Supporting Information for

"Power considerations for generalized estimating equations analyses of four-level cluster randomized trials" by Wang et al.

Web Appendix A

Differences between $\mathbf{R}_i$ and two other correlation structures

An example of the extended nested exchangeable correlation structure for four-level clustered designs, with $M = 2$, $K = 2$, and $L = 2$ for each cluster, is

$$\text{corr}(\mathbf{Y}_i) = \left(\begin{array}{cc|cc|cc|cc}
1 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_2 & \alpha_2 & \alpha_2 \\
\alpha_0 & 1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_2 & \alpha_2 & \alpha_2 \\
\hline
\alpha_1 & \alpha_1 & 1 & \alpha_0 & \alpha_2 & \alpha_2 & \alpha_2 & \alpha_2 \\
\alpha_1 & \alpha_1 & \alpha_0 & 1 & \alpha_2 & \alpha_2 & \alpha_2 & \alpha_2 \\
\hline
\alpha_2 & \alpha_2 & \alpha_2 & \alpha_2 & 1 & \alpha_0 & \alpha_1 & \alpha_1 \\
\alpha_2 & \alpha_2 & \alpha_2 & \alpha_2 & \alpha_0 & 1 & \alpha_1 & \alpha_1 \\
\hline
\alpha_2 & \alpha_2 & \alpha_2 & \alpha_2 & \alpha_1 & \alpha_1 & 1 & \alpha_0 \\
\alpha_2 & \alpha_2 & \alpha_2 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_0 & 1
\end{array}\right).$$

According to Teerenstra et al. (2010), for a three-level CRT, denote Y_{ijk} as the outcome of evaluation $k = 1, \ldots, K$ from subject $j = 1, \ldots, M$ in cluster $i = 1, \ldots, N$, denote $\mathbf{X}_{ijk}$ as a list of covariates, and characterize the degree of similarities among the within-cluster outcomes through the nested exchangeable correlation structure with the following assumptions: (i) the correlation between different evaluations of the same subject is $\text{corr}(Y_{ijk}, Y_{ijk'}|\mathbf{X}_{ijk}, \mathbf{X}_{ijk'}) = \alpha_0$ for $k \neq k'$; (ii) the correlation between evaluations of different subjects but within the same cluster is $\text{corr}(Y_{ijk}, Y_{ij'k'}|\mathbf{X}_{ijk}, \mathbf{X}_{ij'k'}) = \alpha_1$ for $j \neq j'$. Define $\mathbf{Y}_i^{\text{3-level}} = (Y_{i11}, Y_{i12}, \ldots, Y_{iMK})$. An example of the nested exchangeable correlation structure for three-level clustered designs, with $M = 2$ and

$K = 2$ for each cluster, is

$$\text{corr}(\mathbf{Y}_i^{\text{3-level}}) = \left(\begin{array}{cc|cc} 1 & \alpha_0 & \alpha_1 & \alpha_1 \\ \alpha_0 & 1 & \alpha_1 & \alpha_1 \\ \hline \alpha_1 & \alpha_1 & 1 & \alpha_0 \\ \alpha_1 & \alpha_1 & \alpha_0 & 1 \end{array}\right).$$

According to Li et al. (2018), for a cohort stepped wedge design, denote Y_{ijk} as the outcome of individual $k = 1, \ldots, K$ from cluster $i = 1, \ldots, N$ during period $j = 1, \ldots, M$, denote $\mathbf{X}_{ijk}$ as a list of covariates, and characterize the degree of similarities among the within-cluster outcomes through the block exchangeable correlation structure with the following assumptions: (i) the correlation between different individuals within the same cluster during the same period is $\text{corr}(Y_{ijk}, Y_{ijk'}|\mathbf{X}_{ijk}, \mathbf{X}_{ijk'}) = \alpha_0$ for $k \neq k'$; (ii) the correlation between different individuals within the same cluster but across periods is $\text{corr}(Y_{ijk}, Y_{ij'k'}|\mathbf{X}_{ijk}, \mathbf{X}_{ij'k'}) = \alpha_1$ for $j \neq j'$ and $k \neq k'$; (iii) the correlation of the same individual across periods is $\text{corr}(Y_{ijk}, Y_{ij'k}|\mathbf{X}_{ijk}, \mathbf{X}_{ij'k}) = \alpha_2$ for $j \neq j'$. Define $\mathbf{Y}_i^{\text{csw}} = (Y_{i11}, Y_{i12}, \ldots, Y_{iMK})$. An example of the block exchangeable correlation structure for cohort stepped wedge designs, with $M = 2$ and $K = 2$ for each cluster, is

$$\text{corr}(\mathbf{Y}_i^{\text{csw}}) = \left(\begin{array}{cc|cc} 1 & \alpha_0 & \alpha_2 & \alpha_1 \\ \alpha_0 & 1 & \alpha_1 & \alpha_2 \\ \hline \alpha_2 & \alpha_1 & 1 & \alpha_0 \\ \alpha_1 & \alpha_2 & \alpha_0 & 1 \end{array}\right).$$

The block exchangeable correlation structure is also used for cohort parallel arms CRTs (Preisser et al., 2003) and cluster randomized crossover trials (Li et al., 2019).

Web Appendix B

Proof of Theorem 2.1

Proof. Eigenvalues help check the positive definiteness of the matrix. To do so, we first establish the following lemma, the proof of which is directly by Theorem 8.9.1 in Graybill (1983).

Lemma 1. *For a matrix* $S = a\mathbf{I}_{KL} + b\mathbf{I}_K \otimes \mathbf{J}_L + c\mathbf{J}_{KL}$*, the determinant is*

$$\begin{aligned} det(S) &= det[\mathbf{I}_K \otimes \{a\mathbf{I}_L + (b+c)\mathbf{J}_L - c\mathbf{J}_L\} + \mathbf{J}_K \otimes (c\mathbf{J}_L)] \\ &= \{det(a\mathbf{I}_L + b\mathbf{J}_L)\}^{K-1} \times det\{a\mathbf{I}_L + (b+Kc)\mathbf{J}_L\} \\ &= \{a^{L-1}(a+Lb)\}^{K-1} \times a^{L-1}\{a + L(b+Kc)\}. \end{aligned}$$

For the extended nested exchangeable correlation structure, to determine the eigenvalues, we need to solve

$$\begin{aligned} 0 &= \det(\mathbf{R}_i - \lambda\mathbf{I}_{MKL}) \\ &= \det\{(1-\alpha_0-\lambda)\mathbf{I}_{MKL} + (\alpha_0-\alpha_1)\mathbf{I}_{MK} \otimes \mathbf{J}_L + (\alpha_1-\alpha_2)\mathbf{I}_M \otimes \mathbf{J}_{KL} + \alpha_2\mathbf{J}_{MKL}\} \\ &= |A-B|^{M-1}|A+(M-1)B|, \end{aligned}$$

where

$$A - B = (1-\alpha_0-\lambda)\mathbf{I}_{KL} + (\alpha_0-\alpha_1)\mathbf{I}_K \otimes \mathbf{J}_L + (\alpha_1-\alpha_2)\mathbf{J}_{KL},$$

$$A + (M-1)B = (1-\alpha_0-\lambda)\mathbf{I}_{KL} + (\alpha_0-\alpha_1)\mathbf{I}_K \otimes \mathbf{J}_L + (\alpha_1+(M-1)\alpha_2)\mathbf{J}_{KL},$$

both of whose determinant can be calculated using the above Lemma 1 we established. Then

$$\begin{aligned} |A-B| =& [(1-\alpha_0-\lambda)^{L-1}\{(1-\alpha_0-\lambda) + L(\alpha_0-\alpha_1)\}]^{K-1} \\ & \times (1-\alpha_0-\lambda)^{L-1}[(1-\alpha_0-\lambda) + L\{(\alpha_0-\alpha_1) + K(\alpha_1-\alpha_2)\}], \end{aligned}$$

$$|A+(M-1)B| = [(1-\alpha_0-\lambda)^{L-1}\{(1-\alpha_0-\lambda)+L(\alpha_0-\alpha_1)\}]^{K-1}$$
$$\times (1-\alpha_0-\lambda)^{L-1}[(1-\alpha_0-\lambda)+L\{(\alpha_0-\alpha_1)+K(\alpha_1+(M-1)\alpha_2)\}].$$

These two expressions allow us to establish the eigenvalues in closed forms. The eigenvalues are

$$\lambda_1 = 1-\alpha_0 \quad \text{with multiplicity } MK(L-1),$$
$$\lambda_2 = 1+(L-1)\alpha_0 - L\alpha_1 \quad \text{with multiplicity } M(K-1),$$
$$\lambda_3 = 1+(L-1)\alpha_0 + L(K-1)\alpha_1 - LK\alpha_2 \quad \text{with multiplicity } M-1,$$
$$\lambda_4 = 1+(L-1)\alpha_0 + L(K-1)\alpha_1 + LK(M-1)\alpha_2 \quad \text{with multiplicity } 1.$$

The sum of multiplicity is exactly MKL, and the result is established. $\square$

Web Appendix C

Derivation of BC1

Define the cluster leverage (Lu et al., 2007) as $\mathbf{H}_i = \mathbf{D}_i(N\boldsymbol{\Sigma}_1)^{-1}\mathbf{D}_i'\mathbf{V}_i^{-1}$. Setting $\mathbf{C}_i = \mathbf{I}_p$ and $\mathbf{B}_i = (\mathbf{I}_{MKL}-\mathbf{H}_i)^{-1/2}$ provides the finite-sample bias correction of Kauermann and Carroll (2001), or BC1. Scott et al. (2017) proved $\mathbf{D}_i'\mathbf{V}_i^{-1}(\mathbf{I}_{MKL}-\mathbf{H}_i)^{-1/2} = (\mathbf{I}_p-\mathbf{Q}_i)^{-1/2}\mathbf{D}_i'\mathbf{V}_i^{-1}$. So equivalently, setting $\mathbf{C}_i = (\mathbf{I}_p-\mathbf{Q}_i)^{-1/2}$ and $\mathbf{B}_i = \mathbf{I}_{MKL}$ provides BC1.

Derivation of BC2

Setting $\mathbf{C}_i = \mathbf{I}_p$ and $\mathbf{B}_i = (\mathbf{I}_{MKL}-\mathbf{H}_i)^{-1}$ provides the finite-sample bias correction of Mancl and DeRouen (2001), or BC2. Scott et al. (2017) proved $\mathbf{D}_i'\mathbf{V}_i^{-1}(\mathbf{I}_{MKL}-\mathbf{H}_i)^{-1} = (\mathbf{I}_p-\mathbf{Q}_i)^{-1}\mathbf{D}_i'\mathbf{V}_i^{-1}$. So equivalently, setting $\mathbf{C}_i = (\mathbf{I}_p-\mathbf{Q}_i)^{-1}$ and $\mathbf{B}_i = \mathbf{I}_{MKL}$ provides BC2.

Web Appendix D

Derivation of $\mathbf{R}_i^{-1}$

For notational convenience, we write

$$\mathbf{R}_i = a\mathbf{I}_{MK} \otimes \mathbf{I}_L + b\mathbf{I}_{MK} \otimes \mathbf{J}_L + c\mathbf{I}_M \otimes \mathbf{J}_{KL} + d\mathbf{J}_M \otimes \mathbf{J}_{KL},$$

with a, b, c, d as functions of $\boldsymbol{\alpha} = (\alpha_0, \alpha_1, \alpha_2)$ given above. Assume $\mathbf{R}_i$ is invertible, so the coefficients of basis matrices will only take values such that $\min\{\lambda_1, \lambda_2, \lambda_3, \lambda_3\} > 0$. To derive an expression for the inverse, first show that $\mathbf{R}_i^{-1}$ can be expanded by the same set of basis matrices used in constructing $\mathbf{R}_i$. By matrix inverse result (Henderson and Searle, 1981),

$$(\mathbf{A} + \mathbf{B})^{-1} = \mathbf{A}^{-1} - \mathbf{A}^{-1}\mathbf{B}(\mathbf{I} + \mathbf{A}^{-1}\mathbf{B})^{-1}\mathbf{A}^{-1}; \tag{A1}$$

by Theorem 8.3.4 and 8.4.4 in Graybill (1983),

$$(x\mathbf{I}_u + y\mathbf{J}_u)^{-1} = \frac{1}{x}\mathbf{I}_u - \frac{y}{x(x + uy)}\mathbf{J}_u. \tag{A2}$$

Observe that $\mathbf{R}_i = \mathbf{I}_{MK} \otimes \mathbf{S}_L + \mathbf{T}_M \otimes \mathbf{J}_{KL}$, where both $\mathbf{S}_L = a\mathbf{I}_L + b\mathbf{J}_L$ and $\mathbf{T}_M = c\mathbf{I}_M + d\mathbf{J}_M$ are of the exchangeable form. It follows from (A2) that $\mathbf{S}_L^{-1} = e\mathbf{I}_L + f\mathbf{J}_L$ is also of the exchangeable form for some e, f (and same holds for $\mathbf{T}_M^{-1}$). By (A1), the inverse of $\mathbf{R}_i$ is

$$\mathbf{R}_i^{-1} = (\mathbf{I}_{MK} \otimes \mathbf{S}_L^{-1}) - \underbrace{(\mathbf{I}_{MK} \otimes \mathbf{S}_L^{-1})(\mathbf{T}_M \otimes \mathbf{J}_{KL})\{\mathbf{I}_{MKL} + (\mathbf{I}_{MK} \otimes \mathbf{S}_L^{-1})(\mathbf{T}_M \otimes \mathbf{J}_{KL})\}^{-1}(\mathbf{I}_{MK} \otimes \mathbf{S}_L^{-1})}_{\mathbf{G}_{MKL}}.$$

Further $\mathbf{I}_{MK} \otimes \mathbf{S}_L^{-1} = \mathbf{I}_{MK} \otimes (e\mathbf{I}_L + f\mathbf{J}_L) = e\mathbf{I}_{MK} \otimes \mathbf{I}_L + f\mathbf{I}_{MK} \otimes \mathbf{J}_L$, and $\mathbf{T}_M \otimes \mathbf{J}_{KL} = (c\mathbf{I}_M + d\mathbf{J}_M) \otimes \mathbf{J}_{KL} = c\mathbf{I}_M \otimes \mathbf{J}_{KL} + d\mathbf{J}_M \otimes \mathbf{J}_{KL}$. Thus we have

$$\mathbf{I}_{MKL} + (\mathbf{I}_{MK} \otimes \mathbf{S}_L^{-1})(\mathbf{T}_M \otimes \mathbf{J}_{KL}) = \mathbf{I}_{MKL} + (e\mathbf{I}_{MK} \otimes \mathbf{I}_L + f\mathbf{I}_{MK} \otimes \mathbf{J}_L)(c\mathbf{I}_M \otimes \mathbf{J}_{KL} + d\mathbf{J}_M \otimes \mathbf{J}_{KL})$$

$$= \mathbf{I}_{MKL} + (ec + fcL)\mathbf{I}_M \otimes \mathbf{J}_{KL} + (ed + fdL)\mathbf{J}_M \otimes \mathbf{J}_{KL}$$

$$= \mathbf{I}_M \otimes \{\mathbf{I}_{KL} + (ec + fcL)\mathbf{J}_{KL}\} + (ed + fdL)\mathbf{J}_{MKL},$$

whose inverse is $\mathbf{I}_{MKL} + p\mathbf{I}_M \otimes \mathbf{J}_{KL} + q\mathbf{J}_M \otimes \mathbf{J}_{KL}$ for some p, q by using (A1) and (A2) (i.e. treating $\mathbf{I}_T \otimes \{\mathbf{I}_{KL} + (ec + fcL)\mathbf{J}_{KL}\}$ as $\mathbf{A}$ and $(ed + fdL)\mathbf{J}_{KL}$ as $\mathbf{B}$; then $\mathbf{A}^{-1}$ is derived from (A2) and plugged into the right hand side of (A1)). Therefore, $\mathbf{G}_{MKL}$ must be of the form $r\mathbf{I}_M \otimes \mathbf{J}_{KL} + s\mathbf{J}_M \otimes \mathbf{J}_{KL}$, from which we conclude

$$\mathbf{R}_i^{-1} = \tilde{a}\mathbf{I}_{MK} \otimes \mathbf{I}_L + \tilde{b}\mathbf{I}_{MK} \otimes \mathbf{J}_L + \tilde{c}\mathbf{I}_M \otimes \mathbf{J}_{KL} + \tilde{d}\mathbf{J}_M \otimes \mathbf{J}_{KL},$$

for some coefficients $\tilde{a}, \tilde{b}, \tilde{c}, \tilde{d}$. Then solve the full-rank system of equations from $\mathbf{R}_i^{-1}\mathbf{R}_i = \mathbf{I}_{MKL}$ to obtain the coefficients, we have $\tilde{a} = 1/a$, $\tilde{b} = -b/\{a(a + Lb)\}$, $\tilde{c} = -c/\{(a + Lb)(a + Lb + KLc)\}$ and $\tilde{d} = -d/\{(a + Lb + KLc)(a + Lb + KLc + MKLd)\}$. Substituting a, b, c, d with functions of the correlation parameters $\boldsymbol{\alpha}$, we obtain a closed-form matrix inverse

$$\mathbf{R}_i^{-1} = \frac{1}{\lambda_1}\mathbf{I}_{MKL} - \frac{\alpha_0 - \alpha_1}{\lambda_1\lambda_2}\mathbf{I}_{MK} \otimes \mathbf{J}_L - \frac{\alpha_1 - \alpha_2}{\lambda_2\lambda_3}\mathbf{I}_M \otimes \mathbf{J}_{KL} - \frac{\alpha_2}{\lambda_3\lambda_4}\mathbf{J}_{MKL}. \quad \text{(A3)}$$

The significance of the closed-form expression (A3) is in the computational savings arising from not having to invert $\mathbf{R}_i$, which would otherwise be costly for large MKL.

Web Appendix E

Derivation of $\pi_c^{\mathbf{opt}}$

The optimal randomization proportion that leads to the smallest σ_β^2 solves

$$\frac{\partial \sigma_\beta^2}{\partial \pi_c} = -\frac{\rho_c^2}{\pi_c^2} + \frac{\rho_t^2}{(1 - \pi_c)^2} = 0,$$

$$\Rightarrow \; -\rho_c^2(1 - \pi_c)^2 + \rho_t^2\pi_c^2 = 0,$$

$$\Rightarrow (\rho_t^2 - \rho_c^2)\pi_c^2 + 2\rho_c^2\pi_c - \rho_c^2 = 0,$$

because $\partial^2\sigma_\beta^2/\partial\pi_c = 2\rho_c^2/\pi_c^3 + 2\rho_t^2/(1-\pi_c)^3 \geq 0$ for any π_c within the unit interval.

If $\rho_c = \rho_t$, we have $2\pi_c - 1 = 0$, resulting in $\pi_c^{\mathrm{opt}} = 1/2$.

Otherwise, the above quadratic function results in $\pi_c^{\mathrm{opt}} = (\rho_c^2 \pm |\rho_c\rho_t|)/(\rho_c^2 - \rho_t^2)$, depending on which value is contained within the unit interval.

Web Appendix F

Proof of Theorem 3.7

Proof. (1) Randomization at level three

Suppose for each of N clusters, M health facilities are randomized with $\pi_c M$ health facilities assigned to the control arm and $(1-\pi_c)M$ health facilities to the intervention arm. Furthermore, assume there is no interaction effect, i.e., the intervention effect is the same in every cluster. In this case, $\mathbf{X}_i = \left(\mathbf{1}_{MKL}, (\mathbf{0}'_{\pi_c MKL}, \mathbf{1}'_{(1-\pi_c)MKL})'\right)$ for all i.

Using the model-based variance,

$$\mathbf{\Sigma}_1 = N^{-1}\sum_{i=1}^{N}\mathbf{D}_i'\mathbf{V}_i^{-1}\mathbf{D}_i = \begin{pmatrix} \rho_c^{-2}\gamma_1 + 2\rho_c^{-1}\rho_t^{-1}\gamma_2 + \rho_t^{-2}\gamma_3 & \rho_c^{-1}\rho_t^{-1}\gamma_2 + \rho_t^{-2}\gamma_3 \\ \rho_c^{-1}\rho_t^{-1}\gamma_2 + \rho_t^{-2}\gamma_3 & \rho_t^{-2}\gamma_3 \end{pmatrix},$$

$$\mathbf{\Sigma}_1^{-1} = \frac{\rho_c^2\rho_t^2}{\gamma_1\gamma_3 - \gamma_2^2}\begin{pmatrix} \rho_t^{-2}\gamma_3 & -(\rho_c^{-1}\rho_t^{-1}\gamma_2 + \rho_t^{-2}\gamma_3) \\ -(\rho_c^{-1}\rho_t^{-1}\gamma_2 + \rho_t^{-2}\gamma_3) & \rho_c^{-2}\gamma_1 + 2\rho_c^{-1}\rho_t^{-1}\gamma_2 + \rho_t^{-2}\gamma_3 \end{pmatrix},$$

where γ_1 is the sum of elements in first $\pi_c MKL$ rows and first $\pi_c MKL$ columns of $\mathbf{R}^{-1}$, γ_2 is the sum of elements in first $\pi_c MKL$ rows and last $(1-\pi_c)MKL$ columns of $\mathbf{R}^{-1}$, and γ_3 is the sum of elements in last $(1-\pi_c)MKL$ rows and last $(1-\pi_c)MKL$ columns of $\mathbf{R}^{-1}$. For our extended nested exchangeable correlation structure,

$$\gamma_1 = MKL\left\{\frac{\pi_c^2}{\lambda_4} + \frac{\pi_c(1-\pi_c)}{\lambda_3}\right\},$$
$$\gamma_2 = MKL\left\{\frac{\pi_c(1-\pi_c)}{\lambda_4} - \frac{\pi_c(1-\pi_c)}{\lambda_3}\right\},$$
$$\gamma_3 = MKL\left\{\frac{(1-\pi_c)^2}{\lambda_4} + \frac{\pi_c(1-\pi_c)}{\lambda_3}\right\}.$$

Then we have

$$\sigma_\beta^2 = \frac{\lambda_3}{MKL}\left(\frac{\rho_c^2}{\pi_c} + \frac{\rho_t^2}{1-\pi_c}\right) + \frac{(\lambda_4-\lambda_3)(\rho_c-\rho_t)^2}{MKL}.$$

(2) Randomization at level two

Suppose for each of NM health facilities, K providers are randomized with $\pi_c K$ providers assigned to the control arm and $(1-\pi_c)K$ providers to the intervention arm. Furthermore, assume there is no interaction effect, i.e., the intervention effect is the same in every health facility. In this case, $\mathbf{X}_i = \mathbf{1}_M \otimes \mathbf{X}_{hf}$ for all i, where $\mathbf{X}_{hf} = \left(\mathbf{1}_{KL}, (\mathbf{0}'_{\pi_c KL}, \mathbf{1}'_{(1-\pi_c)KL})'\right)$.

