

Estimation of Effects of Endogenous Time-Varying Covariates: A Comparison Of Multilevel Linear Modeling and Generalized Estimating Equations

Research Report

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November 1, 2024

Word count: 728

FETC-approved: 24-2003

Candidate journal: Psychological Methods

Introduction

Across a wide range of disciplines, researchers analyze clustered longitudinal, observational data to investigate prospective causal relationships between variables. When analyzing such data, the psychological sciences most commonly resort to the multilevel linear model (MLM, [McNeish et al., 2017](#)), which—in the context of longitudinal data analysis—separates observed variance into stable between-person differences and within-person fluctuations ([Hamaker & Muthén, 2020](#)). Conversely, other fields, such as biostatistics and econometrics often favour generalized estimating equations (GEE) for the analysis of longitudinal data ([McNeish et al., 2017](#)). Despite some cross-disciplinary efforts to compare these methods ([McNeish et al., 2017](#); [Muth et al., 2016](#); [Yan et al., 2013](#)), their scarcity may leave researchers with limited guidance in choosing the most suitable approach for their application.

Recent evidence has highlighted an issue present in both methods, where controlling for *time-varying endogenous covariates* may lead to biased causal estimates ([Pepe & Anderson, 1994](#); [Qian et al., 2020](#)). A time-varying covariate is *endogenous* if it is directly or indirectly influenced by prior treatment or outcome, meaning its value may be determined by earlier stages of the process ([Qian et al., 2020](#)). As a result of including these covariates in the mentioned models, ordinary interpretations of the coefficients are no longer valid ([Qian et al., 2020, p. 3](#)). According to Diggle ([2002](#)), this issue not only pertains GEE and MLM, but *all* longitudinal data analysis methods.

However, due to a divide between the disciplines that employ these methods, such critiques of the MLM appear to have largely failed to reach the applied researcher in psychology. One specific reason might be that the technical jargon in other disciplines

makes it difficult for researchers to recognize when and how these issues emerge¹. As a result, researchers may address related problems in disconnected literatures but fail to understand each other. For instance, while the MLM literature emphasizes on the distinction between different centering methods and the effect of cross-level interactions on parameter interpretations (e.g., Hamaker & Muthén, 2020), the GEE literature appears to focus more on the marginal and conditional interpretations of model parameters (e.g., Pepe & Anderson, 1994).

Through a cross-fertilization of these literatures, this project aims to (1) explain the issue of including endogenous covariates in analyses involving GEE, MLM and DSEM (a widely used framework in the social sciences based on MLM) in a psychological context and (2) establish guidelines on how researchers can prevent this issue in their longitudinal data analysis. Accordingly, the following research questions will be addressed: *In which cases do the inclusion of endogenous variables in multilevel linear models and generalized estimating equations result in a discrepancy between marginal and conditional estimates?* In line with the literature (Diggle, 2002; Pepe & Anderson, 1994; Qian et al., 2020), we expect that the inclusion of endogenous time-varying covariates in longitudinal data analyses may result in bias that—depending on the circumstances—can promote the potential for faulty inferences. To isolate the issue described in Qian et al. (2020), we will focus on the following sub-questions: (1) When removing the interaction β_1 from generative model 3, is there a difference between the marginal and conditional estimates of the treatment effect? (2) When removing the random slope b_{i2} from generative model 3, is there a difference between the marginal and conditional estimates of the treatment effect?

¹For instance, the term ‘endogeneity’ in econometrics, while related, has a distinct meaning from that of an endogenous variable, which can lead to confusion.

Methods

Simulation Conditions

In the simulation Qian et al. (2020) considered three generative models (GMs), all of which have an endogenous time-varying covariate. In GM1 and GM2, the endogenous covariate X_{it} equals the previous outcome Y_{it} plus some random noise, so the *conditional independence* assumption is valid. In GM3, the endogenous covariate depends directly on b_{i0} , violating the assumption. To isolate the issue described by Qian et al. (2020), we consider 6 models on top of the three models described in the original paper.

AJUST!!! More specifically, we considered models with an “a” suffix, where all random slopes were removed, and models with a “b” suffix, were on top of the removal of random slopes, the interaction terms were removed. AJUST!!!

