gamma_{ux} = \gamma_{rx} = \gamma_{ex} = 0$) reduces the number of parameters to nine, which is not sufficient to identify CACE: when there are always-takers, the additivity assumption needs to be combined with other assumptions, for example with an exclusion restriction for either the never-takers or the always-takers. Thus, speculation about which assumptions are more or less plausible when always-takers are also present is even more difficult without substantial experience with both fitting the models and applying them in substantive areas. One small contribution of ours into this difficult territory is Mealli and Rubin (2002), where we describe how different settings and experimental designs can have very different implications for the plausibility of competing assumptions. An example that makes the exclusion restriction but discusses its plausibility at some length is Barnard et al. (2002).

In conclusion, Jo's paper represents a fine contribution to this demanding and growing area of statistical research, and moreover, it introduces an interesting new class of tools for applied researchers, which illustrates a profitable path for further work.

Additional references

- Baker S.G. (2000). Analyzing a randomized cancer prevention trial with a missing binary outcome, an auxiliary variable, and all-or-none compliance, *Journal of the American Statistical Association*, 95, 43-50.
- Barnard J., Frangakis C., Hill J., and Rubin D.B. (2002). School Choice in NY City: A Bayesian Analysis of an Imperfect Randomized Experiment, in *Case Studies in Bayesian Statistics*, Vol. V, 3-97, C. Gatsonis, B. Carlin and A. Carriquiry (eds.), New York: Springer-Verlag.
- Frangakis C. and Rubin D.B. (1999). Addressing Complications of Intention-To-Treat Analysis in the Combined Presence of All-or-None Treatment-Noncompliance and Subsequent Missing Outcomes, *Biometrika*, 86, 2, 366-379.
- Frangakis C. and Rubin D.B. (2002). Principal Stratification in Causal Inference, *Biometrics*, 58, 1, 21-29.
- Gelman A., Meng X., and Stern H. (1996). Posterior Predictive Assessment of Model Fitness via Realized Discrepancies, *Statistica Sinica*, 6, 733-807.
- Mealli F., Rubin D.B. (2002). Assumptions When Analyzing Randomized Experiments with Noncompliance and Missing Outcomes, Revision to appear in *Health Services Outcome Research Methodology*.
- Rubin D.B. (1976). Inference and Missing Data, *Biometrika*, 63, 3, 581-592, with discussion and reply.
- Rubin D.B. (1984). Bayesianly Justifiable and Relevant Frequency Calculations for the Applied Statistician, *Annals of Statistics*, 12, pp. 1151-1172.

Rejoinder by Booil Jo

I sincerely thank Fabrizia Mealli and Donald B. Rubin for their thorough and constructive commentary on my article. I would like to take this opportunity to clarify a few issues on the basis of their comments, which I find very helpful and reasonable. Most of all, I thank the discussants for several suggestions related to real data examples. I hope that the readers of this paper will note that the analyses for real data examples were focused on illustrating the identification of proposed CACE models without involving other concurrent problems such as missing data in outcomes and covariates. Specific points in the four issues raised by discussants are addressed below.

1. Sensitivity of significant/not significant results

The first issue raised by the discussants is that sensitivity analysis of alternative models seems to be solely based on “significant” and “not significant” results. I agree with the discussants that more information than significance of the results can be provided to better describe sensitivity of the CACE estimate to violation (or relaxation) of the exclusion restriction assumption. I believe that employing a Bayesian paradigm will be very useful in evaluating precision and sensitivity among alternative models, even when CACE models with unique MLE are of concern.

I would like to point out that insensitivity of the CACE estimate in JOBS II is at least partly due to the presence of covariates that are good predictors of compliance (Jo, in press). It was not emphasized in this paper that covariate information may

play an important role not only in models without the exclusion restriction (in identification), but also in models with the exclusion restriction (in reduction of bias). Table 8 shows CACE estimates assuming additive effects of treatment assignment (see Tables 2.a and 2.b for the full results with 9 covariates.). It is shown that the CACE estimate is less sensitive (at least in terms of size) to the exclusion restriction in the presence of covariates associated with compliance (e.g., Mot, Age, Assert). Insensitivity of the CACE estimate in JOBS II is also due to the fact that the exclusion restriction is not severely biased. It would be interesting to see how sensitivity of the CACE estimate differs in various examples in different fields.

Table 8. JOBS II: Sensitivity of the CACE Estimate to the Exclusion Restriction and Covariate Information (SE in parenthesis)

| Present covariates | Exclusion Restriction | |
|------------------------|-----------------------|----------------|
| | Yes | No |
| Dep0 | -0.297 (0.201) | -0.440 (0.150) |
| Dep0, Mot, Age, Assert | -0.340 (0.199) | -0.444 (0.140) |
| All 9 covariates | -0.361 (0.191) | -0.451 (0.131) |

2. Dealing with missing data by listwise deletion

The discussants suggested a better handling of missing data in covariates and outcomes. As they pointed out, noncompliance and missing data can be indeed considered simultaneously. Instead of assuming missing completely at random (MCAR:

Little & Rubin, 1987), noncompliance and missing data can be simultaneously considered by assuming missing at random (MAR: Little & Rubin, 1987) as demonstrated in Yau and Little (2001), or by assuming MAR conditioning on compliance type (latent ignorability), which is less restrictive than the regular MAR assumption (Baker, 2000; Barnard et al., 2002; Frangakis & Rubin, 1999).