Using the model-based variance,

$$\mathbf{\Sigma}_1 = N^{-1}\sum_{i=1}^{N}\mathbf{D}_i'\mathbf{V}_i^{-1}\mathbf{D}_i = \begin{pmatrix} \rho_c^{-2}\eta_1 + 2\rho_c^{-1}\rho_t^{-1}\eta_2 + \rho_t^{-2}\eta_3 & \rho_c^{-1}\rho_t^{-1}\eta_2 + \rho_t^{-2}\eta_3 \\ \rho_c^{-1}\rho_t^{-1}\eta_2 + \rho_t^{-2}\eta_3 & \rho_t^{-2}\eta_3 \end{pmatrix},$$
$$\mathbf{\Sigma}_1^{-1} = \frac{\rho_c^2\rho_t^2}{\eta_1\eta_3 - \eta_2^2}\begin{pmatrix} \rho_t^{-2}\eta_3 & -(\rho_c^{-1}\rho_t^{-1}\eta_2 + \rho_t^{-2}\eta_3) \\ -(\rho_c^{-1}\rho_t^{-1}\eta_2 + \rho_t^{-2}\eta_3) & \rho_c^{-2}\eta_1 + 2\rho_c^{-1}\rho_t^{-1}\eta_2 + \rho_t^{-2}\eta_3 \end{pmatrix},$$

where η_1 is the sum of elements in control rows and control columns of $\mathbf{R}^{-1}$, η_2 is the sum of elements in control rows and intervention columns of $\mathbf{R}^{-1}$, and η_3 is the sum of elements in intervention rows and intervention columns of $\mathbf{R}^{-1}$. For our extended nested exchangeable correlation structure,

$$\eta_1 = MKL\left\{\frac{\pi_c^2}{\lambda_4} + \frac{\pi_c(1-\pi_c)}{\lambda_2}\right\},$$

$$\eta_2 = MKL\left\{\frac{\pi_c(1-\pi_c)}{\lambda_4} - \frac{\pi_c(1-\pi_c)}{\lambda_2}\right\},$$
$$\eta_3 = MKL\left\{\frac{(1-\pi_c)^2}{\lambda_4} + \frac{\pi_c(1-\pi_c)}{\lambda_2}\right\}.$$

Then we have

$$\sigma_\beta^2 = \frac{\lambda_2}{MKL}\left(\frac{\rho_c^2}{\pi_c} + \frac{\rho_t^2}{1-\pi_c}\right) + \frac{(\lambda_4-\lambda_2)(\rho_c-\rho_t)^2}{MKL}.$$

(3) Randomization at level one

Suppose for each of NMK providers, L patients are randomized with $\pi_c L$ patients assigned to the control arm and $(1-\pi_c)L$ patients to the intervention arm. Furthermore, assume there is no interaction effect, i.e., the intervention effect is the same in every provider. In this case, $\mathbf{X}_i = \mathbf{1}_{MK} \otimes \mathbf{X}_{pro}$ for all i, where $\mathbf{X}_{pro} = \left(\mathbf{1}_L, (\mathbf{0}'_{\pi_c L}, \mathbf{1}'_{(1-\pi_c)L})'\right)$.

Using the model-based variance,

$$\mathbf{\Sigma}_1 = N^{-1}\sum_{i=1}^{N}\mathbf{D}_i'\mathbf{V}_i^{-1}\mathbf{D}_i = \begin{pmatrix} \rho_c^{-2}\theta_1 + 2\rho_c^{-1}\rho_t^{-1}\theta_2 + \rho_t^{-2}\theta_3 & \rho_c^{-1}\rho_t^{-1}\theta_2 + \rho_t^{-2}\theta_3 \\ \rho_c^{-1}\rho_t^{-1}\theta_2 + \rho_t^{-2}\theta_3 & \rho_t^{-2}\theta_3 \end{pmatrix},$$
$$\mathbf{\Sigma}_1^{-1} = \frac{\rho_c^2\rho_t^2}{\theta_1\theta_3 - \theta_2^2}\begin{pmatrix} \rho_t^{-2}\theta_3 & -(\rho_c^{-1}\rho_t^{-1}\theta_2 + \rho_t^{-2}\theta_3) \\ -(\rho_c^{-1}\rho_t^{-1}\theta_2 + \rho_t^{-2}\theta_3) & \rho_c^{-2}\theta_1 + 2\rho_c^{-1}\rho_t^{-1}\theta_2 + \rho_t^{-2}\theta_3 \end{pmatrix},$$

where θ_1 is the sum of elements in control rows and control columns of $\mathbf{R}^{-1}$, θ_2 is the sum of elements in control rows and intervention columns of $\mathbf{R}^{-1}$, and θ_3 is the sum of elements in intervention rows and intervention columns of $\mathbf{R}^{-1}$. For our extended nested exchangeable correlation structure,

$$\theta_1 = MKL\left\{\frac{\pi_c^2}{\lambda_4} + \frac{\pi_c(1-\pi_c)}{\lambda_1}\right\},$$
$$\theta_2 = MKL\left\{\frac{\pi_c(1-\pi_c)}{\lambda_4} - \frac{\pi_c(1-\pi_c)}{\lambda_1}\right\},$$
$$\theta_3 = MKL\left\{\frac{(1-\pi_c)^2}{\lambda_4} + \frac{\pi_c(1-\pi_c)}{\lambda_1}\right\}.$$

Then we have

$$\sigma_\beta^2 = \frac{\lambda_1}{MKL}\left(\frac{\rho_c^2}{\pi_c} + \frac{\rho_t^2}{1-\pi_c}\right) + \frac{(\lambda_4-\lambda_1)(\rho_c-\rho_t)^2}{MKL}.$$

$\square$

Web Appendix G

Specific sample size formulas for randomization at lower levels

(1) Randomization at level three

When Y_{ijkl} is continuous, similar to Example 3.4, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2} + t_{\gamma,N-2}\right)^2}{b^2} \times \frac{\phi\lambda_3}{\pi_c(1-\pi_c)MKL}.$$

When Y_{ijkl} is binary, similar to Example 3.5, under the canonical logit link function, the required number of clusters must satisfy

$$\begin{aligned} N \geq \frac{\left(t_{\alpha/2,N-2} + t_{\gamma,N-2}\right)^2}{b^2} \times \Bigg\{ &\frac{\lambda_3}{MKL}\left(\frac{1}{\pi_c \mathrm{P}_0\left(1-\mathrm{P}_0\right)} + \frac{1}{(1-\pi_c)\mathrm{P}_1\left(1-\mathrm{P}_1\right)}\right) \\ &+ \frac{\lambda_4-\lambda_3}{MKL}\left(\frac{1}{\sqrt{\mathrm{P}_0\left(1-\mathrm{P}_0\right)}} - \frac{1}{\sqrt{\mathrm{P}_1\left(1-\mathrm{P}_1\right)}}\right)^2 \Bigg\}; \end{aligned}$$

under the identity link function, the required number of clusters must satisfy

$$\begin{aligned} N \geq \frac{\left(t_{\alpha/2,N-2} + t_{\gamma,N-2}\right)^2}{b^2} \times \Bigg\{ &\frac{\lambda_3}{MKL}\left(\frac{\mathrm{P}_0\left(1-\mathrm{P}_0\right)}{\pi_c} + \frac{\mathrm{P}_1\left(1-\mathrm{P}_1\right)}{1-\pi_c}\right) \\ &+ \frac{\lambda_4-\lambda_3}{MKL}\left(\sqrt{\mathrm{P}_0\left(1-\mathrm{P}_0\right)} - \sqrt{\mathrm{P}_1\left(1-\mathrm{P}_1\right)}\right)^2 \Bigg\}; \end{aligned}$$

under the log link function, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \left\{\frac{\lambda_3}{MKL}\left(\frac{1-\mathrm{P}_0}{\pi_c \mathrm{P}_0}+\frac{1-\mathrm{P}_1}{(1-\pi_c)\mathrm{P}_1}\right)\right.$$
$$\left.+\frac{\lambda_4-\lambda_3}{MKL}\left(\sqrt{\frac{1-\mathrm{P}_0}{\mathrm{P}_0}}-\sqrt{\frac{1-\mathrm{P}_1}{\mathrm{P}_1}}\right)^2\right\}.$$

When Y_{ijkl} is a count outcome, similar to Example 3.6, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \left\{\frac{\lambda_3}{MKL}\left(\frac{1}{\pi_c \exp(\beta_1)}+\frac{1}{(1-\pi_c)\exp(\beta_1+\beta_2)}\right)\right.$$
$$\left.+\frac{\lambda_4-\lambda_3}{MKL}\left(\frac{1}{\sqrt{\exp(\beta_1)}}-\frac{1}{\sqrt{\exp(\beta_1+\beta_2)}}\right)^2\right\}.$$

(2) Randomization at level two

When Y_{ijkl} is continuous, similar to Example 3.4, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \frac{\phi\lambda_2}{\pi_c(1-\pi_c)MKL}.$$

When Y_{ijkl} is binary, similar to Example 3.5, under the canonical logit link function, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \left\{\frac{\lambda_2}{MKL}\left(\frac{1}{\pi_c \mathrm{P}_0\,(1-\mathrm{P}_0)}+\frac{1}{(1-\pi_c)\mathrm{P}_1\,(1-\mathrm{P}_1)}\right)\right.$$
$$\left.+\frac{\lambda_4-\lambda_2}{MKL}\left(\frac{1}{\sqrt{\mathrm{P}_0\,(1-\mathrm{P}_0)}}-\frac{1}{\sqrt{\mathrm{P}_1\,(1-\mathrm{P}_1)}}\right)^2\right\};$$

under the identity link function, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \left\{\frac{\lambda_2}{MKL}\left(\frac{\mathrm{P}_0\,(1-\mathrm{P}_0)}{\pi_c}+\frac{\mathrm{P}_1\,(1-\mathrm{P}_1)}{1-\pi_c}\right)\right.$$
$$\left.+\frac{\lambda_4-\lambda_2}{MKL}\left(\sqrt{\mathrm{P}_0\,(1-\mathrm{P}_0)}-\sqrt{\mathrm{P}_1\,(1-\mathrm{P}_1)}\right)^2\right\};$$

under the log link function, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \left\{ \frac{\lambda_2}{MKL}\left(\frac{1-\mathrm{P}_0}{\pi_c \mathrm{P}_0}+\frac{1-\mathrm{P}_1}{(1-\pi_c)\mathrm{P}_1}\right) + \frac{\lambda_4-\lambda_2}{MKL}\left(\sqrt{\frac{1-\mathrm{P}_0}{\mathrm{P}_0}}-\sqrt{\frac{1-\mathrm{P}_1}{\mathrm{P}_1}}\right)^2 \right\}.$$

When Y_{ijkl} is a count outcome, similar to Example 3.6, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \left\{ \frac{\lambda_2}{MKL}\left(\frac{1}{\pi_c \exp(\beta_1)}+\frac{1}{(1-\pi_c)\exp(\beta_1+\beta_2)}\right) + \frac{\lambda_4-\lambda_2}{MKL}\left(\frac{1}{\sqrt{\exp(\beta_1)}}-\frac{1}{\sqrt{\exp(\beta_1+\beta_2)}}\right)^2 \right\}.$$

(3) Randomization at level one

When Y_{ijkl} is continuous, similar to Example 3.4, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \frac{\phi\lambda_1}{\pi_c(1-\pi_c)MKL}.$$

When Y_{ijkl} is binary, similar to Example 3.5, under the canonical logit link function, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \left\{ \frac{\lambda_1}{MKL}\left(\frac{1}{\pi_c \mathrm{P}_0(1-\mathrm{P}_0)}+\frac{1}{(1-\pi_c)\mathrm{P}_1(1-\mathrm{P}_1)}\right) + \frac{\lambda_4-\lambda_1}{MKL}\left(\frac{1}{\sqrt{\mathrm{P}_0(1-\mathrm{P}_0)}}-\frac{1}{\sqrt{\mathrm{P}_1(1-\mathrm{P}_1)}}\right)^2 \right\};$$

under the identity link function, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2}+t_{\gamma,N-2}\right)^2}{b^2} \times \left\{ \frac{\lambda_1}{MKL}\left(\frac{\mathrm{P}_0(1-\mathrm{P}_0)}{\pi_c}+\frac{\mathrm{P}_1(1-\mathrm{P}_1)}{1-\pi_c}\right) + \frac{\lambda_4-\lambda_1}{MKL}\left(\sqrt{\mathrm{P}_0(1-\mathrm{P}_0)}-\sqrt{\mathrm{P}_1(1-\mathrm{P}_1)}\right)^2 \right\};$$

under the log link function, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2} + t_{\gamma,N-2}\right)^2}{b^2} \times \left\{ \frac{\lambda_1}{MKL} \left(\frac{1-\mathrm{P}_0}{\pi_c \mathrm{P}_0} + \frac{1-\mathrm{P}_1}{(1-\pi_c)\mathrm{P}_1} \right) + \frac{\lambda_4 - \lambda_1}{MKL} \left(\sqrt{\frac{1-\mathrm{P}_0}{\mathrm{P}_0}} - \sqrt{\frac{1-\mathrm{P}_1}{\mathrm{P}_1}} \right)^2 \right\}.$$

When Y_{ijkl} is a count outcome, similar to Example 3.6, the required number of clusters must satisfy

$$N \geq \frac{\left(t_{\alpha/2,N-2} + t_{\gamma,N-2}\right)^2}{b^2} \times \left\{ \frac{\lambda_1}{MKL} \left(\frac{1}{\pi_c \exp(\beta_1)} + \frac{1}{(1-\pi_c)\exp(\beta_1+\beta_2)} \right) + \frac{\lambda_4 - \lambda_1}{MKL} \left(\frac{1}{\sqrt{\exp(\beta_1)}} - \frac{1}{\sqrt{\exp(\beta_1+\beta_2)}} \right)^2 \right\}.$$

Web Appendix H

Proof of Theorem 3.10

Proof. Denote $\epsilon_{ijkl} = y_{ijkl} - \mu_{ijkl}(\boldsymbol{\beta})$, T_0 as the control arm, and T_1 as the intervention arm.

(1) Randomization at level four

We have

$$\begin{aligned}
\hat{\boldsymbol{\Sigma}}_1 &= N^{-1} \sum_{i=1}^{N} \mathbf{D}_i'(\hat{\boldsymbol{\beta}}) \mathbf{V}_i^{-1} \mathbf{D}_i(\hat{\boldsymbol{\beta}}) \\
&= N^{-1} \sum_{i=1}^{N} \mathbf{D}_i'(\boldsymbol{\beta}) \mathbf{V}_i^{-1} \mathbf{D}_i(\boldsymbol{\beta}) + o_p(1) \\
&= \left(\mathbf{1}'\mathbf{I}^{-1}\mathbf{1}\right) \begin{pmatrix} \pi_c \rho_c^{-2} + (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \\ (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \end{pmatrix} + o_p(1).
\end{aligned}$$

Thus as $N \to \infty$, $\hat{\mathbf{\Sigma}}_1$ converges to

$$\mathbf{\Sigma}_1 = MKL \begin{pmatrix} \pi_c \rho_c^{-2} + (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \\ (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \end{pmatrix}.$$

Also,

$$\begin{aligned}
\hat{\mathbf{\Sigma}}_0 &= N^{-1} \sum_{i=1}^{N} \left\{ \sum_{j=1}^{M} \sum_{k=1}^{K} \sum_{l=1}^{L} \frac{\hat{\epsilon}_{ijkl}}{\hat{\mu}_{ijkl}^2 \hat{\kappa}_{ijkl}^2 g'(\hat{\mu}_{ijkl})} \mathbf{X}_{ijkl} \right\}^{\otimes 2} \\
&= N^{-1} \sum_{i=1}^{N} \left\{ \sum_{j=1}^{M} \sum_{k=1}^{K} \sum_{l=1}^{L} \frac{\epsilon_{ijkl}}{\mu_{ijkl}^2 \kappa_{ijkl}^2 g'(\mu_{ijkl})} \mathbf{X}_{ijkl} \right\}^{\otimes 2} + o_p(1) \\
&= \pi_c \omega_c^{-2} (\pi_c N)^{-1} \sum_{i \in T_0} \left\{ \sum_{j=1}^{M} \sum_{k=1}^{K} \sum_{l=1}^{L} \epsilon_{ijkl} \begin{pmatrix} 1 \\ 0 \end{pmatrix} \right\}^{\otimes 2} \\
&\quad + (1-\pi_c)\omega_t^{-2} [(1-\pi_c)N]^{-1} \sum_{i \in T_1} \left\{ \sum_{j=1}^{M} \sum_{k=1}^{K} \sum_{l=1}^{L} \epsilon_{ijkl} \begin{pmatrix} 1 \\ 1 \end{pmatrix} \right\}^{\otimes 2} + o_p(1),
\end{aligned}$$

where $c^{\otimes 2} = cc'$ for a vector c, $\omega_c = \mu_c^2 \kappa_c^2 \{\partial g(\mu_c)/\partial \mu_c\}$, and $\omega_t = \mu_t^2 \kappa_t^2 \{\partial g(\mu_t)/\partial \mu_t\}$.

For $i \in T_0$, we have

$$\begin{aligned}
\mathrm{E}\{(\sum_{j=1}^{M} \sum_{k=1}^{K} \sum_{l=1}^{L} \epsilon_{ijkl})^2\} &= \mu_c^2 \kappa_c^2 MKL\{1 + (L-1)\alpha_0 + (K-1)L\alpha_1 + (M-1)KL\alpha_2\} \\
&= \mu_c^2 \kappa_c^2 MKL\lambda_4.
\end{aligned}$$

For $i \in T_1$, we have

$$\begin{aligned}
\mathrm{E}\{(\sum_{j=1}^{M} \sum_{k=1}^{K} \sum_{l=1}^{L} \epsilon_{ijkl})^2\} &= \mu_t^2 \kappa_t^2 MKL\{1 + (L-1)\alpha_0 + (K-1)L\alpha_1 + (M-1)KL\alpha_2\} \\
&= \mu_t^2 \kappa_t^2 MKL\lambda_4.
\end{aligned}$$

By the central limit theorem, as $N \to \infty$, $\hat{\mathbf{\Sigma}}_0$ converges to

$$\mathbf{\Sigma}_0 = MKL\lambda_4 \begin{pmatrix} \pi_c \rho_c^{-2} + (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \\ (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \end{pmatrix}.$$

As $N \to \infty$, $\mathbf{V}_I^{\text{sandwich}} = \hat{\mathbf{\Sigma}}_1^{-1}\hat{\mathbf{\Sigma}}_0\hat{\mathbf{\Sigma}}_1^{-1} \to \mathbf{\Sigma}^* = \mathbf{\Sigma}_1^{-1}\mathbf{\Sigma}_0\mathbf{\Sigma}_1^{-1}$, and a few steps of algebra show that the $(2,2)$th element of $\mathbf{\Sigma}^*$ has a closed form

$$\sigma_{\beta*}^2 = \frac{\lambda_4}{MKL}\left(\frac{\rho_c^2}{\pi_c} + \frac{\rho_t^2}{1-\pi_c}\right).$$

(2) Randomization at level three

We have

$$\begin{aligned}
\hat{\mathbf{\Sigma}}_1 &= N^{-1}\sum_{i=1}^{N} \mathbf{D}_i'(\hat{\boldsymbol{\beta}})\mathbf{V}_i^{-1}\mathbf{D}_i(\hat{\boldsymbol{\beta}}) \\
&= N^{-1}\sum_{i=1}^{N} \mathbf{D}_i'(\boldsymbol{\beta})\mathbf{V}_i^{-1}\mathbf{D}_i(\boldsymbol{\beta}) + o_p(1) \\
&= \begin{pmatrix} \pi_c MKL\rho_c^{-2} + (1-\pi_c)MKL\rho_t^{-2} & (1-\pi_c)MKL\rho_t^{-2} \\ (1-\pi_c)MKL\rho_t^{-2} & (1-\pi_c)MKL\rho_t^{-2} \end{pmatrix} + o_p(1).
\end{aligned}$$

Thus as $N \to \infty$, $\hat{\mathbf{\Sigma}}_1$ converges to

$$\mathbf{\Sigma}_1 = MKL \begin{pmatrix} \pi_c \rho_c^{-2} + (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \\ (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \end{pmatrix}.$$

Also,

$$\hat{\mathbf{\Sigma}}_0 = N^{-1}\sum_{i=1}^{N}\left\{\sum_{j=1}^{M}\sum_{k=1}^{K}\sum_{l=1}^{L} \frac{\hat{\epsilon}_{ijkl}}{\hat{\mu}_{ijkl}^2\hat{\kappa}_{ijkl}^2 g'(\hat{\mu}_{ijkl})}\mathbf{X}_{ijkl}\right\}^{\otimes 2}$$

$$= N^{-1}\sum_{i=1}^{N}\left\{\sum_{j=1}^{M}\sum_{k=1}^{K}\sum_{l=1}^{L}\frac{\epsilon_{ijkl}}{\mu_{ijkl}^2\kappa_{ijkl}^2 g'(\mu_{ijkl})}\mathbf{X}_{ijkl}\right\}^{\otimes 2} + o_p(1)$$

$$= N^{-1}\sum_{i=1}^{N}\left\{\omega_c^{-1}\sum_{j\in T_0}\sum_{k=1}^{K}\sum_{l=1}^{L}\epsilon_{ijkl}\begin{pmatrix}1\\0\end{pmatrix} + \omega_t^{-1}\sum_{j\in T_1}\sum_{k=1}^{K}\sum_{l=1}^{L}\epsilon_{ijkl}\begin{pmatrix}1\\1\end{pmatrix}\right\}^{\otimes 2} + o_p(1)$$

$$= N^{-1}\sum_{i=1}^{N}\begin{pmatrix}(\omega_c^{-1}\epsilon_{ic_3}+\omega_t^{-1}\epsilon_{it_3})^2 & (\omega_c^{-1}\epsilon_{ic_3}+\omega_t^{-1}\epsilon_{it_3})(\omega_t^{-1}\epsilon_{it_3})\\ (\omega_c^{-1}\epsilon_{ic_3}+\omega_t^{-1}\epsilon_{it_3})(\omega_t^{-1}\epsilon_{it_3}) & (\omega_t^{-1}\epsilon_{it_3})^2\end{pmatrix},$$

where $\epsilon_{ic_3} = \sum_{j\in T_0}\sum_{k=1}^{K}\sum_{l=1}^{L}\epsilon_{ijkl}$, and $\epsilon_{it_3} = \sum_{j\in T_1}\sum_{k=1}^{K}\sum_{l=1}^{L}\epsilon_{ijkl}$.

