Power and Sample Size Calculations for Generalized Estimating Equations via Local Asymptotics

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Supplementary Material

S1 Regularity conditions

(C1) The parameter space $\mathcal{B}$ is compact and $\beta_0$ belongs to its interior.
(C2) There exists $\delta > 1$ such that
$$ c_0 \equiv \sup_{m \geq 1} \max_{i=1,\ldots,m} E_{\beta_m} |h_i(y_i)|^{1+\delta} < \infty \quad \text{and} \quad c_1 \equiv \sup_{m \geq 1} \max_{i=1,\ldots,m} E_{\beta_m} |y_i|^\delta < \infty, $$
where $h_i(y_i) \equiv \sup_{b \in \mathcal{B}} |\Psi_i(y_i, b)|$.
(C3) For any bounded sequence $\{y_i\}$ with $y_i \in \mathbb{R}^n$, the functions $b \mapsto \Psi_i(y_i, b)$ are equicontinuous and uniformly bounded on $\mathcal{B}$.
(C4) $\sup_{m \geq 1} |E_{\delta_0} \{\Psi_i(y_i, b) - E_{\delta_0} \{\Psi_i(y_i, b^*)\}\} | \leq |b_1 - b_1^*| + |b - b^*|$ for all $b_1, b_1^*, b, b^* \in \mathcal{B}$, where “$\lesssim$” means “smaller than up to a constant”.
(C5) For all $\epsilon > 0$, $\inf_{m \geq 1, |b-b_0|>\epsilon} |f_{m,0}(b)| = 0 = |f_{m,0}(\beta_0)|$, where $f_{m,0}(b) = E_{\delta_0} \{m^{-1}s_m(b)\}$.
(C6) $\varphi_i(y, b) = \nabla_b \Psi_i(y, b)$ exists for all $y \in \mathbb{R}^n$, $b \in \mathcal{B}$, and its $j$th row (denoted by $\varphi_{ij}(y, b)$) for further use satisfies conditions (C1)–(C4) in place of $\Psi_i(y, b)$, for each $j = 1, \ldots, k$.
(C7) There exists a neighborhood $N$ of $\beta_0$ such that $\sup_{i \geq 1, j=1,\ldots,k} |V_{ij}(b) - V_{ij}(\beta_0)| \lesssim |b - \beta_0|$ for all $b \in N$, where $V_{ij}(b)$ is the $j$th column of $\text{Var}_{\delta_0}(\Psi_i(y_i, \beta_0))$.
(C8) The elements of $\frac{1}{m} M_m(\beta_0)$ and $\frac{1}{m} \sum_{i=1}^m \text{Var}_{\delta_0}(\Psi_i(y_i, \beta_0))$ converge to finite limits, where $M_m(\beta) = -E_{\delta_0} \{\nabla_\beta s_m(\beta)\}$.
(C9) $M(\beta_0) = \lim_{m \to \infty} \{m^{-1}M_m(\beta_0)\}$ is non-singular.

S2 Detailed formulae under marginal models

To obtain $\hat{\nu}_m$, it is straightforward that we only need to give a derivation of (3.4) and (3.5) from (3.2) and (3.3), for which we need to calculate $M_m(\beta_0)$, $E_{\beta_m}(s_m(\beta_0))$ and $\text{var}_{\beta_m}(s_m(\beta_0))$, with each mean and covariance understood to be conditioned on the covariates (which are suppressed in the notation) and cluster size. Under this setting, we have $\beta_m = (\phi_0, \alpha_T^m, \kappa_0^T, \psi_{\lambda m}^T)^T$ and $\beta_0 = (\phi_0, \alpha_T^0, \kappa_0^T, \psi_{\lambda m}^T)^T$. As discussed at the end of Section 2.1, a combined estimating equation can be used to estimate $\beta$ (see Fitzmaurice et al., 2009, Chap 3):
$$s_m(\beta) = \sum_{i=1}^{m} (\tilde{U}_i^T, u_i^T, U_i^T)^T = 0,$$

with \(\tilde{U}_i\) and \(u_i\) defined as follows:

$$\tilde{U}_i(\theta, \phi) = 1_{n_i \times 1}{\{\tilde{W}_i(\theta) - 1_{n_i \times 1}\}}$$

and

$$u_i(\theta, \alpha, \phi) = E_i^T{\{W_i(\theta, \phi) - \rho_i(\alpha)\}},$$

where \(\tilde{W}_i\) is the \(n_i\)-dimensional vector with \(j\)th element \(\tilde{W}_{ij} = (y_{ij} - \mu_{ij})^2/\nu(\mu_{ij})\), \(E_i = \partial \rho_i(\alpha)/\partial \alpha\), and \(\rho_i(\alpha)\) is the vector [of dimension \(n_i(n_i-1)/2\)] consisting of the upper-triangular entries of \(R_i(\alpha)\) in lexicographic order and \(W_i\) is defined in the same way as \(\rho_i(\alpha)\) except from the matrix with \(jk\)th entry.

Thus, in the general setting described in Section 2.2, we have \(\Psi_i(y_i) = (\tilde{U}_i^T, u_i^T, U_i^T)^T\), where \(U_i = D_i^T V_i(y_i - \mu_i(\theta))\), \(D_i = \partial \mu_i/\partial \theta\), and \(\theta = (\kappa^T, \psi^T)^T\). It can now be shown that \(M_m(\beta_0)\) has the form

$$M_m(\beta_0) = -\sum_{i=1}^{m} E_{\beta_0} \begin{pmatrix} \frac{\partial \tilde{U}_i}{\partial \phi} & \frac{\partial \tilde{U}_i}{\partial u_i} & \frac{\partial \tilde{U}_i}{\partial \theta} \\ \frac{\partial u_i}{\partial \phi} & \frac{\partial u_i}{\partial u_i} & \frac{\partial u_i}{\partial \theta} \\ \frac{\partial \tilde{U}_i}{\partial \phi} & \frac{\partial \tilde{U}_i}{\partial u_i} & \frac{\partial \tilde{U}_i}{\partial \theta} \end{pmatrix} = \begin{pmatrix} F & G \\ 0 & H \end{pmatrix},$$

where, writing \(W_i = D_i^T V_i^{-1}\) and denoting the \(j\)th row of \(W_i\) by \(W_{ij}\),

$$H = -\sum_{i=1}^{m} E_{\beta_0} \left( \partial U_i/\partial \theta \right)$$

$$= -\sum_{i=1}^{m} E_{\beta_0} [\partial \{W_i(y_i - \mu_i)\}/\partial \theta]$$

