Untangling Bias in Multilevel Linear Models: The Role of Endogenous Time-Varying Covariates

Research Report

Ward B. Eiling (9294163)

Supervisors: Ellen Hamaker and Jeroen Mulder

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Utrecht University

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1 Introduction

Across a wide range of disciplines, researchers analyze clustered longitudinal, observational data to investigate prospective causal relationships between variables. When analyzing such data, psychological researchers most commonly use the multilevel linear model[1] (MLM, Bauer & Sterba, 2011), which—in the context of longitudinal data analysis—partitions observed variance into stable between-person differences and within-person fluctuations (Hamaker & Muthén, 2020). Research questions explored with the MLM commonly lead to the availability of time invariant and/or time-varying covariates, the latter measured repeatedly over time. The inclusion of covariates is a common strategy to improve parameter precision (Boruvka et al., 2018) and address bias introduced by (time-varying) confounders (Daniel et al., 2013; Robins et al., 2000; Wodtke, 2020). Nevertheless, this approach is not universally beneficial, as conditioning on endogenous covariates—those influenced by (prior) treatment/exposure or outcome—can create challenges for standard methods like MLMs, which implicitly assume the exogeneity of covariates (Erler et al., 2019).

Dating back to the work of Pepe & Anderson (1994), this assumption has proven to be non-trivial when endogenous covariates vary over time. In fact, their inclusion in longitudinal studies can lead to biased treatment effect estimates, an issue that, despite its significance, has received limited attention in psychological research. Building on this foundation, a recent paper by Qian et al. (2020) examined the suitability of MLM for estimating the causal effect of a time-varying exposure or treatment. Specifically, they focused on settings where the exposure is randomly assigned at each occasion within individuals. Such randomized exposures may include, for example, prompts delivered through push notifications to remind participants of cognitive or mindfulness-based strategies (Nahum-Shani et al., 2021; Walton et al., 2018). While random assignment with a constant probability might seem sufficient to identify (the presence

[1]The MLM is known by various names in different substantive fields, including: linear mixed model, hierarchical linear model, random-effect model and mixed-effects model.

and absence of) causal effects, Qian et al. (2020) showed that model fitting issues and parameter bias can arise when a *time-varying endogenous covariate* is present.

However, due to a divide between the disciplines that employ the MLM, such critiques 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 emerge. This report aims to explore why Qian et al. (2020) observed biased estimates of the treatment effect in certain data-generating mechanisms containing endogenous covariates, while not for others. Additionally, it seeks to explain this issue to an audience of psychologists. The study will first employ graphical diagrams to assess two criteria across various scenarios involving an endogenous time-varying covariate and randomized treatment: (a) path diagrams to evaluate the conditional independence assumption introduced by Qian et al. (2020) and (b) directed acyclic graphs (DAGs) to assess the backdoor criterion (Pearl, 1988, 2009). Subsequently, data simulations based on Qian et al. (2020)'s original scenarios, along with additional ones, will be performed to reproduce and isolate the underlying issue and evaluate whether these criteria can effectively detect bias in the treatment effect. The following research question will be addressed: *When does the inclusion of endogenous variables in multilevel linear models result in biased estimates of the treatment effect?*

2 Methods

In this section, the GMs will be formulated and specifications will be defined for the simulation study.

2.1 Data Generation

We consider two GMs from Qian et al. (2020), one (GM A) being a special case of the general model (GM G) where bias was detected. To further isolate the source of bias, we introduce two additional special cases, labeled GM B and C. Table 1 summarizes the differences between the

generative models. Compared to the general model G, GM A is not directly determined by the random intercept b_{i0}; GM B is does not have a random slope b_{i2} for treatment; and GM C does not have a fixed interaction effect β_1 between covariate and treatment.

Table 1: Generative Models: Summary of Differences

Generative Model	Name in Qian et al. (2020)	dependency b_{i0} and X_{it}	random slope treatment b_{i2}	interaction β_1
G(eneral)	3	✓	✓	✓
A	1	×	✓	✓
B	NA	✓	×	✓
C	NA	✓	✓	×

The details of the generative models are described below.

