Treatment Effect Bias in Multilevel Linear Models under Time-Varying Endogeneity: A New Look at Qian et al. (2020)

Research Report

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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 model¹ (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 often result in 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 confounders (Daniel et al., 2013; Robins et al., 2000). 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 and Anderson (1994) in the biostatistics literature, this assumption has been shown 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 and absence of) causal effects, Qian et al. (2020) showed that model

¹The MLM is known by various names in different substantive fields, including: linear mixed model, hierarchical linear model, random-effect model and mixed-effects 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 models 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, we first formulate four generative models (GMs) that incorporate a time-varying endogenous covariate and a randomized treatment. We then outline the methodology used to investigate treatment effect bias across different settings.

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 GM-C. We first describe the general generative

model (GM-G) in detail, and then proceed to its three special cases: GM-A, GM-B, and GM-C.

2.1.1 General Model: GM-G

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

$$Y_{it+1} = \alpha_0 + \alpha_1 X_{it} + b_{i0} + A_{it} (\beta_0 + \beta_1 X_{it} + b_{i2}) + \epsilon_{it+1}$$
(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 rewritten in the multilevel notation of Raudenbush and Bryk (2002), with at the within-person level (level 1):

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

and at the between-person level (level 2):

$$\begin{split} \pi_{0i} &= \alpha_0 + b_{i0}, \quad \text{where} \quad b_{i0} \sim \mathcal{N}(0, \sigma_{b0}^2), \\ \pi_{1i} &= \alpha_1, \\ \\ \pi_{2i} &= \beta_0 + b_{i2}, \quad \text{where} \quad b_{i2} \sim \mathcal{N}(0, \sigma_{b2}^2), \\ \\ \pi_{3i} &= \beta_1. \end{split}$$

The parameters $\alpha_0 = -2$, $\alpha_1 = -0.3$, $\beta_0 = 1$, and $\beta_1 = 0.3$ are fixed effects that are constant across individuals. Conversely, b_{i0} and b_{i2} are independent random effects that capture individual-specific deviations from population parameters α_0 and β_0 respectively. 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} . The random intercept b_{i0} and random slope

 b_{i2} are assumed to be normally distributed with mean zero and variance $\sigma_{b0}^2 = 4$ and $\sigma_{b2}^2 = 1$, respectively. The exogenous noise ϵ_{it+1} in the outcome is normally distributed with mean zero and variance $\sigma_{\epsilon}^2 = 1$.

The covariate is generated as:

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

The treatment randomization probability is constant at $p_t = 0.5$, so $A_{it} \sim \text{Bernoulli}(0.5)$, implying that for every given person i and every timepoint t, the probability that treatment is assigned is equivalent to a fair coinflip. Relationships between the (observed and latent) variables are illustrated in Figure 1a.

2.1.2 Special Cases: GM-A, GM-B and GM-C

We consider three special cases of GM-G, namely GM-A, GM-B and GM-C. The relation of each special case to GM-G is summarized in Table 1. The specifics of each special case are described below.

Table 1: Summary of Differences Between Generative Models

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

GM-A is a special case of GM-G, where the effect of b_{i0} on X_{it} is set to zero, which implies that X_{it} is not directly determined by b_{i0} (see Figure 1b). Instead, the endogenous covariate

 X_{it} equals the previous outcome Y_{it} plus some random noise:

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

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

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

The composite model then becomes:

$$Y_{it+1} = (\alpha_0 + b_{i0}) + \alpha_1 X_{it} + \beta_0 A_{it} + \beta_1 A_{it} X_{it} + \epsilon_{it+1}$$
 (2)

GM-C is a special case of GM-G, where β_1 is set to zero, which implies the removal of the interaction term $\beta_1 A_{it} X_{it}$ (see Figure 1d) and π_{3i} . Therefore, the within-person model from GM-G changes into:

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

Since the between-person model of π_{0i} , π_{1i} and π_{2i} remains the same as GM-G, the composite model becomes:

$$Y_{it+1} = \alpha_0 + \alpha_1 X_{it} + b_{i0} + A_{it}(\beta_0 + b_{i2}) + \epsilon_{it+1}. \tag{3}$$

2.2 Data Analysis

Data generation and estimation were performed in R, version 4.4.2 (Team, 2024), following Qian et al. (2020)'s methodology for consistency. After data generation, analytical MLMs with restricted maximum likelihood estimation were fit using the lmer function from the lme4 package (Bates et al., 2015). Specifically, the MLM from Equation 1 was fit for GM-G and A, the MLM from Equation 2 for GM-B, and the MLM from Equation 3 for GM-C².