The details of the generative models are described below. We follow the notation of Qian et al. (2020) to allow for direct comparison, but rewrite the equations into within- and between-person models (see Raudenbusch & Bryk, 2002). We accompany the equations of the GMs with graphical representations, where latent variables are represented by circles, observed variables by squares and relationships across variables by arrows. The path diagrams of the three data generating models shows the discrepancies between the different generative models—especially concerning the interaction effects—more clearly than DAGs.

Generative Model 1

In GM1, we considered a simple case with only a random intercept and a random slope for X_{it} . The outcome is generated according to the following repeated-observations or within-person model (level 1):

$$Y_{it+1} = \pi_{0i} + \pi_{1i}X_{it} + \pi_{2i}A_{it} + \pi_{3i}A_{it}X_{it} + \epsilon_{it+1}$$

with the person-level or between-person model (level 2):

$$\pi_{0i} = \alpha_0 + b_{i0}, \quad b_{i0} \sim \mathcal{N}(0, \sigma_{b0}^2),$$

$$\pi_{1i} = \alpha_1,$$

$$\pi_{2i} = \beta_0 + b_{i2}, \quad b_{i2} \sim \mathcal{N}(0, \sigma_{b2}^2),$$

$$\pi_{3i} = \beta_1.$$

By substitution, we get the single equation model:

$$\begin{aligned} Y_{it+1} &= \pi_{0i} + \pi_{1i}X_{it} + \pi_{2i}A_{it} + \pi_{3i}A_{it}X_{it} + \epsilon_{it+1} \\ &= (\alpha_0 + b_{i0}) + \alpha_1X_{it} + (\beta_0 + b_{i2})A_{it} + \beta_1A_{it}X_{it} + \epsilon_{it+1} \\ &= \alpha_0 + \alpha_1X_{it} + b_{i0} + A_{it}(\beta_0 + \beta_1X_{it} + b_{i2}) + \epsilon_{it+1}. \end{aligned}$$

The random effects $b_{i0} \sim \mathcal{N}(0, \sigma_{b0}^2)$ and $b_{i2} \sim \mathcal{N}(0, \sigma_{b2}^2)$ are independent of each other.

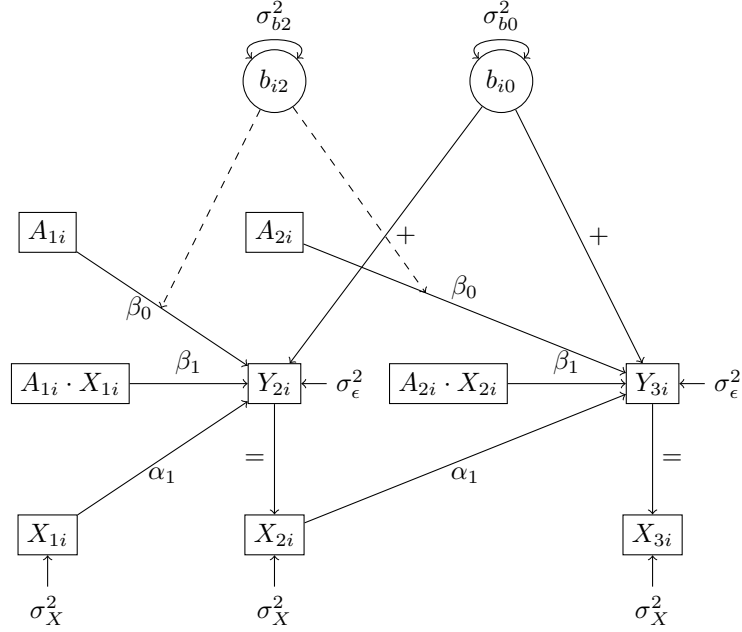
The covariate is generated as $X_{i1} \sim \mathcal{N}(0, 1)$, and for $t \geq 2$,

$$X_{it} = Y_{it} + \mathcal{N}(0, 1).$$

The randomization probability $p_t = P(A_{it} = 1 \mid H_{it})$ is constant at $1/2$. Thus, $A_{it} \sim \text{Bernoulli}(0.5)$ for $i = 1, \dots, N$ and $t = 1, \dots, T$. The exogenous noise is $\epsilon_{it+1} \sim \mathcal{N}(0, \sigma_\epsilon^2)$.