2.1.1 General Generative Model

Following the original notation of Qian et al. (2020), the outcome of GM G was generated as:

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

where Y_{it+1} is the outcome for person i at time $t+1$, X_{it} is the covariate for person i at time t, A_{it} is the treatment for person i at time t, b_{i0} is the random intercept, b_{i2} is the random slope for the treatment, and ϵ_{it+1} is the error term. Alternatively, the model can be represented in the multilevel notation of Raudenbush & Bryk (2002) with at the within-person level (level 1)

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

and at the between-person level (level 2)

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

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

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

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

The parameters α_0, α_1, β_0, and β_1 are fixed effects that are constant across individuals, while b_{i0} and b_{i2} are independent random effects that capture individual-specific deviations from population parameters. The presence of the interaction term β_1 implies treatment heterogeneity: the effect of the treatment A_{it} on the outcome depends on the value of the covariate X_{it}. b_{i0} represents deviations from the population intercept α_0, and b_{i2} represents deviations from the population slope β_0.

The covariate is generated as:

$$X_{it} = \begin{cases} b_{i0} + \epsilon_{X_{it}} & \text{if } t = 1, \\ b_{i0} + Y_{it} + \epsilon_{X_{it}} & \text{if } t \geq 2, \end{cases} \quad \text{where} \quad \epsilon_{X_{it}} \sim \mathcal{N}(0, 1)$$

The treatment randomization probability is constant at $p_t = 0.5$, so $A_{it} \sim \text{Bernoulli}(0.5)$ for all i and t. In other words, for every given person i and every timepoint t, the probability that treatment is assigned is equivalent to a fair coinflip. The exogenous noise is $\epsilon_{it+1} \sim \mathcal{N}(0, \sigma^2_\epsilon)$.

Figure 1a shows the path diagram for GM G.

The following parameter values were adapted from Qian et al. (2020):

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

$$\sigma^2_{b0} = 4, \quad \sigma^2_{b2} = 1, \quad \sigma^2_\epsilon = 1.$$

2.1.2 Special Cases

GM A is a special case of GM G, where the effect of the random intercept b_{i0} on the covariate X_{it} is set to zero. This results in a model where the covariate X_{it} is not directly determined by the random intercept b_{i0} (see Figure 1b). Instead, the endogenous covariate X_{it} equals the previous outcome Y_{it} plus some random noise:

$$X_{it} = \begin{cases} \epsilon_{X_{it}} & \text{if } t = 1, \\ Y_{it} + \epsilon_{X_{it}} & \text{if } t \geq 2, \end{cases} \quad \text{where} \quad \epsilon_{X_{it}} \sim \mathcal{N}(0, 1)$$

GM B is a special case of GM G in which the random slope b_{i2} was removed (see Figure 1c) by setting the random slope variance σ^2_{b2} to zero. While the within-person model is the same as GM G, there is a slight alteration in the between-person model:

$$\pi_{2i} = \beta_0.$$

The composite model then becomes:

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

GM C is a special case of GM G, where the fixed interaction parameter β_1 is set to zero, which implies the removal of the interaction term $\beta_1 A_{it} X_{it}$ (see Figure 1d). This, in turn, removed π_{3i}, thereby creating a discrepancy in within-person model of GM C and GM G:

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

Nevertheless, the between-person model of π_{0i}, π_{1i} and π_{2i} remains the same as GM G. The single equation model then becomes:

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

2.2 Data Analysis

All data generation and estimation was performed in `R`, version 4.4.2 (Team, 2024). After the generation of data generation for any given setting, analytical MLMs were fit that contain all the fixed and random parameters present in each of the respective data generating models. To fit the MLM, the `lmer` function from the R-package `lme4` (Bates et al., 2015) was employed with restricted maximum likelihood estimation.

