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Second term improvement to generalized linear mixed model asymptotics

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Summary

A recent article by Jiang et al. (2022) on generalized linear mixed model asymptotics derived the rates of convergence for the asymptotic variances of maximum likelihood estimators. If m denotes the number of groups and n is the average within-group sample size then the asymptotic variances have orders m^{-1} and $(mn)^{-1}$, depending on the parameter. We extend this theory to provide explicit forms of the $(mn)^{-1}$ second terms of the asymptotically harder-to-estimate parameters. Improved accuracy of statistical inference and planning are consequences of our theory.

Some key words: Longitudinal data analysis; Maximum likelihood estimation; Sample size calculation.

1. Introduction

Generalized linear mixed models are a vehicle for regression analysis of grouped data with non-Gaussian responses such as counts and categorical labels. Until recently, the precise asymptotic behaviour of the conditional maximum likelihood estimators were not known for these models. Jiang et al. (2022) derived leading term asymptotic variances and showed that they have orders m^{-1} and $(mn)^{-1}$, depending on the parameter, where m is the number of groups and n is the average within-group sample size. The main contribution of this article is to extend the asymptotic variance and covariance approximations to terms in $(mn)^{-1}$ for all parameters. This constitutes second term improvement to generalized linear mixed model asymptotics. The potential statistical pay-offs are improved accuracy of confidence intervals, hypothesis tests, sample size calculations and optimal design.

The essence of generalized linear mixed models is the extension of general linear models via the addition of random effects that allow for the handling of correlations arising from repeated measures. There are numerous types of random effect structures. The most common is the two-level nested structure, corresponding to repeated measures within each of m distinct groups. This version of generalized linear mixed models, with frequentist inference via maximum likelihood and its quasilikelihood extension, is our focus here.

Suppose that a fixed effect parameter in a two-level generalized linear mixed model is accompanied by a random effect. Jiang et al. (2022) showed that the variance of its maximum likelihood estimator, conditional on the predictor data, is asymptotic to $C_1 m^{-1}$ for some deterministic constant C_1

that depends on the true model parameter values. The crux of this article is to extend the asymptotic variance approximation to $C_1 m^{-1} + C_2 (mn)^{-1}$ for an additional deterministic constant C_2. We derive the explicit form of C_2 for two-level nested generalized linear mixed models for both maximum likelihood and maximum quasilikelihood situations. Even though, in general, C_2 does not have a succinct form, it is still usable in that operations such as studentization are straightforward and result in improvements in statistical utility.

For two-level nested mixed models, $(mn)^{-1}$ is the best possible rate of convergence for the asymptotic variance of the estimator of a model parameter. Such a rate is achieved by maximum likelihood estimators of fixed effect parameters unaccompanied by random effects and dispersion parameters; see, e.g., Bhaskaran & Wand (2023). The current article closes the problem of obtaining the precise asymptotic forms of the variances, up to terms in $(mn)^{-1}$, for estimation of all model parameters. To achieve this goal, three-dimensional arrays and their combination with regular matrices play a central role. We introduce a new type of array multiplication that streamlines the required manipulations.

2. Model description and maximum likelihood estimation

Consider the class of two-parameter exponential family of density, or probability mass, functions with generic form

$$p(y; \eta, \phi) = \exp[\{y\eta - b(\eta) + c(y)\}/\phi + d(y, \phi)]h(y), \quad (1)$$

where η is the natural parameter and $\phi > 0$ is the dispersion parameter. Examples include the Gaussian density for which $b(x) = \frac{1}{2}x^2$, $c(x) = -\frac{1}{2}x^2$, $d(x_1, x_2) = -\frac{1}{2}\log(2\pi x_2)$ and $h(x) = I(x \in \mathbb{R})$ and the gamma density function for which $b(x) = -\log(-x)$, $c(x) = \log(x)$, $d(x_1, x_2) = -\log(x_1) - \log(x_2)/x_2 - \log\Gamma(1/x_2)$ and $h(x) = I(x > 0)$. Here $I(\mathcal{P}) = 1$ if condition $\mathcal{P}$ is true and $I(\mathcal{P}) = 0$ if $\mathcal{P}$ is false. The binomial and Poisson probability mass functions are also special cases of (1), but with ϕ fixed at 1. When (1) is used in regression contexts, a common modelling extension for count and proportion responses, usually to account for overdispersion, is to remove the $\phi = 1$ restriction and replace it with $\phi > 0$. In these circumstances

$$\{y\eta - b(\eta) + c(y)\}/\phi + d(y, \phi) \quad (2)$$

is labelled a quasilikelihood function since it is not the logarithm of a probability mass function for $\phi \neq 1$. We use the more general quasilikelihood terminology for the remainder of this article.