The potential relationship between noncompliance and missing data may introduce more complex issues in identifying CACE models, which I did not want to include within the scope of the current paper. In fact, in JOBS II, a substantial number of individuals did not respond at follow-up surveys, and observed nonresponse rates in the treatment condition were quite different for compliers and noncompliers, implying potential correlation between noncompliance and nonresponse. To maintain identifiability of CACE models allowing for this correlation (latent ignorability: Frangakis & Rubin, 1999), the exclusion restriction is imposed not only on outcomes, but also on missing indicators of outcomes (compound exclusion restriction). This situation raises a question of how the exclusion restriction assumption should be tested with an increased number of parameters and increased complexity in bias mechanisms. An interesting next step will be to investigate how proposed alternative assumptions can be applied to build identifiability in this situation, whether resulting model properties lead to reasonable and interpretable estimates, and whether model estimates maintain a practical level of accuracy and precision.

3. Language that tends to confuse subpopulation differences and treatment effects

This confusion resulted from mechanical interpretation of interaction effects without considering the difference between pretreatment covariates and treatment assignment.

In regard to Table 3.a., the statement “However, high motivation and being married had a negative impact on individuals who would have complied with the intervention if offered, but were assigned to the control condition” needs to be disregarded. In regard to Table 3.b., the statement “However, being single and less assertive had a negative impact on individuals who would have complied with the intervention if offered, but were assigned to the control condition” needs to be disregarded.

4. Scientific rationale for various specifications

Finally, the discussants raised the issue of scientific plausibility of the alternative models and the resulting estimates. In some situations, it may be relatively clear which assumptions (and therefore which models) are more plausible, possibly based on scientific evidence, previous studies, and experts’ opinion. In many situations, however, plausibility of model assumptions is often questionable. The second best thing one can expect under this uncertainty is to have assumptions that will yield clear and consistent bias mechanisms when violated so that inferences can be made considering possible ranges of bias in parameter estimates. For example, the bias mechanism in CACE models assuming the exclusion restriction is quite straightfor-

ward in the absence of covariates. However, in the presence of covariates, the bias mechanism becomes very complicated, which makes interpretation of analysis results very difficult when plausibility of the exclusion restriction is questionable. Similarly, CACE models assuming constant effects of covariates (Model C) involve complex bias mechanisms when the assumption is violated. Therefore, inferences made in these two models depend heavily on the scientific plausibility of model assumptions (i.e., exclusion restriction or constant effects of covariates).

The advantage of CACE models assuming the additive effect of treatment assignment (Model B) is that the bias mechanism is relatively simple when the assumption is violated. The simplicity of the bias mechanism provides a couple of convenient properties in Model B. First, the bias mechanism of compliers is separated from that of never-takers. As a result, regardless of violation of additivity, at least combined (main and interaction) effects of treatment assignment can be estimated without introducing bias due to violation of the exclusion restriction. Second, if there are multiple covariates, the additivity assumption is not completely unverifiable. As shown in Tables 3.a and 3.b, some interaction effects are estimable. On the basis of these two properties, Model B can be creatively used to explore more plausible and parsimonious sets of model assumptions. For example, in the presence of multiple covariates, one can estimate interaction effects for most covariates in each class, and then decide whether additivity or a constant effect assumption is appropriate.

Model B including only compliers and never-takers is useful in more controlled experiments such as JOBS II and Hopkins PIRC. However, in other large scale exper-

iments or randomized encouragement studies, for practical and ethical reasons, it may be difficult to prohibit study participants assigned to the control condition from receiving treatment (e.g., Barnard et al., 2002; Hirano et al., 2000). As the discussants pointed out, Model B cannot be identified with both never-takers and always-takers when there is only one covariate. One way to build identifiability in this situation is to relax the exclusion restriction for either never-takers or always-takers, but not for both. In doing so, however, Model B loses its unique properties unless there is strong scientific plausibility that the exclusion restriction should hold either for never-takers or for always-takers. I agree with the discussants that it is more difficult to retain interpretability when the exclusion restriction has to be partially imposed in conjunction with the additivity assumption. Here, the information from multiple covariates comes into play. If there are multiple covariates, the number of subpopulations for which the exclusion restriction can be relaxed increases in Model B. For example, assume there are two binary covariates X_1 and X_2 . Compared to the number of parameters and directly estimable population means based on equation (11a), the number of parameters increases by three (i.e., λ_{nX_2} , λ_{aX_2} , λ_{cX_2}), whereas the number of directly estimable population means increases by four (i.e., $\mu_{1n, X_1=0, X_2=1}$, $\mu_{0a, X_1=0, X_2=1}$, $\mu_{00, X_1=0, X_2=1}$, $\mu_{11, X_1=0, X_2=1}$), which results in a just identified model. In principle, Model B with always-takers can be identified with one less degree of freedom compared to Model B without always-takers. However, whether resulting parameter estimates will retain a practical level of precision is another interesting issue to be studied.