In the simulation study, we evaluated the performance of the analytical models across a total of 24 different settings, each replicated 1,000 times, by systematically varying the following factors:

- **Generative Models (GM):** G, A, B, C
- **Number of timepoints (T):** 10, 30
- **Sample size (N):** 30, 100, 200

3 Results

3.1 Conditional Independence and Path Diagrams

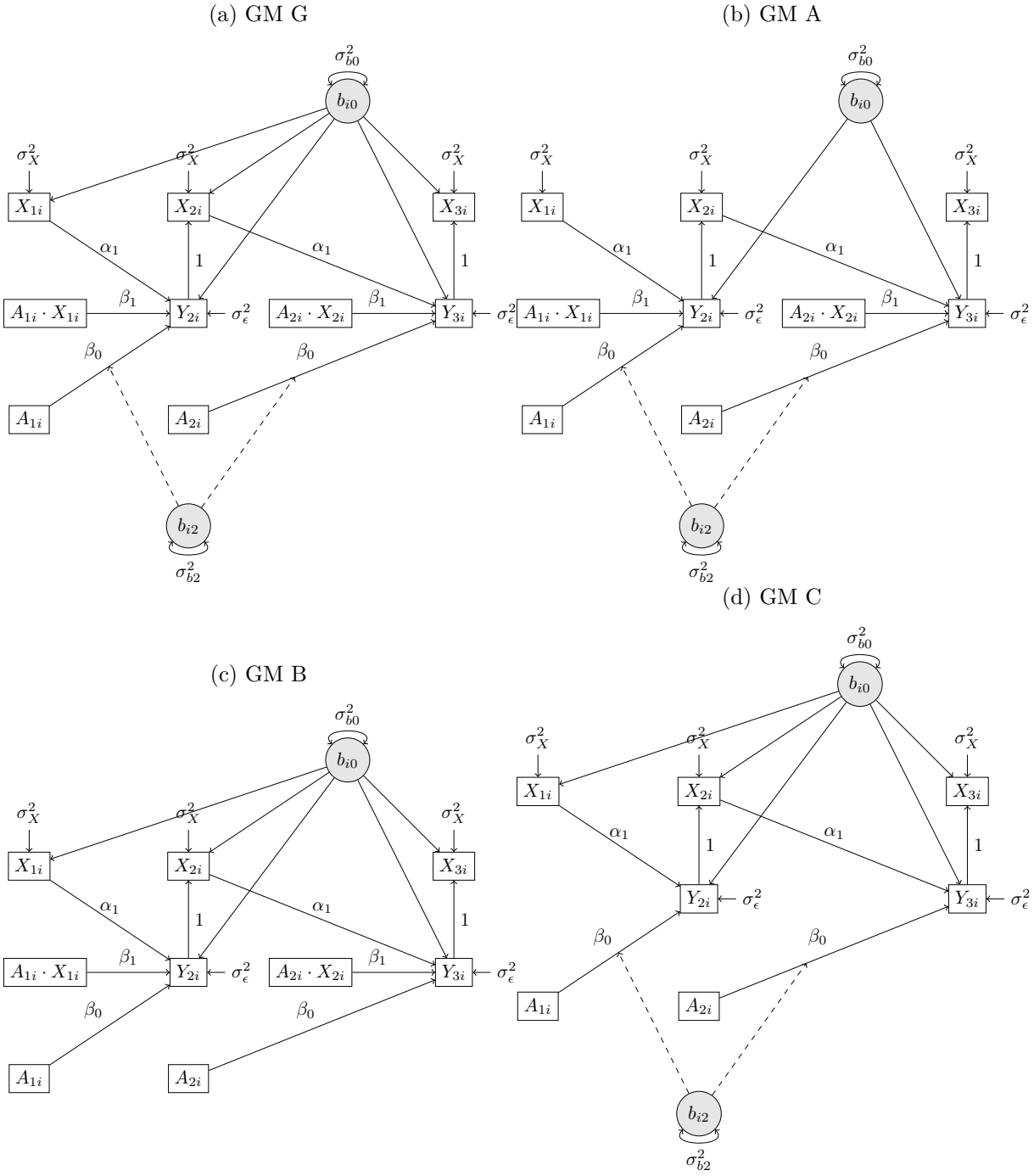
The first criterion for evaluating the presence of bias in treatment effect estimates is the *conditional independence assumption*, introduced by Qian et al. (2020) and based on the work of Sitlani et al. (2012). According to Qian et al. (2020), this assumption should identify whether estimators of the treatment effect are consistent and unbiased under randomized treatment assignment. The conditional independence assumption states that the covariate at time t (X_{it}) should be independent of the individual's random effects (intercept b_{i0} and slope(s) b_{i1}) once we