$$= -\sum_{i=1}^{m} \begin{pmatrix} E_{\beta_0} [\partial \{W_{i1}(y_i - \mu_i)\}/\partial \theta] \\ \vdots \\ E_{\beta_0} [\partial \{W_{ip+q}(y_i - \mu_i)\}/\partial \theta] \end{pmatrix}$$

$$= -\sum_{i=1}^{m} \begin{pmatrix} (y_i - \mu_i)^T \partial W_{i1}^T/\partial \theta - W_{i1} \partial \mu_i/\partial \theta \\ \vdots \\ (y_i - \mu_i)^T \partial W_{ip+q}^T/\partial \theta - W_{ip+q} \partial \mu_i/\partial \theta \end{pmatrix}$$

$$= \sum_{i=1}^{m} D_i^T V_i^{-1} D_i.$$
The zero submatrix at the bottom left-hand corner of $M_m(\beta_0)$ is due to the fact that $\partial U_i/\partial \phi$ and $\partial U_i/\partial \alpha$ are linear functions of $y_i - \mu_i(\theta_0)$, which has zero expectation when $\beta = \beta_0$. Then

$$\{M_m(\beta_0)\}^{-1} = \begin{pmatrix} F^{-1} & -F^{-1}GH^{-1} \\ 0 & H^{-1} \end{pmatrix}$$

and substituting into (2), we obtain

$$\xi_{m\psi} = B\{M_m(\beta_0)\}^{-1}E_{\beta_m}\{s_m(\beta_0)\}$$

$$= (0_{p\times(k-q-p)} \ B) \left( F^{-1} - F^{-1}GH^{-1} \right) E_{\beta_m}\{s_m(\beta_0)\}$$

$$= BH^{-1}\sum_{i=1}^{m} E_{\beta_m}(U_i)$$

$$= BA_m^{-1}\left\{ \frac{1}{m} \sum_{i=1}^{m} D_i^TV_i^{-1}(\mu_i(\theta_m) - \mu_i(\theta_0)) \right\},$$

where $A_m = \frac{1}{m} \sum_{i=1}^{m} D_i^TV_i^{-1}D_i$, $B = (0_{p\times k-q-p})$, and we used $E_{\beta_m}(U_i) = D_i^TV_i^{-1}(\mu_i(\theta_m) - \mu_i(\theta_0))$ in the last step. Here $A_m$, $D_i$ and $V_i$ are evaluated under $H_0$. Similarly, we have

$$\Sigma_{m\psi} = BA_m^{-1}\left\{ \frac{1}{m} \sum_{i=1}^{m} D_i^TV_i^{-1}\text{var}_{\beta_m}(y_i|x_i,v_i^{-1}D_i) \right\} A_m^{-1}B^T$$

by noticing that $\text{var}_{\beta_m}(U_i) = D_i^TV_i^{-1}\text{var}_{\beta_m}(y_i|x_i,v_i^{-1}D_i)$. Again, $A_m$, $D_i$ and $V_i$ are evaluated under $H_0$. Now we replace $h$ in the expressions of $\xi_{m\psi}$ and $\Sigma_{m\psi}$ by $\sqrt{m}(\psi_A - \psi_0)$. They become

$$\xi_{m\psi} = BA_m^{-1}\left\{ \frac{1}{m} \sum_{i=1}^{m} D_i^TV_i^{-1}(\mu_i(\theta_A) - \mu_i(\theta_0)) \right\}$$

and

$$\Sigma_{m\psi} = BA_m^{-1}\left\{ \frac{1}{m} \sum_{i=1}^{m} D_i^TV_i^{-1}\text{var}_{\beta_A}(y_i|x_i,v_i^{-1}D_i) \right\} A_m^{-1}B^T.$$
where \( \{(u_l, w_l), l = 1, \ldots, L\} \) are the \( L \) different possible values of covariates. LL also assumed that the structure of the true conditional correlation matrix of the outcome is known. The quasi-score test statistic \( T_m \) is given by

\[
T_m = S_m^T(\kappa_0, \psi_0) \hat{\Sigma}_m^{-1} S_m(\kappa_0, \psi_0),
\]

where \( S_m(\kappa_0, \psi_0) = \sum_{i=1}^m \left( \frac{\partial \mu_i}{\partial \psi} \right)^T V_i^{-1} (y_i - \mu_i) \mid_{\kappa=\kappa_0, \psi=\psi_0} \), \( \hat{\Sigma}_m = \text{cov}_H \{ S_m(\kappa_0, \psi_0) \} \)
and \( \kappa_0 \) is an estimator of \( \kappa \) obtained by solving

\[
S_m(\kappa, \psi_0) = \sum_{i=1}^m \left( \frac{\partial \mu_i}{\partial \psi} \right)^T V_i^{-1} (y_i - \mu_i) \mid_{\psi=\psi_0}.
\]

Under \( \psi = \psi_A \) and \( \kappa = \kappa_0 \), note that \( \kappa_0 \) is generally not a consistent estimator of \( \kappa_0 \) and it will converge to some value \( \kappa^*_0 \), namely the solution of

\[
\lim_{m \to \infty} m^{-1} \text{E}\{ S_m(\kappa^*_0, \psi_0); \kappa_0, \psi_A \} = 0.
\]

LL used standard Taylor series arguments to obtain an approximation to \( S_m(\kappa_0, \psi_0) \). This approximation is \( G(\kappa^*_0, \psi_0) = S_m(\kappa^*_0, \psi_0) - I_{\psi \kappa}^* (I_{\lambda \kappa}^*)^{-1} S_m(\kappa^*_0, \psi_0) \), where

\[
I_{\psi \kappa}^* = \sum_i \left( \frac{\partial \mu_i}{\partial \psi} \right)^T V_i^{-1} \left( \frac{\partial \mu_i}{\partial \kappa} \right) \mid_{\kappa=\kappa^*_0, \psi=\psi_0},
\]

and

\[
I_{\lambda \kappa}^* = \sum_i \left( \frac{\partial \mu_i}{\partial \kappa} \right)^T V_i^{-1} \left( \frac{\partial \mu_i}{\partial \kappa} \right) \mid_{\kappa=\kappa^*_0, \psi=\psi_0}.
\]