Figure 1 shows the path diagram for GM3.

Figure 1: Path diagram for Generative Model 1



Generative Model 1A

GM1A is the same as GM1, except that the random slope b_{i2} for the treatment A_{it} is removed. The single equation model thus becomes:

$$Y_{it+1} = \alpha_0 + \alpha_1 X_{it} + b_{i0} + A_{it}(\beta_0 + \beta_1 X_{it}) + \epsilon_{it+1}.$$

Generative Model 1B

GM1B is the same as GM1A, except that the interaction term $\beta_1 A_{it} X_{it}$ is removed. The single equation model thus becomes:

$$Y_{it+1} = \alpha_0 + \alpha_1 X_{it} + b_{i0} + \beta_0 A_{it} + \epsilon_{it+1}.$$

Generative Model 2

In GM2, we considered the case with a random intercept and random slopes for (1) covariate X_{it} , (2) treatment A_{it} , and (3) the interaction between A_{it} and X_{it} ; and with a time-varying randomization probability for treatment. The outcome is generated according to the same repeated-observations model presented in GM1. However, the person-level model is different:

$$\pi_{0i} = \alpha_0 + b_{i0}, \quad b_{i0} \sim \mathcal{N}(0, \sigma_{b0}^2),$$

$$\pi_{1i} = \alpha_1 + b_{i1}, \quad b_{i1} \sim \mathcal{N}(0, \sigma_{b1}^2),$$

$$\pi_{2i} = \beta_0 + b_{i2}, \quad b_{i2} \sim \mathcal{N}(0, \sigma_{b2}^2),$$

$$\pi_{3i} = \beta_1 + b_{i3}, \quad b_{i3} \sim \mathcal{N}(0, \sigma_{b3}^2).$$

By substitution, we get the single equation model:

$$\begin{aligned} Y_{it+1} &= \pi_{0i} + \pi_{1i}X_{it} + \pi_{2i}A_{it} + \pi_{3i}A_{it}X_{it} + \epsilon_{it+1} \\ &= (\alpha_0 + b_{i0}) + (\alpha_1 + b_{i1})X_{it} + (\beta_0 + b_{i2})A_{it} + (\beta_1 + b_{i3})A_{it}X_{it} + \epsilon_{it+1} \\ &= \alpha_0 + \alpha_1X_{it} + b_{i0} + b_{i1}X_{it} + A_{it}(\beta_0 + \beta_1X_{it} + b_{i2} + b_{i3}X_{it}) + \epsilon_{it+1}. \end{aligned}$$

The random effects $b_{ij} \sim \mathcal{N}(0, \sigma_{bj}^2)$, for $j = 0, 1, 2, 3$, are independent of each other.

The covariate is generated as $X_{i1} \sim \mathcal{N}(0, 1)$, and for $t \geq 2$,

$$X_{it} = Y_{it} + \mathcal{N}(0, 1).$$

The randomization probability depends on X_{it} :

$$p_t = P(A_{it} = 1 \mid H_{it}) = \begin{cases} 0.7 & \text{if } X_{it} > -1.27, \\ 0.3 & \text{if } X_{it} \leq -1.27, \end{cases}$$

where the cutoff -1.27 was chosen so that p_t equals 0.7 or 0.3 for about half of the time. In other words, if the value of the covariate for any given person and time point is above the cutoff, the probability of receiving the treatment p_t is 0.7; otherwise, it is 0.3. Accordingly, $A_{it} \sim \text{Bernoulli}(p_t)$ for $i = 1, \dots, N$ and $t = 1, \dots, T$. The exogenous noise is $\epsilon_{it+1} \sim \mathcal{N}(0, \sigma_\epsilon^2)$.

Generative Model 2A

GM2A is the same as GM2, except that the random slopes b_{i1} , b_{i2} and b_{i3} are removed. The single equation model then becomes the same as GM1A, but with the time-varying randomization probabilities of GM2.