Consider, for observations of the random pairs (X_{ij}, Y_{ij}), $1 \leqslant i \leqslant m$, $1 \leqslant j \leqslant n_i$, generalized linear mixed models of the form

$$Y_{ij} \mid X_{ij}, U_i \text{ independent having quasilikelihood function (2) with natural parameter}$$
$$\left(\beta^0 + \begin{bmatrix} U_i \\ 0 \end{bmatrix}\right)^{\mathrm{T}} X_{ij} \text{ such that the } U_i \text{ are independent } N(0, \Sigma^0) \text{ random vectors.} \quad (3)$$

The X_{ij} are $d_{\mathrm{F}} \times 1$ random vectors corresponding to predictors. The U_i are $d_{\mathrm{R}} \times 1$ unobserved random effect vectors, where $d_{\mathrm{R}} \leqslant d_{\mathrm{F}}$. Under this set-up, the first d_{R} entries of the X_{ij} are partnered by a random effect. The remaining entries correspond to predictors that have a fixed effect only. We assume that the X_{ij} and U_i for $1 \leqslant i \leqslant m$ and $1 \leqslant j \leqslant n_i$ are totally independent, with the X_{ij} each having the same distribution as the $d_{\mathrm{F}} \times 1$ random vector X and the U_i each having the same distribution as the $d_{\mathrm{R}} \times 1$ random vector U. Also, $X = [X_{\mathrm{A}}^{\mathrm{T}}, X_{\mathrm{B}}^{\mathrm{T}}]^{\mathrm{T}}$ where X_{A} is $d_{\mathrm{R}} \times 1$.

For any β ($d_{\rm F} \times 1$) and Σ ($d_{\rm R} \times d_{\rm R}$) that is symmetric and positive definite and conditional on the X_{ij} data, the quasilikelihood is

$$\ell(\beta, \Sigma) = \sum_{i=1}^{m} \sum_{j=1}^{n_i} \left[\frac{Y_{ij}\beta^{\rm T} X_{ij} + c(Y_{ij})}{\phi} + d(Y_{ij}, \phi) \right] - \frac{m}{2} \log |2\pi \Sigma|$$
$$+ \sum_{i=1}^{m} \log \int_{\mathbb{R}^{d_{\rm R}}} \exp \left(\frac{1}{\phi} \sum_{j=1}^{n_i} \left[Y_{ij} \begin{bmatrix} u \\ 0 \end{bmatrix}^{\rm T} X_{ij} - b\left\{ \left(\beta + \begin{bmatrix} u \\ 0 \end{bmatrix} \right)^{\rm T} X_{ij} \right\} \right] \right.$$
$$\left. - \frac{1}{2} u^{\rm T} \Sigma^{-1} u \right) {\rm d}u.$$

The maximum quasilikelihood estimator of (β^0, Σ^0) is $(\hat{\beta}, \hat{\Sigma}) = \arg\max_{\beta,\Sigma} \ell(\beta, \Sigma)$. In practice, computation of $(\hat{\beta}, \hat{\Sigma})$ can be challenging due to intractable $d_{\rm R}$-dimensional integrals, although ongoing advances tend to alleviate this problem. We ignore this aspect here and study the theoretical properties of the exact maximum quasilikelihood estimator rather than approximations to them.

