Supplement to: Bias from cluster-specific time trajectories in cluster-randomized stepped wedge trials

February 26, 2026

1 Theorems

Theorem 1 (Non-identifiability Theorem). *Consider a generalized linear model (GLM) of the form:*

$$g(Y_{ijk}) = \alpha_i + \delta X_{ij} + \beta_j + \alpha\beta_{ij}, \tag{1}$$

where α_i are the cluster effects, β_j are the time effects, X_{ij} is the treatment indicator for cluster i at time j and $\alpha\beta_{ij}$ are the interaction effects. Assume the balanced setting with $i = 1, ..., a$, $j = 1, ..., b$, $k = 1, ..., n$. If data are generated from a SWT design, then the model of Equation 1 is not identifiable.

Proof. The model is not identifiable if two different sets of parameter values result in the same likelihood function.

First, without loss of generality, consider the reparametrized model with no intercept and no main effects, and therefore no constraint equations, which we can write as

$$g(Y_{ijk}) = \alpha\beta_{ij} + \delta X_{ij}. \tag{2}$$

The likelihood function for a generalized linear model is

$$L = \prod_{k=1}^{n} \prod_{i=1}^{a} \prod_{j=1}^{b} f(y_{ijk}; \alpha\beta_{ij}, \delta).$$

Now consider the following two parametrizations of the model:

$$\begin{aligned} P_0 &= (\delta = 0, \alpha\beta_{11} + 2X_{11}, ..., \alpha\beta_{ab} + 2X_{ab})^T \\ P_1 &= (\delta = 2, \alpha\beta_{11}, ..., \alpha\beta_{ab})^T . \end{aligned}$$

Then, noting that $g_{P_0}(Y_{ijk}) = \alpha\beta_{ij} + 2X_{ij}$ and $g_{P_1}(Yijk) = \alpha\beta_{ij} + 2X_{ij}$, clearly P_0 and P_2 result in the same likelihood function. However, the parameters in the two models are not equal. Therefore, the model is not identifiable. QED. □

Theorem 2 (Identifiability Theorem)**.** *Consider a generalized linear model (GLM) of the form in Equation 1, which is written again here:*

$$g(Y_{ijk}) = \alpha_i + \delta X_{ij} + \beta_j + \alpha\beta_{ij},$$

where α_i are the cluster effects, β_j are the time effects, X_{ij} is the treatment indicator for cluster i at time j and $\alpha\beta_{ij}$ are the interaction effects. Assume the balanced model $i = 1, ..., a,\ j = 1, ..., b,\ k = 1, ..., n$. If data are generated from a complete replication design, then the model of Equation 1 is identifiable.

Proof. Add a new factor ζ_h with two levels, $\zeta_h = 0$ if $X_{ij} = 0$ and $\zeta_h = 1$ if $X_{ij} = 1$. Then consider the three-factor model

$$g(Y_{ijhk}) = \alpha_i + \beta_j + \delta \cdot \zeta_h + \alpha\beta_{ij} \qquad (3)$$

Then notice that the design with respect to (α, β, ζ) is a complete three-way layout with replication (assuming $n > 2$). Therefore, all effects in Equation 3 will be identifiable. And these effects correspond to effects in Equation 1. Therefore, the latter model is identifiable. Q.E.D. □

Theorem 3 (SWT mixed main effects bias theorem). *Assume a SWT design with a continuous response, and mean function given by Equation 1 of Theorem 1. Further assume data are fit with the Hussey/Hughes (HH) model* $Y_{ijk} = (\alpha)_i + \delta X_{ij} + \beta_j + \epsilon_{ijk}$ *using generalized least squares (GLS). Then the GLS estimator* $\hat{\delta}_{GLS}$ *will be a linear function of the cell means* $\overline{Y}_{ij\cdot}$ *of form*

$$\hat{\delta} \;=\; \sum_{i=1}^{a}\sum_{j=1}^{b} w_{ij}(\tau^2,\sigma^2)\overline{Y}_{ij\cdot}$$

where $w_{ij}(\tau^2,\sigma^2), i = 1, ..., a; j = 1, ..., b$ *are functions of* τ^2 *and* σ^2*.*