account for their history of covariates up to timepoint $t-1$ (H_{it-1}), previous treatments (A_{it-1}), and prior outcomes (Y_{it}).

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

This assumption allows for X_{it} to be influenced by earlier variables (e.g., outcomes or treatments) but not directly by unobserved individual characteristics (i.e., random effects). However, as Qian et al. (2020) highlights, ensuring this assumption holds requires careful consideration of theory and domain knowledge. To clarify the application of the conditional independence assumption, we pair the equations of the generative models (GMs) with path diagrams (Duncan, 1966; Wright, 1934) illustrating the first three timepoints (t) for each model (see Figure 1).

Figure 1: Path Diagrams for Generative Models G, A, B and C (t = 1, 2, 3)



Note. Random effects are represented by grey circles, observed variables by squares and relationships across variables by arrows, where dashed lines are reserved for random slopes.

In GM G, the covariate X_{it} is directly influenced by unobserved individual factors (represented by the random effects, b_{i0}). Consequently, conditioning on prior variables, such as the

outcome at the previous timepoint Y_{it}, does not fully block or eliminate the influence of these unobserved factors. As a result, X_{it} remains dependent on the random effects, violating the assumption. This violation of the conditional independence assumption aligns with the biased estimates of the treatment effect observed in GM G, as identified by Qian et al. (2020).

In contrast, GM A, a special case of GM G where no bias was found by Qian et al. (2020), removes the direct link between X_{it} and the random effects b_{i0}. In this case, X_{it} is simply the previous outcome Y_{it} plus some random noise. While there remains an indirect connection between X_{it} and b_{i0} through Y_{it}, conditioning on Y_{it} effectively "breaks the link" between X_{it} and the random effects, satisfying the conditional independence assumption.

For GM B and GM C, the direct link between the random effects and X_{it} remains, as in GM G. As a result, these models also violate the conditional independence assumption, suggesting the presence of bias in treatment effect estimates.

3.2 Backdoor Criterion and DAGs

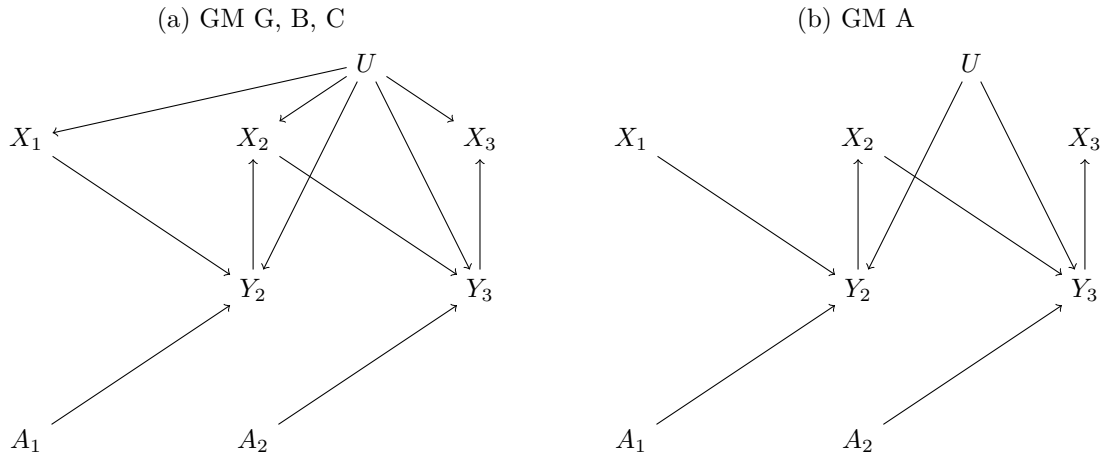
The second criterion for evaluating bias in treatment effect estimates is the *backdoor criterion* (Pearl, 1988, 2009). This addresses the classical problem in causal inference: causal effects cannot be directly observed and must be inferred from associations, which often include both causal and non-causal or *spurious* components (Holland, 1986). When causal effects can be isolated under ideal conditions (e.g., no measurement error, infinite sample size), they are said to be *identified*. According to the backdoor criterion, causal effects can be identified by blocking non-causal paths through conditioning on appropriate variables, such as relevant confounders—common causes that induce spurious relationships. If spurious backdoor paths remain unblocked, bias persists in treatment effect estimates (Kim & Steiner, 2021).

