Estimation of Intervention Effects with Noncompliance: Alternative Model Specifications

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This study examines alternative ways of specifying models in the complier average causal effect (CACE) 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 pretreatment 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 pretreatment 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.

Treatment noncompliance is a common problem in randomized intervention trials. Standard intent-to-treat (ITT) 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 complier average causal effect (CACE), 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 Public School Preventive Intervention 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 pretreatment 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.

Modeling Options in Estimating CACE

Common Setting

Assume the simplest experimental setting where there is only one outcome measure (Y), the treatment assignment (Z) is binary $(1 = \text{treatment}, 0 = \text{control})$, and the treatment received (D) has only two levels $(1 = \text{received}, 0 = \text{not received})$. 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

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

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

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

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 stable unit treatment value (SUTVA) (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 ($ITT_c = \text{CACE}$) 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, then the complete-data likelihood function is

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

$$\times \prod_{i \in \{C(n), Z_i=0\}} \pi_n f(y_i \mid \mu_{0n}, \sigma_n^2) \times \prod_{i \in \{C(c), Z_i=0\}} \pi_c f(y_i \mid \mu_{0c}, \sigma_c^2), \tag{2}$$

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 $f(y_i | \mu, \sigma^2)$ 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

$$L(\theta | data) \propto \prod_{i \in \{Z_i = 1, D_i = 0\}} \pi_n f(y_i | \mu_{1n}, \sigma_n^2) \times \prod_{i \in \{Z_i = 1, D_i = 1\}} \pi_c f(y_i | \mu_{1c}, \sigma_c^2)$$

$$\times \prod_{i \in \{Z_i = 0, D_i = 0\}} [\pi_n f(y_i | \mu_{0n}, \sigma_n^2) + \pi_c f(y_i | \mu_{0c}, \sigma_c^2)]. \tag{3}$$

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, 2002; McLachlan & Krishnan, 1997; Tanner, 1996). π_c and π_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 M*plus* 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.

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

$$\mu_{1n} = \alpha_n + \gamma_n, \tag{4}$$

$$\mu_{1c} = \alpha_c + \gamma_c, \tag{5}$$

$$\mu_0 = \pi_n \alpha_n + \pi_c \alpha_c, \tag{6}$$

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 ($ITT_c = \text{CACE}$).

From Equation 4, α_n can be defined as

$$\alpha_n = \mu_{1n} - \gamma_n. \tag{7}$$

From Equations 6 and 7, α_c can be defined as

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

From Equations 5 and 8, γ_c can then be defined as

$$\gamma_c = \frac{\mu_1 - \mu_0}{\pi_c} - \frac{\pi_n\gamma_n}{\pi_c}. \tag{9}$$

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, 2002a). 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, 2002a). 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.

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, Rubin, & Zhou, 2002; Hirano et al., 2000). In the ML estimation method, it has been demonstrated that covariate information may increase statistical power (Jo, 2002b) and reduce bias due to model misspecification (Jo, 2002a). The current study focuses on the role of covariate information in identifying CACE models.

If pretreatment 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 x be a vector of pretreatment covariates. The logistic regression of compliance on covariates is described as

$$P[i \in C(c)|x_i] = \pi_{ci},$$

$$P[i \in C(n)|x_i] = 1 - \pi_{ci},$$

$$logit(\pi_{ci}) = \beta_0 + \beta_1' x_i, \tag{10}$$

where β_0 represents a logit intercept, and β_1 is a vector of logit coefficients. The level of association between compliance and covariates is represented by β_1.

Pretreatment 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,

$$Y_i = \alpha_n n_i + \alpha_c c_i + \gamma_n n_i Z_i + \gamma_c c_i Z_i + \gamma_{nx}' n_i Z_i x_i + \gamma_{cx}' c_i Z_i x_i$$

$$+ \lambda_n' n_i x_i + \lambda_c' c_i x_i + \varepsilon_{in} n_i + \varepsilon_{ic} c_i, \tag{11}$$

where α_n is the intercept for never-takers, and α_c is the intercept for compliers. λ_n denotes the main effect of covariates for never-takers, and λ_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}, λ_n, and λ_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}, λ_n, and λ_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 3 can be modified as

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

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

$$\mu_{1n,\,X=0} = \alpha_n + \gamma_n, \tag{13}$$

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

$$\mu_{1c,\,X=0} = \alpha_c + \gamma_c, \tag{15}$$

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

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

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

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.

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.

$$\mu_{1n,\,X=0} = \alpha_n, \tag{19}$$

$$\mu_{1n,\,X=1} = \alpha_n + \lambda_n, \tag{20}$$

$$\mu_{1c,\,X=0} = \alpha_c + \gamma_c, \tag{21}$$

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

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

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

From Equation 19, the estimator of α_n is directly defined as

$$\hat{\alpha}_n = \hat{\mu}_{1n,\,X=0}, \tag{25}$$

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

$$\hat{\lambda}_n = \hat{\mu}_{1n,\,X=1} - \hat{\mu}_{1n,\,X=0}, \tag{26}$$

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

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

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

$$\hat{\gamma}_c = \hat{\mu}_{1c,\,X=0} - \hat{\alpha}_c, \tag{28}$$

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

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

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:

$$\hat{\gamma}_{cx} = \hat{\mu}_{1c,\,X=1} - \hat{\alpha}_c - \hat{\gamma}_c - \hat{\lambda}_c, \tag{30}$$

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).