Let

\[
\mu^1_{ij} = g^{-1}(\kappa_0 + x_{ij} \psi_A),
\]

\[
\mu^*_{ij} = g^{-1}(\kappa^*_0 + x_{ij} \psi_0),
\]

\[
\mu^1_i = (\mu^1_{i1}, \mu^1_{i1}, \ldots, \mu^1_{in})^T,
\]

\[
\mu^*_i = (\mu^*_{i1}, \mu^*_{i1}, \ldots, \mu^*_n)^T,
\]

\[
P_i^* = \left\{ \left( \frac{\partial \mu_i}{\partial \psi} \right)^T - I_{\psi \kappa}^* I_{\lambda \kappa}^* \left( \frac{\partial \mu_i}{\partial \kappa} \right)^T \right\} \mid_{\kappa=\kappa^*_0, \psi=\psi_0},
\]

and \( V_i^* = V_i \mid_{\kappa=\kappa^*_0, \psi=\psi_0} \).
Notice that $G(\kappa_0, \psi_0) = \sum_i \mathbf{P}_i^*(V_i^*)^{-1}(y_i - \mu_i^*)$. Under the allocation scheme specified in (S3.1), and $\psi = \psi_A$ and $\kappa = \kappa_0$, LL claim that $G(\kappa_0, \psi_0)$ is approximately normal with mean and variance given by $m\xi$ and $m\Sigma$, respectively, where

$$\dot{\xi} = \sum_{i=1}^L \omega_i \mathbf{P}_i^*(V_i^*)^{-1}(\mu_i^1 - \mu_i^*) \quad (S3.11)$$

and

$$\dot{\Sigma} = \sum_{i=1}^L \omega_i \mathbf{P}_i^* (V_i^*)^{-1} \mathbf{cov}(y_i; \kappa_0, \psi_A) (V_i^*)^{-1} \mathbf{P}_i^{*T}. \quad (S3.12)$$

Here $\mu_i^1, \mu_i^1, \mathbf{P}_i^*$ and $V_i^*$ are defined as in (S3.8), (S3.9), (S3.10) and $V_i^*$ with $(x_i, z_i) = (u_i, w_i)$, and $\mathbf{cov}(y_i; \kappa_0, \psi_A)$ equals $\mathbf{cov}(y_i; \kappa_0, \psi_A)$ with $(x_i, z_i) = (u_i, w_i)$. So the distribution of $S_{m\psi}(\kappa_0, \psi_0)$ is approximated by $N(m\xi, m\Sigma)$, which implies that the distribution of $T_m$ is approximated by a noncentral chi-square distribution with $p$ degrees of freedom since $T_m$ has $p$ dimensions. The non-centrality parameter is given by

$$\dot{\nu}_m = (m\dot{\xi})^T (m\dot{\Sigma})^{-1} (m\dot{\xi}). \quad (S3.13)$$

The sample size $m$ for achieving nominal power $1 - \eta$ at significance level $\zeta$ is obtained by solving the equation $\dot{\nu}_m = \bar{\nu}$, which implies that

$$m = \frac{\bar{\nu}}{\xi^T \dot{\Sigma}^{-1} \xi}. \quad (S3.14)$$

Under the allocation scheme (S3.1), equation (S3.3) becomes

$$\sum_{i=1}^L \omega_i \left( \frac{\partial \mu_i^*}{\partial \kappa} \right)^T (V_i^*)^{-1}(\mu_i^1 - \mu_i^*) = 0, \quad (S3.15)$$

where $\frac{\partial \mu_i^*}{\partial \kappa} = \frac{\partial \mu_i}{\partial \kappa} |_{\kappa = \kappa_0, \psi = \psi_0}$, and $\mu_i$ is defined to be the mean vector $\mu_i$ with $(x_i, z_i) = (u_i, w_i)$. This equation corresponds to equation (12) in LL, which needs to be solved to derive explicit formulae for $\xi$ and $\Sigma$.

Two potential problems of this method were pointed out by Self and Mauritsen (1988):

1. Since $\tilde{\kappa}_0$ is not a consistent estimator of $\kappa$ under the alternative hypothesis, $\tilde{\Sigma}$ is not the asymptotic variance of $\frac{1}{\sqrt{m}} S_{m\psi}(\tilde{\kappa}_0, \psi_0)$. Thus the condition needed for the distributional result mentioned above does not hold, even asymptotically.

2. Even though the distribution of $\frac{1}{\sqrt{m}} S_{m\psi}(\tilde{\kappa}_0, \psi_0)$ approaches multivariate normality, the expected value of $S_{m\psi}(\tilde{\kappa}_0, \psi_0)$ is simultaneously going to infinity. Therefore, the result relies on the quality of the chi-square approximation at a sequence of points that move progressively farther out in the tail of the distribution as $m$ becomes large.

The first problem is caused by inconsistency of the estimator under fixed alternatives. The second problem is caused by the test statistic converging in probability to a degenerate distribution (infinity) under fixed alternatives. Our approach using local asymptotic theory succeeds in overcoming both of these problems.
S4  Approach of Shih (1997)

Shih considered the case $p = 1$, with the working covariance identical to the true covariance, and approximated the distribution of $W_m$ under the fixed alternative $\psi = \psi_A$ by a noncentral $\chi^2$ with non-centrality parameter $\tilde{v}_m = m\psi_A^2/v$, where $v$ is the asymptotic variance of $\hat{\psi}$ (cf. Remark 2 in Section A) when $\psi = \psi_A$. This is similar to the approach discussed in Remark 4 of Section 3.2, where the asymptotic power function is used, except that the variance now depends on the value of parameter under a fixed alternative. In this approach, the sample size for achieving nominal power $1 - \eta$ at significance level $\zeta$ based on a two-sided test is simply given by $m = v(z_{1-\zeta/2} + z_{1-\eta})^2/(\psi_A - \psi_0)^2$.

S5  Two lemmas

The following lemmas are crucial for proving our main results.

**Lemma 1** Let $H_m(b) = m^{-1}\sum_{i=1}^m \{ \Psi_i(y_i, b) - E_{\beta_m}(\Psi_i(y_i, b)) \}$. Under conditions (C1)–(C3),

$$\sup_{b \in B} |H_m(b)| \xrightarrow{P_m} 0.$$

This lemma is a routine extension of a uniform law of large numbers of Shao (Lemma 5.3) to a triangular array. The result is similar to a Glivenko–Cantelli theorem in that the convergence holds uniformly over a class of functions. The relative compactness condition (C3) plays a crucial role in the proof. The proof is similar to that for Lemma 5.3 in Shao.