For all i, we have

$$\begin{aligned}
\mathrm{E}\{(\omega_c^{-1}\epsilon_{ic_3}+\omega_t^{-1}\epsilon_{it_3})^2\} &= \omega_c^{-2}\mu_c^2\kappa_c^2\gamma_4 + 2\omega_c^{-1}\mu_c\kappa_c\omega_t^{-1}\mu_t\kappa_t\gamma_5 + \omega_t^{-2}\mu_t^2\kappa_t^2\gamma_6\\
&= \rho_c^{-2}\gamma_4 + 2\rho_c^{-1}\rho_t^{-1}\gamma_5 + \rho_t^{-2}\gamma_6,\\
\mathrm{E}\{(\omega_c^{-1}\epsilon_{ic_3}+\omega_t^{-1}\epsilon_{it_3})(\omega_t^{-1}\epsilon_{it_3})\} &= \rho_c^{-1}\rho_t^{-1}\gamma_5 + \rho_t^{-2}\gamma_6,\\
\mathrm{E}\{(\omega_t^{-1}\epsilon_{it_3})^2\} &= \rho_t^{-2}\gamma_6,
\end{aligned}$$

where γ_4 is the sum of elements in first $\pi_c MKL$ rows and first $\pi_c MKL$ columns of $\mathbf{R}$, γ_5 is the sum of elements in first $\pi_c MKL$ rows and last $(1-\pi_c)MKL$ columns of $\mathbf{R}$, and γ_6 is the sum of elements in last $(1-\pi_c)MKL$ rows and last $(1-\pi_c)MKL$ columns of $\mathbf{R}$. For our extended nested exchangeable correlation structure,

$$\begin{aligned}
\gamma_4 &= (1-\alpha_0)\pi_c MKL + (\alpha_0-\alpha_1)\pi_c MKL^2 + (\alpha_1-\alpha_2)\pi_c MK^2L^2 + \alpha_2(\pi_c M)^2K^2L^2\\
&= MKL\left\{\pi_c^2\lambda_4 + \pi_c(1-\pi_c)\lambda_3\right\},\\
\gamma_5 &= MKL\left\{\pi_c(1-\pi_c)\lambda_4 - \pi_c(1-\pi_c)\lambda_3\right\},\\
\gamma_6 &= MKL\left\{(1-\pi_c)^2\lambda_4 + \pi_c(1-\pi_c)\lambda_3\right\}.
\end{aligned}$$

By the central limit theorem, as $N \to \infty$, $\hat{\mathbf{\Sigma}}_0$ converges to

$$\mathbf{\Sigma}_0 = \begin{pmatrix} \rho_c^{-2}\gamma_4 + 2\rho_c^{-1}\rho_t^{-1}\gamma_5 + \rho_t^{-2}\gamma_6 & \rho_c^{-1}\rho_t^{-1}\gamma_5 + \rho_t^{-2}\gamma_6 \\ \rho_c^{-1}\rho_t^{-1}\gamma_5 + \rho_t^{-2}\gamma_6 & \rho_t^{-2}\gamma_6 \end{pmatrix}.$$

As $N \to \infty$, $\mathbf{V}_I^{\text{sandwich}} = \hat{\mathbf{\Sigma}}_1^{-1}\hat{\mathbf{\Sigma}}_0\hat{\mathbf{\Sigma}}_1^{-1} \to \mathbf{\Sigma}^* = \mathbf{\Sigma}_1^{-1}\mathbf{\Sigma}_0\mathbf{\Sigma}_1^{-1}$, and a few steps of algebra show that the $(2,2)$th element of $\mathbf{\Sigma}^*$ has a closed form

$$\sigma_{\beta *}^2 = \frac{\lambda_3}{MKL}\left(\frac{\rho_c^2}{\pi_c} + \frac{\rho_t^2}{1-\pi_c}\right) + \frac{(\lambda_4 - \lambda_3)(\rho_c - \rho_t)^2}{MKL}.$$

(3) Randomization at level two

Similar to the derivation in (2), we have

$$\mathbf{\Sigma}_1 = MKL \begin{pmatrix} \pi_c\rho_c^{-2} + (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \\ (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \end{pmatrix},$$

$$\mathbf{\Sigma}_0 = \begin{pmatrix} \rho_c^{-2}\eta_4 + 2\rho_c^{-1}\rho_t^{-1}\eta_5 + \rho_t^{-2}\eta_6 & \rho_c^{-1}\rho_t^{-1}\eta_5 + \rho_t^{-2}\eta_6 \\ \rho_c^{-1}\rho_t^{-1}\eta_5 + \rho_t^{-2}\eta_6 & \rho_t^{-2}\eta_6 \end{pmatrix},$$

where η_4 is the sum of elements in control rows and control columns of $\mathbf{R}$, η_5 is the sum of elements in control rows and intervention columns of $\mathbf{R}$, and η_6 is the sum of elements in intervention rows and intervention columns of $\mathbf{R}$, when the randomization takes place at the second level. For our extended nested exchangeable correlation structure,

$$\eta_4 = MKL\left\{\pi_c^2\lambda_4 + \pi_c(1-\pi_c)\lambda_2\right\},$$

$$\eta_5 = MKL\left\{\pi_c(1-\pi_c)\lambda_4 - \pi_c(1-\pi_c)\lambda_2\right\},$$

$$\eta_6 = MKL\left\{(1-\pi_c)^2\lambda_4 + \pi_c(1-\pi_c)\lambda_2\right\}.$$

As $N \to \infty$, $\mathbf{V}_I^{\text{sandwich}} = \hat{\mathbf{\Sigma}}_1^{-1}\hat{\mathbf{\Sigma}}_0\hat{\mathbf{\Sigma}}_1^{-1} \to \mathbf{\Sigma}^* = \mathbf{\Sigma}_1^{-1}\mathbf{\Sigma}_0\mathbf{\Sigma}_1^{-1}$, and a few steps of algebra show that the $(2,2)$th element of $\mathbf{\Sigma}^*$ has a closed form

$$\sigma^2_{\beta *} = \frac{\lambda_2}{MKL}\left(\frac{\rho_c^2}{\pi_c} + \frac{\rho_t^2}{1-\pi_c}\right) + \frac{(\lambda_4 - \lambda_2)(\rho_c - \rho_t)^2}{MKL}.$$

(4) Randomization at level one

Similar to the derivation in (2), we have

$$\mathbf{\Sigma}_1 = MKL\begin{pmatrix} \pi_c\rho_c^{-2} + (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \\ (1-\pi_c)\rho_t^{-2} & (1-\pi_c)\rho_t^{-2} \end{pmatrix},$$

$$\mathbf{\Sigma}_0 = \begin{pmatrix} \rho_c^{-2}\theta_4 + 2\rho_c^{-1}\rho_t^{-1}\theta_5 + \rho_t^{-2}\theta_6 & \rho_c^{-1}\rho_t^{-1}\theta_5 + \rho_t^{-2}\theta_6 \\ \rho_c^{-1}\rho_t^{-1}\theta_5 + \rho_t^{-2}\theta_6 & \rho_t^{-2}\theta_6 \end{pmatrix},$$

where θ_4 is the sum of elements in control rows and control columns of $\mathbf{R}$, θ_5 is the sum of elements in control rows and intervention columns of $\mathbf{R}$, and θ_6 is the sum of elements in intervention rows and intervention columns of $\mathbf{R}$, when the randomization takes place at the first level. For our extended nested exchangeable correlation structure,

$$\theta_4 = MKL\left\{\pi_c^2\lambda_4 + \pi_c(1-\pi_c)\lambda_1\right\},$$

$$\theta_5 = MKL\left\{\pi_c(1-\pi_c)\lambda_4 - \pi_c(1-\pi_c)\lambda_1\right\},$$

$$\theta_6 = MKL\left\{(1-\pi_c)^2\lambda_4 + \pi_c(1-\pi_c)\lambda_1\right\}.$$

As $N \to \infty$, $\mathbf{V}_I^{\text{sandwich}} = \hat{\mathbf{\Sigma}}_1^{-1}\hat{\mathbf{\Sigma}}_0\hat{\mathbf{\Sigma}}_1^{-1} \to \mathbf{\Sigma}^* = \mathbf{\Sigma}_1^{-1}\mathbf{\Sigma}_0\mathbf{\Sigma}_1^{-1}$, and a few steps of algebra show that the $(2,2)$th element of $\mathbf{\Sigma}^*$ has a closed form

$$\sigma^2_{\beta *} = \frac{\lambda_1}{MKL}\left(\frac{\rho_c^2}{\pi_c} + \frac{\rho_t^2}{1-\pi_c}\right) + \frac{(\lambda_4 - \lambda_1)(\rho_c - \rho_t)^2}{MKL}.$$

$\square$

Web Appendix I

Proof of Remark 4.1

Proof. Under balanced designs, the sum of each column of $\mathbf{R}^{-1}$ is same, denoted as h, where $h = (\mathbf{1}'\mathbf{R}^{-1}\mathbf{1})/(MKL)$. When the randomization is carried out at the 4th level, we have

$$
\begin{aligned}
\sum_{i=1}^{N} \mathbf{D}_i'\mathbf{V}_i^{-1}(\mathbf{Y}_i - \boldsymbol{\mu}_i) &= \sum_{i\in T_0} \mathbf{D}_i'\mathbf{V}_i^{-1}\boldsymbol{\epsilon}_i + \sum_{i\in T_1} \mathbf{D}_i'\mathbf{V}_i^{-1}\boldsymbol{\epsilon}_i \\
&= \omega_c^{-1}\mathbf{X}_c'\mathbf{R}^{-1}\sum_{i\in T_0}\boldsymbol{\epsilon}_i + \omega_t^{-1}\mathbf{X}_t'\mathbf{R}^{-1}\sum_{i\in T_1}\boldsymbol{\epsilon}_i \\
&= h\omega_c^{-1}\left(\sum_{i\in T_0}\mathbf{1}'\boldsymbol{\epsilon}_i\right)\begin{pmatrix}1\\0\end{pmatrix} + h\omega_t^{-1}\left(\sum_{i\in T_1}\mathbf{1}'\boldsymbol{\epsilon}_i\right)\begin{pmatrix}1\\1\end{pmatrix} \\
&= h\begin{pmatrix}\omega_c^{-1}\sum_{i\in T_0}\mathbf{1}'\boldsymbol{\epsilon}_i + \omega_t^{-1}\sum_{i\in T_1}\mathbf{1}'\boldsymbol{\epsilon}_i \\ \omega_t^{-1}\sum_{i\in T_1}\mathbf{1}'\boldsymbol{\epsilon}_i\end{pmatrix}.
\end{aligned}
$$

Thus solving the $\boldsymbol{\beta}$-estimating equations $\sum_{i=1}^{N}\mathbf{D}_i'\mathbf{V}_i^{-1}(\mathbf{Y}_i - \boldsymbol{\mu}_i) = \mathbf{0}$ is independent of h, or independent of the correlation matrix. That is, GEE analysis using the extended nested exchangeable working correlation matrix or using an independence working correlation matrix result in the same estimator $\hat{\boldsymbol{\beta}}$.

For $i \in T_0$, we have

$$
\begin{aligned}
\mathbf{Q}_i &= \mathbf{D}_i'\mathbf{V}_i^{-1}\mathbf{D}_i(N\boldsymbol{\Sigma}_1)^{-1} \\
&= \rho_c^{-2}\left(\mathbf{1}'\mathbf{R}^{-1}\mathbf{1}\right)\begin{pmatrix}1 & 0\\ 0 & 0\end{pmatrix}\frac{1}{N\left(\mathbf{1}'\mathbf{R}^{-1}\mathbf{1}\right)\pi_c\rho_c^{-2}(1-\pi_c)\rho_t^{-2}}\begin{pmatrix}(1-\pi_c)\rho_t^{-2} & -(1-\pi_c)\rho_t^{-2}\\ -(1-\pi_c)\rho_t^{-2} & \pi_c\rho_c^{-2} + (1-\pi_c)\rho_t^{-2}\end{pmatrix} \\
&= \frac{1}{\pi_c N}\begin{pmatrix}1 & -1\\ 0 & 0\end{pmatrix}.
\end{aligned}
$$

For $i \in T_1$, we have

$$\begin{aligned}
\mathbf{Q}_i &= \mathbf{D}_i'\mathbf{V}_i^{-1}\mathbf{D}_i(N\boldsymbol{\Sigma}_1)^{-1} \\
&= \rho_t^{-2}\left(\mathbf{1}'\mathbf{R}^{-1}\mathbf{1}\right)\begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} \frac{1}{N\left(\mathbf{1}'\mathbf{R}^{-1}\mathbf{1}\right)\pi_c\rho_c^{-2}(1-\pi_c)\rho_t^{-2}} \begin{pmatrix} (1-\pi_c)\rho_t^{-2} & -(1-\pi_c)\rho_t^{-2} \\ -(1-\pi_c)\rho_t^{-2} & \pi_c\rho_c^{-2} + (1-\pi_c)\rho_t^{-2} \end{pmatrix} \\
&= \frac{1}{(1-\pi_c)N}\begin{pmatrix} 0 & 1 \\ 0 & 1 \end{pmatrix}.
\end{aligned}$$

Thus $\mathbf{Q}_i$ is independent of the correlation matrix. That is, GEE analysis using the extended nested exchangeable working correlation matrix or using an independence working correlation matrix result in the same $\mathbf{C}_i$ for BC0, BC1, BC2, and BC3, respectively.

In addition,

$$\begin{aligned}
\boldsymbol{\Sigma}_1^{-1} &= \frac{1}{\left(\mathbf{1}'\mathbf{R}^{-1}\mathbf{1}\right)\pi_c\rho_c^{-2}(1-\pi_c)\rho_t^{-2}} \begin{pmatrix} (1-\pi_c)\rho_t^{-2} & -(1-\pi_c)\rho_t^{-2} \\ -(1-\pi_c)\rho_t^{-2} & \pi_c\rho_c^{-2} + (1-\pi_c)\rho_t^{-2} \end{pmatrix}, \\
\boldsymbol{\Sigma}_0 &= \frac{1}{N}\left[\sum_{i\in T_0}\left\{\mathbf{C}_i h\omega_c^{-1}\left(\mathbf{1}'\hat{\boldsymbol{\epsilon}}_i\right)\begin{pmatrix} 1 \\ 0 \end{pmatrix}\right\}^{\otimes 2} + \sum_{i\in T_1}\left\{\mathbf{C}_i h\omega_t^{-1}\left(\mathbf{1}'\hat{\boldsymbol{\epsilon}}_i\right)\begin{pmatrix} 1 \\ 1 \end{pmatrix}\right\}^{\otimes 2}\right] \\
&= \frac{h^2}{N}\left[\omega_c^{-2}\sum_{i\in T_0}\left\{\left(\mathbf{1}'\hat{\boldsymbol{\epsilon}}_i\right)\mathbf{C}_i\begin{pmatrix} 1 \\ 0 \end{pmatrix}\right\}^{\otimes 2} + \omega_t^{-2}\sum_{i\in T_1}\left\{\left(\mathbf{1}'\hat{\boldsymbol{\epsilon}}_i\right)\mathbf{C}_i\begin{pmatrix} 1 \\ 1 \end{pmatrix}\right\}^{\otimes 2}\right].
\end{aligned}$$

Denote

$$\begin{aligned}
\mathbf{T} &= \frac{1}{\pi_c\rho_c^{-2}(1-\pi_c)\rho_t^{-2}} \begin{pmatrix} (1-\pi_c)\rho_t^{-2} & -(1-\pi_c)\rho_t^{-2} \\ -(1-\pi_c)\rho_t^{-2} & \pi_c\rho_c^{-2} + (1-\pi_c)\rho_t^{-2} \end{pmatrix}, \\
\mathbf{L} &= \frac{1}{N}\left[\omega_c^{-2}\sum_{i\in T_0}\left\{\left(\mathbf{1}'\hat{\boldsymbol{\epsilon}}_i\right)\mathbf{C}_i\begin{pmatrix} 1 \\ 0 \end{pmatrix}\right\}^{\otimes 2} + \omega_t^{-2}\sum_{i\in T_1}\left\{\left(\mathbf{1}'\hat{\boldsymbol{\epsilon}}_i\right)\mathbf{C}_i\begin{pmatrix} 1 \\ 1 \end{pmatrix}\right\}^{\otimes 2}\right],
\end{aligned}$$

where $\mathbf{T}$ and $\mathbf{L}$ are both independent of the correlation matrix. Then

$$\begin{aligned}
\mathbf{V}_R^{\text{sandwich}} &= \hat{\mathbf{\Sigma}}_1^{-1}\hat{\mathbf{\Sigma}}_0\hat{\mathbf{\Sigma}}_1^{-1} \\
&= \frac{1}{\mathbf{1}'\mathbf{R}^{-1}\mathbf{1}}\mathbf{T}\left(\frac{\mathbf{1}'\mathbf{R}^{-1}\mathbf{1}}{MKL}\right)^2\mathbf{L}\frac{1}{\mathbf{1}'\mathbf{R}^{-1}\mathbf{1}}\mathbf{T} \\
&= \left(\frac{1}{MKL}\right)^2\mathbf{TLT},
\end{aligned}$$

which is independent of the correlation matrix. Therefore, GEE analysis using the extended nested exchangeable working correlation matrix or using an independence working correlation matrix result in the same estimators BC0, BC1, BC2, AVG, and BC3. □

Web Appendix J: Web tables from simulation study

Web Table 1: Convergence rates (out of 1000) of GEE/MAEE analyses, using the extended nested exchangeable working correlation structure under balanced four-level CRTs.

P_0	P_1	$\boldsymbol{\alpha}$[a]	n	m	k	l	Convergence (Size)[b]	Convergence (Power)[c]
0.2	0.5	A1	14	2	3	5	998	1000
0.2	0.5	A1	14	2	3	10	1000	999
0.2	0.5	A1	14	2	4	5	999	1000
0.2	0.5	A1	12	3	3	5	1000	1000
0.2	0.5	A2	10	2	3	5	1000	994
0.2	0.5	A2	10	2	3	10	1000	998
0.2	0.5	A2	10	2	4	5	998	998
0.2	0.5	A2	8	3	3	5	954	948
0.2	0.5	A3	8	2	3	5	922	894
0.2	0.5	A3	8	3	3	5	911	913
0.2	0.5	A4	8	3	3	5	944	928
0.1	0.3	A1	22	2	3	5	983	985
0.1	0.3	A1	20	2	3	10	990	990
0.1	0.3	A1	20	2	4	5	995	995
0.1	0.3	A1	16	3	3	5	1000	999
0.1	0.3	A2	16	2	3	5	997	995
0.1	0.3	A2	14	2	3	10	997	995
0.1	0.3	A2	14	2	4	5	995	994
0.1	0.3	A2	12	3	3	5	1000	998
0.1	0.3	A3	12	2	3	5	991	991
0.1	0.3	A3	10	3	3	5	992	989
0.1	0.3	A4	10	3	3	5	993	991
0.5	0.7	A1	26	2	4	5	1000	1000
0.5	0.7	A2	16	3	3	5	1000	1000
0.5	0.7	A3	12	2	4	5	998	998
0.5	0.7	A4	14	3	3	5	999	1000
0.8	0.9	A2	30	3	3	5	1000	1000
0.8	0.9	A3	22	2	4	5	1000	1000
0.8	0.9	A4	28	2	4	5	1000	1000
0.8	0.9	A4	24	3	3	5	1000	1000

[a] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[b] Convergence rates (out of 1000) in simulation scenarios for assessing the empirical type I error rate.

[c] Convergence rates (out of 1000) in simulation scenarios for assessing the empirical power.