Generative Model 2B

GM2B is the same as GM2A, except that the interaction term $\beta_1 A_{it} X_{it}$ is removed. The single equation model then becomes the same as GM1B, but with the time-varying randomization probabilities of GM2.

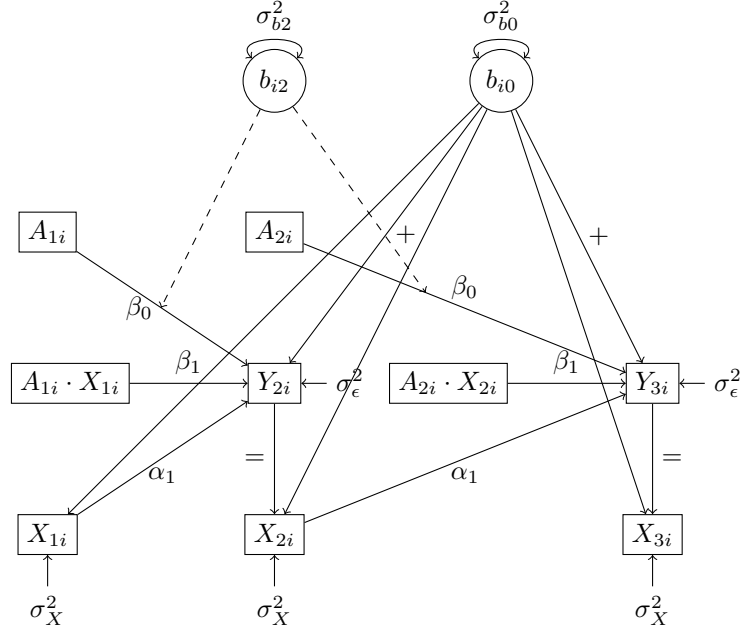
Generative Model 3

GM3 is the same as GM1, except that the covariate X_{it} depends directly on b_{i0} :

$$X_{i1} \sim \mathcal{N}(b_{i0}, 1), \quad X_{it} = Y_{it} + \mathcal{N}(b_{i0}, 1) \text{ for } t \geq 2.$$

Figure 2 shows the path diagram for GM3.

Figure 2: Path diagram for Generative Model 3



Generative Model 3A

GM3A is the same as GM3, except that the random slope b_{i2} for the treatment A_{it} is removed. The single equation model then becomes the same as GM1A, but including the dependency of the covariate X_{it} on the random intercept b_{i0} present in GM3.

Generative Model 3B

GM3B is the same as GM3A, except that the interaction term $\beta_1 A_{it} X_{it}$ is removed. The single equation model then becomes the same as GM1B, but including the dependency of the covariate X_{it} on the random intercept b_{i0} present in GM3.

Parameter Values

The following parameter values were chosen:

$$\alpha_0 = -2, \quad \alpha_1 = -0.3, \quad \beta_0 = 1, \quad \beta_1 = 0.3,$$