**Proof.** Since we only need to consider components of $\Psi_i$’s, without loss of generality we can assume that $\Psi_i$’s are functions from $\mathbb{R}^{m_i} \times B$ to $\mathbb{R}$. For any fixed $\epsilon > 0$ and any fixed subset $O \subset B$,

$$P_m \left( \sup_{b \in O} |H_m(b)| > \epsilon \right) \leq P_m \left( \sup_{b \in O} H_m(b) > \epsilon \right) + P_m \left( \inf_{b \in O} H_m(b) < -\epsilon \right) \quad (S5.1)$$

We will show the first term on the right hand side converges to zero; the second term converges to zero by a similar argument. Clearly,

$$P_m \left( \sup_{b \in O} H_m(b) > \epsilon \right) \leq P_m \left[ m^{-1} \sum_{i=1}^m \left\{ \sup_{b \in O} \Psi_i(y_i, b) - E_{\beta_m}(\inf_{b \in O} \Psi_i(y_i, b)) \right\} > \epsilon \right]$$

$$= P_m \left[ m^{-1} \sum_{i=1}^m \Psi_i^{(m)} + m^{-1} \sum_{i=1}^m E_{\beta_m} \left\{ \sup_{b \in O} \Psi_i(y_i, b) - \inf_{b \in O} \Psi_i(y_i, b) \right\} > \epsilon \right], \quad (S5.2)$$

where $\Psi_i^{(m)} = \sup_{b \in O} \Psi_i(y_i, b) - E_{\beta_m}(\sup_{b \in O} \Psi_i(y_i, b))$. Since

$$\sup_{m \geq 1} \max_{i=1,\ldots,m} E_{\beta_m} |h_i(y_i)|^{1+\delta} \leq \sup_{m \geq 1} \max_{i=1,\ldots,m} E_{\beta_m} |h_i(y_i)|^{1+\delta} < c_0,$$
where \( h_i(y_i) \) is defined in condition (C2), then \( m^{-1} \sum_{i=1}^{m} \Psi_i^{(m)} = o_{P_m}(1) \) by Lemma 2. If we show that

\[
\frac{1}{m} \sum_{i=1}^{m} E_{\beta_m} \left\{ \sup_{b \in O} \Psi_i(y_i, b) - \inf_{b \in O} \Psi_i(y_i, b) \right\} < \bar{\epsilon},
\]

for all \( m \geq 1 \) where \( 0 < \bar{\epsilon} < \epsilon \), then (S5.2) converges to zero. Next we show that the above equation holds when the subset \( O \) is sufficiently small.

Using the Hölder and Markov inequalities, and condition (C2), for any \( c > 0 \)

\[
E_{\beta_m} \left\{ \frac{1}{m} \sum_{i=1}^{m} h_i(y_i) I_{(c, \infty)}(|y_i|) \right\} \\
\leq \max_{i=1, \ldots, m} E_{\beta_m} \left\{ h_i(y_i) I_{(c, \infty)}(|y_i|) \right\} \\
\leq \max_{i=1, \ldots, m} \left\{ E_{\beta_m} |h_i(y_i)|^{1+\delta} \right\}^{1/(1+\delta)} \left\{ P_m(|y_i| > c) \right\}^{\delta/(1+\delta)} \\
\leq \max_{i=1, \ldots, m} \left\{ E_{\beta_m} |h_i(y_i)|^{1+\delta} \right\}^{1/(1+\delta)} \left\{ \frac{E_{\beta_m} |y_i|^\delta}{c^\delta} \right\}^{\delta/(1+\delta)} \\
= \left\{ \max_{i=1, \ldots, m} \left\{ E_{\beta_m} |h_i(y_i)|^{1+\delta} \right\}^{1/(1+\delta)} \right\} \left\{ \max_{i=1, \ldots, m} E_{\beta_m} |y_i|^\delta \right\}^{\delta/(1+\delta)} c^{-\delta^2/(1+\delta)} \\
\leq c_0 \frac{1}{c_1} \frac{\delta/(1+\delta)}{\delta^2/(1+\delta)} c^{-\delta^2/(1+\delta)}
\]

for all \( m \geq 1 \). Thus for any \( \epsilon > \bar{\epsilon} > \epsilon/2 \), there exists \( c > 0 \) such that

\[
E_{\beta_m} \left\{ \frac{1}{m} \sum_{i=1}^{m} h_i(y_i) I_{(c, \infty)}(|y_i|) \right\} < \bar{\epsilon}/2 - \epsilon/4
\]

for all \( m \geq 1 \). For this value of \( c \),

\[
E_{\beta_m} \left\{ \frac{1}{m} \sum_{i=1}^{m} h_i(y_i) I_{(c, \infty)}(|y_i|) \right\} \\
\leq E_{\beta_m} \left\{ \frac{1}{m} \sum_{i=1}^{m} \sup_{b \in \mathbb{A}} \Psi_i(y_i, b) - \inf_{b \in \mathbb{A}} \Psi_i(y_i, b) \right\} I_{(c, \infty)}(|y_i|) \\
\leq E_{\beta_m} \left\{ \frac{1}{m} \sum_{i=1}^{m} \sup_{b \in \mathbb{A}} \Psi_i(y_i, b) I_{(c, \infty)}(|y_i|) + m^{-1} \sum_{i=1}^{m} \inf_{b \in \mathbb{A}} \Psi_i(y_i, b) I_{(c, \infty)}(|y_i|) \right\} \\
\leq E_{\beta_m} \left\{ \frac{1}{m} \sum_{i=1}^{m} h_i(y_i) I_{(c, \infty)}(|y_i|) + m^{-1} \sum_{i=1}^{m} h_i(y_i) I_{(c, \infty)}(|y_i|) \right\} \\
= 2E_{\beta_m} \left\{ \frac{1}{m} \sum_{i=1}^{m} h_i(y_i) I_{(c, \infty)}(|y_i|) \right\} \\
< \bar{\epsilon} - \epsilon/2 \quad \text{(S5.3)}
\]
for all $m \geq 1$. By the equicontinuity of $\{\Psi_i(\mathbf{y}, b)\}$ in condition (C3), there exists a $\delta_\epsilon > 0$ such that
\[
m^{-1} \sum_{i=1}^{m} \left\{ \sup_{b \in O_{c}} \Psi_i(\mathbf{y}, b) - \inf_{b \in O_{c}} \Psi_i(\mathbf{y}, b) \right\} I_{[0,\epsilon]}(|y|) < \epsilon/2
\]
for all $m \geq 1$, where $O_{c}$ is any subset of $\mathbb{B}$ with $\text{diam}(O_{c}) < \delta_\epsilon$. Here $\text{diam}(O_{c})$ is defined as the supremum of the distances between pairs of points in $O_{c}$. The inequality (S5.3) holds with $O$ replaced by $O_{c}$ which together with the above inequality implies
\[
m^{-1} \sum_{i=1}^{m} E_{\beta_{m}} \left\{ \sup_{b \in O_{c}} \Psi_i(\mathbf{y}, b) - \inf_{b \in O_{c}} \Psi_i(\mathbf{y}, b) \right\}
\]
\[= E_{\beta_{m}} \left[ m^{-1} \sum_{i=1}^{m} \left\{ \sup_{b \in O_{c}} \Psi_i(\mathbf{y}, b) - \inf_{b \in O_{c}} \Psi_i(\mathbf{y}, b) \right\} I_{(c,\infty)}(|y|) \right]
\]
\[+ E_{\beta_{m}} \left[ m^{-1} \sum_{i=1}^{m} \left\{ \sup_{b \in O_{c}} \Psi_i(\mathbf{y}, b) - \inf_{b \in O_{c}} \Psi_i(\mathbf{y}, b) \right\} I_{[0,c]}(|y|) \right]
\]
\[< \tilde{\epsilon} - \epsilon/2 + \epsilon/2 = \tilde{\epsilon} < \epsilon
\]
for all $m \geq 1$. The right hand side of (S5.2) with $O$ replaced by $O_{c}$ converges to zero since it is bounded above by