Web Table 2: Simulation scenarios and empirical type I error rates[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under balanced four-level CRTs. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	0.281	0.070	**0.049**	**0.043**	**0.047**	**0.046**	**0.046**	1000
0.2	0.5	A1	14	2	3	10	0.427	0.078	**0.056**	**0.041**	**0.047**	**0.049**	**0.046**	1000
0.2	0.5	A1	14	2	4	5	0.337	0.070	**0.051**	**0.037**	**0.045**	**0.048**	**0.047**	1000
0.2	0.5	A1	12	3	3	5	0.310	0.070	**0.049**	0.033	**0.042**	**0.038**	**0.042**	1000
0.2	0.5	A2	10	2	3	5	0.145	**0.060**	**0.044**	0.024	0.032	0.033	0.030	1000
0.2	0.5	A2	10	2	3	10	0.293	0.077	**0.054**	0.032	**0.041**	**0.040**	**0.039**	1000
0.2	0.5	A2	10	2	4	5	0.184	0.069	**0.050**	0.034	**0.041**	**0.045**	**0.039**	1000
0.2	0.5	A2	8	3	3	5	0.148	0.074	**0.041**	0.024	0.033	0.034	0.030	1000
0.2	0.5	A3	8	2	3	5	**0.064**	**0.058**	**0.042**	0.020	0.028	0.035	0.022	1000
0.2	0.5	A3	8	3	3	5	0.071	0.076	**0.041**	0.024	0.031	0.035	0.025	1000
0.2	0.5	A4	8	3	3	5	0.104	0.070	**0.047**	0.028	**0.039**	**0.039**	0.032	1000
0.1	0.3	A1	22	2	3	5	0.334	0.074	**0.059**	**0.051**	**0.052**	**0.054**	**0.051**	999
0.1	0.3	A1	20	2	3	10	0.458	0.084	0.072	**0.051**	**0.061**	**0.063**	**0.057**	1000
0.1	0.3	A1	20	2	4	5	0.356	0.077	**0.059**	**0.048**	**0.053**	**0.054**	**0.053**	1000
0.1	0.3	A1	16	3	3	5	0.329	0.073	**0.050**	**0.036**	**0.043**	**0.040**	**0.042**	1000
0.1	0.3	A2	16	2	3	5	0.182	0.075	**0.056**	**0.041**	**0.047**	**0.048**	**0.045**	1000
0.1	0.3	A2	14	2	3	10	0.308	0.073	**0.059**	**0.041**	**0.050**	**0.045**	**0.047**	1000
0.1	0.3	A2	14	2	4	5	0.211	0.080	**0.055**	**0.040**	**0.050**	**0.048**	**0.047**	999
0.1	0.3	A2	12	3	3	5	0.186	0.083	**0.056**	**0.040**	**0.049**	**0.048**	**0.046**	1000
0.1	0.3	A3	12	2	3	5	0.086	0.076	**0.063**	**0.048**	**0.055**	**0.053**	**0.050**	1000
0.1	0.3	A3	10	3	3	5	0.083	**0.062**	**0.041**	0.030	0.032	0.032	0.029	1000
0.1	0.3	A4	10	3	3	5	0.114	0.067	**0.043**	0.026	0.035	0.033	0.030	1000
0.5	0.7	A1	26	2	4	5	0.354	0.066	**0.063**	**0.049**	**0.055**	**0.057**	**0.055**	1000
0.5	0.7	A2	16	3	3	5	0.228	0.065	**0.057**	**0.041**	**0.049**	**0.049**	**0.049**	1000
0.5	0.7	A3	12	2	4	5	0.108	0.070	**0.055**	**0.038**	**0.042**	**0.041**	**0.039**	1000
0.5	0.7	A4	14	3	3	5	0.154	**0.061**	**0.039**	0.033	0.035	0.035	0.035	1000
0.8	0.9	A2	30	3	3	5	0.211	**0.053**	**0.047**	**0.041**	**0.044**	**0.046**	**0.045**	1000
0.8	0.9	A3	22	2	4	5	0.139	**0.056**	**0.047**	**0.037**	**0.039**	**0.039**	**0.040**	1000
0.8	0.9	A4	28	2	4	5	0.190	**0.057**	**0.051**	**0.037**	**0.042**	**0.043**	**0.042**	1000
0.8	0.9	A4	24	3	3	5	0.179	**0.056**	**0.049**	**0.041**	**0.046**	**0.046**	**0.047**	1000

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 3: Simulation scenarios, predicted power, and empirical power[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under balanced four-level CRTs. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	0.986	0.857	**0.822**	0.767	**0.798**	**0.795**	**0.798**	1000
0.2	0.5	A1	14	2	3	10	0.845	0.994	**0.876**	**0.833**	0.790	0.811	0.806	0.813	1000
0.2	0.5	A1	14	2	4	5	0.866	0.996	0.909	**0.884**	**0.854**	**0.871**	**0.869**	**0.872**	1000
0.2	0.5	A1	12	3	3	5	0.857	0.994	0.891	**0.851**	0.793	0.824	0.821	0.827	1000
0.2	0.5	A2	10	2	3	5	0.808	0.977	0.882	**0.812**	0.745	**0.783**	0.777	**0.784**	1000
0.2	0.5	A2	10	2	3	10	0.870	0.996	0.907	**0.863**	0.792	0.829	0.827	0.834	1000
0.2	0.5	A2	10	2	4	5	0.852	0.986	0.897	**0.853**	0.784	0.823	0.820	**0.827**	1000
0.2	0.5	A2	8	3	3	5	0.800	0.983	0.896	**0.826**	0.716	**0.779**	**0.778**	**0.787**	1000
0.2	0.5	A3	8	2	3	5	0.851	0.973	0.923	**0.859**	0.769	0.810	0.811	0.820	1000
0.2	0.5	A3	8	3	3	5	0.936	0.999	0.983	**0.954**	**0.912**	**0.933**	**0.936**	**0.937**	1000
0.2	0.5	A4	8	3	3	5	0.892	0.996	0.960	**0.914**	0.839	**0.877**	**0.874**	**0.882**	1000
0.1	0.3	A1	22	2	3	5	0.829	0.991	0.879	0.856	**0.831**	**0.845**	**0.840**	**0.844**	999
0.1	0.3	A1	20	2	3	10	0.818	0.994	0.866	**0.843**	**0.815**	**0.832**	**0.829**	**0.832**	1000
0.1	0.3	A1	20	2	4	5	0.841	0.991	0.886	**0.858**	**0.830**	**0.844**	**0.840**	**0.844**	1000
0.1	0.3	A1	16	3	3	5	0.805	0.983	0.851	**0.817**	**0.783**	**0.804**	**0.803**	**0.806**	1000
0.1	0.3	A2	16	2	3	5	0.844	0.985	0.907	0.876	**0.834**	**0.858**	**0.853**	**0.860**	1000
0.1	0.3	A2	14	2	3	10	0.849	0.998	0.895	**0.855**	0.808	**0.828**	**0.827**	**0.831**	1000
0.1	0.3	A2	14	2	4	5	0.829	0.984	0.898	0.870	**0.823**	**0.850**	**0.842**	**0.851**	999
0.1	0.3	A2	12	3	3	5	0.826	0.989	0.892	**0.844**	0.798	**0.828**	**0.825**	**0.828**	1000
0.1	0.3	A3	12	2	3	5	0.873	0.978	0.931	**0.893**	**0.855**	**0.878**	**0.875**	**0.878**	1000
0.1	0.3	A3	10	3	3	5	0.898	0.989	0.959	**0.917**	**0.872**	**0.893**	**0.891**	**0.896**	1000
0.1	0.3	A4	10	3	3	5	0.837	0.986	0.919	0.878	0.800	**0.840**	**0.830**	**0.845**	1000
0.5	0.7	A1	26	2	4	5	0.823	0.988	0.854	**0.838**	**0.814**	**0.825**	**0.825**	**0.825**	1000
0.5	0.7	A2	16	3	3	5	0.831	0.976	0.864	**0.831**	0.789	**0.810**	**0.813**	**0.811**	1000
0.5	0.7	A3	12	2	4	5	0.827	0.937	0.860	**0.825**	0.778	0.800	**0.806**	0.799	1000
0.5	0.7	A4	14	3	3	5	0.868	0.974	**0.894**	**0.861**	0.814	0.835	0.835	0.835	1000
0.8	0.9	A2	30	3	3	5	0.804	0.967	0.838	**0.818**	**0.800**	**0.810**	**0.810**	**0.811**	1000
0.8	0.9	A3	22	2	4	5	0.804	0.938	**0.829**	**0.810**	**0.788**	**0.801**	**0.805**	**0.803**	1000
0.8	0.9	A4	28	2	4	5	0.824	0.967	**0.850**	**0.839**	**0.826**	**0.836**	**0.837**	**0.836**	1000
0.8	0.9	A4	24	3	3	5	0.813	0.957	0.847	**0.823**	**0.799**	**0.810**	**0.811**	**0.812**	1000

[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

Web Table 4: Simulation scenarios and empirical type I error rates[a] of GEE/MAEE analyses based on different variance estimators, using the extended nested exchangeable working correlation structure under unbalanced four-level CRTs with CV = 0.25. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	**0.048**	0.073	**0.054**	**0.042**	**0.048**	**0.050**	**0.045**	997
0.2	0.5	A1	14	2	3	10	**0.040**	0.070	**0.053**	0.035	**0.045**	**0.044**	**0.040**	999
0.2	0.5	A1	14	2	4	5	**0.039**	0.072	**0.049**	0.033	**0.041**	**0.043**	**0.036**	999
0.2	0.5	A1	12	3	3	5	**0.046**	0.071	**0.055**	**0.038**	**0.049**	**0.047**	**0.046**	998
0.2	0.5	A2	10	2	3	5	**0.039**	0.067	**0.047**	0.022	0.031	0.032	0.029	998
0.2	0.5	A2	10	2	3	10	**0.045**	0.082	**0.050**	**0.036**	**0.038**	**0.039**	**0.038**	998
0.2	0.5	A2	10	2	4	5	**0.046**	0.077	**0.059**	0.032	**0.042**	**0.038**	**0.037**	997
0.2	0.5	A2	8	3	3	5	0.033	0.070	**0.046**	0.022	0.028	0.033	0.023	943
0.2	0.5	A3	8	2	3	5	0.023	**0.055**	0.030	0.014	0.019	0.020	0.017	860
0.2	0.5	A3	8	3	3	5	0.034	**0.053**	0.034	0.018	0.025	0.028	0.024	888
0.2	0.5	A4	8	3	3	5	0.035	0.066	0.035	0.016	0.027	0.025	0.022	925
0.1	0.3	A1	22	2	3	5	0.033	**0.060**	**0.054**	**0.046**	**0.049**	**0.049**	**0.046**	980
0.1	0.3	A1	20	2	3	10	**0.038**	0.076	**0.062**	**0.045**	**0.053**	**0.053**	**0.049**	988
0.1	0.3	A1	20	2	4	5	0.035	0.068	**0.054**	**0.044**	**0.047**	**0.048**	**0.045**	993
0.1	0.3	A1	16	3	3	5	**0.047**	0.078	**0.061**	**0.046**	**0.054**	**0.054**	**0.051**	998
0.1	0.3	A2	16	2	3	5	**0.037**	**0.063**	**0.053**	**0.036**	**0.044**	**0.042**	**0.039**	994
0.1	0.3	A2	14	2	3	10	**0.046**	0.078	0.067	**0.048**	**0.058**	**0.057**	**0.054**	998
0.1	0.3	A2	14	2	4	5	**0.041**	0.074	**0.056**	**0.042**	**0.049**	**0.047**	**0.045**	997
0.1	0.3	A2	12	3	3	5	**0.037**	0.072	**0.055**	0.035	**0.043**	**0.043**	**0.037**	997
0.1	0.3	A3	12	2	3	5	**0.047**	0.077	**0.056**	**0.037**	**0.048**	**0.044**	**0.041**	989
0.1	0.3	A3	10	3	3	5	**0.045**	0.077	**0.051**	0.030	**0.041**	**0.043**	**0.036**	987
0.1	0.3	A4	10	3	3	5	**0.044**	0.072	**0.052**	**0.036**	**0.042**	**0.042**	**0.038**	989
0.5	0.7	A1	26	2	4	5	**0.053**	**0.060**	**0.056**	**0.047**	**0.052**	**0.052**	**0.052**	1000
0.5	0.7	A2	16	3	3	5	**0.053**	**0.064**	**0.050**	**0.037**	**0.042**	**0.041**	**0.042**	1000
0.5	0.7	A3	12	2	4	5	**0.061**	0.081	**0.059**	**0.038**	**0.049**	**0.051**	**0.045**	996
0.5	0.7	A4	14	3	3	5	**0.051**	0.072	**0.049**	**0.036**	**0.039**	**0.041**	**0.039**	1000
0.8	0.9	A2	30	3	3	5	**0.048**	**0.053**	**0.051**	**0.043**	**0.048**	**0.048**	**0.048**	1000
0.8	0.9	A3	22	2	4	5	**0.049**	**0.060**	**0.050**	**0.042**	**0.047**	**0.045**	**0.046**	1000
0.8	0.9	A4	28	2	4	5	**0.039**	**0.043**	**0.040**	**0.038**	**0.040**	**0.040**	**0.040**	1000
0.8	0.9	A4	24	3	3	5	**0.058**	0.069	0.065	**0.048**	**0.055**	**0.056**	**0.053**	1000

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 5: Simulation scenarios, predicted power, and empirical power[a] of GEE/MAEE analyses based on different variance estimators, using the extended nested exchangeable working correlation structure under unbalanced four-level CRTs with CV = 0.25. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	**0.805**	**0.841**	**0.798**	0.761	0.773	0.778	0.774	997
0.2	0.5	A1	14	2	3	10	0.845	**0.855**	0.891	**0.858**	0.812	**0.835**	**0.832**	**0.827**	1000
0.2	0.5	A1	14	2	4	5	0.866	**0.873**	0.901	**0.870**	0.826	**0.846**	**0.845**	**0.846**	999
0.2	0.5	A1	12	3	3	5	0.857	**0.852**	0.891	**0.845**	0.799	0.823	0.822	0.821	1000
0.2	0.5	A2	10	2	3	5	0.808	**0.834**	0.880	**0.826**	0.754	**0.794**	**0.793**	**0.789**	985
0.2	0.5	A2	10	2	3	10	0.870	**0.885**	0.925	**0.880**	0.816	**0.849**	**0.850**	**0.845**	996
0.2	0.5	A2	10	2	4	5	0.852	**0.877**	0.925	**0.869**	0.810	**0.844**	**0.840**	**0.839**	995
0.2	0.5	A2	8	3	3	5	0.800	**0.807**	0.876	**0.800**	0.691	0.750	0.746	0.742	920
0.2	0.5	A3	8	2	3	5	0.851	**0.844**	0.912	**0.855**	0.732	0.791	0.785	0.777	867
0.2	0.5	A3	8	3	3	5	0.936	**0.945**	0.971	**0.944**	0.894	**0.922**	**0.919**	**0.913**	877
0.2	0.5	A4	8	3	3	5	0.892	**0.911**	0.951	**0.910**	0.830	**0.873**	**0.873**	0.862	932
0.1	0.3	A1	22	2	3	5	0.829	0.859	0.878	**0.852**	**0.827**	**0.839**	**0.838**	**0.839**	985
0.1	0.3	A1	20	2	3	10	0.818	0.859	0.877	0.849	**0.827**	**0.836**	**0.834**	**0.836**	985
0.1	0.3	A1	20	2	4	5	0.841	**0.857**	0.879	**0.848**	**0.817**	**0.834**	**0.831**	**0.835**	991
0.1	0.3	A1	16	3	3	5	0.805	0.837	0.870	0.835	**0.799**	**0.817**	**0.814**	**0.816**	992
0.1	0.3	A2	16	2	3	5	0.844	0.880	0.894	0.871	**0.841**	**0.854**	**0.852**	**0.852**	993
0.1	0.3	A2	14	2	3	10	0.849	**0.874**	0.901	0.876	**0.834**	**0.857**	**0.853**	**0.853**	998
0.1	0.3	A2	14	2	4	5	0.829	0.858	0.880	**0.843**	**0.806**	**0.825**	**0.824**	**0.825**	996
0.1	0.3	A2	12	3	3	5	0.826	0.867	0.901	0.860	**0.802**	**0.828**	**0.829**	**0.828**	996
0.1	0.3	A3	12	2	3	5	0.873	0.910	0.934	0.906	**0.856**	**0.884**	**0.879**	**0.884**	989
0.1	0.3	A3	10	3	3	5	0.898	**0.921**	0.953	**0.920**	0.871	**0.902**	**0.895**	**0.892**	972
0.1	0.3	A4	10	3	3	5	0.837	0.873	0.914	0.865	0.810	**0.839**	**0.840**	**0.837**	977
0.5	0.7	A1	26	2	4	5	0.823	**0.832**	**0.849**	**0.834**	**0.809**	**0.823**	**0.823**	**0.822**	1000
0.5	0.7	A2	16	3	3	5	0.831	**0.817**	**0.846**	**0.816**	0.779	0.804	0.803	0.801	1000
0.5	0.7	A3	12	2	4	5	0.827	**0.834**	0.880	**0.827**	0.784	**0.807**	**0.809**	**0.803**	996
0.5	0.7	A4	14	3	3	5	0.868	**0.877**	0.905	**0.870**	0.831	**0.852**	**0.851**	**0.850**	1000
0.8	0.9	A2	30	3	3	5	0.804	**0.822**	0.836	**0.821**	**0.798**	**0.811**	**0.813**	**0.808**	1000
0.8	0.9	A3	22	2	4	5	0.804	**0.804**	**0.830**	**0.800**	0.773	**0.784**	**0.788**	**0.783**	999
0.8	0.9	A4	28	2	4	5	0.824	**0.832**	**0.846**	**0.827**	**0.801**	**0.815**	**0.816**	**0.812**	998
0.8	0.9	A4	24	3	3	5	0.813	**0.812**	**0.832**	**0.807**	**0.790**	**0.801**	**0.803**	**0.800**	999

[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

Web Table 6: Simulation scenarios and empirical type I error rates[a] of GEE/MAEE analyses based on different variance estimators, using the extended nested exchangeable working correlation structure under unbalanced four-level CRTs with CV = 0.50. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	**0.047**	**0.064**	**0.050**	**0.037**	**0.043**	**0.039**	**0.039**	996
0.2	0.5	A1	14	2	3	10	**0.053**	0.085	**0.060**	**0.047**	**0.050**	**0.051**	**0.049**	1000
0.2	0.5	A1	14	2	4	5	**0.056**	0.079	**0.060**	**0.048**	**0.056**	**0.054**	**0.049**	999
0.2	0.5	A1	12	3	3	5	**0.042**	0.069	**0.054**	0.034	**0.044**	**0.041**	**0.039**	998
0.2	0.5	A2	10	2	3	5	**0.039**	0.066	**0.045**	0.030	**0.039**	**0.037**	**0.038**	974
0.2	0.5	A2	10	2	3	10	**0.043**	0.079	**0.050**	0.032	**0.039**	**0.039**	**0.036**	984
0.2	0.5	A2	10	2	4	5	**0.036**	0.074	**0.046**	0.027	0.035	0.035	0.030	990
0.2	0.5	A2	8	3	3	5	0.032	0.070	**0.037**	0.012	0.025	0.024	0.018	884
0.2	0.5	A3	8	2	3	5	0.025	**0.045**	0.025	0.011	0.018	0.017	0.016	760
0.2	0.5	A3	8	3	3	5	0.028	**0.054**	0.030	0.017	0.022	0.022	0.021	827
0.2	0.5	A4	8	3	3	5	0.017	**0.050**	0.024	0.009	0.015	0.018	0.013	848
0.1	0.3	A1	22	2	3	5	**0.041**	**0.064**	**0.049**	**0.042**	**0.046**	**0.047**	**0.046**	967
0.1	0.3	A1	20	2	3	10	**0.038**	0.068	**0.049**	**0.041**	**0.045**	**0.041**	**0.040**	977
0.1	0.3	A1	20	2	4	5	0.034	**0.064**	**0.053**	**0.046**	**0.049**	**0.049**	**0.046**	989
0.1	0.3	A1	16	3	3	5	**0.036**	0.069	**0.056**	**0.043**	**0.045**	**0.045**	**0.043**	988
0.1	0.3	A2	16	2	3	5	**0.037**	0.065	**0.053**	**0.037**	**0.048**	**0.046**	**0.044**	988
0.1	0.3	A2	14	2	3	10	0.034	0.069	**0.050**	**0.038**	**0.040**	**0.039**	**0.039**	985
0.1	0.3	A2	14	2	4	5	0.034	0.072	**0.052**	**0.044**	**0.047**	**0.043**	**0.043**	992
0.1	0.3	A2	12	3	3	5	**0.051**	0.075	**0.055**	**0.040**	**0.049**	**0.045**	**0.045**	993
0.1	0.3	A3	12	2	3	5	**0.049**	0.072	**0.056**	**0.038**	**0.048**	**0.047**	**0.044**	963
0.1	0.3	A3	10	3	3	5	**0.041**	0.067	**0.056**	**0.037**	**0.042**	**0.040**	**0.037**	956
0.1	0.3	A4	10	3	3	5	**0.041**	0.080	**0.052**	0.033	**0.040**	**0.038**	**0.039**	960
0.5	0.7	A1	26	2	4	5	**0.045**	**0.051**	**0.040**	0.031	0.035	0.035	0.035	1000
0.5	0.7	A2	16	3	3	5	**0.048**	**0.058**	**0.045**	0.033	**0.037**	**0.037**	**0.037**	999
0.5	0.7	A3	12	2	4	5	**0.047**	0.070	**0.046**	0.032	**0.039**	**0.039**	**0.037**	992
0.5	0.7	A4	14	3	3	5	**0.056**	0.071	**0.056**	**0.037**	**0.044**	**0.045**	**0.044**	998
0.8	0.9	A2	30	3	3	5	**0.056**	**0.064**	**0.056**	**0.043**	**0.048**	**0.049**	**0.048**	1000
0.8	0.9	A3	22	2	4	5	**0.050**	**0.061**	**0.050**	**0.041**	**0.045**	**0.046**	**0.044**	1000
0.8	0.9	A4	28	2	4	5	**0.042**	**0.050**	**0.045**	**0.037**	**0.042**	**0.040**	**0.042**	1000
0.8	0.9	A4	24	3	3	5	**0.048**	**0.060**	**0.048**	**0.044**	**0.045**	**0.045**	**0.045**	1000

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 7: Simulation scenarios, predicted power, and empirical power[a] of GEE/MAEE analyses based on different variance estimators, using the extended nested exchangeable working correlation structure under unbalanced four-level CRTs with CV = 0.50. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	**0.841**	0.879	**0.834**	0.787	**0.811**	**0.810**	**0.807**	994
0.2	0.5	A1	14	2	3	10	0.845	**0.843**	0.874	**0.843**	0.797	**0.827**	**0.824**	**0.823**	999
0.2	0.5	A1	14	2	4	5	0.866	**0.873**	0.903	**0.870**	0.821	**0.848**	**0.848**	**0.848**	997
0.2	0.5	A1	12	3	3	5	0.857	**0.865**	0.902	**0.861**	0.808	0.830	**0.832**	0.829	999
0.2	0.5	A2	10	2	3	5	0.808	**0.799**	0.861	**0.799**	0.724	0.761	0.760	0.755	975
0.2	0.5	A2	10	2	3	10	0.870	**0.868**	0.926	**0.879**	0.816	**0.851**	**0.847**	0.842	988
0.2	0.5	A2	10	2	4	5	0.852	**0.872**	0.916	**0.861**	0.774	**0.829**	0.820	0.819	991
0.2	0.5	A2	8	3	3	5	0.800	**0.796**	0.861	**0.782**	0.688	0.746	0.733	0.734	890
0.2	0.5	A3	8	2	3	5	0.851	**0.834**	0.896	**0.838**	0.724	0.786	0.781	0.778	767
0.2	0.5	A3	8	3	3	5	0.936	**0.942**	0.969	**0.942**	0.883	**0.918**	**0.912**	**0.913**	814
0.2	0.5	A4	8	3	3	5	0.892	**0.901**	0.946	**0.895**	0.811	0.854	0.859	0.850	856
0.1	0.3	A1	22	2	3	5	0.829	**0.849**	0.866	**0.840**	**0.815**	**0.827**	**0.826**	**0.828**	967
0.1	0.3	A1	20	2	3	10	0.818	0.854	0.875	0.847	**0.822**	**0.832**	**0.829**	**0.832**	967
0.1	0.3	A1	20	2	4	5	0.841	**0.853**	0.872	**0.852**	**0.819**	**0.837**	**0.835**	**0.834**	989
0.1	0.3	A1	16	3	3	5	0.805	**0.818**	0.859	**0.814**	0.760	**0.789**	**0.784**	**0.784**	991
0.1	0.3	A2	16	2	3	5	0.844	**0.869**	0.897	**0.867**	**0.823**	**0.843**	**0.844**	**0.840**	991
0.1	0.3	A2	14	2	3	10	0.849	**0.866**	0.890	**0.863**	**0.832**	**0.851**	**0.854**	**0.854**	996
0.1	0.3	A2	14	2	4	5	0.829	**0.848**	0.879	**0.846**	0.800	**0.827**	**0.822**	**0.824**	991
0.1	0.3	A2	12	3	3	5	0.826	**0.846**	0.883	**0.844**	0.796	**0.816**	**0.820**	**0.821**	995
0.1	0.3	A3	12	2	3	5	0.873	**0.896**	0.914	**0.885**	0.839	**0.866**	**0.863**	**0.862**	975
0.1	0.3	A3	10	3	3	5	0.898	**0.910**	0.944	**0.904**	0.859	**0.886**	**0.878**	**0.880**	959
0.1	0.3	A4	10	3	3	5	0.837	0.867	0.910	**0.858**	0.806	**0.833**	**0.829**	**0.827**	971
0.5	0.7	A1	26	2	4	5	0.823	**0.828**	0.851	**0.828**	**0.807**	**0.820**	**0.818**	**0.817**	1000
0.5	0.7	A2	16	3	3	5	0.831	0.802	**0.846**	**0.805**	0.765	0.786	0.785	0.781	1000
0.5	0.7	A3	12	2	4	5	0.827	**0.810**	0.859	**0.806**	0.757	0.778	0.782	0.776	989
0.5	0.7	A4	14	3	3	5	0.868	**0.883**	0.913	**0.881**	0.837	**0.863**	**0.868**	**0.859**	999
0.8	0.9	A2	30	3	3	5	0.804	**0.803**	**0.813**	**0.797**	**0.783**	**0.789**	**0.789**	**0.790**	1000
0.8	0.9	A3	22	2	4	5	0.804	**0.813**	0.833	**0.811**	**0.779**	**0.796**	**0.798**	**0.794**	999
0.8	0.9	A4	28	2	4	5	0.824	**0.820**	**0.834**	**0.821**	0.795	**0.806**	**0.809**	**0.806**	998
0.8	0.9	A4	24	3	3	5	0.813	**0.821**	0.845	**0.818**	**0.795**	**0.808**	**0.809**	**0.807**	1000