Proof. Note that, under the GLS estimation framework $\tau^2 = Var(\alpha_i)$ and $\sigma^2 = var(\epsilon_{ijk})$ are known. Therefore, the vector of means

$$(\overline{Y}_{11\cdot}, ..., \overline{Y}_{ab\cdot})$$

is sufficient for the fixed effect parameters under the HH model. After reducing the model to eliminate redundancies in the parametrization (Hocking, 1996) the HH model can be written in the form

$$\overline{Y} \;=\; X_{red.}B_{red.} + Zu + \eta$$

where $X_{red.}$ is a design matrix of full rank, $B_{red.}$ is the corresponding vector of non-redundant parameters, Z is an incidence matrix for the cluster random effects, and $u \sim MVN(0, \tau^2 I_a)$ is a vector of random cluster effects, and $\eta \sim MVN(0, (\sigma^2/n)I_{ab})$ is the error term. The u and η are independent. Assume that the dimension has been reduced in such a way that the treatment effect δ is an element of the vector $B_{red.}$. For this model,

$$\begin{aligned} V &= Var(\overline{Y}) \\ &= (\tau^2 ZZ^T + (\sigma^2/n)I_{ab}) \end{aligned}$$

Then the GLS estimator of the vector of fixed parameters $B_{red.}$ is

$$\hat{B}_{GLS} \;=\; (X_{red.}^T V^{-1} X_{red.})^{-1} X_{red.}^T V^{-1}\overline{Y}.$$

Note that each row of $\hat{B}_{GLS}$ is a function of (τ^2, σ^2) for fixed design settings and sample size n. From this, it follows that we can write the estimator of the element of $\hat{B}_{GLS}$ that corresponds to $\hat{\delta}_{GLS}$ in the form:

$$\hat{\delta}_{GLS} = \sum_{i=1}^{a}\sum_{j=1}^{b} w_{ij}\overline{Y}_{ij\cdot}.$$

where, for fixed design settings (Z, I_{ab}), and sample size n, the variance w_{ij} is a function of (τ^2, σ^2) only. Thus, we can write

$$\hat{\delta}_{GLS} = \sum_{i=1}^{a}\sum_{j=1}^{b} w_{ij}(\tau^2, \sigma^2)\overline{Y}_{ij\cdot}.$$

Q.E.D. □

1.1 Example of an unbiased design: The flip-over paired design

Theorem 3 suggests a design that will result in unbiased estimation, but that requires strong *a priori* knowledge of cluster-specific time effects expected over the course of the study. To describe the design concisely, define a canonical SWT table as a two-way table with rows representing clusters and columns representing time periods, with the time period columns ordered from earliest to latest, and the cluster rows ordered so that all rows below a given row, say i, have cross-over times identical to or later than row i. Example canonical SWT tables are given in Figure **??**.

Theorem 3 can be used to show that w_i and w_{a+1-i} are related. The sum of the biases from these two clusters will equal zero if:

$$\begin{aligned} 0 &= CG_i + CG_{a+1-i} \\ &= w_i^T\gamma_i + w_{a+1-i}^T\gamma_{a+1-i} \\ &= w_i^T\gamma_i + [(-1)\cdot R_b \cdot w_i]^T\gamma_{a+1-i} && [Theorem\ 1] \\ &= w_i^T[\gamma_i - R_b\gamma_{a+1-i}] \end{aligned}$$

Therefore, the bias of these two clusters will cancel out if

$$\gamma_i = R_b\gamma_{a+1-i}.$$

So that if $\gamma_i = R_b\gamma_{a+1-i}$ for each i, then

$$Bias(\hat{\delta}) = 0$$

and the Hussey/Hughes estimates will be unbiased.

Definition 1.1. The Flip-over paired SWT design: Assume the setting of Theorem 2. Assume a is even. For each of the a clusters available, match each cluster with another cluster which has a reverse ordering of the time-by-cluster interaction effects. Call these cluster pairs (c_i, c_i^*) for $i = 1, 2, ...(a/2)$. In the canonical SWT table, pick a cluster pair at random and assign those clusters to rows 1 and $a+1-1$ of the table. Repeat the process for $i = 2, ..., a/2$, assigning cluster pairs to rows i and $a + 1 - i$, and randomly selecting one for row i.

While the flip-over paired SWT design follows naturally from Theorem 2, it requires knowledge of cluster-specific time effects that is not likely to be available in practice.