\[
P_{m} \left( m^{-1} \sum_{i=1}^{m} \Psi_i^m > \epsilon - \tilde{\epsilon} \right) \rightarrow 0,
\]
and we conclude that $P_{m} \left( \sup_{b \in O_{c}} H_m(b) > \epsilon \right) \rightarrow 0$. By a similar argument,
\[
P_{m} \left( \inf_{b \in O_{c}} H_m(b) < -\epsilon \right) \rightarrow 0.
\]
Thus by (S5.1), we have
\[
P_{m} \left( \sup_{b \in O_{c}} |H_m(b)| > \epsilon \right) \rightarrow 0.
\]
(S5.4)

Due to the compactness of $\mathbb{B}$, there exist finitely many open balls $\{O_{c}^j\}_{j=1,...,n_\epsilon}$ with $\text{diam}(O_{c}^j) < \delta_\epsilon$ in $\mathbb{R}^k$ to cover $\mathbb{B}$. That implies
\[
\left\{ \sup_{b \in \mathbb{B}} |H_m(b)| > \epsilon \right\} \subset \bigcup_{j=1}^{n_\epsilon} \left\{ \sup_{b \in O_{c}^j \cap \mathbb{B}} |H_m(b)| > \epsilon \right\},
\]
which together with (S5.4) indicates
\[
P_{m} \left( \sup_{b \in \mathbb{B}} |H_m(b)| > \epsilon \right) \leq \sum_{j=1}^{n_\epsilon} P_{m} \left( \sup_{b \in O_{c}^j \cap \mathbb{B}} |H_m(b)| > \epsilon \right) \rightarrow 0,
\]
concluding the proof.

**Lemma 2** Let $\{X_{mi}\}_{i=1,...,m}$ be independent random variables. If there is a constant $r > 1$ such that
\[
L = \sup_{m \geq 1} \max_{i=1,...,m} E|X_{mi}|^r < \infty,
\]
then
\[ \frac{1}{m} \sum_{i=1}^{m} \{ X_{mi} - E(X_{mi}) \} \xrightarrow{P} 0. \]

This lemma is a version of the WLLN (see, e.g., Theorem 1.14 (ii) in Shao) in the setting of a triangular array. The proof is straightforward by Lyapounov’s inequality, Jensen’s inequality and Theorem 2 of von Bahr and Esseen (1965).

**Proof.** By Liapounov’s inequality, it suffices to consider \( r \in (1, 2] \). For any \( \epsilon > 0 \), by Markov’s inequality
\[
P \left[ \frac{1}{m} \left| \sum_{i=1}^{m} \{ X_{mi} - E(X_{mi}) \} \right| > \epsilon \right] = P \left[ \frac{1}{m} \left( \sum_{i=1}^{m} \{ X_{mi} - E(X_{mi}) \} \right)^r > \epsilon^r \right] \leq \frac{1}{\epsilon^r m^r} E \left( \left( \sum_{i=1}^{m} \{ X_{mi} - E(X_{mi}) \} \right)^r \right).
\]  
(S5.5)

By the inequality \( |a + b|^r \leq 2^{r-1}(|a|^r + |b|^r) \) (Jensen’s inequality) and Lyapounov’s inequality,
\[
\max_{i=1,\ldots,m} E|X_{mi} - E(X_{mi})|^r \leq \max_{i=1,\ldots,m} 2^{r-1} \{ E|X_{mi}|^r + E|E(X_{mi})|^r \} \leq 2^r \max_{i=1,\ldots,m} E|X_{mi}|^r 
\]
\[
\leq 2^r L.
\]

Then, according to Theorem 2 of von Bahr and Esseen (1965), we have
\[
E \left[ \sum_{i=1}^{m} \{ X_{mi} - E(X_{mi}) \} \right]^r \leq 2 \sum_{i=1}^{m} E|X_{mi} - E(X_{mi})|^r \leq 2^{r+1} m L.
\]

Combining the above inequality and (S5.5),
\[
P \left[ \frac{1}{m} \left( \sum_{i=1}^{m} (X_{mi} - E(X_{mi})) \right) > \epsilon \right] \leq \frac{2^{r+1} L}{\epsilon^r m^{r-1}} \rightarrow 0,
\]
concluding the proof.