To detect backdoor paths, directed acyclic graphs (DAGs) (Pearl, 1995, 2009) are invaluable tools. DAGs generalize conventional path diagrams (Duncan, 1966; Wright, 1934) within a fully nonparametric framework. Unlike traditional diagrams, DAGs make no assumptions about

distributional properties (e.g., multivariate normality) or functional forms (e.g., linearity). They encode qualitative causal assumptions about the data-generating process, where arrows indicate direct causal effects that may vary across individuals (effect heterogeneity) or depend on other variables (effect interaction or modification) (Elwert & Winship, 2014). Notably, random slopes from random-effects models and interaction effects are not explicitly represented in DAGs, which precludes their use for evaluating the conditional independence assumption.

Using the direct causal effects specified in each generative model (GM), we can formulate DAGs for the first three observations, representing the random disturbance b_{0i} as the node U (e.g., Kim & Steiner, 2021, see Figure 2). These diagrams confirm that random slopes and fixed interaction effects are absent. Indeed, this absence explains why the DAGs for GMs G, B, and C are equivalent.

Figure 2: DAGs for Generative Models G, A, B and C (t = 1, 2, 3)



Note. The red arrows show the biased backdoor path(s) in the treatment efffect (before controlling for X_{it}).

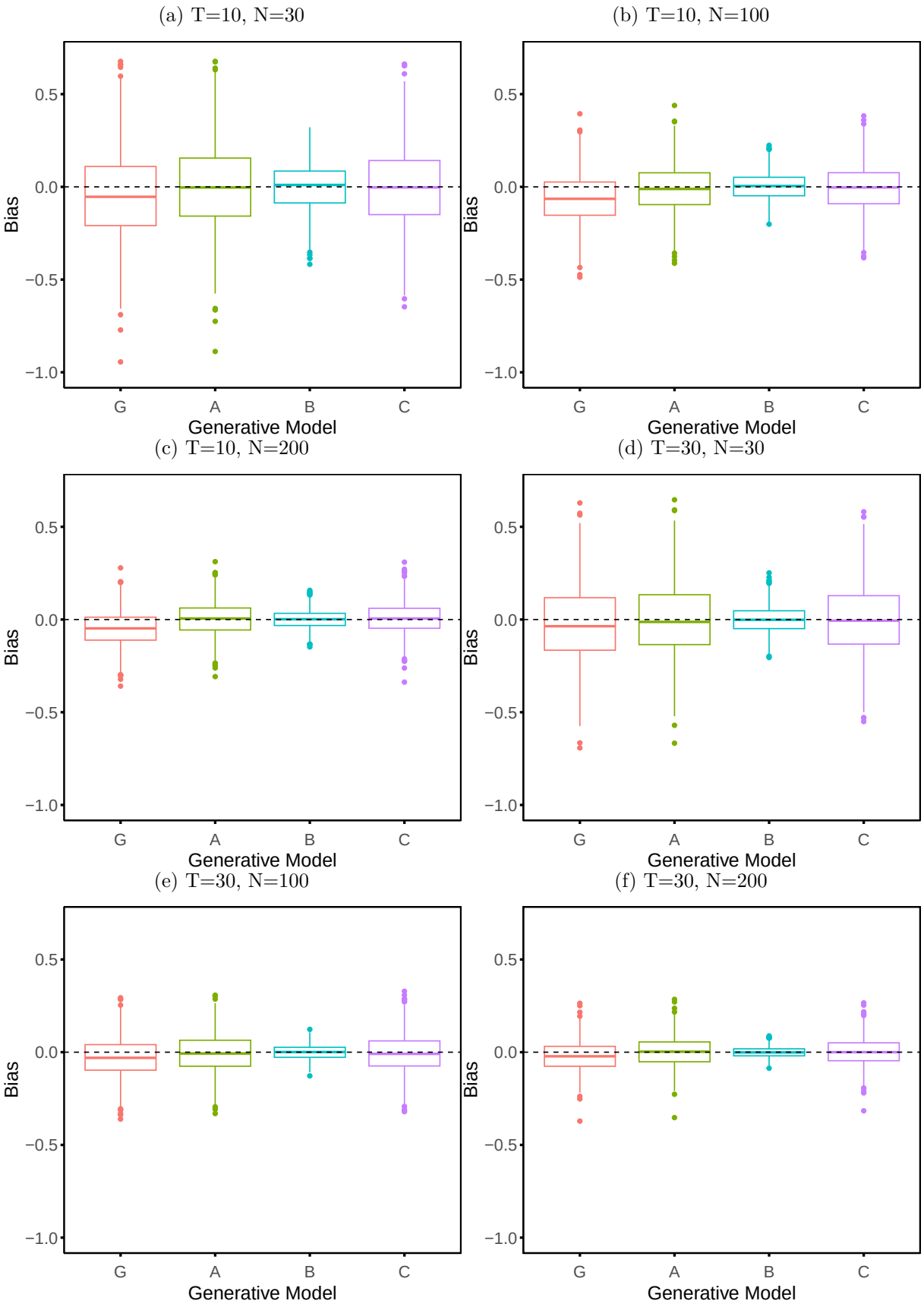
We now apply the backdoor criterion to these DAGs to assess potential bias in the treatment effect. For all GMs, there are no backdoor paths in the treatment effect $A_t \rightarrow Y_{t+1}$, as A_t lacks any parent nodes. Consequently, covariate X_t need not be controlled to obtain an unbiased total effect. Importantly, including X_{it} does not introduce identification issues, as it is neither