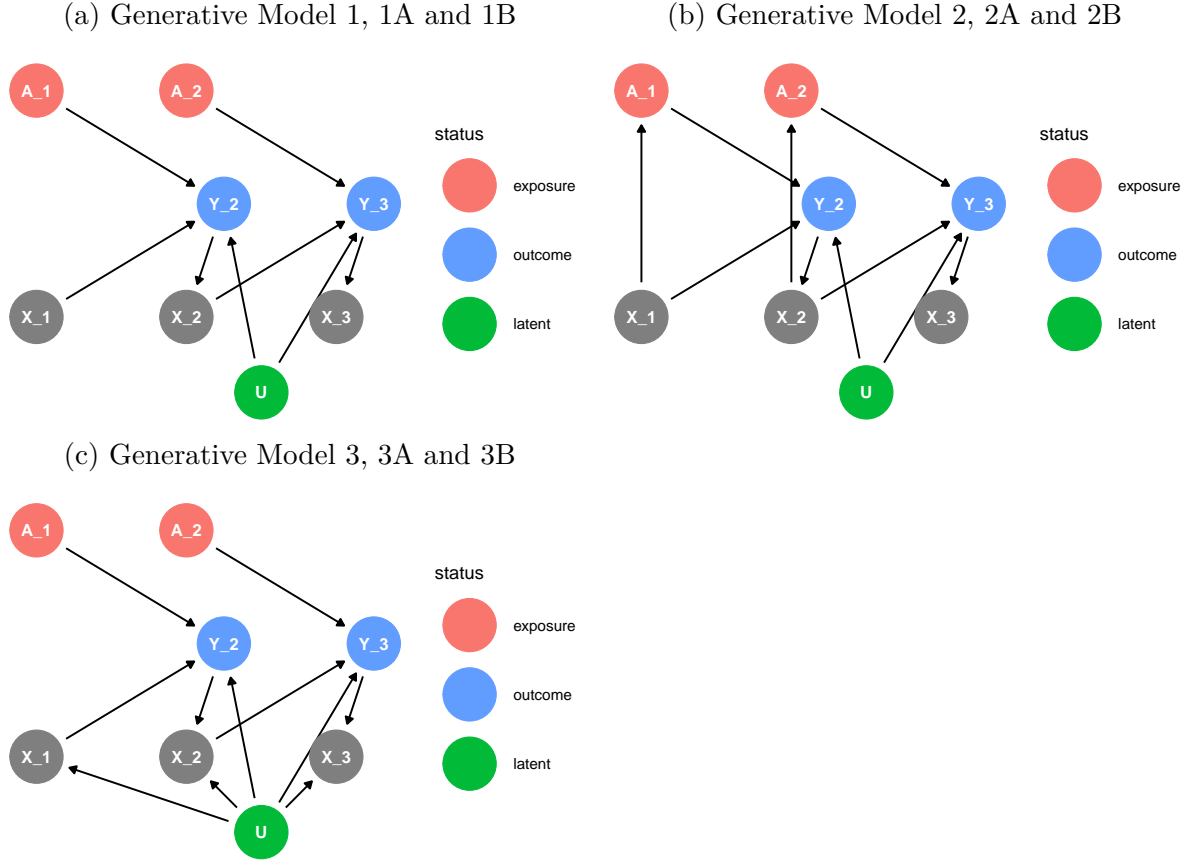
$$\sigma_{b0}^2 = 4, \quad \sigma_{b1}^2 = \frac{1}{4}, \quad \sigma_{b2}^2 = 1, \quad \sigma_{b3}^2 = \frac{1}{4}, \quad \sigma_\epsilon^2 = 1.$$

Graphical representations of Data Generating Models

Directed Acyclic Graphs (DAGs)

The DAGs for the first three observations of the three data generating models are presented in Figure 3. The red arrows show the biased paths after controlling for the covariate X_{it} .

Figure 3: DAG for Generative Model 1



We may notice that the DAGs for GM1 and GM2 are identical (there are only differences in random effects and randomization probabilities), while GM3 has a different structure due to the dependency of the covariate X_{it} on the random intercept b_{i0} .

Paraphrasing Qian et al. (2020), the conditional independence assumption is:

$$X_{it} \perp (b_{i0}, b_{i1}) \mid H_{it-1}, A_{it-1}, Y_{it}.$$

This allows X_{it} to be endogenous, but the endogenous covariate X_{it} can only depend on the random effects through variables observed prior to X_{it} : H_{it-1} , A_{it-1} , and Y_{it} . If the only endogenous covariates are functions of prior treatments and prior outcomes, then the assumption automatically holds.

When inspecting Figure 3, we can see that this assumption is violated in GM3, as

X_{it} depends directly on b_{i0} and is thus not independent of the random effects b_{i0} and b_{i1} . Notice that GM1 and GM2 are also not marginally independent of b_{i0} and b_{i1} , but they are conditionally independent given H_{it-1} , A_{it-1} , and Y_{it} .