**S6 Proof of Theorem 1**

We first show that \( \widehat{\psi} \xrightarrow{P} \psi_0 \) under conditions (C1)–(C5) by adapting the proof of Theorem 5.7 of van der Vaart (1998). Let \( f_{m,m}(b) = E_{\hat{\beta}_m} \{ m^{-1} s_{m}(b) \} \). By Lemma 1,
\[
\left| m^{-1} s_{m} (\hat{\beta}) - f_{m,m}(\hat{\beta}) \right| \leq \sup_{b \in \mathcal{B}} |H_m(b)| \xrightarrow{P} 0.
\]
Since $s_m(\hat{\beta}) = 0$, it follows that $f_{m,m}(\hat{\beta}) \overset{P_m}{\rightarrow} 0$, which together with condition (C4) shows that there exists $L > 0$ such that

$$|f_{m,0}(\hat{\beta})| \leq |f_{m,0}(\hat{\beta}) - f_{m,m}(\hat{\beta})| + |f_{m,m}(\hat{\beta})| \leq L|\hat{\beta}_m - \beta_0| + o_{P_m}(1) = o_{P_m}(1),$$

where $f_{m,0}$ is defined in (C5). According to (C5), which indicates that the solution $\beta_0$ of $f_m(b) = 0$ is well-separated from other points in $\mathbb{B}$, for all $\epsilon > 0$ there exists $\delta > 0$ such that

$$\{|\hat{\beta} - \beta_0| > \epsilon\} \subset \{|f_{m,0}(\hat{\beta})| > \delta\}$$

for all $m \geq 1$, which together with (S6.1) implies that $|\hat{\beta} - \beta_0| \overset{P_m}{\rightarrow} 0$. Therefore, $\hat{\beta} \overset{P_m}{\rightarrow} \beta_0$ and $\hat{\psi} \overset{P_m}{\rightarrow} \psi_0$.

Next, assuming conditions (C1)–(C9), we will show $\sqrt{m}(\hat{\psi} - \psi_0)$ converges to $N_p(h, B\Sigma\beta_0 B^T)$ in distribution under $P_m$. It suffices to consider $\sqrt{m}(\hat{\beta} - \beta_0)$, since $\hat{\psi}$ is a subvector of $\hat{\beta}$. By the fundamental theorem of calculus, the chain rule, and the fact that $s_m(\hat{\beta}) = 0$, in terms of $g(t) = s_m(\beta_0 + t(\hat{\beta} - \beta_0)), 0 \leq t \leq 1$, we have

$$-s_m(\beta_0) = s_m(\hat{\beta}) - s_m(\beta_0) = g(1) - g(0) = \int_0^1 g'(t) \, dt$$

$$= \left\{ \int_0^1 \nabla s_m(\beta_0 + t(\hat{\beta} - \beta_0)) \, dt \right\} (\hat{\beta} - \beta_0).$$

(S6.2)

We also have

$$\left| m^{-1} \left[ \int_0^1 \nabla s_m(\beta_0 + t(\hat{\beta} - \beta_0)) \, dt - E_{\beta_m} \{\nabla s_m(\beta_0)\} \right] \right|$$

$$\leq \int_0^1 \left| m^{-1} \left[ \nabla s_m(\beta_0 + t(\hat{\beta} - \beta_0)) - E_{\beta_m} \{\nabla s_m(\beta_0)\} \right] \right| \, dt,$$

(S6.3)

where $\| \cdot \|$ denotes the Frobenius matrix norm, that is $\|A\| = \sqrt{\text{tr}(AA^T)}$ for any matrix $A$. We will show that (S6.3) has order $o_{P_m}(1)$, for which it suffices to show that

$$\int_0^1 m^{-1} \left| \sum_{i=1}^m \varphi_{ij}(y_i, \beta_0 + t(\hat{\beta} - \beta_0)) - \sum_{i=1}^m E_{\beta_m} \{\varphi_{ij}(y_i, \beta_0)\} \right| \, dt = o_{P_m}(1),$$

(S6.4)

for $j = 1, \ldots, k$. The integrand in the above expression is (uniformly) bounded by

$$\sup_{b \in \mathbb{B}} m^{-1} \left| \sum_{i=1}^m \varphi_{ij}(y_i, b) - \sum_{i=1}^m E_{\beta_m} \{\varphi_{ij}(y_i, b)\} \right|$$

$$+ \sup_{0 \leq t \leq 1} m^{-1} \left| \sum_{i=1}^m E_{\beta_m} \{\varphi_{ij}(y_i, \beta_0 + t(\hat{\beta} - \beta_0))\} - \sum_{i=1}^m E_{\beta_m} \{\varphi_{ij}(y_i, \beta_0)\} \right|.$$ (S6.5)

Using an argument similar to the proof of Lemma 1, we can show that under conditions (C1)–(C3) and (C6), (S6.5) = $o_{P_m}(1)$. By conditions (C4) and (C6), there exists a $L > 0$ such that
(S6.6) ≤ \sup_{0 \leq t \leq 1} L|\tilde{\beta} - \beta_0| = L|\tilde{\beta} - \beta_0| = o_{P_m}(1) by the first part of the proof. Thus (S6.3) = o_{P_m}(1), and since under conditions (C4) and (C6) we have \( m^{-1}||E_{\beta_m}\{\nabla s_m(\beta_0)\} - \) \( M_m(\beta_0)|| = o(1), \) it follows that

\[
m^{-1}\left\| \int_0^1 \nabla s_m(\beta_0 + t(\beta - \beta_0))dt \right\| - M_m(\beta_0) \right\| = o_{P_m}(1).
\]

The above display together with (S6.2) and conditions (C8) and (C9) give

\[
\sqrt{m}\{M_m(\beta_0)\}^{-1}s_m(\beta_0) = (1 + o_{P_m}(1))\sqrt{m}(\tilde{\beta} - \beta_0).
\]  

(S6.7)

The result then follows if the left hand side above converges in distribution under \( P_m \) to \( N(h^*, \Sigma_{\beta_0}) \), where \( h^* = (0_{k-p}^T, h^*)^T \) and \( 0_{k-p} \) is the \((k - p)\)-dimensional zero vector. We will establish this using the Lindeberg–Feller theorem and the Cramér–Wold device. Fix a nonzero \( k \)-vector \( l \) and \( \epsilon > 0 \). The Lindeberg condition is checked using condition (C2) and the Hölder and Markov inequalities:

\[
\sum_{i=1}^m E_{\beta_m}\sqrt{ml^T}\{M_m(\beta_0)\}^{-1}\Psi_i(y_i, \beta_0)^2\{\sqrt{ml^T}\{M_m(\beta_0)\}^{-1}\Psi_i(y_i, \beta_0)\} > \epsilon
\]

\[
\leq \sum_{i=1}^m \left[ E_{\beta_m}\sqrt{ml^T}\{M_m(\beta_0)\}^{-1}\Psi_i(y_i, \beta_0)^{2+\tilde{\delta}} \right]^\frac{1}{2+\tilde{\delta}}
\]

\[
\times [P_m(\{\sqrt{ml^T}\{M_m(\beta_0)\}^{-1}\Psi_i(y_i, \beta_0)\} > \epsilon)]^{\frac{\epsilon}{2+\tilde{\delta}}}
\]