Suppose that $d_{\rm F} > d_{\rm R}$ and consider the partition $\beta = [\beta_{\rm A}^{\rm T}, \beta_{\rm B}^{\rm T}]^{\rm T}$ of the fixed effect parameter vector, where $\beta_{\rm A}$ is $d_{\rm R} \times 1$ and $\beta_{\rm B}$ is $(d_{\rm F} - d_{\rm R}) \times 1$. The $d_{\rm F} = d_{\rm R}$ boundary case is such that $\beta_{\rm B}$ is null. Also, let $\mathcal{X} \equiv \{X_{ij} : 1 \leqslant i \leqslant m,\ 1 \leqslant j \leqslant n_i\}$. Theorem 1 of Jiang et al. (2022) implies that, under some mild conditions, the covariance matrices of $\hat{\beta}_{\rm A}$, $\hat{\beta}_{\rm B}$ and vech$(\hat{\Sigma})$ have leading term behaviour given by

$$\text{cov}(\hat{\beta}_{\rm A} \mid \mathcal{X}) = \frac{\Sigma^0\{1 + o_p(1)\}}{m}, \qquad \text{cov}(\hat{\beta}_{\rm B} \mid \mathcal{X}) = \frac{\phi \Lambda_{\beta_{\rm B}}\{1 + o_p(1)\}}{mn}, \tag{4}$$

where $n \equiv (1/m) \sum_{i=1}^{m} n_i$, and

$$\text{cov}(\text{vech}(\hat{\Sigma}) \mid \mathcal{X}) = \frac{2D_{d_{\rm R}}^{+}(\Sigma^0 \otimes \Sigma^0) D_{d_{\rm R}}^{+{\rm T}}\{1 + o_p(1)\}}{m}. \tag{5}$$

Here $\Lambda_{\beta_{\rm B}}$ is a $(d_{\rm F} - d_{\rm R}) \times (d_{\rm F} - d_{\rm R})$ matrix that depends on β and the (X, U) distribution, $D_{d_{\rm R}}$ is the matrix of zeroes and ones such that $D_{d_{\rm R}} \text{vech}(A) = \text{vec}(A)$ for all $d_{\rm R} \times d_{\rm R}$ symmetric matrices A and $D_{d_{\rm R}}^{+} = (D_{d_{\rm R}}^{\rm T} D_{d_{\rm R}})^{-1} D_{d_{\rm R}}^{\rm T}$ is the Moore–Penrose inverse of $D_{d_{\rm R}}$. The theory of Jiang et al. (2022) also indicates a degree of asymptotic orthogonality between $\beta_{\rm A}$ and $\beta_{\rm B}$ in that $E\{(\hat{\beta}_{\rm A} - \beta_{\rm A}^0)(\hat{\beta}_{\rm B} - \beta_{\rm B}^0)^{\rm T} \mid \mathcal{X}\}$ has $O_p\{(mn)^{-1}\}$ entries, which implies that the correlations between the entries of $\hat{\beta}_{\rm A}$ and $\hat{\beta}_{\rm B}$ are asymptotically negligible. For Gaussian responses, Lyu & Welsh (2022) considered an extension of (3) for which some entries of X_{ij} are constrained to be constant across all n_i measurements within the ith group. For such constant-within-group predictors, they showed that the asymptotic variances of the corresponding fixed effect parameters are of order m^{-1} rather than $(mn)^{-1}$. This type of extension is worthy of future consideration.

The leading term approximations of the variability in $\hat{\beta}_{\rm A}$ and vech$(\hat{\Sigma})$, given by (4) and (5), are somewhat crude. Unlike the asymptotic covariance of $\hat{\beta}_{\rm B}$, they do not show the effect of the average within-group sample size n. In the next section we investigate their second term improvements.