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 treatment 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.

$$\mu_{1n,\,X=0} = \alpha_n + \gamma_n, \tag{31}$$

$$\mu_{1n,\,X=1} = \alpha_n + \gamma_n + \lambda_n, \tag{32}$$

$$\mu_{1c,\,X=0} = \alpha_c + \gamma_c, \tag{33}$$

$$\mu_{1c,\,X=1} = \alpha_c + \gamma_c + \lambda_c, \tag{34}$$

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

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

From Equations 31 and 32, the estimator of λ_n can be defined as

$$\hat{\lambda}_n = \hat{\mu}_{1n, X=1} - \hat{\mu}_{1n, X=0}, \tag{37}$$

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

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

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, 37, and 38, the estimator of α_n can be defined as

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

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

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

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

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

Finally, from Equations 33 and 40, the estimator of γ_c is defined as

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

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 the exclusion restriction. In Model B, the γ_c estimate is not sensitive to violation of $\gamma_n = 0$. 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 $\gamma_n \neq 0$ 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 4 and 5, 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.

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.

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

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

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

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

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

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

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

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

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

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

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

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

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

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 $\mu_{0,\, X_1=1, X_2=0}$, $\mu_{0,\, X_1=0, X_2=0}$, $\pi_{c,\, X_1=0, X_2=0}$, and $\pi_{c,\, X_1=1, X_2=0}$.

From Equations 49 and 53, the estimator of α_c can be defined as

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

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

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

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

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

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.

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 four or five sessions ($M = 4.3$ sessions, $Mdn = 5$ 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 6 months after the intervention was 87%. In the CACE analyses shown in this section, the level of depression 6 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 2 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, nega-

TABLE 1
JOBS II: Sample Statistics (N = 486)

Variable	M	SD	Description
Z	0.67	0.47	Intervention assignment (0 = control, 1 = treatment)
c	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

JOBS II: CACE Estimation Assuming Additive Effect of Intervention Assignment

Exclusion Restriction	With		Without	
Parameter	Estimate	SE	Estimate	SE
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

tive 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.

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 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 3 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 3 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 4 demonstrates how parameter estimates in Table 2 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 and 3 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 4 and 5, only parameters that are related to treatment assignment are listed.

The results in Table 4 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

TABLE 3

JOBS II: Logistic Regression of Compliance on Covariates (Compliers vs. Never-takers)

Parameter	Estimate	SE
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 4

JOBS II: Relaxing Additivity of Treatment Effect for Compliers ($\gamma_{nx} = 0$ for all Covariates)

γ_{cx}	0 relaxed		4 relaxed		8 relaxed	
Parameter	Estimate	SE	Estimate	SE	Estimate	SE
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

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. Inter-vention 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 nega-tive impact on individuals who would have complied with the intervention if offered, but were assigned to the control condition.

Table 5 demonstrates how parameter estimates in Table 2 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 and 3 for full results). In the second analysis, γ_{nx} is relaxed for four

TABLE 5

JOBS II: Relaxing Additivity of Treatment Effect for Never-takers ($\gamma_{cx} = 0$ for all Covariates)

γ_{nx}	0 relaxed		4 relaxed		8 relaxed	
Parameter	Estimate	SE	Estimate	SE	Estimate	SE
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

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.

The results in Table 5 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 6 shows results from CACE estimation assuming constant effects of covariates. For all nine covariates, it is assumed that $\lambda_n = \lambda_c$, and $\gamma_{nx} = \gamma_{cx}$. Addi-

TABLE 6

JOBS II: CACE Estimation Assuming Constant Effects of Covariates

Parameter	Estimate	SE
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

tionally, 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 6 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 3. Individuals complied more if they were older, more motivated, more educated, and less assertive.

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 6 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 Teacher Observation of Classroom Adaptation-Revised score (TOCA-R) (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 7 describes the variables used in this example.

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 8 shows results from CACE models assuming an additive effect of treatment assignment. Eight covariates are included in CACE analyses shown in this

TABLE 7
Johns Hopkins PIRC: Sample Statistics (N = 284)

Variable	M	SD	Description
Z	0.50	0.50	Intervention assignment (0 = control, 1 = treatment)
c	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 8
Johns Hopkins PIRC: CACE Estimation Assuming Additive Effect of Intervention Assignment

Exclusion Restriction	With		Without	
Parameter	Estimate	SE	Estimate	SE
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

section ($X_1 = $ Shy0, $X_2 = $ Agg0, $X_3 = $ Male, $X_4 = $ Lunch, $X_5 = $ Phealth, $X_6 = $ Page, $X_7 = $ Pmale, $X_8 = $ 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 8 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 9 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 nonWhite 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 10 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 10 that the main effect of intervention assignment was not significant either for high compliers

TABLE 9

Johns Hopkins PIRC: Logistic Regression of Compliance on Covariates (High Compliers vs. Low Compliers)

Parameter	Estimate	SE
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 10

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_r	1.417	0.424
α_n	0.448	0.508
σ_c^2	0.931	0.116
σ_n^2	0.642	0.121

($\widehat{ITT_c} = -0.382$, effect size $= 0.377$) or for low compliers ($\widehat{ITT_n} = 0.240$, 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 ($\hat{\gamma}_{nX2} = \hat{\gamma}_{cX2} = -0.358$, 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.

Conclusion

The current study demonstrated alternative ways of modeling CACE in the presence of pretreatment 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 exclu-

sion 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 subpopulations 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.

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