\[
\leq m\{M_m(\beta_0)\}^{-1}l^2 \sum_{i=1}^m E_{\beta_m}\Psi_i(y_i, \beta_0)^{2+\tilde{\delta}} \]

\[
\times \left[ (\sqrt{m}\{M_m(\beta_0)\}^{-1}l)^{2+\tilde{\delta}} E_{\beta_m}\Psi_i(y_i, \beta_0)^{2+\tilde{\delta}} \right]\frac{1}{2+\tilde{\delta}}
\]

\[
= m^{1+\tilde{\delta}/2}\{M_m(\beta_0)\}^{-1}l^{2+\tilde{\delta}} \sum_{i=1}^m E_{\beta_m}\Psi_i(y_i, \beta_0)^{2+\tilde{\delta}}
\]

\[
\leq \frac{m^{2+\tilde{\delta}/2}\{M_m(\beta_0)\}^{-1}l^{2+\tilde{\delta}} \epsilon_0}{\epsilon^{\tilde{\delta}}} = \frac{|\{m^{-1}M_m(\beta_0)\}^{-1}l^{2+\tilde{\delta}} \epsilon_0}{m^{\delta/2}\epsilon^{\delta}} \rightarrow 0,
\]

where \( 1\{\cdot\} \) is an indicator function, \( \tilde{\delta} = \delta - 1 \) and the last step is from condition (C9). Also under condition (C7),

\[
\sum_{i=1}^m \Var_{\beta_m}(\sqrt{ml^T}\{M_m(\beta_0)\}^{-1}\Psi_i(y_i, \beta_0))
\]

\[
= \sum_{i=1}^m m l^T\{M_m(\beta_0)\}^{-1} \Var_{\beta_m}(\Psi_i(y_i, \beta_0)) \{M_m(\beta_0)\}^{-1}l
\]

\[
= l^T\{m^{-1}M_m(\beta_0)\}^{-1}\{m^{-1} \Var_{\beta_m}(s_m(\beta_0))\} \{m^{-1}M_m(\beta_0)\}^{-1}l \rightarrow l^T \Sigma_{\beta_0} l.
\]

Thus \( \sqrt{ml^T}\{M_m(\beta_0)\}^{-1}\{s_m(\beta_0) - E_{\beta_m}(s_m(\beta_0))\} \) converges to \( N(0, l^T \Sigma_{\beta_0} l) \) in distribution under \( P_m \). Now we show that \( \sqrt{ml^T}\{M_m(\beta_0)\}^{-1}E_{\beta_m}(s_m(\beta_0)) \rightarrow l^T h^* \). From condition
(C6),

$$\sup_{m \geq 1} \max_{i=1,...,m} E_{\beta_m} \left\{ \sup_{b \in \mathbb{B}} |\varphi_{ij}(y_i, b)| \right\} < \infty, \quad (S6.8)$$

$$\sup_{0 \leq t \leq 1} \left| m^{-1} E_{\beta_m} \left\{ \sum_{i=1}^{m} \varphi_{ij}(y_i, \beta_m + th^* / \sqrt{m}) \right\} - m^{-1} E_{\beta_0} \left\{ \sum_{i=1}^{m} \varphi_{ij}(y_i, \beta_0) \right\} \right| \lesssim \sup_{0 \leq t \leq 1} (|\beta_m - \beta_0| + |th^* / \sqrt{m}|) \to 0 \quad (S6.9)$$

for $j = 1, \ldots, k$. Since $m^{-1} \sum_{i=1}^{m} \varphi_{ij}(y_i, b)$ is the $j$th row of $\nabla b_s(b)$, by (S6.8) and (S6.9)

$$l^T \sqrt{m} \{M_m(\beta_0)\}^{-1} E_{\beta_m} \{s_m(\beta_0)\} = l^T \sqrt{m} \{M_m(\beta_0)\}^{-1} E_{\beta_m} \{s_m(\beta_0) - s_m(\beta_m)\} = l^T \sqrt{m} \{M_m(\beta_0)\}^{-1} E_{\beta_m} \left\{ \int_0^1 \nabla \beta s_m(\beta_0 + th^* / \sqrt{m}) dt \right\} \frac{-h^*}{\sqrt{m}}$$

$$= l^T \{M_m(\beta_0)\}^{-1} \int_0^1 E_{\beta_m} \left\{ -\nabla \beta s_m(\beta_0 + th^* / \sqrt{m}) \right\} dt h^* \quad (S6.10)$$

$$= l^T \{M_m(\beta_0)\}^{-1} \int_0^1 m^{-1} E_{\beta_m} \left\{ -\nabla \beta s_m(\beta_0 + th^* / \sqrt{m}) \right\} dt h^*$$

$$\to l^T \{M_m(\beta_0)\}^{-1} \int_0^1 M(\beta_0) dt h^* = l^T h^*, \quad (S6.11)$$

where (S6.10) and (S6.11) use Fubini’s theorem and the dominated convergence theorem, respectively, and $\nabla \beta s_m(\beta_0 + th^* / \sqrt{m}) = \partial s_m(b) / \partial b |_{b=\beta_0 + th^* / \sqrt{m}}$. Combining the above result and that $\sqrt{m} l^T \{M_m(\beta_0)\}^{-1} s_m(\beta_0) - E_{\beta_m} \{s_m(\beta_m)\}$ converges in distribution to $N(0, l^T \Sigma_{\beta_0} l)$ under $P_m$, we have that $\sqrt{m} l^T \{M_m(\beta_0)\}^{-1} s_m(\beta_0)$ converges under $P_m$ in distribution to $N(l^T h^*, l^T \Sigma_{\beta_0} l)$ for any non-zero $k$-vector $l$. Thus $\sqrt{m} \{M_m(\beta_0)\}^{-1} s_m(\beta_0)$ converges in distribution to $N(h^*, \Sigma_{\beta_0})$ under $P_m$, and from (S6.7) and using Slutsky’s lemma, $\sqrt{m}(\hat{\beta} - \beta_0)$ converges in distribution under $P_m$ to $N(h^*, \Sigma_{\beta_0})$. The proof is completed by noticing that $\psi = B \beta$.