a mediator (i.e., on the pathway from A_t to Y_{t+1}) nor a collider (i.e., a common effect of A_t and Y_{t+1}) in the treatment effect. Therefore, according to the backdoor criterion, the inclusion of the time-varying covariate X_{it} should not result in biased estimates of the treatment effect in any of the generative models.

3.3 Simulation Study

Table 2 and Figure 3 present the simulation results for each of the generative models. The bias in Table 2 refers to the difference between the mean of the estimated parameter values $\bar{\hat{\beta}}_0$ and the prespecified treatment effect β_0. As $\beta_0 = 1$, an absolute bias of 0.05 implies a 5% relative bias.

Figure 3: Estimation bias for the fixed treatment effect β_0 of each generative model for different combinations of sample size N and number of timepoints T over 1000 simulation replications



In this reproduction of Qian et al. (2020), the overall pattern was consistent with the original study (see Figure 3): we observed substantial absolute bias ranging from 0.023 (2.3%) to 0.064 (6.4%) for the most general generative model (GM G), and much smaller bias of ≤ 0.015 (1.5%) for GM A. These results align with expectations based on the conditional independence assumption, which predicts that the treatment effect would be unbiased for GM A and biased for GM G. However, the findings contradict the backdoor criterion, which predicts no bias for any of the generative models (GMs). Notably, we found 4 times greater treatment effect bias for GM A in the scenario with $T = 10$ and $N = 100$ than reported by Qian et al. (2020), with a maximum bias of -0.012 (1.2%; (see Table 2), compared to -0.003 (0.3%) found by Qian et al. (2020). For GM G, the size of the bias decreased as the number of time points increased.