3. Two-term asymptotic covariance results

3.1. *Definition of two-term asymptotic covariance*

We define the two-term asymptotic covariance matrix problem to be the determination of the unique deterministic matrices M_β and M_Σ such that, under reasonably mild conditions,

$$\text{cov}(\hat{\beta} \mid \mathcal{X}) = \frac{1}{m}\begin{bmatrix} \Sigma^0 & O \\ O & O \end{bmatrix} + \frac{M_\beta\{1 + o_p(1)\}}{mn}$$

$$\text{and} \quad \text{cov}(\text{vech}(\hat{\Sigma}) \mid \mathcal{X}) = \frac{2D^+_{d_\text{R}}(\Sigma^0 \otimes \Sigma^0)D^{+\text{T}}_{d_\text{R}}}{m} + \frac{M_\Sigma\{1 + o_p(1)\}}{mn}.$$

An example for which a solution to the two-term asymptotic covariance problem can be expressed relatively simply is the $d_\text{F} = 2$, $d_\text{R} = 1$ Poisson quasilikelihood special case of (3), with parameters $\beta = (\beta_0, \beta_1)$ and $\Sigma = \sigma^2$ and predictor variable $[1, X]^\text{T}$ for a scalar random variable X. Define

$$a_1(\beta_0, \beta_1, \sigma^2) \equiv e^{\beta_0 + \sigma^2/2}[E(X^2 e^{\beta_1 X})E(e^{\beta_1 X}) - \{E(Xe^{\beta_1 X})\}^2]$$

$$\text{and} \quad a_2(\beta_1, \sigma^2) \equiv \frac{e^{\sigma^2}E(X^2 e^{\beta_1 X})E(e^{\beta_1 X}) + (1 - e^{\sigma^2})\{E(Xe^{\beta_1 X})\}^2}{E(e^{\beta_1 X})}.$$

Then the two-term covariance matrix of $(\hat{\beta}_0, \hat{\beta}_1)$ is

$$\text{cov}\left(\begin{bmatrix} \hat{\beta}_0 \\ \hat{\beta}_1 \end{bmatrix} \,\middle|\, \mathcal{X}\right) = \frac{1}{m}\begin{bmatrix} (\sigma^2)^0 & 0 \\ 0 & 0 \end{bmatrix} + \frac{\phi\{1 + o_p(1)\}}{a_1\{\beta_0^0, \beta_1^0, (\sigma^2)^0\}mn}\begin{bmatrix} a_2\{\beta_1^0, (\sigma^2)^0\} & -E(Xe^{\beta_1^0 X}) \\ -E(Xe^{\beta_1^0 X}) & E(e^{\beta_1^0 X}) \end{bmatrix}.$$

Studentization of the two-term asymptotic covariance matrix for obtaining confidence intervals and Wald hypothesis tests is straightforward. For example, $E(X^2 e^{\beta_1^0 X})$ can be replaced by the estimator $(mn)^{-1}\sum_{i=1}^m \sum_{j=1}^{n_i} X_{ij}^2 e^{\hat{\beta}_1 X_{ij}}$.

The remainder of this section is concerned with the theoretical problem of obtaining the forms of M_β and M_Σ for model (3) in general. The score asymptotic approximation approach used in Jiang et al. (2022) requires higher numbers of terms to obtain valid two-term covariance matrix approximations. Some of these terms can only be expressed using three-dimensional arrays rather than with matrices. A succinct statement of M_β and M_Σ is only possible with well-designed nested function notation. A novel notation for multiplicative combining of three-dimensional arrays with compatible matrices is also beneficial. The next subsection focusses on these notational aspects.

3.2. *Notation for the main result*

Let $\mathcal{A}$ be a $d_1 \times d_2 \times d_3$ array and M be a $d_1 \times d_2$ matrix. Then we let $\mathcal{A} \bigstar M$ denote the $d_3 \times 1$ vector with tth entry given by $\sum_{r=1}^{d_1}\sum_{s=1}^{d_2}(\mathcal{A})_{rst}(M)_{rs}$. Next, for $U \sim N(0, \Sigma^0)$, define

$$\Omega_\text{AA}(U) \equiv E[b''\{(\beta_\text{A}^0 + U)^\text{T}X_\text{A} + (\beta_\text{B}^0)^\text{T}X_\text{B}\}X_\text{A}X_\text{A}^\text{T} \mid U],$$
$$\Omega_\text{AB}(U) \equiv E[b''\{(\beta_\text{A}^0 + U)^\text{T}X_\text{A} + (\beta_\text{B}^0)^\text{T}X_\text{B}\}X_\text{A}X_\text{B}^\text{T} \mid U],$$
$$\Omega_\text{BB}(U) \equiv E[b''\{(\beta_\text{A}^0 + U)^\text{T}X_\text{A} + (\beta_\text{B}^0)^\text{T}X_\text{B}\}X_\text{B}X_\text{B}^\text{T} \mid U].$$