[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

Web Table 8: Simulation scenarios and empirical type I error rates[a] of GEE/MAEE analyses based on different variance estimators, using the extended nested exchangeable working correlation structure under unbalanced four-level CRTs with CV = 0.75. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	**0.056**	0.067	**0.048**	0.033	**0.042**	**0.039**	**0.040**	983
0.2	0.5	A1	14	2	3	10	**0.060**	0.074	**0.053**	**0.043**	**0.046**	**0.047**	**0.046**	973
0.2	0.5	A1	14	2	4	5	**0.047**	0.065	**0.049**	**0.039**	**0.043**	**0.043**	**0.041**	989
0.2	0.5	A1	12	3	3	5	**0.050**	**0.062**	**0.048**	0.034	**0.042**	**0.041**	**0.039**	983
0.2	0.5	A2	10	2	3	5	**0.045**	0.075	**0.058**	**0.038**	**0.044**	**0.046**	**0.042**	933
0.2	0.5	A2	10	2	3	10	**0.060**	0.091	**0.056**	**0.039**	**0.045**	**0.049**	**0.040**	946
0.2	0.5	A2	10	2	4	5	**0.044**	0.065	**0.045**	0.031	**0.038**	**0.038**	0.031	956
0.2	0.5	A2	8	3	3	5	0.034	0.070	**0.039**	0.017	0.028	0.027	0.023	816
0.2	0.5	A3	8	2	3	5	0.027	**0.044**	0.024	0.014	0.017	0.015	0.017	662
0.2	0.5	A3	8	3	3	5	0.027	**0.058**	0.027	0.011	0.015	0.016	0.014	739
0.2	0.5	A4	8	3	3	5	0.031	**0.057**	**0.037**	0.021	0.026	0.030	0.024	776
0.1	0.3	A1	22	2	3	5	**0.036**	**0.061**	**0.048**	**0.040**	**0.043**	**0.042**	**0.040**	934
0.1	0.3	A1	20	2	3	10	**0.039**	**0.063**	**0.049**	**0.042**	**0.046**	**0.047**	**0.043**	945
0.1	0.3	A1	20	2	4	5	0.035	**0.060**	**0.049**	**0.037**	**0.040**	**0.043**	**0.039**	968
0.1	0.3	A1	16	3	3	5	**0.044**	0.073	**0.062**	**0.049**	**0.056**	**0.053**	**0.046**	968
0.1	0.3	A2	16	2	3	5	0.033	0.070	**0.053**	**0.038**	**0.048**	**0.042**	**0.041**	966
0.1	0.3	A2	14	2	3	10	**0.039**	0.071	**0.047**	0.035	**0.044**	**0.041**	**0.038**	964
0.1	0.3	A2	14	2	4	5	**0.041**	0.075	**0.054**	**0.038**	**0.048**	**0.044**	**0.043**	978
0.1	0.3	A2	12	3	3	5	**0.044**	0.079	**0.064**	**0.049**	**0.053**	**0.053**	**0.048**	973
0.1	0.3	A3	12	2	3	5	0.027	**0.062**	**0.039**	0.023	0.031	0.028	0.024	932
0.1	0.3	A3	10	3	3	5	0.035	0.074	**0.048**	0.028	**0.037**	0.034	0.031	917
0.1	0.3	A4	10	3	3	5	0.032	0.073	**0.045**	0.028	0.035	0.032	0.030	902
0.5	0.7	A1	26	2	4	5	**0.047**	**0.053**	**0.046**	**0.037**	**0.041**	**0.042**	**0.038**	1000
0.5	0.7	A2	16	3	3	5	**0.054**	0.068	**0.051**	**0.036**	**0.041**	**0.042**	**0.042**	997
0.5	0.7	A3	12	2	4	5	**0.051**	0.071	**0.046**	0.035	**0.038**	**0.039**	**0.038**	971
0.5	0.7	A4	14	3	3	5	0.067	0.077	0.069	**0.053**	**0.059**	**0.059**	**0.057**	985
0.8	0.9	A2	30	3	3	5	**0.053**	**0.058**	**0.048**	**0.040**	**0.044**	**0.043**	**0.044**	1000
0.8	0.9	A3	22	2	4	5	0.034	**0.049**	**0.038**	0.028	0.033	0.034	0.031	999
0.8	0.9	A4	28	2	4	5	**0.042**	**0.051**	**0.041**	0.033	**0.036**	**0.038**	**0.036**	1000
0.8	0.9	A4	24	3	3	5	0.035	**0.051**	**0.040**	0.030	0.033	0.034	0.033	997

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 9: Simulation scenarios, predicted power, and empirical power[a] of GEE/MAEE analyses based on different variance estimators, using the extended nested exchangeable working correlation structure under unbalanced four-level CRTs with CV = 0.75. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	**0.814**	0.845	**0.811**	0.747	0.783	0.779	0.777	984
0.2	0.5	A1	14	2	3	10	0.845	**0.840**	0.887	**0.858**	0.807	**0.827**	**0.828**	**0.822**	979
0.2	0.5	A1	14	2	4	5	0.866	**0.862**	0.900	**0.857**	0.818	0.838	0.839	0.834	994
0.2	0.5	A1	12	3	3	5	0.857	**0.848**	0.891	**0.855**	0.798	0.827	0.826	0.821	981
0.2	0.5	A2	10	2	3	5	0.808	**0.797**	0.871	**0.801**	0.728	0.768	0.768	0.759	935
0.2	0.5	A2	10	2	3	10	0.870	**0.871**	0.911	**0.870**	0.800	0.840	0.834	0.828	948
0.2	0.5	A2	10	2	4	5	0.852	**0.846**	0.911	**0.860**	0.791	0.824	0.823	0.818	973
0.2	0.5	A2	8	3	3	5	0.800	**0.788**	0.883	**0.797**	0.681	0.744	0.732	0.730	831
0.2	0.5	A3	8	2	3	5	0.851	**0.833**	0.893	0.821	0.720	0.778	0.767	0.758	653
0.2	0.5	A3	8	3	3	5	0.936	**0.935**	0.968	**0.940**	0.876	**0.913**	**0.913**	0.908	739
0.2	0.5	A4	8	3	3	5	0.892	**0.886**	0.929	**0.900**	0.822	**0.868**	0.865	0.856	763
0.1	0.3	A1	22	2	3	5	0.829	**0.853**	0.877	0.860	**0.832**	**0.841**	**0.842**	**0.843**	955
0.1	0.3	A1	20	2	3	10	0.818	**0.825**	0.861	**0.824**	**0.793**	**0.810**	**0.808**	**0.807**	962
0.1	0.3	A1	20	2	4	5	0.841	0.868	0.890	0.870	**0.845**	**0.862**	**0.855**	**0.858**	975
0.1	0.3	A1	16	3	3	5	0.805	**0.818**	0.866	**0.829**	**0.782**	**0.810**	**0.805**	**0.801**	984
0.1	0.3	A2	16	2	3	5	0.844	**0.870**	0.900	0.871	**0.836**	**0.855**	**0.851**	**0.852**	980
0.1	0.3	A2	14	2	3	10	0.849	**0.861**	0.893	**0.868**	0.820	**0.842**	**0.839**	**0.839**	969
0.1	0.3	A2	14	2	4	5	0.829	**0.832**	0.868	**0.827**	0.782	**0.808**	0.801	**0.803**	984
0.1	0.3	A2	12	3	3	5	0.826	**0.837**	0.891	**0.844**	0.786	**0.820**	**0.810**	**0.812**	983
0.1	0.3	A3	12	2	3	5	0.873	**0.880**	0.923	**0.886**	0.838	**0.864**	**0.851**	**0.860**	920
0.1	0.3	A3	10	3	3	5	0.898	**0.914**	0.944	**0.915**	0.854	**0.890**	**0.882**	**0.885**	910
0.1	0.3	A4	10	3	3	5	0.837	**0.863**	0.900	**0.863**	0.798	**0.830**	**0.831**	**0.827**	913
0.5	0.7	A1	26	2	4	5	0.823	**0.809**	**0.833**	**0.807**	0.784	**0.797**	**0.797**	**0.797**	1000
0.5	0.7	A2	16	3	3	5	0.831	0.799	**0.842**	0.792	0.757	0.776	0.779	0.774	999
0.5	0.7	A3	12	2	4	5	0.827	0.777	**0.831**	0.784	0.727	0.761	0.766	0.754	973
0.5	0.7	A4	14	3	3	5	0.868	**0.869**	**0.889**	**0.867**	0.838	**0.852**	**0.854**	**0.850**	985
0.8	0.9	A2	30	3	3	5	0.804	**0.804**	**0.821**	**0.797**	**0.786**	**0.789**	**0.789**	**0.789**	1000
0.8	0.9	A3	22	2	4	5	0.804	**0.802**	**0.825**	**0.794**	0.767	0.777	**0.781**	**0.779**	999
0.8	0.9	A4	28	2	4	5	0.824	**0.812**	**0.827**	**0.815**	**0.798**	**0.808**	**0.810**	**0.806**	1000
0.8	0.9	A4	24	3	3	5	0.813	**0.820**	0.841	**0.821**	**0.796**	**0.806**	**0.810**	**0.805**	990

[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

Web Table 10: Simulation scenarios and empirical type I error rates[a] of GEE/MAEE analyses based on different variance estimators, using the extended nested exchangeable working correlation structure under unbalanced four-level CRTs with CV = 1.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	**0.048**	0.072	**0.051**	**0.036**	**0.045**	**0.042**	**0.042**	929
0.2	0.5	A1	14	2	3	10	**0.048**	**0.060**	**0.046**	0.035	**0.040**	**0.043**	**0.039**	932
0.2	0.5	A1	14	2	4	5	**0.052**	**0.061**	**0.043**	0.033	0.035	**0.038**	0.034	967
0.2	0.5	A1	12	3	3	5	**0.052**	0.072	**0.053**	**0.038**	**0.047**	**0.049**	**0.042**	958
0.2	0.5	A2	10	2	3	5	**0.038**	**0.059**	**0.038**	0.019	0.027	0.026	0.025	877
0.2	0.5	A2	10	2	3	10	**0.050**	0.084	**0.056**	**0.036**	**0.042**	**0.044**	**0.040**	858
0.2	0.5	A2	10	2	4	5	**0.040**	0.069	**0.043**	0.025	**0.036**	**0.037**	0.033	917
0.2	0.5	A2	8	3	3	5	0.023	**0.053**	0.023	0.005	0.008	0.012	0.005	767
0.2	0.5	A3	8	2	3	5	0.026	0.067	**0.040**	0.012	0.022	0.019	0.012	581
0.2	0.5	A3	8	3	3	5	0.016	**0.047**	0.019	0.007	0.010	0.012	0.009	684
0.2	0.5	A4	8	3	3	5	0.023	**0.053**	0.023	0.014	0.017	0.019	0.014	694
0.1	0.3	A1	22	2	3	5	0.032	**0.050**	**0.042**	0.035	**0.036**	0.034	0.032	895
0.1	0.3	A1	20	2	3	10	**0.045**	0.071	**0.061**	**0.049**	**0.056**	**0.052**	**0.049**	890
0.1	0.3	A1	20	2	4	5	**0.043**	**0.064**	**0.046**	0.035	**0.040**	**0.038**	**0.038**	936
0.1	0.3	A1	16	3	3	5	**0.041**	**0.061**	**0.045**	0.034	**0.036**	0.032	0.032	937
0.1	0.3	A2	16	2	3	5	**0.041**	0.065	**0.050**	**0.039**	**0.041**	**0.040**	**0.037**	941
0.1	0.3	A2	14	2	3	10	**0.042**	0.071	**0.053**	**0.038**	**0.042**	**0.038**	**0.041**	903
0.1	0.3	A2	14	2	4	5	**0.047**	0.077	**0.057**	**0.045**	**0.051**	**0.047**	**0.047**	952
0.1	0.3	A2	12	3	3	5	**0.039**	0.072	**0.051**	**0.037**	**0.043**	**0.044**	**0.038**	954
0.1	0.3	A3	12	2	3	5	**0.036**	**0.062**	**0.036**	0.022	0.028	0.029	0.027	861
0.1	0.3	A3	10	3	3	5	0.033	**0.060**	**0.044**	0.025	0.030	0.031	0.030	868
0.1	0.3	A4	10	3	3	5	**0.040**	0.084	**0.053**	0.029	**0.039**	**0.037**	0.033	829
0.5	0.7	A1	26	2	4	5	**0.050**	**0.062**	**0.052**	**0.047**	**0.051**	**0.051**	**0.051**	999
0.5	0.7	A2	16	3	3	5	**0.038**	**0.054**	**0.038**	0.029	0.033	0.033	0.032	996
0.5	0.7	A3	12	2	4	5	**0.054**	0.087	0.069	**0.047**	**0.055**	**0.060**	**0.053**	924
0.5	0.7	A4	14	3	3	5	**0.057**	0.069	**0.056**	**0.042**	**0.052**	**0.053**	**0.051**	961
0.8	0.9	A2	30	3	3	5	**0.046**	**0.049**	**0.045**	**0.040**	**0.043**	**0.042**	**0.043**	1000
0.8	0.9	A3	22	2	4	5	**0.059**	0.071	**0.062**	**0.052**	**0.056**	**0.057**	**0.056**	994
0.8	0.9	A4	28	2	4	5	0.028	**0.039**	0.030	0.025	0.025	0.025	0.025	994
0.8	0.9	A4	24	3	3	5	**0.038**	**0.060**	**0.046**	0.032	**0.036**	0.034	0.035	988

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 11: Simulation scenarios, predicted power, and empirical power[a] of GEE/MAEE analyses based on different variance estimators, using the extended nested exchangeable working correlation structure under unbalanced four-level CRTs with CV = 1.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	**0.834**	0.879	0.844	0.788	**0.813**	**0.807**	**0.806**	953
0.2	0.5	A1	14	2	3	10	0.845	**0.838**	0.878	**0.847**	0.798	0.815	0.813	0.810	939
0.2	0.5	A1	14	2	4	5	0.866	**0.881**	0.922	0.894	**0.844**	**0.868**	**0.867**	**0.862**	977
0.2	0.5	A1	12	3	3	5	0.857	**0.869**	0.912	**0.876**	0.829	**0.859**	**0.849**	**0.848**	969
0.2	0.5	A2	10	2	3	5	0.808	**0.791**	0.860	**0.808**	0.717	0.758	0.752	0.747	879
0.2	0.5	A2	10	2	3	10	0.870	**0.845**	0.912	**0.861**	0.795	0.827	0.821	0.821	877
0.2	0.5	A2	10	2	4	5	0.852	**0.861**	0.910	**0.867**	0.807	**0.841**	**0.842**	**0.835**	922
0.2	0.5	A2	8	3	3	5	0.800	**0.790**	0.876	**0.807**	0.697	0.749	0.745	0.728	753
0.2	0.5	A3	8	2	3	5	0.851	0.801	0.887	0.817	0.708	0.763	0.771	0.765	558
0.2	0.5	A3	8	3	3	5	0.936	**0.930**	0.975	**0.938**	0.869	0.906	**0.910**	0.900	647
0.2	0.5	A4	8	3	3	5	0.892	**0.897**	0.953	**0.904**	0.817	0.858	0.860	0.849	677
0.1	0.3	A1	22	2	3	5	0.829	**0.830**	**0.852**	**0.835**	**0.805**	**0.821**	**0.823**	**0.819**	924
0.1	0.3	A1	20	2	3	10	0.818	**0.809**	0.846	**0.808**	0.784	**0.794**	**0.794**	**0.794**	911
0.1	0.3	A1	20	2	4	5	0.841	0.869	0.888	0.869	**0.836**	**0.850**	**0.847**	**0.845**	954
0.1	0.3	A1	16	3	3	5	0.805	**0.824**	0.854	**0.818**	0.776	**0.790**	**0.795**	**0.793**	961
0.1	0.3	A2	16	2	3	5	0.844	**0.844**	0.888	**0.848**	0.809	**0.830**	**0.825**	**0.825**	954
0.1	0.3	A2	14	2	3	10	0.849	**0.862**	0.890	**0.857**	0.799	**0.835**	**0.829**	**0.826**	937
0.1	0.3	A2	14	2	4	5	0.829	**0.829**	0.874	**0.827**	0.778	**0.805**	**0.806**	**0.805**	967
0.1	0.3	A2	12	3	3	5	0.826	**0.837**	0.867	**0.834**	0.779	**0.807**	**0.805**	**0.808**	974
0.1	0.3	A3	12	2	3	5	0.873	**0.868**	0.917	**0.871**	0.820	0.845	0.841	0.841	866
0.1	0.3	A3	10	3	3	5	0.898	**0.911**	0.941	**0.904**	0.856	**0.880**	**0.881**	**0.878**	869
0.1	0.3	A4	10	3	3	5	0.837	0.871	0.922	0.875	0.810	**0.843**	**0.835**	**0.835**	859
0.5	0.7	A1	26	2	4	5	0.823	0.766	0.790	0.767	0.744	0.753	0.755	0.754	1000
0.5	0.7	A2	16	3	3	5	0.831	**0.812**	**0.842**	**0.809**	0.770	0.790	0.792	0.783	995
0.5	0.7	A3	12	2	4	5	0.827	0.792	0.856	**0.807**	0.740	0.774	0.780	0.765	938
0.5	0.7	A4	14	3	3	5	0.868	**0.889**	0.917	**0.890**	**0.852**	**0.872**	**0.873**	**0.869**	955
0.8	0.9	A2	30	3	3	5	0.804	**0.802**	**0.820**	**0.791**	0.769	**0.780**	**0.783**	**0.779**	999
0.8	0.9	A3	22	2	4	5	0.804	**0.799**	**0.828**	**0.802**	0.770	**0.783**	**0.787**	**0.784**	993
0.8	0.9	A4	28	2	4	5	0.824	**0.829**	**0.846**	**0.834**	**0.811**	**0.823**	**0.825**	**0.822**	985
0.8	0.9	A4	24	3	3	5	0.813	**0.833**	0.855	**0.829**	**0.802**	**0.814**	**0.815**	**0.812**	982

[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

Web Table 12: Simulation scenarios and empirical type I error rates[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under unbalanced four-level CRTs with CV = 0.25. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	0.309	0.078	**0.058**	**0.042**	**0.047**	**0.046**	**0.048**	1000
0.2	0.5	A1	14	2	3	10	0.417	0.073	**0.055**	**0.041**	**0.048**	**0.047**	**0.048**	1000
0.2	0.5	A1	14	2	4	5	0.321	0.070	**0.048**	0.035	**0.040**	**0.040**	**0.041**	1000
0.2	0.5	A1	12	3	3	5	0.309	0.073	**0.054**	**0.037**	**0.043**	**0.043**	**0.044**	1000
0.2	0.5	A2	10	2	3	5	0.146	0.071	**0.048**	0.023	0.032	0.032	0.029	1000
0.2	0.5	A2	10	2	3	10	0.289	0.079	**0.054**	0.033	**0.045**	**0.045**	**0.047**	1000
0.2	0.5	A2	10	2	4	5	0.187	0.077	**0.058**	0.033	**0.043**	**0.045**	**0.042**	1000
0.2	0.5	A2	8	3	3	5	0.133	0.075	**0.044**	0.024	0.033	0.034	0.029	1000
0.2	0.5	A3	8	2	3	5	**0.056**	0.075	**0.042**	0.026	0.030	0.031	0.024	1000
0.2	0.5	A3	8	3	3	5	0.070	0.082	**0.052**	0.029	**0.042**	**0.042**	0.033	1000
0.2	0.5	A4	8	3	3	5	0.088	0.081	**0.045**	0.025	0.032	0.032	0.026	1000
0.1	0.3	A1	22	2	3	5	0.283	0.075	**0.063**	**0.048**	**0.054**	**0.051**	**0.053**	1000
0.1	0.3	A1	20	2	3	10	0.457	0.082	**0.064**	**0.051**	**0.059**	**0.061**	**0.057**	1000
0.1	0.3	A1	20	2	4	5	0.323	0.068	**0.051**	**0.044**	**0.048**	**0.049**	**0.048**	1000
0.1	0.3	A1	16	3	3	5	0.334	0.079	0.067	**0.049**	**0.056**	**0.058**	**0.056**	1000
0.1	0.3	A2	16	2	3	5	0.184	0.071	**0.053**	**0.041**	**0.049**	**0.046**	**0.047**	1000
0.1	0.3	A2	14	2	3	10	0.300	0.081	**0.062**	**0.047**	**0.056**	**0.053**	**0.054**	1000
0.1	0.3	A2	14	2	4	5	0.213	0.076	**0.057**	**0.046**	**0.050**	**0.049**	**0.048**	1000
0.1	0.3	A2	12	3	3	5	0.183	0.081	**0.057**	**0.038**	**0.048**	**0.042**	**0.045**	1000
0.1	0.3	A3	12	2	3	5	0.100	0.079	**0.058**	**0.040**	**0.046**	**0.049**	**0.044**	1000
0.1	0.3	A3	10	3	3	5	0.090	0.077	**0.055**	0.033	**0.040**	**0.042**	**0.038**	1000
0.1	0.3	A4	10	3	3	5	0.126	0.074	**0.051**	**0.036**	**0.041**	**0.043**	**0.039**	1000
0.5	0.7	A1	26	2	4	5	0.338	0.067	**0.056**	**0.042**	**0.051**	**0.051**	**0.051**	1000
0.5	0.7	A2	16	3	3	5	0.230	0.065	**0.048**	0.035	**0.039**	**0.039**	**0.041**	1000
0.5	0.7	A3	12	2	4	5	0.133	0.092	0.066	**0.043**	**0.051**	**0.053**	**0.048**	1000
0.5	0.7	A4	14	3	3	5	0.145	0.074	**0.053**	**0.036**	**0.043**	**0.042**	**0.041**	1000
0.8	0.9	A2	30	3	3	5	0.238	**0.055**	**0.051**	**0.043**	**0.046**	**0.046**	**0.046**	1000
0.8	0.9	A3	22	2	4	5	0.150	0.065	**0.054**	**0.043**	**0.047**	**0.047**	**0.047**	1000
0.8	0.9	A4	28	2	4	5	0.182	**0.044**	**0.040**	**0.037**	**0.038**	**0.038**	**0.038**	1000
0.8	0.9	A4	24	3	3	5	0.191	0.070	**0.061**	**0.054**	**0.058**	**0.059**	**0.058**	1000