Data Estimation/Analysis

For the multilevel linear model, the analytical models are equivalent to each of the respective data-generating models. The multilevel linear models were fitted using the `lmer` function in R. As a reminder, the analytical *multilevel model* for GM1 and GM3 is given by:

$$Y_{it+1} = (\alpha_0 + b_{i0}) + \alpha_1 X_{it} + (\beta_0 + b_{i2}) A_{it} + \beta_1 A_{it} X_{it} + \epsilon_{it+1}.$$

which is fitted as `lmer(Y ~ X * A + (1 + A | id), data = data)` in R.

The analytical *multilevel model* for GM2 is given by:

$$Y_{it+1} = (\alpha_0 + b_{i0}) + (\alpha_1 + b_{i1}) X_{it} + (\beta_0 + b_{i2}) A_{it} + (\beta_1 + b_{i3}) A_{it} X_{it} + \epsilon_{it+1}.$$

which is fitted as `lmer(Y ~ X * A + (X * A | id), data = data)` in R.

The analytical *multilevel model* for GM1A, GM2A, and GM3A is given by:

$$Y_{it+1} = \alpha_0 + b_{i0} + \alpha_1 X_{it} + \beta_0 A_{it} + \beta_1 A_{it} X_{it} + \epsilon_{it+1}.$$

which is fitted as `lmer(Y ~ X * A + (1 | id), data = data)` in R.

The analytical *multilevel model* for GM1B, GM2B, and GM3B is given by:

$$Y_{it+1} = \alpha_0 + b_{i0} + \alpha_1 X_{it} + \beta_0 A_{it} + \epsilon_{it+1}.$$

which is fitted as `lmer(Y ~ X + A + (1 | id), data = data)` in R.

The specification of the GEE models related to each of the generative models is unsurprisingly different considering that GEE does not explicitly model random effects. For each of the generative models, we will fit three GEE models: one with an exchangeable correlation structure, one with an independent correlation structure, and one with an AR(1) correlation structure. The GEE models were fitted using the `geeglm` function in R. Since the fixed effects modeled in GM1, GM1a, GM2, GM2a, GM3, GM3a are the same (the only differences pertain to the modeling of random effects), the analytical *GEE model* is identical across these three conditions. The analytical *GEE model* is given by:

$$Y_{it+1} = \alpha_0 + \alpha_1 X_{it} + \beta_0 A_{it} + \beta_1 A_{it} X_{it} + \epsilon_{it+1}.$$

The GEE models were fitted as `geeglm(Y ~ X * A, id = id, data = data, family = gaussian, corstr = "exchangeable")`, `geeglm(Y ~ X * A, id = id, data = data, family = gaussian, corstr = "independence")`, and `geeglm(Y ~ X * A, id = id, data = data, family = gaussian, corstr = "ar1")` in R.

In GM1b, GM2b, GM3b, the fixed interaction effect is removed, so the analytical *GEE model* is given by:

$$Y_{it+1} = \alpha_0 + \alpha_1 X_{it} + \beta_0 A_{it} + \epsilon_{it+1}.$$

The GEE models were fitted as `geeglm(Y ~ X + A, id = id, data = data, family = gaussian, corstr = "exchangeable")`, `geeglm(Y ~ X + A, id = id,`

`data = data, family = gaussian, corstr = "independence")`, and `geeglm(Y ~ X + A, id = id, data = data, family = gaussian, corstr = "ar1")` in R.

Results

As shown in Table X, GM3 results in bias

Discussion

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Appendix

Original Section from Qian et al. (2020): “4. Simulation”

In the simulation, we considered three generative models (GMs), all of which have an endogenous covariate. In the first two GMs, the endogenous covariate X_{it} equals the previous outcome Y_{it} plus some random noise, so the conditional independence assumption (10) is valid. In GM 3, the endogenous covariate depends directly on b_i , violating assumption (10). The details of the generative models are described below.

In GM1, we considered a simple case with only a random intercept and a random slope for A_{it} , so that $Z_{i(t_0)} = Z_{i(t_2)} = 1$ in model (7). The outcome is generated as:

$$Y_{it+1} = \alpha_0 + \alpha_1 X_{it} + b_{i0} + A_{it}(\beta_0 + \beta_1 X_{it} + b_{i2}) + \epsilon_{it+1}.$$

The random effects $b_{i0} \sim N(0, \sigma_{b0}^2)$ and $b_{i2} \sim N(0, \sigma_{b2}^2)$ are independent of each other. The covariate is generated as $X_{i1} \sim N(0, 1)$, and for $t \geq 2$,

$$X_{it} = Y_{it} + N(0, 1).$$

The randomization probability p_t is constant at $1/2$. The exogenous noise is $\epsilon_{it+1} \sim N(0, \sigma_\epsilon^2)$.