Also, let $\Omega'_\text{AAA}(U)$ be the $d_\text{R} \times d_\text{R} \times d_\text{R}$ array with (r, s, t) entry equal to

$$E[b'''\{(\beta_\text{A}^0 + U)^\text{T}X_\text{A} + (\beta_\text{B}^0)^\text{T}X_\text{B}\}(X_\text{A})_r(X_\text{A})_s(X_\text{A})_t \mid U]$$

and $\Omega'_\text{AAB}(U)$ be the $d_\text{R} \times d_\text{R} \times (d_\text{F} - d_\text{R})$ array with (r, s, t) entry equal to

$$E[b'''\{(\beta_\text{A}^0 + U)^\text{T}X_\text{A} + (\beta_\text{B}^0)^\text{T}X_\text{B}\}(X_\text{A})_r(X_\text{A})_s(X_\text{B})_t \mid U].$$

Define the random vectors

$$\begin{aligned}
\psi_1(U) &\equiv \mathrm{vech}(\Sigma^0 - UU^{\mathrm{T}}),\\
\psi_2(U) &\equiv \Omega'_{\mathrm{AAA}}(U) \bigstar \Omega_{\mathrm{AA}}(U)^{-1},\\
\psi_3(U) &\equiv \Omega'_{\mathrm{AAB}}(U) \bigstar \Omega_{\mathrm{AA}}(U)^{-1},\\
\psi_4(U) &\equiv D^{+}_{d_{\mathrm{R}}} \mathrm{vec}\{\Omega_{\mathrm{AA}}(U)^{-1}(\Sigma^0)^{-1}[\Sigma^0 - UU^{\mathrm{T}} - \Sigma^0\psi_2(U)U^{\mathrm{T}}]\}.
\end{aligned}$$

Then define the random matrices

$$\begin{aligned}
\Psi_5(U) &\equiv \Omega_{\mathrm{AA}}(U)^{-1}\Omega_{\mathrm{AB}}(U),\\
\Psi_6(U) &\equiv \Omega_{\mathrm{BB}}(U) - \Psi_5(U)^{\mathrm{T}}\Omega_{\mathrm{AB}}(U),\\
\Psi_7(U) &\equiv UU^{\mathrm{T}}(\Sigma^0)^{-1}\Omega_{\mathrm{AA}}(U)^{-1},\\
\Psi_8(U) &\equiv D^{+}_{d_{\mathrm{R}}}[(UU^{\mathrm{T}}) \otimes \{\Omega_{\mathrm{AA}}(U)^{-1}\}]D^{+\mathrm{T}}_{d_{\mathrm{R}}},\\
\Psi_9(U) &\equiv \psi_1(U)\psi_4(U)^{\mathrm{T}} + \psi_4(U)\psi_1(U)^{\mathrm{T}}.
\end{aligned}$$

Lastly, define the expectation matrices

$$\begin{aligned}
\Lambda_{\mathrm{AA}} &\equiv E\{\Psi_7(U) + \Psi_7(U)^{\mathrm{T}} - \Omega_{\mathrm{AA}}(U)^{-1} + \Omega_{\mathrm{AA}}(U)^{-1}\psi_2(U)U^{\mathrm{T}} + U\psi_2(U)^{\mathrm{T}}\Omega_{\mathrm{AA}}(U)^{-1}\},\\
\Lambda_{\mathrm{AB}} &\equiv E\{UU^{\mathrm{T}}(\Sigma^0)^{-1}\Psi_5(U) + U\psi_2(U)^{\mathrm{T}}\Psi_5(U) - U\psi_3(U)^{\mathrm{T}}\},\\
\Delta &\equiv E([\Psi_5(U)^{\mathrm{T}}\{(\Sigma^0)^{-1}U + \psi_2(U)\} - \psi_3(U)]\psi_1(U)^{\mathrm{T}}).
\end{aligned}$$