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 13: Simulation scenarios, predicted power, and empirical power[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under unbalanced four-level CRTs with CV = 0.25. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	0.978	**0.835**	**0.793**	0.755	0.778	0.777	0.778	1000
0.2	0.5	A1	14	2	3	10	0.845	0.994	0.887	**0.846**	0.796	0.818	0.816	**0.819**	1000
0.2	0.5	A1	14	2	4	5	0.866	0.994	0.896	**0.862**	0.818	**0.841**	**0.842**	**0.842**	1000
0.2	0.5	A1	12	3	3	5	0.857	0.993	0.884	**0.847**	0.787	0.815	0.815	0.816	1000
0.2	0.5	A2	10	2	3	5	0.808	0.977	0.886	**0.823**	0.745	**0.792**	**0.789**	**0.794**	1000
0.2	0.5	A2	10	2	3	10	0.870	0.997	0.919	**0.877**	0.801	**0.844**	0.843	**0.847**	1000
0.2	0.5	A2	10	2	4	5	0.852	0.990	0.921	**0.867**	0.816	**0.836**	**0.835**	**0.837**	1000
0.2	0.5	A2	8	3	3	5	0.800	0.979	0.887	**0.802**	0.695	0.749	0.751	0.759	1000
0.2	0.5	A3	8	2	3	5	0.851	0.979	0.920	**0.858**	0.758	0.810	0.800	0.816	1000
0.2	0.5	A3	8	3	3	5	0.936	0.994	0.975	**0.953**	0.902	**0.928**	**0.930**	**0.933**	1000
0.2	0.5	A4	8	3	3	5	0.892	0.993	0.951	**0.911**	0.841	**0.885**	**0.887**	**0.889**	1000
0.1	0.3	A1	22	2	3	5	0.829	0.988	0.870	**0.845**	**0.818**	**0.829**	**0.828**	**0.830**	1000
0.1	0.3	A1	20	2	3	10	0.818	0.996	0.863	0.845	**0.815**	**0.831**	**0.828**	**0.835**	1000
0.1	0.3	A1	20	2	4	5	0.841	0.988	0.872	**0.846**	0.812	**0.831**	**0.824**	**0.831**	1000
0.1	0.3	A1	16	3	3	5	0.805	0.988	0.856	0.833	**0.792**	**0.813**	**0.809**	**0.816**	1000
0.1	0.3	A2	16	2	3	5	0.844	0.988	0.893	0.876	**0.845**	**0.860**	**0.857**	**0.860**	1000
0.1	0.3	A2	14	2	3	10	0.849	0.991	0.895	**0.867**	0.822	**0.849**	**0.846**	**0.851**	1000
0.1	0.3	A2	14	2	4	5	0.829	0.985	0.884	**0.850**	**0.805**	**0.825**	**0.823**	**0.829**	1000
0.1	0.3	A2	12	3	3	5	0.826	0.984	0.892	0.858	**0.806**	**0.838**	**0.834**	**0.838**	1000
0.1	0.3	A3	12	2	3	5	0.873	0.977	0.932	0.905	**0.856**	**0.880**	**0.876**	**0.884**	1000
0.1	0.3	A3	10	3	3	5	0.898	0.994	0.953	**0.924**	**0.877**	**0.899**	**0.893**	**0.903**	1000
0.1	0.3	A4	10	3	3	5	0.837	0.982	0.916	0.871	**0.816**	**0.851**	**0.845**	**0.851**	1000
0.5	0.7	A1	26	2	4	5	0.823	0.983	**0.849**	**0.830**	**0.803**	**0.815**	**0.818**	**0.817**	1000
0.5	0.7	A2	16	3	3	5	0.831	0.956	**0.849**	**0.815**	0.774	0.798	0.800	0.799	1000
0.5	0.7	A3	12	2	4	5	0.827	0.944	0.871	**0.835**	0.781	**0.807**	**0.808**	**0.808**	1000
0.5	0.7	A4	14	3	3	5	0.868	0.972	0.902	**0.873**	0.824	**0.848**	**0.851**	**0.852**	1000
0.8	0.9	A2	30	3	3	5	0.804	0.958	0.832	**0.816**	**0.797**	**0.811**	**0.813**	**0.810**	1000
0.8	0.9	A3	22	2	4	5	0.804	0.938	**0.821**	**0.799**	0.768	**0.782**	**0.787**	**0.784**	1000
0.8	0.9	A4	28	2	4	5	0.824	0.966	**0.843**	**0.820**	**0.799**	**0.811**	**0.814**	**0.814**	1000
0.8	0.9	A4	24	3	3	5	0.813	0.948	**0.827**	**0.809**	**0.788**	**0.800**	**0.804**	**0.800**	1000

[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

Web Table 14: Simulation scenarios and empirical type I error rates[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under unbalanced four-level CRTs with CV = 0.50. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	0.296	0.069	**0.053**	**0.041**	**0.047**	**0.044**	**0.047**	1000
0.2	0.5	A1	14	2	3	10	0.456	0.086	**0.060**	**0.039**	**0.055**	**0.052**	**0.055**	1000
0.2	0.5	A1	14	2	4	5	0.360	0.081	**0.064**	**0.046**	**0.056**	**0.054**	**0.056**	1000
0.2	0.5	A1	12	3	3	5	0.311	0.067	**0.049**	**0.036**	**0.045**	**0.041**	**0.044**	1000
0.2	0.5	A2	10	2	3	5	0.181	0.072	**0.051**	0.035	**0.040**	**0.040**	**0.037**	1000
0.2	0.5	A2	10	2	3	10	0.311	0.081	**0.051**	0.034	**0.039**	**0.038**	**0.039**	1000
0.2	0.5	A2	10	2	4	5	0.199	0.075	**0.051**	0.030	**0.040**	**0.038**	**0.038**	1000
0.2	0.5	A2	8	3	3	5	0.168	0.078	**0.046**	0.027	**0.036**	**0.036**	0.032	1000
0.2	0.5	A3	8	2	3	5	**0.061**	0.072	**0.044**	0.028	**0.040**	**0.037**	0.028	1000
0.2	0.5	A3	8	3	3	5	0.079	0.068	**0.049**	0.031	**0.041**	**0.036**	0.030	1000
0.2	0.5	A4	8	3	3	5	0.104	**0.063**	0.033	0.021	0.027	0.027	0.023	1000
0.1	0.3	A1	22	2	3	5	0.326	0.085	0.073	**0.057**	0.066	**0.060**	**0.064**	1000
0.1	0.3	A1	20	2	3	10	0.495	0.083	0.072	**0.062**	0.069	**0.064**	0.066	1000
0.1	0.3	A1	20	2	4	5	0.364	0.075	**0.058**	**0.046**	**0.048**	**0.049**	**0.049**	1000
0.1	0.3	A1	16	3	3	5	0.339	0.081	0.066	**0.051**	**0.055**	**0.055**	**0.052**	1000
0.1	0.3	A2	16	2	3	5	0.198	0.079	**0.061**	**0.042**	**0.046**	**0.051**	**0.048**	1000
0.1	0.3	A2	14	2	3	10	0.318	0.070	**0.050**	**0.042**	**0.045**	**0.045**	**0.045**	1000
0.1	0.3	A2	14	2	4	5	0.228	0.078	**0.062**	**0.044**	**0.051**	**0.047**	**0.049**	1000
0.1	0.3	A2	12	3	3	5	0.201	0.081	**0.056**	**0.040**	**0.045**	**0.044**	**0.044**	1000
0.1	0.3	A3	12	2	3	5	0.091	0.076	**0.059**	**0.037**	**0.048**	**0.044**	**0.044**	1000
0.1	0.3	A3	10	3	3	5	0.098	0.082	**0.061**	**0.042**	**0.047**	**0.048**	**0.041**	1000
0.1	0.3	A4	10	3	3	5	0.138	0.086	**0.057**	0.033	**0.040**	**0.038**	**0.038**	1000
0.5	0.7	A1	26	2	4	5	0.368	**0.047**	**0.038**	0.032	0.035	**0.036**	**0.036**	1000
0.5	0.7	A2	16	3	3	5	0.218	**0.059**	**0.043**	**0.036**	**0.038**	**0.039**	**0.039**	1000
0.5	0.7	A3	12	2	4	5	0.132	0.067	**0.052**	0.032	**0.039**	**0.041**	**0.037**	1000
0.5	0.7	A4	14	3	3	5	0.161	0.068	**0.051**	0.033	**0.043**	**0.043**	**0.042**	1000
0.8	0.9	A2	30	3	3	5	0.259	**0.057**	**0.050**	**0.041**	**0.049**	**0.048**	**0.049**	1000
0.8	0.9	A3	22	2	4	5	0.156	**0.063**	**0.051**	**0.045**	**0.048**	**0.048**	**0.048**	1000
0.8	0.9	A4	28	2	4	5	0.190	**0.052**	**0.039**	0.035	**0.038**	**0.037**	**0.038**	1000
0.8	0.9	A4	24	3	3	5	0.196	**0.064**	**0.051**	**0.043**	**0.050**	**0.050**	**0.049**	1000

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 15: Simulation scenarios, predicted power, and empirical power[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under unbalanced four-level CRTs with CV = 0.50. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	0.984	0.850	**0.813**	0.748	0.782	0.778	0.788	1000
0.2	0.5	A1	14	2	3	10	0.845	0.995	**0.842**	0.793	0.741	0.776	0.773	0.782	1000
0.2	0.5	A1	14	2	4	5	0.866	0.985	**0.885**	**0.852**	0.798	0.829	0.825	0.837	1000
0.2	0.5	A1	12	3	3	5	0.857	0.992	0.884	**0.843**	0.767	0.806	0.807	0.813	1000
0.2	0.5	A2	10	2	3	5	0.808	0.968	0.849	**0.785**	0.707	0.748	0.745	0.754	1000
0.2	0.5	A2	10	2	3	10	0.870	0.991	0.911	**0.859**	0.794	0.834	0.828	0.839	1000
0.2	0.5	A2	10	2	4	5	0.852	0.990	0.913	**0.854**	0.768	0.813	0.810	0.823	1000
0.2	0.5	A2	8	3	3	5	0.800	0.975	0.868	**0.790**	0.685	0.744	0.727	0.750	1000
0.2	0.5	A3	8	2	3	5	0.851	0.963	0.903	**0.841**	0.740	0.791	0.789	0.798	1000
0.2	0.5	A3	8	3	3	5	0.936	0.993	0.971	**0.947**	0.874	**0.914**	**0.915**	**0.920**	1000
0.2	0.5	A4	8	3	3	5	0.892	0.991	0.947	**0.903**	0.823	0.860	0.858	0.865	1000
0.1	0.3	A1	22	2	3	5	0.829	0.987	0.858	**0.834**	**0.804**	**0.817**	**0.815**	**0.821**	1000
0.1	0.3	A1	20	2	3	10	0.818	0.990	0.846	**0.812**	0.772	**0.792**	0.788	**0.798**	1000
0.1	0.3	A1	20	2	4	5	0.841	0.992	**0.852**	**0.828**	0.802	**0.815**	**0.815**	**0.819**	1000
0.1	0.3	A1	16	3	3	5	0.805	0.986	0.833	**0.789**	0.739	0.764	0.761	0.770	1000
0.1	0.3	A2	16	2	3	5	0.844	0.986	0.893	**0.860**	0.811	**0.837**	**0.836**	**0.842**	1000
0.1	0.3	A2	14	2	3	10	0.849	0.995	0.880	**0.846**	0.804	0.816	0.820	**0.823**	1000
0.1	0.3	A2	14	2	4	5	0.829	0.984	0.876	**0.832**	0.786	**0.813**	0.800	**0.810**	1000
0.1	0.3	A2	12	3	3	5	0.826	0.986	0.877	**0.841**	0.789	**0.816**	**0.804**	**0.818**	1000
0.1	0.3	A3	12	2	3	5	0.873	0.975	0.918	**0.884**	0.828	**0.851**	0.840	**0.855**	1000
0.1	0.3	A3	10	3	3	5	0.898	0.989	0.942	**0.907**	0.846	**0.878**	0.870	**0.883**	1000
0.1	0.3	A4	10	3	3	5	0.837	0.983	0.913	**0.859**	0.805	**0.828**	**0.831**	**0.834**	1000
0.5	0.7	A1	26	2	4	5	0.823	0.981	**0.820**	**0.801**	0.780	0.785	0.787	0.787	1000
0.5	0.7	A2	16	3	3	5	0.831	0.961	**0.833**	0.797	0.752	0.772	0.774	0.778	1000
0.5	0.7	A3	12	2	4	5	0.827	0.938	**0.849**	0.798	0.744	0.772	0.777	0.779	1000
0.5	0.7	A4	14	3	3	5	0.868	0.974	0.905	**0.872**	0.818	**0.845**	**0.850**	**0.849**	1000
0.8	0.9	A2	30	3	3	5	0.804	0.962	**0.807**	**0.789**	0.774	**0.779**	**0.781**	**0.780**	1000
0.8	0.9	A3	22	2	4	5	0.804	0.936	**0.820**	**0.789**	0.756	0.774	**0.778**	0.776	1000
0.8	0.9	A4	28	2	4	5	0.824	0.951	**0.830**	**0.806**	0.786	**0.798**	**0.800**	**0.799**	1000
0.8	0.9	A4	24	3	3	5	0.813	0.949	**0.833**	**0.815**	0.781	**0.801**	**0.804**	**0.804**	1000

[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

Web Table 16: Simulation scenarios and empirical type I error rates[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under unbalanced four-level CRTs with CV = 0.75. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	0.332	0.079	**0.056**	**0.041**	**0.046**	**0.043**	**0.047**	1000
0.2	0.5	A1	14	2	3	10	0.476	0.094	0.070	**0.041**	**0.052**	**0.048**	**0.054**	1000
0.2	0.5	A1	14	2	4	5	0.347	0.079	**0.063**	**0.045**	**0.055**	**0.057**	**0.055**	1000
0.2	0.5	A1	12	3	3	5	0.348	0.080	**0.061**	**0.036**	**0.046**	**0.045**	**0.046**	1000
0.2	0.5	A2	10	2	3	5	0.185	0.073	**0.051**	0.031	**0.038**	**0.038**	**0.038**	1000
0.2	0.5	A2	10	2	3	10	0.322	0.092	**0.064**	**0.039**	**0.054**	**0.046**	**0.052**	1000
0.2	0.5	A2	10	2	4	5	0.196	0.070	**0.051**	**0.036**	**0.043**	**0.042**	**0.043**	1000
0.2	0.5	A2	8	3	3	5	0.186	0.079	**0.049**	0.028	0.034	0.034	0.034	1000
0.2	0.5	A3	8	2	3	5	0.070	0.072	**0.049**	0.033	**0.041**	**0.039**	0.034	1000
0.2	0.5	A3	8	3	3	5	0.102	0.082	**0.045**	0.024	0.032	0.032	0.025	1000
0.2	0.5	A4	8	3	3	5	0.115	0.079	**0.045**	0.026	0.032	0.034	0.030	1000
0.1	0.3	A1	22	2	3	5	0.344	0.086	0.067	**0.054**	**0.058**	**0.054**	**0.058**	1000
0.1	0.3	A1	20	2	3	10	0.514	0.082	0.065	**0.051**	**0.056**	**0.054**	**0.058**	1000
0.1	0.3	A1	20	2	4	5	0.385	0.077	**0.057**	**0.047**	**0.051**	**0.048**	**0.051**	1000
0.1	0.3	A1	16	3	3	5	0.349	0.080	0.066	**0.058**	**0.064**	**0.059**	**0.061**	1000
0.1	0.3	A2	16	2	3	5	0.213	0.077	**0.064**	**0.052**	**0.057**	**0.055**	**0.055**	1000
0.1	0.3	A2	14	2	3	10	0.334	0.081	**0.060**	**0.043**	**0.048**	**0.050**	**0.050**	1000
0.1	0.3	A2	14	2	4	5	0.257	0.074	**0.060**	**0.048**	**0.054**	**0.052**	**0.055**	1000
0.1	0.3	A2	12	3	3	5	0.231	0.093	**0.062**	**0.045**	**0.054**	**0.053**	**0.052**	999
0.1	0.3	A3	12	2	3	5	0.090	0.069	**0.048**	0.028	0.033	0.033	0.034	1000
0.1	0.3	A3	10	3	3	5	0.123	0.080	**0.054**	0.031	**0.043**	**0.038**	**0.044**	1000
0.1	0.3	A4	10	3	3	5	0.136	0.071	**0.046**	0.033	**0.038**	**0.036**	**0.036**	1000
0.5	0.7	A1	26	2	4	5	0.382	**0.055**	**0.049**	**0.038**	**0.043**	**0.042**	**0.045**	1000
0.5	0.7	A2	16	3	3	5	0.229	**0.064**	**0.046**	**0.039**	**0.044**	**0.044**	**0.044**	1000
0.5	0.7	A3	12	2	4	5	0.136	0.081	**0.051**	**0.039**	**0.045**	**0.043**	**0.044**	1000
0.5	0.7	A4	14	3	3	5	0.176	0.077	**0.060**	**0.050**	**0.052**	**0.054**	**0.054**	1000
0.8	0.9	A2	30	3	3	5	0.258	**0.062**	**0.050**	**0.045**	**0.047**	**0.047**	**0.047**	1000
0.8	0.9	A3	22	2	4	5	0.164	**0.050**	**0.043**	0.032	**0.037**	**0.037**	**0.037**	1000
0.8	0.9	A4	28	2	4	5	0.197	**0.054**	**0.046**	**0.039**	**0.045**	**0.043**	**0.045**	1000
0.8	0.9	A4	24	3	3	5	0.200	**0.048**	0.030	0.025	0.027	0.027	0.027	1000

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 17: Simulation scenarios, predicted power, and empirical power[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under unbalanced four-level CRTs with CV = 0.75. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	0.978	**0.799**	0.751	0.674	0.706	0.702	0.720	1000
0.2	0.5	A1	14	2	3	10	0.845	0.986	**0.819**	0.760	0.700	0.728	0.720	0.741	1000
0.2	0.5	A1	14	2	4	5	0.866	0.993	**0.850**	0.801	0.742	0.763	0.762	0.775	1000
0.2	0.5	A1	12	3	3	5	0.857	0.984	**0.836**	0.790	0.740	0.767	0.763	0.772	1000
0.2	0.5	A2	10	2	3	5	0.808	0.975	0.845	**0.786**	0.684	0.740	0.736	0.759	1000
0.2	0.5	A2	10	2	3	10	0.870	0.992	**0.892**	0.824	0.742	0.795	0.782	0.805	1000
0.2	0.5	A2	10	2	4	5	0.852	0.984	0.898	**0.835**	0.764	0.801	0.794	0.807	1000
0.2	0.5	A2	8	3	3	5	0.800	0.978	0.863	**0.784**	0.655	0.726	0.713	0.734	1000
0.2	0.5	A3	8	2	3	5	0.851	0.969	0.906	**0.828**	0.703	0.773	0.768	0.793	1000
0.2	0.5	A3	8	3	3	5	0.936	0.994	0.967	**0.939**	0.869	0.908	**0.910**	**0.915**	1000
0.2	0.5	A4	8	3	3	5	0.892	0.988	0.938	**0.904**	0.828	**0.868**	0.863	**0.880**	1000
0.1	0.3	A1	22	2	3	5	0.829	0.984	**0.821**	0.794	0.757	0.775	0.774	0.782	1000
0.1	0.3	A1	20	2	3	10	0.818	0.990	**0.801**	0.757	0.718	0.739	0.735	0.749	1000
0.1	0.3	A1	20	2	4	5	0.841	0.988	**0.840**	0.810	0.783	0.798	0.791	0.804	1000
0.1	0.3	A1	16	3	3	5	0.805	0.982	**0.818**	**0.781**	0.726	0.755	0.747	0.760	1000
0.1	0.3	A2	16	2	3	5	0.844	0.980	0.881	**0.853**	0.814	**0.837**	**0.829**	**0.839**	1000
0.1	0.3	A2	14	2	3	10	0.849	0.984	**0.868**	**0.830**	0.770	0.799	0.793	0.817	1000
0.1	0.3	A2	14	2	4	5	0.829	0.987	**0.853**	**0.806**	0.761	0.788	0.778	0.790	1000
0.1	0.3	A2	12	3	3	5	0.826	0.988	0.868	**0.825**	0.767	0.794	0.780	**0.800**	999
0.1	0.3	A3	12	2	3	5	0.873	0.980	0.906	**0.869**	0.807	0.839	0.833	**0.853**	1000
0.1	0.3	A3	10	3	3	5	0.898	0.986	0.934	**0.905**	0.843	**0.878**	**0.873**	**0.886**	1000
0.1	0.3	A4	10	3	3	5	0.837	0.983	0.901	**0.855**	0.786	**0.818**	**0.822**	**0.832**	1000
0.5	0.7	A1	26	2	4	5	0.823	0.967	0.788	0.760	0.729	0.744	0.746	0.747	1000
0.5	0.7	A2	16	3	3	5	0.831	0.962	**0.815**	0.783	0.735	0.761	0.763	0.763	1000
0.5	0.7	A3	12	2	4	5	0.827	0.940	**0.824**	0.765	0.688	0.722	0.726	0.732	1000
0.5	0.7	A4	14	3	3	5	0.868	0.975	**0.889**	**0.856**	0.813	0.836	0.836	**0.842**	1000
0.8	0.9	A2	30	3	3	5	0.804	0.956	**0.806**	**0.786**	0.761	0.775	**0.779**	**0.778**	1000
0.8	0.9	A3	22	2	4	5	0.804	0.939	**0.797**	0.769	0.739	0.756	0.759	0.758	1000
0.8	0.9	A4	28	2	4	5	0.824	0.956	**0.823**	**0.808**	0.782	0.791	0.794	0.792	1000
0.8	0.9	A4	24	3	3	5	0.813	0.953	**0.828**	**0.802**	0.779	**0.789**	**0.793**	**0.795**	1000