In the simulation study, we evaluated the bias of the analytical models across different settings by systematically varying the following 3 factors: Generative Model (GM) with the levels G, A, B, and C; number of timepoints (T) with the levels 10 and 30; and sample size (N) with the levels 30, 100, and 200. By varying these factors, we created a total of 24 unique settings, each of which was replicated 10,000 times. Bias estimates were calculated as the difference between the mean of the estimated parameter values $\bar{\beta}_0$ (across replications) and the prespecified treatment effect $\beta_0 = 1$.

3 Results

This section begins by constructing predictions about treatment effect bias for each GM, guided by the conditional independence assumption and the backdoor criterion. These predictions are then compared with the simulation study results, which present the estimated bias across the different GMs.

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

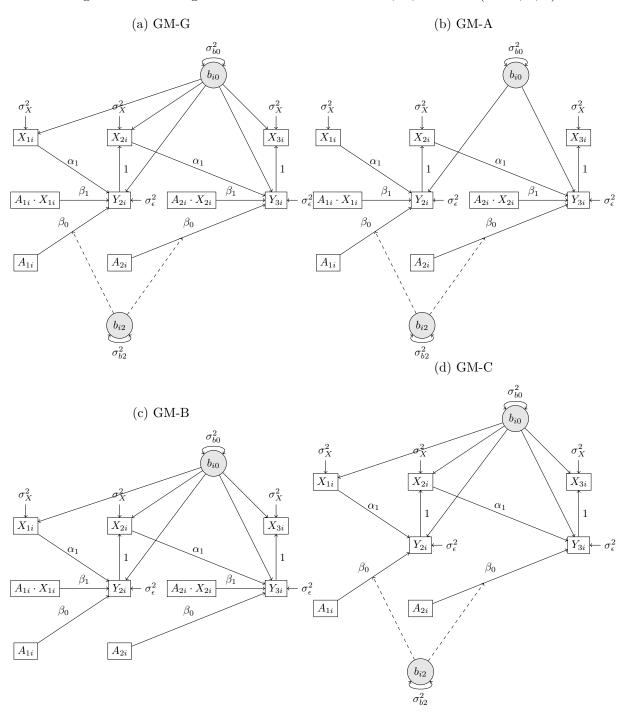
²Contrary to the data generating models, the analytical models do not model the covariate X_{it} and the treatment A_{it} .

estimators of the treatment effect are consistent and unbiased under randomized treatment assignment. The 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 treatment (A_{it-1}), and prior outcome (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 but not directly by random effects (i.e., unobserved individual characteristics). Evaluation of this assumption must be done based on domain knowledge (Qian et al., 2020). To clarify the application of the conditional independence assumption, we pair the equations of the GMs with path diagrams (Duncan, 1966; Wright, 1934) (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 the random intercept b_{i0} . Consequently, conditioning on prior variables, such as the outcome at the previous timepoint Y_{it} , does not fully

block the influence of the random effects. 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} . 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.

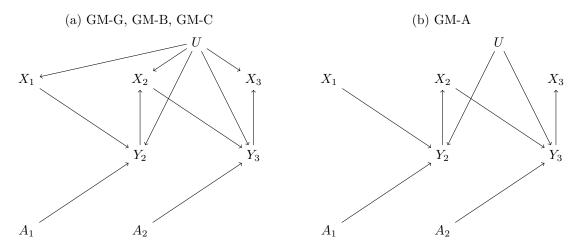
3.2 Backdoor Criterion and DAGs

The second criterion for evaluating bias in treatment effect estimates is the backdoor criterion (Pearl, 1988, 2009), which can help us decide which variables to control for. To detect backdoor paths, DAGs (Pearl, 1995, 2009) are invaluable tools³. Unlike conventional linear path diagrams (Duncan, 1966; Wright, 1934) and structural equation models, DAGs are non-parametric. They encode 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). Hence, random slopes and interaction effects are not explicitly represented in DAGs, which precluded their use for evaluating the conditional independence assumption.