3.3. *Assumptions for the main result*

The main result depends on the following sample size asymptotic assumptions: the number of groups m diverges to ∞; the within-group sample sizes n_i diverge to ∞ in such a way that $n_i/n \to C_i$ for constants $0 < C_i < \infty$, $1 \leqslant i \leqslant m$; the ratio n/m converges to zero. The last of these conditions is in keeping with the number of groups being large compared with the within-group sample sizes, as often arises in practice. For our asymptotics, it ensures that, for the harder-to-estimate parameters, the asymptotic variances of the maximum likelihood estimators have leading terms of the form $K_1m^{-1} + K_2(mn)^{-1}$. In addition, it ensures that the Fisher information is sufficiently dominant for obtaining asymptotic variances.

We also assume that the (X, U) joint distribution is such that all required convergence in probability limits that appear in the deterministic order $(mn)^{-1}$ terms are justified. The determination of sufficient conditions on the (X, U) distribution that guarantee the validity of the main result is challenging, involving the determination of at least 18 additional moment-type conditions for results similar to Lemma A1 of Jiang et al. (2022), and beyond the scope of this article.

3.4. *Statement of the main result*

Using the notation presented in § 3.2 and under the assumptions described in § 3.3, and assuming that $d_{\mathrm{F}} > d_{\mathrm{R}}$, we have

$$\mathrm{cov}(\hat{\beta} \mid \mathcal{X}) = \frac{1}{m}\begin{bmatrix} \Sigma^0 & O \\ O & O \end{bmatrix} + \frac{\phi}{mn}\begin{bmatrix} \Lambda_{\mathrm{AA}}^{-1} & \Lambda_{\mathrm{AA}}^{-1}\Lambda_{\mathrm{AB}} \\ \Lambda_{\mathrm{AB}}^{\mathrm{T}}\Lambda_{\mathrm{AA}}^{-1} & \Lambda_{\mathrm{AB}}^{\mathrm{T}}\Lambda_{\mathrm{AA}}^{-1}\Lambda_{\mathrm{AB}} + E\{\Psi_6(U)\} \end{bmatrix}^{-1}\{1 + o_p(1)\}, \tag{6}$$

$$\mathrm{cov}(\mathrm{vech}(\hat{\Sigma}) \mid \mathcal{X}) = \frac{2D_{d_R}^{+}(\Sigma^0 \otimes \Sigma^0)D_{d_R}^{+\mathrm{T}}}{m} + \frac{\phi}{mn}(2E\{\Psi_9(U) - 2\Psi_8(U)\} + \Delta^{\mathrm{T}}[E\{\Psi_6(U)\}]^{-1}\Delta) \times \{1 + o_p(1)\}.$$

For the $d_F = d_R$ boundary case, the first term of $\mathrm{cov}(\hat{\beta} \mid \mathcal{X})$ is simply Σ^0/m. A full derivation of (6) can be found in the Supplementary Material.

In the Gaussian response special case we have $b''(x) = 1$ and $b'''(x) = 0$ and the main results reduce to the following succinct forms:

$$\mathrm{cov}(\hat{\beta} \mid \mathcal{X}) = \frac{1}{m}\begin{bmatrix} \Sigma^0 & O \\ O & O \end{bmatrix} + \frac{\phi\{E(XX^{\mathrm{T}})\}^{-1}\{1 + o_p(1)\}}{mn},$$

$$\mathrm{cov}(\mathrm{vech}(\hat{\Sigma}) \mid \mathcal{X}) = \frac{2D_{d_R}^{+}(\Sigma^0 \otimes \Sigma^0)D_{d_R}^{+\mathrm{T}}}{m} + \frac{4\phi D_{d_R}^{+}[\Sigma^0 \otimes \{E(X_A X_A^{\mathrm{T}})\}^{-1}]D_{d_R}^{+\mathrm{T}}\{1 + o_p(1)\}}{mn}.$$

We are not aware of any previous appearances of this result in the linear mixed model literature.