[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

Web Table 18: Simulation scenarios and empirical type I error rates[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under unbalanced four-level CRTs with CV = 1.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[c]
0.2	0.5	A1	14	2	3	5	0.371	0.092	**0.064**	**0.047**	**0.051**	**0.048**	**0.055**	1000
0.2	0.5	A1	14	2	3	10	0.504	0.084	0.067	**0.052**	**0.061**	**0.057**	**0.061**	1000
0.2	0.5	A1	14	2	4	5	0.389	0.070	**0.047**	0.033	**0.038**	**0.039**	**0.042**	1000
0.2	0.5	A1	12	3	3	5	0.368	0.081	**0.055**	**0.037**	**0.047**	**0.047**	**0.047**	1000
0.2	0.5	A2	10	2	3	5	0.213	0.079	**0.048**	0.031	**0.037**	**0.037**	**0.038**	1000
0.2	0.5	A2	10	2	3	10	0.355	0.102	0.070	**0.041**	**0.048**	**0.050**	**0.049**	1000
0.2	0.5	A2	10	2	4	5	0.228	0.067	**0.044**	0.025	**0.042**	0.035	**0.042**	1000
0.2	0.5	A2	8	3	3	5	0.189	0.084	**0.052**	0.027	0.035	**0.036**	0.035	1000
0.2	0.5	A3	8	2	3	5	0.101	0.075	**0.048**	0.028	**0.039**	**0.037**	0.031	1000
0.2	0.5	A3	8	3	3	5	0.111	0.089	**0.051**	0.027	**0.036**	**0.037**	0.032	1000
0.2	0.5	A4	8	3	3	5	0.122	0.079	**0.047**	0.027	**0.037**	**0.038**	0.034	1000
0.1	0.3	A1	22	2	3	5	0.381	0.085	0.071	**0.057**	0.065	0.066	0.066	1000
0.1	0.3	A1	20	2	3	10	0.531	0.106	0.087	0.079	0.081	0.078	0.083	1000
0.1	0.3	A1	20	2	4	5	0.407	0.086	0.070	**0.053**	0.067	0.065	0.066	1000
0.1	0.3	A1	16	3	3	5	0.388	0.079	**0.059**	**0.041**	**0.050**	**0.048**	**0.049**	1000
0.1	0.3	A2	16	2	3	5	0.256	0.085	**0.061**	**0.046**	**0.056**	**0.053**	**0.054**	1000
0.1	0.3	A2	14	2	3	10	0.372	0.091	**0.064**	**0.043**	**0.054**	**0.055**	**0.057**	1000
0.1	0.3	A2	14	2	4	5	0.283	0.086	0.068	**0.052**	**0.058**	**0.059**	**0.059**	1000
0.1	0.3	A2	12	3	3	5	0.262	0.084	**0.056**	**0.043**	**0.049**	**0.046**	**0.046**	1000
0.1	0.3	A3	12	2	3	5	0.112	0.071	**0.049**	0.031	**0.038**	**0.038**	0.035	1000
0.1	0.3	A3	10	3	3	5	0.131	0.080	**0.054**	0.031	**0.039**	**0.039**	**0.038**	1000
0.1	0.3	A4	10	3	3	5	0.147	0.093	**0.060**	0.032	**0.045**	**0.046**	**0.045**	1000
0.5	0.7	A1	26	2	4	5	0.394	**0.058**	**0.044**	**0.038**	**0.041**	**0.041**	**0.041**	1000
0.5	0.7	A2	16	3	3	5	0.230	**0.053**	**0.038**	0.029	0.035	0.034	**0.036**	1000
0.5	0.7	A3	12	2	4	5	0.152	0.079	**0.060**	**0.039**	**0.051**	**0.051**	**0.050**	1000
0.5	0.7	A4	14	3	3	5	0.187	0.072	**0.057**	**0.045**	**0.051**	**0.052**	**0.053**	1000
0.8	0.9	A2	30	3	3	5	0.266	**0.049**	**0.042**	0.034	**0.038**	**0.037**	**0.039**	1000
0.8	0.9	A3	22	2	4	5	0.177	0.070	**0.056**	**0.047**	**0.049**	**0.049**	**0.050**	1000
0.8	0.9	A4	28	2	4	5	0.202	**0.039**	0.030	0.025	0.028	0.028	0.028	1000
0.8	0.9	A4	24	3	3	5	0.202	**0.050**	**0.044**	0.031	0.034	0.035	**0.036**	1000

[a] Bold text indicates acceptable empirical type I error rate (from 3.6% to 6.4%).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

[c] CR: Convergence rate (out of 1000) for assessing the empirical type I error rate.

Web Table 19: Simulation scenarios, predicted power, and empirical power[a] of GEE analyses based on different variance estimators, using an independence working correlation matrix under unbalanced four-level CRTs with CV = 1.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

P_0	P_1	$\boldsymbol{\alpha}$[b]	n	m	k	l	Pred[c]	MB	BC0	BC1	BC2	AVG	BC3	BC4	CR[d]
0.2	0.5	A1	14	2	3	5	0.817	0.978	**0.802**	0.740	0.669	0.700	0.689	0.720	1000
0.2	0.5	A1	14	2	3	10	0.845	0.984	0.777	0.708	0.646	0.681	0.675	0.696	1000
0.2	0.5	A1	14	2	4	5	0.866	0.993	**0.845**	0.803	0.744	0.772	0.767	0.784	1000
0.2	0.5	A1	12	3	3	5	0.857	0.984	**0.850**	0.800	0.715	0.755	0.752	0.776	1000
0.2	0.5	A2	10	2	3	5	0.808	0.976	0.838	0.764	0.665	0.717	0.707	0.744	1000
0.2	0.5	A2	10	2	3	10	0.870	0.988	**0.868**	0.794	0.703	0.745	0.738	0.770	1000
0.2	0.5	A2	10	2	4	5	0.852	0.985	**0.876**	0.822	0.729	0.774	0.774	0.797	1000
0.2	0.5	A2	8	3	3	5	0.800	0.986	0.858	0.756	0.631	0.684	0.679	0.710	1000
0.2	0.5	A3	8	2	3	5	0.851	0.967	0.879	0.807	0.693	0.763	0.753	0.781	1000
0.2	0.5	A3	8	3	3	5	0.936	0.996	**0.962**	**0.918**	0.835	0.878	0.873	0.891	1000
0.2	0.5	A4	8	3	3	5	0.892	0.992	0.949	**0.897**	0.823	0.863	0.862	**0.877**	1000
0.1	0.3	A1	22	2	3	5	0.829	0.982	0.780	0.746	0.706	0.728	0.719	0.736	1000
0.1	0.3	A1	20	2	3	10	0.818	0.982	0.745	0.710	0.661	0.682	0.672	0.696	1000
0.1	0.3	A1	20	2	4	5	0.841	0.986	**0.827**	0.787	0.748	0.771	0.762	0.777	1000
0.1	0.3	A1	16	3	3	5	0.805	0.984	**0.781**	0.725	0.674	0.697	0.685	0.710	1000
0.1	0.3	A2	16	2	3	5	0.844	0.977	**0.853**	0.808	0.755	0.787	0.774	0.800	1000
0.1	0.3	A2	14	2	3	10	0.849	0.983	**0.850**	0.800	0.751	0.777	0.769	0.790	1000
0.1	0.3	A2	14	2	4	5	0.829	0.986	**0.850**	**0.811**	0.753	0.783	0.771	0.794	1000
0.1	0.3	A2	12	3	3	5	0.826	0.979	0.860	**0.807**	0.733	0.769	0.757	0.783	1000
0.1	0.3	A3	12	2	3	5	0.873	0.977	0.903	**0.858**	0.784	0.819	0.810	0.833	1000
0.1	0.3	A3	10	3	3	5	0.898	0.984	0.930	**0.887**	0.824	0.862	0.846	**0.874**	1000
0.1	0.3	A4	10	3	3	5	0.837	0.980	0.912	**0.856**	0.789	**0.828**	**0.820**	**0.837**	1000
0.5	0.7	A1	26	2	4	5	0.823	0.968	0.724	0.692	0.657	0.673	0.674	0.681	1000
0.5	0.7	A2	16	3	3	5	0.831	0.967	**0.814**	0.771	0.721	0.744	0.747	0.754	1000
0.5	0.7	A3	12	2	4	5	0.827	0.930	**0.819**	0.760	0.688	0.726	0.732	0.738	1000
0.5	0.7	A4	14	3	3	5	0.868	0.972	0.906	**0.861**	0.803	0.834	0.838	**0.848**	1000
0.8	0.9	A2	30	3	3	5	0.804	0.969	0.772	0.751	0.724	0.737	0.743	0.745	1000
0.8	0.9	A3	22	2	4	5	0.804	0.927	**0.787**	0.763	0.720	0.741	0.748	0.746	1000
0.8	0.9	A4	28	2	4	5	0.824	0.966	**0.831**	**0.807**	0.778	0.795	**0.799**	**0.799**	1000
0.8	0.9	A4	24	3	3	5	0.813	0.962	**0.836**	**0.813**	0.778	**0.799**	**0.802**	**0.803**	1000

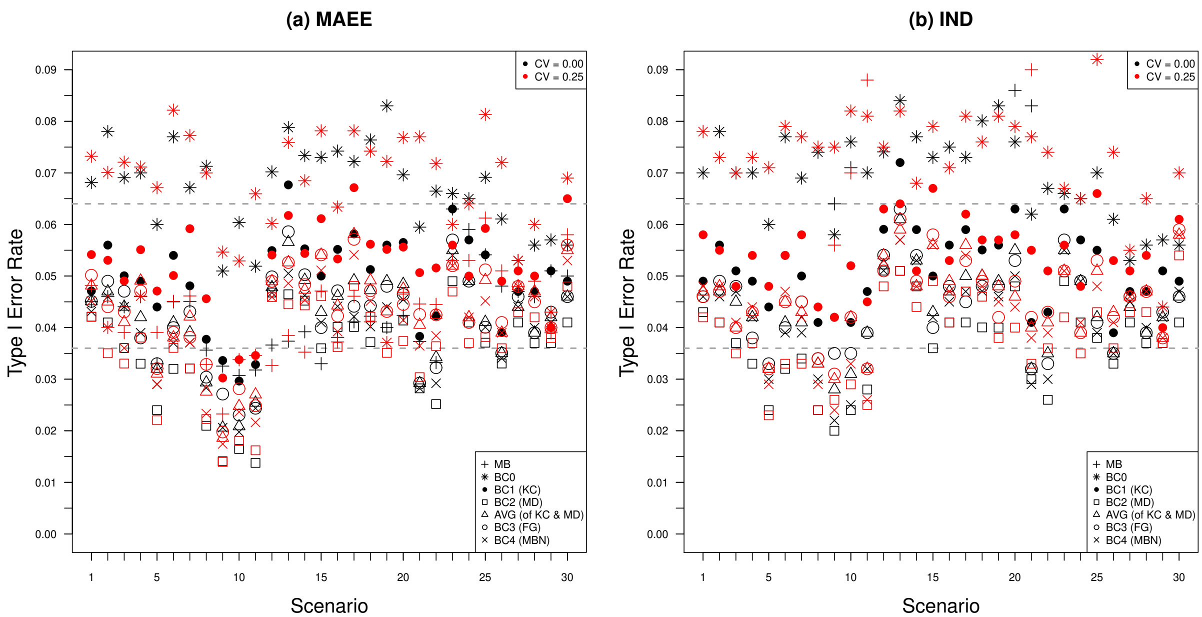
[a] Bold text indicates acceptable empirical power (differing at most 2.6% from the predicted power).

[b] A1: $\boldsymbol{\alpha} = (0.4, 0.1, 0.03)$; A2: $\boldsymbol{\alpha} = (0.15, 0.08, 0.02)$; A3: $\boldsymbol{\alpha} = (0.1, 0.02, 0.01)$; A4: $\boldsymbol{\alpha} = (0.05, 0.05, 0.02)$.

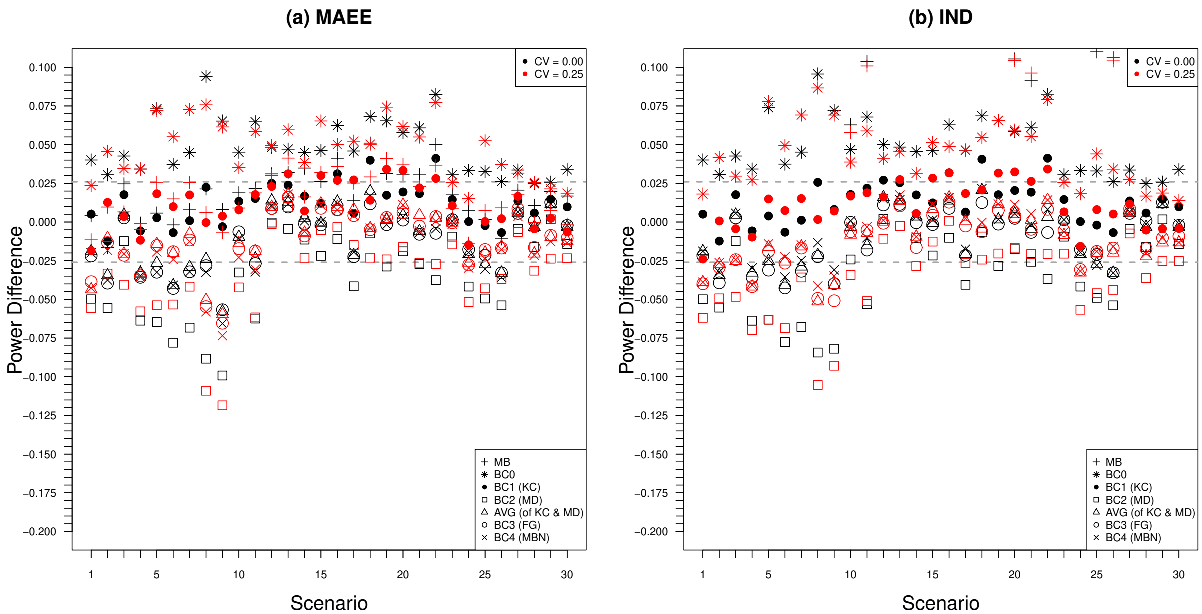
[c] Pred: Predicted power based on t-test.

[d] CR: Convergence rate (out of 1000) for assessing the empirical power.

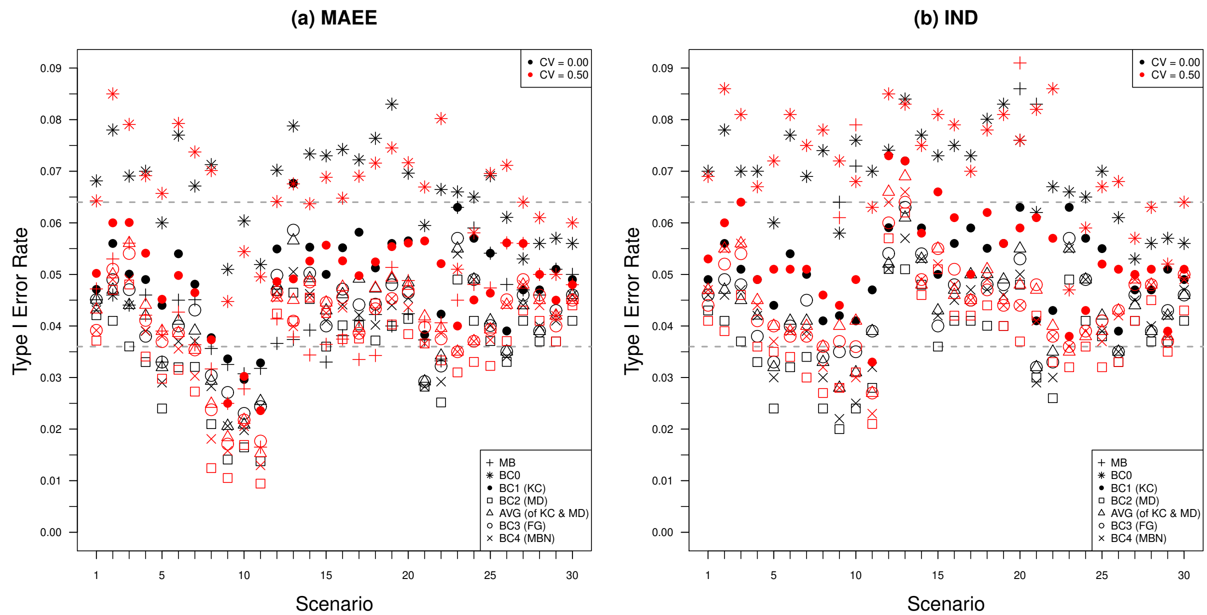
Web Appendix K: Web figures from simulation study



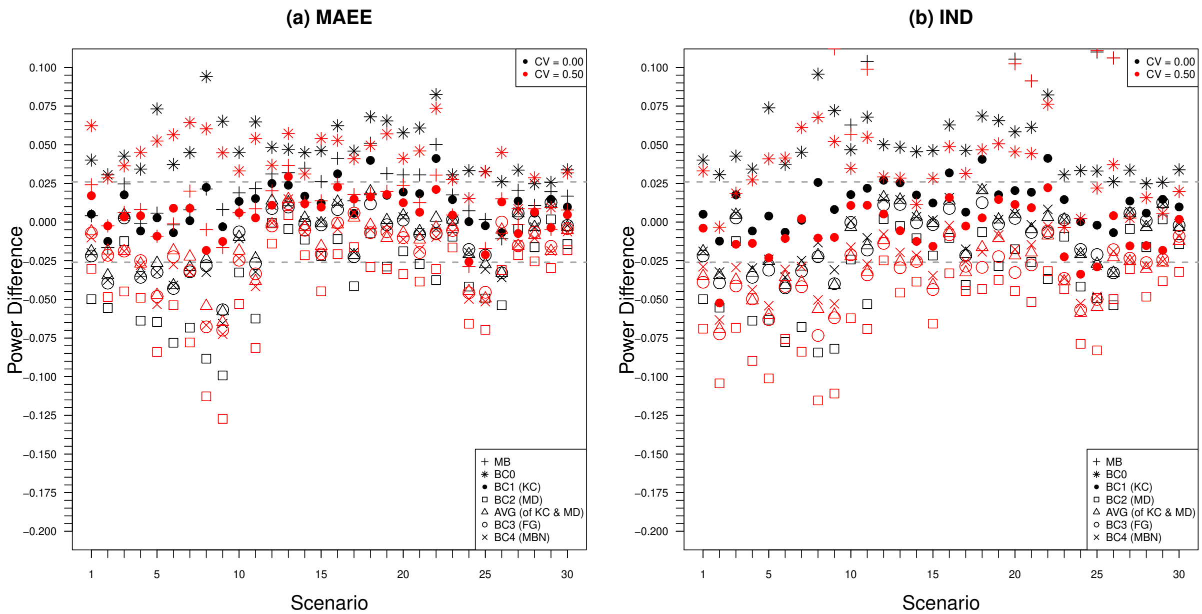
Web Figure 1: Empirical type I error rates of GEE analyses based on different variance estimators, using (a) the extended nested exchangeable working correlation structure with MAEE and (b) an independence working correlation matrix, under four-level CRTs with CV = 0.25 compared to CV = 0.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).



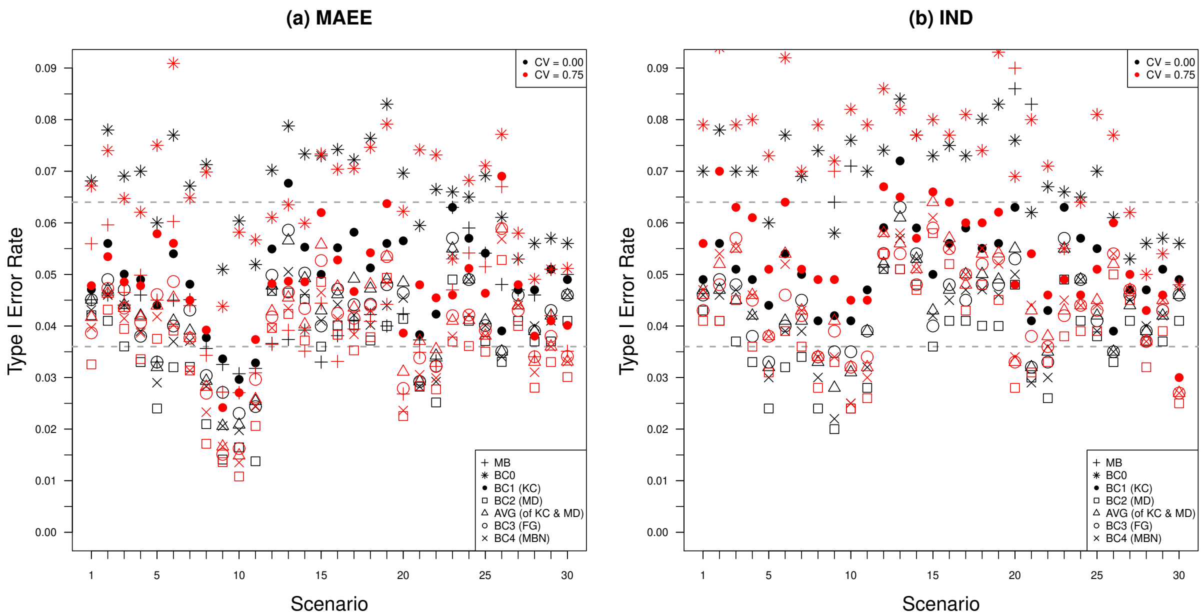
Web Figure 2: Difference between the empirical power and the predicted power of GEE analyses based on different variance estimators, using (a) the extended nested exchangeable working correlation structure with MAEE and (b) an independence working correlation matrix, under four-level CRTs with CV = 0.25 compared to CV = 0.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).