The DAGs for each GM are formulated in Figure 2, which 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.

³An accessible introduction into DAGs and backdoor paths can be found in Rohrer (2018).

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



Note. The node U represents the random disturbance b_{0i} in the generative models.

Application of the backdoor criterion begins by identifying all paths that connect A_t to Y_{t+1} , excluding the direct treatment effect $A_t \to Y_{t+1}$ itself. Next, we determine whether these paths can transmit association by applying the d-separation rules⁴. A path that contains an arrow pointing to the treatment A_t is considered a backdoor path.

Examining the DAGs presented in Figure 2, we observe that none of the GMs contains any path connecting A_t to Y_{t+1} other than $A_t \to Y_{t+1}$ itself. This confirms that there are no backdoor paths in $A_t \to Y_{t+1}$, as A_t lacks any parent nodes. Indeed, the random assignment of the treatment ensures, by design, the absence of backdoor paths. Consequently, X_t does not need to be controlled for to obtain an unbiased estimate of the total effect. Nevertheless, the inclusion of X_t should not introduce bias in the treatment effect⁵, as it does not lay on a pathway connecting A_t to Y_{t+1} .

⁴For an accessible introduction to d-separation, see (Hayduk et al., 2003).

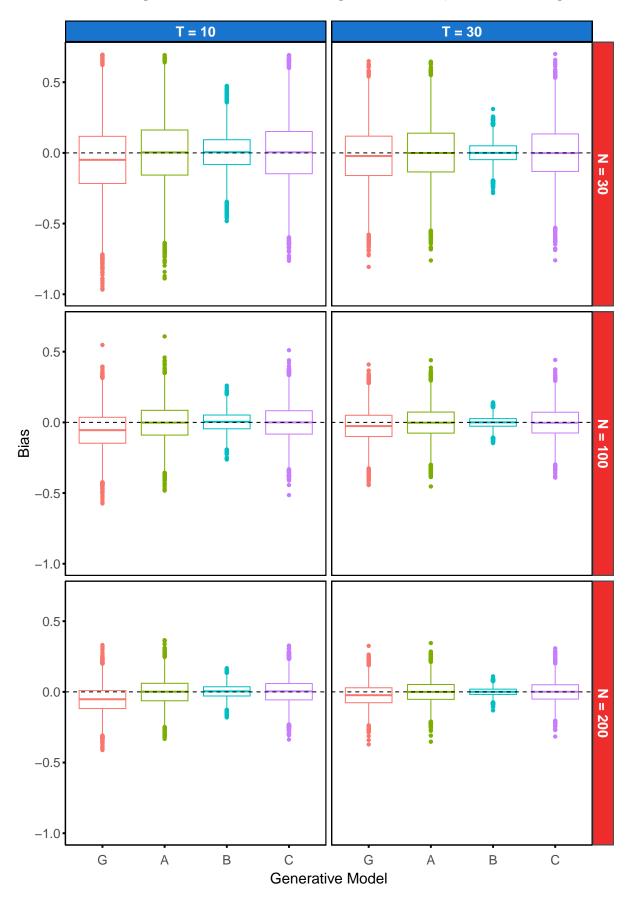
⁵Inclusion of the covariate may, however, increase the power to detect the treatment effect.

3.3 Simulation Study

Figure 3 present the bias estimates for each of the GMs⁶, where an absolute bias of 0.05 implies a 5% relative bias, since $\beta_0 = 1$.