4. UTILITY OF THE SECOND TERM IMPROVEMENTS

The second term improvements of (6) have ready and straightforward applications to confidence intervals, Wald hypothesis tests and sample size calculations. Optimal design is another possible utility, but would require second term improvements of the type of theory given in § 5 of Jiang et al. (2022). In order to understand potential practical impacts of second term improvements to generalized linear mixed model asymptotics, we present an illustration on sample size calculations for a Poisson-response mixed model. In the Supplementary Material we report results from simulation exercises involving confidence intervals for the parameters of a logistic regression model. These assess the improvements afforded by our two-term asymptotic covariance expressions against the theory of Jiang et al. (2022) and also serve as a comparison to existing software.

Consider the following $d_F = d_R = 2$ Poisson quasilikelihood special case of (3):

$$Y_{ij} \mid X_{ij}, U_{0i}, U_{1i},\ 1 \leqslant i \leqslant m,\ 1 \leqslant j \leqslant n, \text{ independently distributed as}$$
$$\mathrm{Po}[\exp\{\beta_0^0 + U_{0i} + (\beta_1^0 + U_{1i})X_{ij}\}], \text{ where the } \begin{bmatrix} U_{0i} \\ U_{1i} \end{bmatrix}^{\mathrm{T}} \text{ are independent } N(0, \Sigma^0) \tag{7}$$
$$\text{random vectors and the } X_{ij} \text{ are independently drawn from } X \sim \mathrm{Ber}(p).$$

Suppose that the model above is expected to be adopted in a study involving m subjects. Now suppose that we would like to determine the required number of subjects m to detect a possibly positive effect of the binary predictor X at a global level by testing

$$H_0: \beta_1^0 = 0 \quad \text{versus} \quad H_1: \beta_1^0 > 0 \tag{8}$$

with a significance level α and at least P power. If $\beta_1^a > 0$ is a particular alternative value of β_1^0 and $\hat{\beta}_1$ an estimate of β_1^0, then standard arguments lead to the sample size being the solution to

$$\frac{\beta_1^a}{\{\mathrm{var}(\hat{\beta}_1)\}^{1/2}} = \Phi^{-1}(\alpha) + \Phi^{-1}(1 - P), \tag{9}$$

Table 1. *The results from the illustrative sample size calculation and corresponding checks of empirical power (as a percentage) for the simulation study described in the text with* $n = 20$ *and for various combinations of* β_0^0, β_1^0 *and* Σ^0 *values. The values of the minimum number of subjects m correspond to an advertised power of 90% and are calculated using both* $\text{asy.var}(\hat{\beta}_1) = \Sigma_{11}^0/m$ *('1-term var.') and* $\text{asy.var}(\hat{\beta}_1) = \Sigma_{11}^0/m + \phi c(\beta^0, \Sigma^0)/(mn)$ *('2-term var.'). The 95% confidence intervals of power are also provided.*

	$\beta_1^0 = 0.3$, $\Sigma^0 = \text{vech}^{-1}([0.5, 0.1, 0.25]^{\mathrm{T}})$					
	$\beta_0^0 = -1.5$		$\beta_0^0 = -0.5$		$\beta_0^0 = 0.5$	
	1-term var.	2-term var.	1-term var.	2-term var.	1-term var.	2-term var.
Minimum m	24	130	24	63	24	39
Power estimate	37.0	88.0	58.5	90.1	75.8	89.8
Power conf. int.	(34.0, 40.0)	(86.0, 90.0)	(55.4, 61.6)	(88.2, 92.0)	(73.1, 78.5)	(87.9, 91.7)
	$\beta_0^0 = -1.5$, $\Sigma^0 = \text{vech}^{-1}([0.5, 0.1, 0.25]^{\mathrm{T}})$					
	$\beta_1^0 = 0.2$		$\beta_1^0 = 0.4$		$\beta_1^0 = 0.5$	
	1-term var.	2-term var.	1-term var.	2-term var.	1-term var.	2-term var.
Minimum m	54	304	14	71	9	44
Power estimate	32.8	88.5	40.5	89.7	41.6	89.8
Power conf. int.	(29.9, 35.7)	(86.5, 90.5)	(37.5, 43.5)	(87.8, 91.6)	(38.5, 44.7)	(87.9, 91.7)
	$\beta_0^0 = -1.5, \beta_1^0 = 0.3$					
	$\Sigma^0 = \text{vech}^{-1}([0.5, -0.1, 0.25]^{\mathrm{T}})$		$\Sigma^0 = \text{vech}^{-1}([1, 0.2, 0.5]^{\mathrm{T}})$		$\Sigma^0 = \text{vech}^{-1}([1, -0.2, 0.5]^{\mathrm{T}})$	
	1-term var.	2-term var.	1-term var.	2-term var.	1-term var.	2-term var.
Minimum m	24	121	48	200	48	173
Power estimate	33.5	88.4	46.5	92.2	47.1	91.2
Power conf. int.	(30.6, 36.4)	(86.4, 90.4)	(43.4, 49.6)	(90.5, 93.9)	(44.0, 50.2)	(89.4, 93.0)