For the two additional special cases of GM G, namely GM B and GM C, we observed even smaller absolute bias than for GM A: ≤ 0.010 (1%) for GM C and ≤ 0.005 (0.5%) for GM B (see Table 2). These findings align with the backdoor criterion's prediction of no bias but contradict the expectations based on the conditional independence assumption, which suggests the presence of bias. Additionally, GM B exhibited the smallest absolute bias overall and showed much smaller variability across simulation replications compared to all other GMs. In contrast, the remaining models exhibited comparable levels of variability (see Figure 3 and Table 2).

In summary, these findings suggest that if the underlying GM did not include the direct dependency of the random intercept on the covariate (GM A), the random slope b_{i2} (GM B), or the interaction term β_1 (GM C), as in GM G, the bias either disappears or becomes negligible. However, neither the backdoor criterion nor the conditional independence assumption provided consistent predictions of treatment effect bias across all models.

4 Discussion

4.1 Main Findings

In this research report, we evaluated several GMs to investigate when endogenous time-varying covariates bias treatment effect estimates in MLMs under randomized treatment. We also assessed the ability of the conditional independence assumption and the backdoor criterion to predict this bias. Consistent with Qian et al. (2020) and the conditional independence assumption, we observed substantially greater bias in the most general model (GM G) compared to a special case (GM A), where the direct effect of the random intercept on the covariate was removed. However, one unexpected result was the fourfold increase in maximum bias for GM A compared to Qian et al. (2020). This discrepancy may stem from differences in the simulation setup (e.g., random number generation or handling of warnings/errors). The two additional special cases of GM G, where the random slope for treatment (GM B) or the interaction term between treatment and covariate (GM C) was removed, exhibited even smaller bias in the treatment effect—despite violations of the conditional independence assumption. These findings tell us that—at least in this particular instance—the dependency between the covariate and treatment, the random slope for treatment, and the interaction effect are all essential for bias to occur.

This naturally raises important questions: why was no discernible bias observed in GM B and GM C, as predicted by the conditional independence assumption, and can this pattern generalize beyond the current generative models? One possibility is that, while bias may exist as predicted, it was canceled out by parameter removal in these specific models. Alternatively, heterogeneity in the treatment effect—whether unexplained via the random slope or explained via the covariate—may both be necessary for bias to occur. This explanation aligns with the statement by Qian et al. (2020) that "applying linear mixed models is problematic because potential moderators of the treatment effect are frequently endogenous" (p. 375). If treatment

effect moderation by a covariate is indeed a prerequisite for bias, it could explain the absence of bias in GM C, where no interaction term was included. However, it remains unclear why Qian et al. (2020) does not explicitly mention this condition (e.g., when introducing the conditional independence assumption). Further research is needed to determine whether these findings generalize or are specific to the evaluated GMs, thereby informing practical recommendations for using MLMs with endogenous time-varying covariates.

Regarding the backdoor criterion and DAGs (Pearl, 1988, 2009), our results suggest that the classical non-parametric DAG may be insufficient to identify bias in GM G. While DAGs account for direct causal effects, they do not impose restrictions on random slopes or interaction effects[2], which are central to the conditional independence assumption. Similar concerns regarding the use of the DAG with Pearl's backdoor criterion in situations with interaction effects have been raised (Attia et al., 2022; Weinberg, 2007). Future research could explore to what extent proposed extensions of the DAG—that incorperate interaction effects—may allow the backdoor criterion to identify bias in the treatment effect estimates.