 $^{^6}$ The supplemental table with additional information can be found at the OSF repository: $\frac{1}{8} \frac{1}{100} = \frac{1}{100} = \frac{1}{100} \frac{1}{100} = \frac{1}{100$

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 10,000 simulation replications



Note. bias refers to the difference between the mean of the estimated parameter values $\bar{\beta}_0$ and the prespecified treatment effect $\beta_0 = 1$.

In this reproduction of Qian et al. (2020), the overall pattern was consistent with the original study: we observed bias for GM-G (0.023-0.056 or 2.3%-5.6%), but not for GM-A (≤ 0.002 or 0.2%). These results align with expectations based on the conditional independence assumption, but contradict the backdoor criterion, which predicted the absence of bias for all the GMs. As shown in Figure 3, the bias in GM-G decreased as T increased. In contrast, the bias remained stable across different levels of N, implying that the estimates are inconsistent (i.e. they do not converge to the true value as N increases).

Similar to GM-A, we observed no discernible bias for GM-B (≤ 0.005 or 0.5%) and GM-C (≤ 0.003 or 0.3%). These findings align with the backdoor criterion's prediction of no bias but contradict the expectations based on the conditional independence assumption, which suggested the presence of bias. Additionally, GM-B showed much smaller variability across simulation replications compared to the other GMs (see Figure 3).

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 disappears. However, neither the backdoor criterion nor the conditional independence assumption provided consistent predictions of treatment effect bias across all models.

4 Discussion

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 when this bias will occur. We observed biased and inconsistent estimates in the most

general model (GM-G), but not in the three special cases, that either did not contain a direct effect of the random intercept on the covariate (GM-A), a random slope for treatment (GM-B), or an interaction term between treatment and covariate (GM-C). The conditional independence assumption correctly predicted bias in GM-G and GM-A, but not in GM-B and GM-C. The backdoor criterion predicted no bias in any of the GMs, which was inconsistent with the bias found in GM-G. These findings suggest that, at least in this 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 GMs? One possibility is that heterogeneity in the treatment effect—both explained by the covariate and influenced by the random slope—is necessary for bias to occur. Both factors appear to be essential in driving the bias, rather than either factor alone. This aligns with Qian et al. (2020)'s assertion 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 this would not explain why the bias disappears in the model without the random slope (GM-B). More generally, note of caution is due here since the current study only considered a specific set of GMs. 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 DAG arrows can represent interaction effects⁷ and effect heterogeneity, these are not explicitly defined as such,

⁷Note that the term "effect modification", while often used interchangeably with "interaction", has a distinct definition in the counterfactual framework (VanderWeele, 2009).

precluding them from evaluating the conditional independence assumption. Similar concerns about using DAGs with the backdoor criterion in situations involving interaction effects have been raised (Attia et al., 2022; Weinberg, 2007). Future research could explore how extensions of the DAG, which incorporate interaction effects, may allow the backdoor criterion to identify bias in treatment effect estimates.

Another avenue for future investigation is the role of centering approaches (see Hamaker and Muthén (2020) for an overview). According to Antonakis et al. (2021), the assumption of uncorrelated random effects and level 1 covariates can be relaxed using Mundlak's contextual model⁸ (Mundlak, 1978), which adds cluster means of each covariate as predictors of the random intercept. This approach, which explicitly models the source of endogeneity as suggested by Bell and Jones (2015), could provide new insights into the treatment effect bias in GM-G and its absence in GM-A, GM-B and GM-C.

Finally, Qian et al. (2020) only considered the independence between the random intercept and random slope, and perfect correlation between the random intercept of the outcome and the covariate. These assumptions may be violated in practice. Exploring cases where the random intercept and random slope are correlated or where the random intercepts differ across covariate and outcome could provide further insight.

5 Conclusion

Dating all the way back to the work of Pepe and Anderson (1994) it has been known that the endogeneity of time-varying covariates can result in biased parameter estimates. This research report is a first step towards understanding the work of Qian et al. (2020), who illustrated that this issue can even affect MLMs with randomized treatment. To recognize and understand completely when and why endogenous covariates may trouble an empirical investigation, further research is needed.

⁸This is referred to as the Correlated Random Effects (CRE) approach by Wooldridge (2002).

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