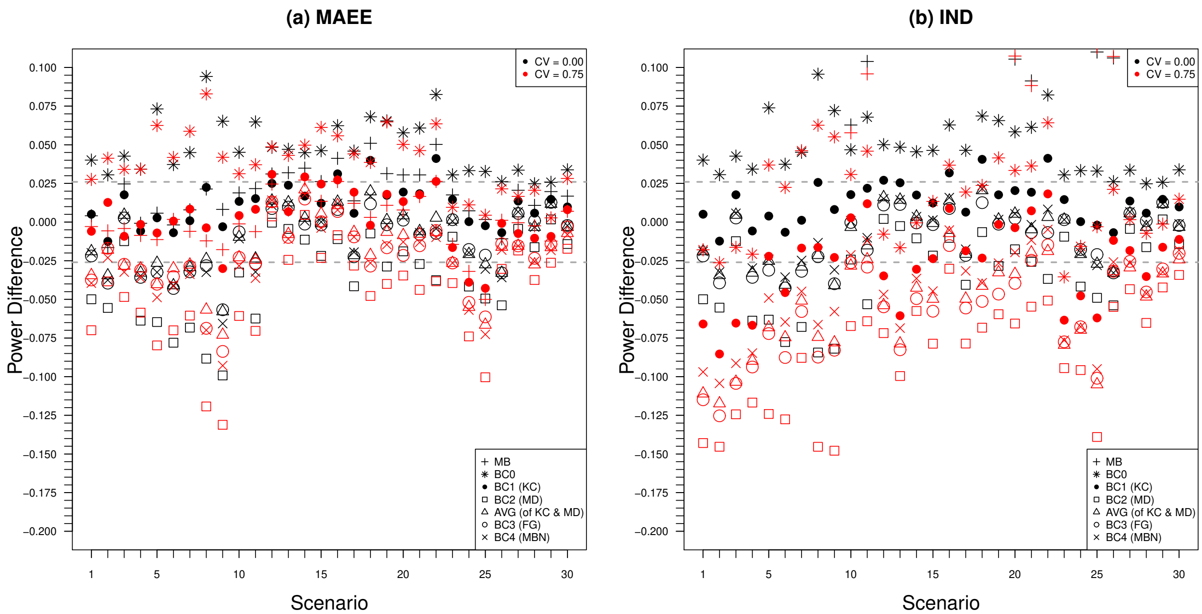
Web Figure 3: Empirical type I error rates of GEE analyses based on different variance estimators, using (a) the extended nested exchangeable working correlation structure with MAEE and (b) an independence working correlation matrix, under four-level CRTs with CV = 0.50 compared to CV = 0.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).



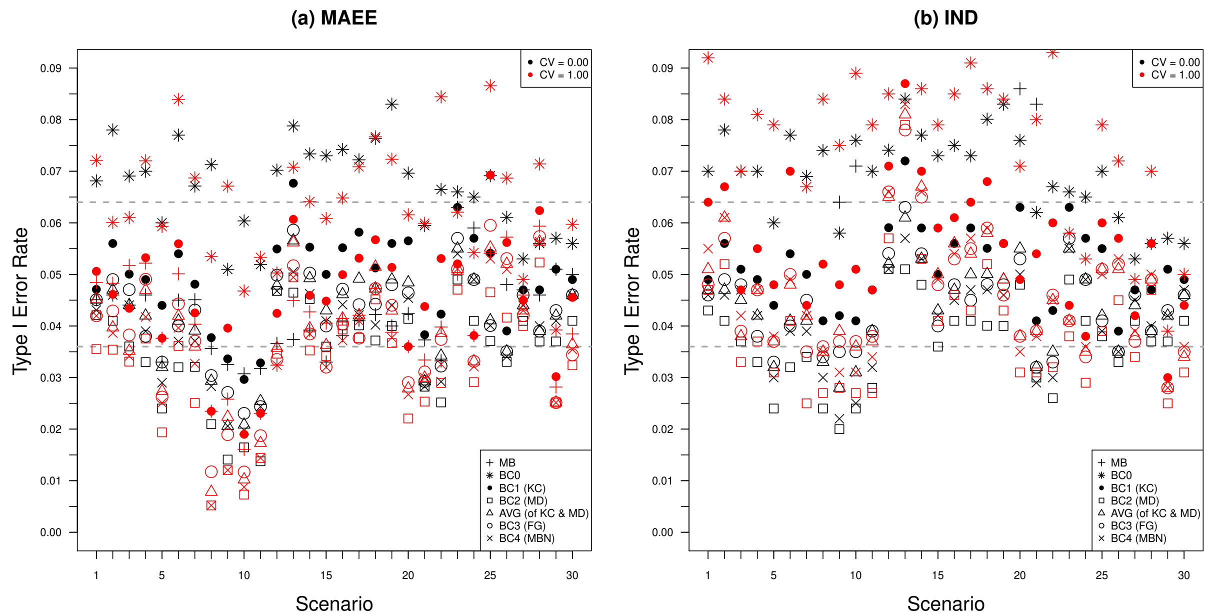
Web Figure 4: Difference between the empirical power and the predicted power of GEE analyses based on different variance estimators, using (a) the extended nested exchangeable working correlation structure with MAEE and (b) an independence working correlation matrix, under four-level CRTs with CV = 0.50 compared to CV = 0.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).



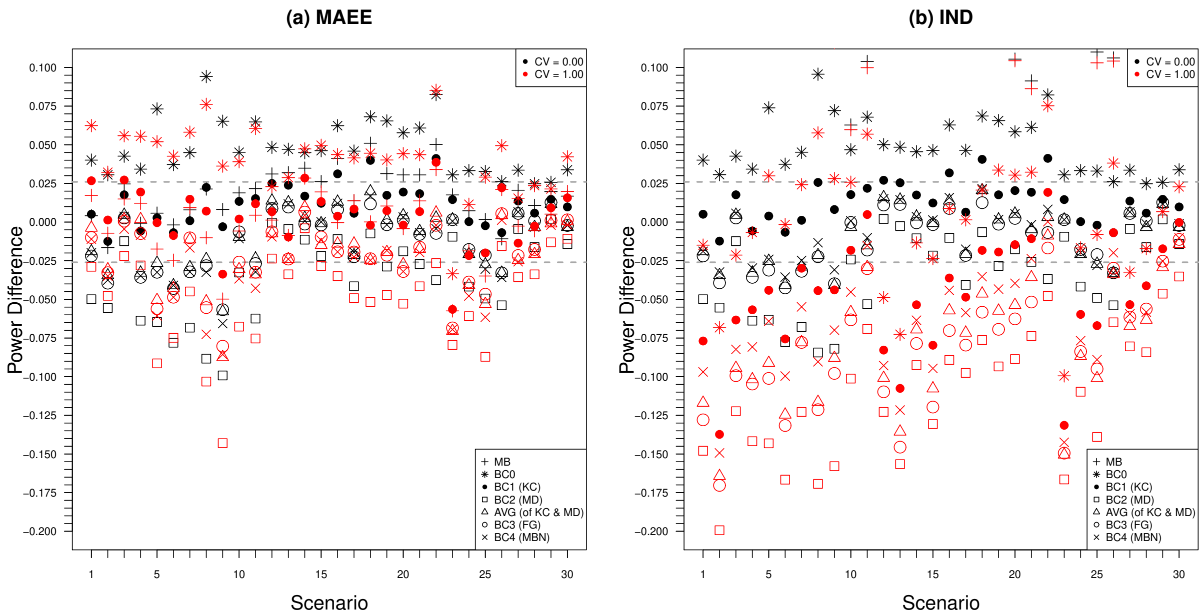
Web Figure 5: Empirical type I error rates of GEE analyses based on different variance estimators, using (a) the extended nested exchangeable working correlation structure with MAEE and (b) an independence working correlation matrix, under four-level CRTs with CV = 0.75 compared to CV = 0.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).



Web Figure 6: Difference between the empirical power and the predicted power of GEE analyses based on different variance estimators, using (a) the extended nested exchangeable working correlation structure with MAEE and (b) an independence working correlation matrix, under four-level CRTs with CV = 0.75 compared to CV = 0.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).



Web Figure 7: Empirical type I error rates of GEE analyses based on different variance estimators, using (a) the extended nested exchangeable working correlation structure with MAEE and (b) an independence working correlation matrix, under four-level CRTs with CV = 1.00 compared to CV = 0.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

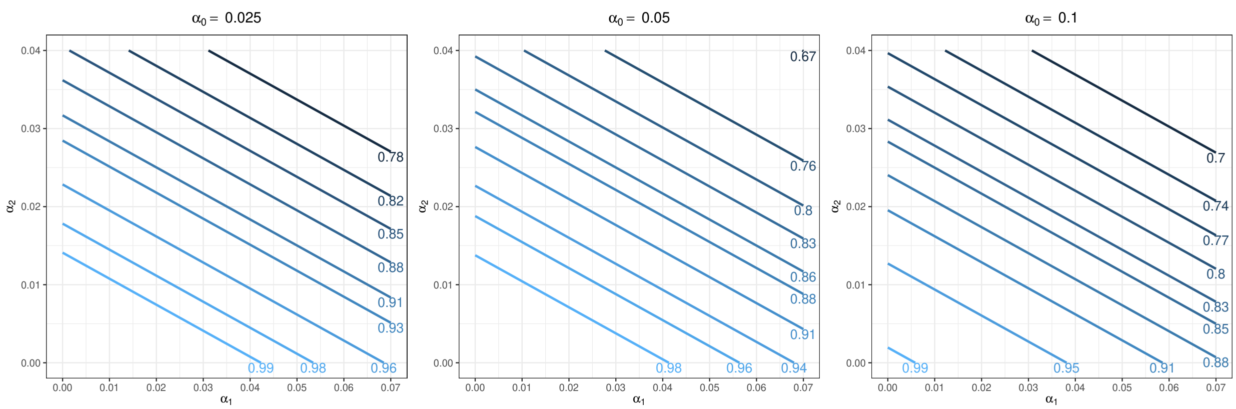


Web Figure 8: Difference between the empirical power and the predicted power of GEE analyses based on different variance estimators, using (a) the extended nested exchangeable working correlation structure with MAEE and (b) an independence working correlation matrix, under four-level CRTs with CV = 1.00 compared to CV = 0.00. MB: Model-based variance estimator; BC0: Uncorrected sandwich estimator of Liang and Zeger (1986); BC1: Bias-corrected sandwich estimator of Kauermann and Carroll (2001); BC2: Bias-corrected sandwich estimator of Mancl and DeRouen (2001); AVG: Bias-corrected sandwich estimator with standard error as the average of those from BC1 and BC2; BC3: Bias-corrected sandwich estimator of Fay and Graubard (2001); BC4: Bias-corrected sandwich estimator of Morel et al. (2003).

Web Appendix L

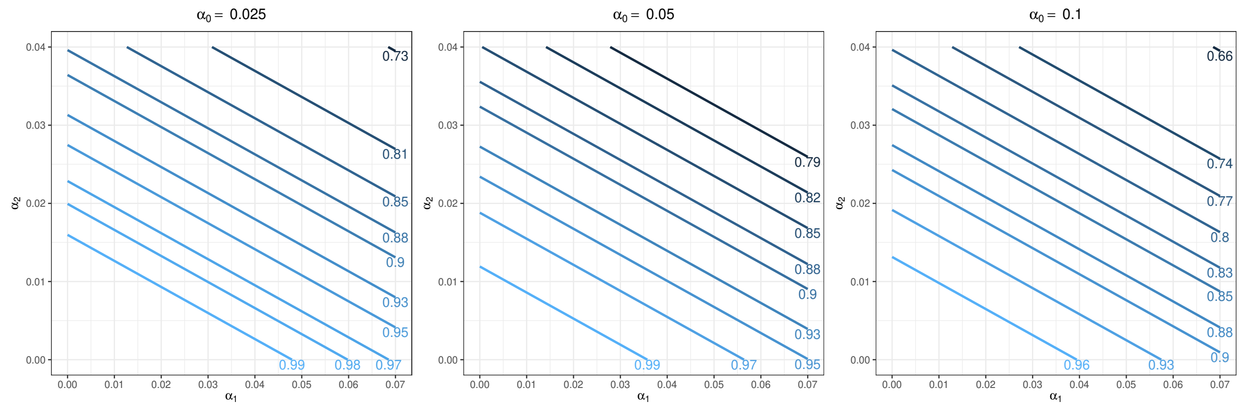
Application of the proposed method to the RESHAPE trial under different link functions

Given the same assumptions for the RESHAPE trial as in Section 5.1 of the main paper, under the identity link function, Equation (10) and (4) of the main paper suggested that the required number of municipalities is $N = 20$ with power of 80.10%. Web Figure 9 shows the sensitivity of power as a function of α_1 and α_2 at $\alpha_0 = \{0.025, 0.05, 0.1\}$, assuming $N = 20$ under the identity link function.



Web Figure 9: Predicted power contours as a function of α_1 and α_2 at $\alpha_0 = \{0.025, 0.05, 0.1\}$, with $N = 20, M = 3, K = 3, L = 36, \mathrm{P}_0 = 78.5\%, \mathrm{P}_1 = 88\%$ for the RESHAPE trial, under the identity link function.

Under the log link function, Equation (11) and (4) of the main paper suggested that the required number of municipalities is $N = 22$ with power of 82.91%. Web Figure 10 shows the sensitivity of power as a function of α_1 and α_2 at $\alpha_0 = \{0.025, 0.05, 0.1\}$, assuming $N = 22$ under the log link function.



Web Figure 10: Predicted power contours as a function of α_1 and α_2 at $\alpha_0 = \{0.025, 0.05, 0.1\}$, with $N = 22, M = 3, K = 3, L = 36, \mathrm{P}_0 = 78.5\%, \mathrm{P}_1 = 88\%$ for the RESHAPE trial, under the log link function.

Randomization at lower levels under the RESHAPE trial context

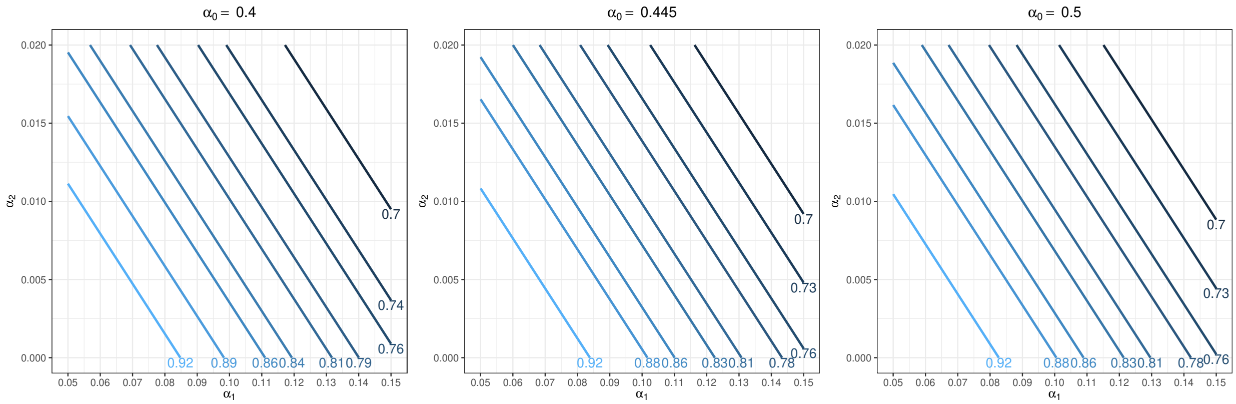
Web Table 20: Required number of municipalities (N) with $M = 3, K = 3, L = 36, \mathrm{P}_0 = 78.5\%, \mathrm{P}_1 = 88\%, \boldsymbol{\alpha} = (0.05, 0.04, 0.03)$ under the RESHAPE trial context, when randomization is hypothetically carried out in different levels.

Randomization Level	Logit Link		Identity Link		Log Link	
	N	Power	N	Power	N	Power
4	22	82.65%	20	80.10%	22	82.91%
3	8	91.78%	8	92.66%	8	90.55%
2	6	92.83%	6	93.57%	6	90.64%
1	6	96.69%	6	97.04%	6	95.11%

Application of the proposed method to the HALI trial under a different effect size

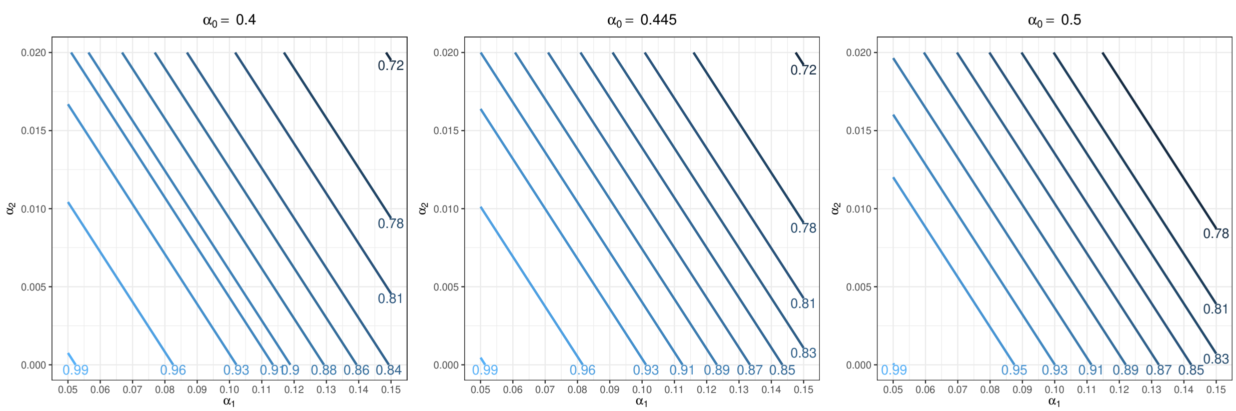
According to the results reported in Table 5 of Juke's paper (Jukes et al., 2017), the effect size was 0.25 SD for spelling scores. Given $M = 4, K = 25, L = 2, b = 0.25\sqrt{\phi}$, and $\boldsymbol{\alpha} = (0.445, 0.104, 0.008)$, Equation (8) and (4) of the main paper suggested that the required number of TAC tutor zones was $N = 22$ with power of 81.43%. Web Figure 11 shows the sensitivity of power as a function of α_1 and α_2 at $\alpha_0 = \{0.4, 0.445, 0.5\}$, assuming $N = 22$.

Since there were 26 TAC tutor zones in the actual trial sample, we also calculated the power of the actual trial. Given $N = 26, M = 4, K = 25, L = 2, b = 0.25\sqrt{\phi}$, and $\boldsymbol{\alpha} = (0.445, 0.104, 0.008)$,



Web Figure 11: Predicted power contours as a function of α_1 and α_2 at $\alpha_0 = \{0.4, 0.445, 0.5\}$, with $N = 22, M = 4, K = 25, L = 2, b = 0.25\sqrt{\phi}$ for the HALI trial.

using Equation (4) of the main paper, the power of the actual trial was 87.87%. Web Figure 12 shows the sensitivity of power as a function of α_1 and α_2 at $\alpha_0 = \{0.4, 0.445, 0.5\}$.



Web Figure 12: Predicted power contours as a function of α_1 and α_2 at $\alpha_0 = \{0.4, 0.445, 0.5\}$, with $N = 26, M = 4, K = 25, L = 2, b = 0.25\sqrt{\phi}$ for the HALI trial.

Randomization at lower levels under the HALI trial context

Web Table 21: Required number of TAC tutor zones (N) with $M = 4, K = 25, L = 2, \boldsymbol{\alpha} = (0.445, 0.104, 0.008)$ under the HALI trial context, when randomization is hypothetically carried out in different levels[a].

Effect Size per SD ($b/\sqrt{\phi}$)	Randomization Level	N	Power
0.19	4	36	80.87%
	3	30	82.40%
	2	8	81.52%
0.25	4	22	81.43%
	3	18	81.75%
	2	6	83.67%

[a] For the HALI trial, we cannot randomize at level one because there are repeated measures at that level.

References

Fay, M. P. and Graubard, B. I. (2001). Small-sample adjustments for wald-type tests using sandwich estimators. *Biometrics* **57,** 1198–1206.

Graybill, F. A. (1983). *Matrices with applications in statistics.* Number 512.896 G7 1983.

Henderson, H. V. and Searle, S. R. (1981). On deriving the inverse of a sum of matrices. *Siam Review* **23,** 53–60.

Jukes, M. C., Turner, E. L., Dubeck, M. M., Halliday, K. E., Inyega, H. N., Wolf, S., et al. (2017). Improving literacy instruction in kenya through teacher professional development and text messages support: A cluster randomized trial. *Journal of Research on Educational Effectiveness* **10,** 449–481.

Kauermann, G. and Carroll, R. J. (2001). A note on the efficiency of sandwich covariance matrix estimation. *Journal of the American Statistical Association* **96,** 1387–1396.

Li, F., Forbes, A. B., Turner, E. L., and Preisser, J. S. (2019). Power and sample size requirements for gee analyses of cluster randomized crossover trials. *Statistics in Medicine* **38,** 636–649.

Li, F., Turner, E. L., and Preisser, J. S. (2018). Sample size determination for gee analyses of stepped wedge cluster randomized trials. *Biometrics* **74,** 1450–1458.

Liang, K.-Y. and Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika* **73,** 13–22.

Lu, B., Preisser, J. S., Qaqish, B. F., Suchindran, C., Bangdiwala, S. I., and Wolfson, M. (2007). A comparison of two bias-corrected covariance estimators for generalized estimating equations. *Biometrics* **63,** 935–941.

Mancl, L. A. and DeRouen, T. A. (2001). A covariance estimator for gee with improved small-sample properties. *Biometrics* **57,** 126–134.

Morel, J. G., Bokossa, M., and Neerchal, N. K. (2003). Small sample correction for the variance of gee estimators. *Biometrical Journal: Journal of Mathematical Methods in Biosciences* **45,** 395–409.

Preisser, J. S., Young, M. L., Zaccaro, D. J., and Wolfson, M. (2003). An integrated population-averaged approach to the design, analysis and sample size determination of cluster-unit trials. *Statistics in medicine* **22,** 1235–1254.

Scott, J. M., deCamp, A., Juraska, M., Fay, M. P., and Gilbert, P. B. (2017). Finite-sample corrected generalized estimating equation of population average treatment effects in stepped wedge cluster randomized trials. *Statistical methods in medical research* **26,** 583–597.

Teerenstra, S., Lu, B., Preisser, J. S., Van Achterberg, T., and Borm, G. F. (2010). Sample size considerations for gee analyses of three-level cluster randomized trials. *Biometrics* **66,** 1230–1237.