It should also be noted that the current investigation takes for granted that the marginal (population-averaged) interpretation of the treatment effect estimators of the MLM may not be valid due to the presence of endogenous time-varying covariates Pepe & Anderson (1994). While, the conditional-on-the-random-effect interpretation of the parameters is often aligned with the scientific interest in psychology, future research would benefit from a more comprehensive intergration of insights from the literature on marginal effects.

Another avenue for future investigation is the role of centering approaches (see Hamaker & Muthén (2020) for an overview). Namely, Antonakis et al. (2021) notes that the assumption of uncorrelatedness between the random effects and level 1 covariates can be relaxed by using Mundlak's contextual model[3] (Mundlak, 1978): adding the cluster means of each covariate

[2]Note that the term "effect modification", while often used interchangeably with "interaction", has a distinct definition in the counterfactual framework (VanderWeele, 2009).

[3]This is referred to as the Correlated Random Effects (CRE) approach by Wooldridge (2002).

as predictor of the random intercept. Such an approach of explicitly modeling the source of endogeneity, as advocated by Bell & Jones (2015), may further clarify the treatment effect bias in GM G.

Finally, Qian et al. (2020) only considered independent random effects, a restrictive assumption that may be violated in practice. Exploring correlated random effects using structural equation modeling frameworks (Rovine & Molenaar, 2000) could provide further insight.

4.2 Conclusion

This report is a first step towards understanding the implications of endogenous covariates in multilevel linear models. However, to recognize and understand completely when and why endogenous covariates may trouble an empirical investigation, further research is needed.

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6 Appendix (MAAK SUPPLEMTAL MATERIALS AAN!!!)

Table 2: Treatment effect bias for Generative Models G, A, B and C over 1000 replications

			β_0			
GM	T	N	Bias	SD	MC-SE	SR
G	10	30	-0.052	0.245	0.008	0.999
		100	-0.064	0.134	0.004	1.000
		200	-0.051	0.096	0.003	1.000
	30	30	-0.024	0.206	0.007	0.997
		100	-0.030	0.108	0.003	0.996
		200	-0.023	0.080	0.003	0.997
A	10	30	0.000	0.238	0.008	0.998
		100	-0.012	0.129	0.004	1.000
		200	0.003	0.093	0.003	0.999
	30	30	-0.001	0.203	0.006	0.998
		100	-0.007	0.107	0.003	0.996
		200	0.001	0.079	0.003	0.996
B	10	30	0.000	0.126	0.004	1.000
		100	0.004	0.073	0.002	1.000
		200	0.002	0.048	0.002	1.000
	30	30	-0.001	0.071	0.002	1.000
		100	0.000	0.040	0.001	1.000
		200	0.000	0.028	0.001	1.000
C	10	30	0.001	0.217	0.007	0.999
		100	-0.008	0.121	0.004	1.000
		200	0.005	0.087	0.003	1.000
	30	30	0.000	0.193	0.006	1.000
		100	-0.008	0.103	0.003	0.997
		200	0.001	0.075	0.002	0.999

Note. GM: generative model. T: number of timepoints. N: sample size. SD: $\sqrt{\frac{1}{(n_{\text{sim}}-1)}\sum_{i=1}^{n_{\text{sim}}}\left(\hat{\beta}_{0i}-\bar{\beta}_0\right)^2}$, which is the standard deviation of estimates across replications. SR: model fitting success rate. Bias: $\frac{1}{n_{\text{sim}}}\sum_{i=1}^{n_{\text{sim}}}\hat{\beta}_{0i}-\beta_0$ (Morris et al., 2019), which represents the difference between the mean of the estimated parameter values $\hat{\beta}_0$ and the prespecified treatment effect $\beta_0 = 1$. MC-SE: $\sqrt{\frac{1}{n_{\text{sim}}(n_{\text{sim}}-1)}\sum_{i=1}^{n_{\text{sim}}}\left(\hat{\beta}_{0i}-\bar{\beta}_0\right)^2} = \frac{\text{SD}}{\sqrt{n_{\text{sim}}}}$, which represents the Monte Carlo SE of bias (Morris et al., 2019).