In GM2, we considered the case where $Z_{i(t_0)} = Z_{i(t_2)} = 1$, with time-varying randomization probability. The outcome is generated as:

$$Y_{it+1} = \alpha_0 + \alpha_1 X_{it} + b_{i0} + b_{i1} X_{it} + A_{it}(\beta_0 + \beta_1 X_{it} + b_{i2} + b_{i3} X_{it}) + \epsilon_{it+1}.$$

The random effects $b_{ij} \sim N(0, \sigma_{b_j}^2)$, for $0 \leq j \leq 3$, are independent of each other. The covariate is generated as $X_{i1} \sim N(0, 1)$, and for $t \geq 2$,

$$X_{it} = Y_{it} + N(0, 1).$$

The randomization probability depends on X_{it} :

$$p_t = 0.7 \cdot 1(X_{it} > -1.27) + 0.3 \cdot 1(X_{it} \leq -1.27),$$

where $1(\cdot)$ represents the indicator function, and the cutoff -1.27 was chosen so that p_t equals 0.7 or 0.3 for about half of the time. The exogenous noise is $\epsilon_{it+1} \sim N(0, \sigma_\epsilon^2)$.

GM3 is the same as GM 1, except that the covariate X_{it} depends directly on b_i :

$$X_{i1} \sim N(b_{i0}, 1), \quad X_{it} = Y_{it} + N(b_{i0}, 1) \text{ for } t \geq 2.$$

We chose the following parameter values:

$$\alpha_0 = -2, \quad \alpha_1 = -0.3, \quad \beta_0 = 1, \quad \beta_1 = 0.3,$$

$$\sigma_{b0}^2 = 4, \quad \sigma_{b1}^2 = \frac{1}{4}, \quad \sigma_{b2}^2 = 1, \quad \sigma_{b3}^2 = \frac{1}{4}, \quad \sigma_{\epsilon}^2 = 1.$$

Overview of Variations on Generative Model 3

Table 1: Models with 1 Parameter Less

Generative	random slope	interactie β_1	fixed slope	bias
Model	treatment b_{i2}		covariate α_1	
3	yes	yes	yes	yes, negative
3a	no	yes	yes	no
3d	yes	no	yes	no
3h	yes	yes	no	yes, positive

Generative	random slope	interactie β_1	fixed slope	bias
Model	treatment b_{i2}		covariate α_1	
3	yes	yes	yes	yes, negative
3b	no	no	yes	no
3i	no	yes	no	
3j	yes	no	no	

Simulation Plan Proposal

To uncover the undesirable effects of endogenous covariates and investigate robustness against these effects, we will carry out simulations in which data will be generated according to several increasingly complex scenarios. These scenarios will be visually represented using directed acyclic graphs and analyzed using GEE, MLM and DSEM. We will start out with a scenario of the basic MLM—where a time-varying outcome Y is regressed on a single time-varying predictor X and in the presence of stable between person differences

in the intercept—and increase the complexity until we reach the scenario that includes a time-varying endogenous covariate. The primary interest of this simulation study is the comparative performance of different specifications of the MLM and GEE in terms of bias in the estimation of the effect of X to Y . The secondary interest is the efficiency in mean squared error (MSE). We consider settings with timepoints $T = 10, 30$ and sample size $N = 30, 100, 200$.

Statistical analyses pertaining to the GEE and basic MLM will be performed in R, version 4.4.2 (?). To fit the GEE, the R-package `geepack` ([Halekoh et al., 2006](#)) will evaluate several different working correlation structures, including independent, exchangeable, AR(1) and unstructured. To fit the basic MLM, the R-package `lme4` ([Bates et al., 2015](#)) will be employed, where we will use restricted maximum likelihood estimation.