where Φ^{-1} is the $N(0, 1)$ quantile function. Application of the main result (6) to model (7) and the derivations provided in the Supplementary Material lead to the two-term asymptotic variance of $\hat{\beta}_1$ being

$$\text{asy.var}(\hat{\beta}_1) = \frac{\Sigma_{11}^0}{m} + \frac{\phi c(\beta^0, \Sigma^0)}{mn}$$

with

$$c(\beta^0, \Sigma^0) \equiv \frac{1}{p} \exp\left\{ -\beta_0^0 - \beta_1^0 + \frac{1}{2}(\Sigma_{00}^0 + 2\Sigma_{01}^0 + \Sigma_{11}^0) \right\} + \frac{1}{1-p} \exp\left\{ -\beta_0^0 + \frac{\Sigma_{00}^0}{2} \right\},$$

where $\beta^0 = [\beta_0^0, \beta_1^0]$ and $\Sigma^0 = \text{vech}^{-1}([\Sigma_{00}^0, \Sigma_{01}^0, \Sigma_{11}^0]^{\mathrm{T}})$. This can be used to replace $\text{var}(\hat{\beta}_1)$ in (9), providing the following lower bound for the number of subjects required to achieve at least P power in test (8) at the α significance level:

$$m = \left\lceil \frac{1}{(\beta_1^a)^2} \left\{ \Sigma_{11}^0 + \frac{\phi c(\beta^0, \Sigma^0)}{n} \right\} \{\Phi^{-1}(\alpha) + \Phi^{-1}(1 - P)\}^2 \right\rceil. \quad (10)$$

Here, for any $x \in \mathbb{R}$, $\lceil x \rceil$ denotes the smallest integer greater than or equal to x.

We conducted a simulation exercise aimed at understanding whether the number of subjects m chosen according to the two-term asymptotic variance of $\hat{\beta}_1$ leads to the advertised power for hypothesis tests. The simulation study involved producing 1000 replicates corresponding to (7) with $p = 0.5$ and average group size $n = 20$ for various combinations of β_0^0, β_1^0 and Σ^0 according to Table 1. We then fitted model (7) to each simulated dataset via the `glmmTMB` package in `R` (Brooks et al., 2023; R Development Core Team, 2024), and assumed that $\phi = 1$, $\alpha = 0.05$ and $P = 0.9$. Table 1 shows the empirical estimates of P and corresponding 95% confidence intervals resulting from both the fully asymptotic theory of Jiang et al. (2022) and our two-term asymptotic results. For this illustration, we see that the sample size formula (10) performs very well with regards to the actual power delivered, with the true power value P falling inside of all the confidence intervals. When the other parameters are held fixed, the required number of subjects decreases for increasing values of $\exp(\beta_0^0)$, larger β_1^0 values or smaller within-group variation. On the other hand, the minimum number of subject values obtained by substituting the one-term asymptotic variance of $\hat{\beta}_1$ into (9) is substantially different from those computed using (10) and produced empirical estimates of power that are well below the advertised level P for all the β_0^0, β_1^0 and Σ^0 combinations.

Simulation results such as those summarized by Table 1 provide an appreciation for the practical utility of our second term improvement to generalized linear mixed model asymptotics.

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Supplementary material

The Supplementary Material contains derivational details and additional simulation results.

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