**S7 Proof of Theorem 2**

**Asymptotic distribution of $W_m$**

To prove $W_m$ converges in distribution under $H_{1m}$ to $\chi^2_2(\nu)$, the key step is to show that $\hat{\Sigma}$ converges in probability under $H_{1m}$ to $\Sigma_{\beta_0}$, which implies that $B\Sigma B^T$ converges in probability under $H_{1m}$ to $B\Sigma_{\beta_0} B^T$. Note that, under conditions (C7)–(C9),

$$\Sigma_{\beta_0} = \{M(\beta_0)\}^{-1} \left[ \lim_{m \to \infty} m^{-1} \sum_{i=1}^{m} \text{Var}_{\beta_0} \{\Psi_i(y_i, \beta_0)\} \right] \{M(\beta_0)\}^{-1}. $$
Write
\[ \hat{\Sigma} = \left\{ m^{-1} M_m(\hat{\beta}) \right\}^{-1} \left\{ m^{-1} \sum_{i=1}^{m} \Psi_i(y_i, \hat{\beta})\Psi_i(y_i, \hat{\beta})^T \right\} \left\{ m^{-1} M_m(\hat{\beta}) \right\}^{-1}. \]

We will show that
\[ m^{-1} M_m(\hat{\beta}) = M(\beta_0) + o_P(1) \quad (S7.1) \]
and
\[ m^{-1} \sum_{i=1}^{m} \Psi_i(y_i, \hat{\beta})\Psi_i(y_i, \hat{\beta})^T - m^{-1} \sum_{i=1}^{m} \text{Var}_{\beta_0} \{\Psi_i(y_i, \beta_0)\} = o_P(1). \quad (S7.2) \]

The proof of (S7.1) is straightforward using conditions (C4), (C6) and (C9) and the consistency of \( \beta \) shown in Section B:
\[
\| m^{-1} M_m(\hat{\beta}) - M(\beta_0) \| = \| m^{-1} M_m(\hat{\beta}) - m^{-1} M_m(\beta_0) \|
+ \| m^{-1} M_m(\beta_0) - M(\beta_0) \|
\leq |\hat{\beta} - \beta_0| + o(1) = o_P(1).
\]

Write the left hand side of (S7.2) as:
\[
m^{-1} \sum_{i=1}^{m} \Psi_i(y_i, \hat{\beta})\Psi_i(y_i, \hat{\beta})^T - m^{-1} \sum_{i=1}^{m} \Psi_i(y_i, \beta_0)\Psi_i(y_i, \beta_0)^T \quad (S7.3)
+ m^{-1} \sum_{i=1}^{m} \left[ \Psi_i(y_i, \beta_0)\Psi_i(y_i, \beta_0)^T - E_{\beta_m} \left\{ \Psi_i(y_i, \beta_0)\Psi_i(y_i, \beta_0)^T \right\} \right] \quad (S7.4)
+ m^{-1} \sum_{i=1}^{m} \left( E_{\beta_m} - E_{\beta_0} \right) \left\{ \Psi_i(y_i, \beta_0)\Psi_i(y_i, \beta_0)^T \right\} \quad (S7.5)
\]

Let \( \Psi_{ij}(y_i, \beta_0) \) be the \( j \)th element of the vector \( \Psi_i(y_i, \beta_0) \) for \( j = 1, \ldots, k \). The term (S7.4) converges to zero in probability under \( H_{1m} \) by Lemma 2; the condition needed to apply that lemma can be shown to hold using the Cauchy–Schwarz inequality and condition (C2). It can be shown that (S7.5) = \( o(1) \) since under conditions (C2), (C4) and (C7)
\[
|E_{\beta_m} - E_{\beta_0}| \left\{ \Psi_{ij}(y_i, \beta_0)\Psi_{il}(y_i, \beta_0) \right\}
\leq |\text{cov}_{\beta_m}(\Psi_{ij}(y_i, \beta_0), \Psi_{il}(y_i, \beta_0)) - \text{cov}_{\beta_0}(\Psi_{ij}(y_i, \beta_0), \Psi_{il}(y_i, \beta_0))|
+ |E_{\beta_m}(\Psi_{ij}(y_i, \beta_0))| |E_{\beta_0}(\Psi_{il}(y_i, \beta_0)) - E_{\beta_0}(\Psi_{il}(y_i, \beta_0))|
+ |E_{\beta_0}(\Psi_{il}(y_i, \beta_0))| |E_{\beta_m}(\Psi_{ij}(y_i, \beta_0)) - E_{\beta_0}(\Psi_{ij}(y_i, \beta_0))|
\leq |\beta_m - \beta_0| = o(1).
\]

Next consider the matrix (S7.3). If each component can be shown to converge in probability under \( H_{1m} \) to zero, then we have completed the proof of (S7.2). Let
\[
g_{ijl}(y_i, b) = \frac{\partial}{\partial b} \{ \Psi_{ij}(y_i, b)\Psi_{il}(y_i, b) \}
= \varphi_{ij}(y_i, b)\Psi_{il}(y_i, b) + \varphi_{il}(y_i, b)\Psi_{ij}(y_i, b) \equiv g_{ijl}(y_i, b) + g_{ijl}(y_i, b).
\]
As in (S6.2), but with the role of \( g(t) \) now played by \( m^{-1} \sum_{i=1}^{m} \psi_{ij}(y_i, \beta_0 + t(\hat{\beta} - \beta_0))/\psi_{ij}(y_i, \beta_0 + t(\hat{\beta} - \beta_0)), 0 \leq t \leq 1, \) for any fixed \( \varepsilon > 0, \) the \( j \)th entry of (S7.3) is bounded above by

\[
\left\lvert \int_0^1 m^{-1} \sum_{i=1}^{m} g_{ij}(y_i, \beta_0 + t(\hat{\beta} - \beta_0)) \, dt \right\rvert (\hat{\beta} - \beta_0) \leq \sup_{b \in \mathbb{B}} \left\lvert m^{-1} \sum_{i=1}^{m} g_{ij}(y_i, b) \right\rvert o_{P_m}(1) + \sup_{b \in \mathbb{B}} \left\lvert m^{-1} \sum_{i=1}^{m} g^2_{ij}(y_i, b) \right\rvert o_{P_m}(1). \tag{S7.6}
\]

Next we show that the supremum terms above are of order \( o_{P_m}(1) \). The first of these terms

\[
\sup_{b \in \mathbb{B}} \left\lvert \frac{1}{m} \sum_{i=1}^{m} g_{ij}^1(y_i, b) \right\rvert \leq \sup_{b \in \mathbb{B}} \left\lvert m^{-1} \sum_{i=1}^{m} g_{ij}(y_i, b) - E_{\beta_m} \left\{ m^{-1} \sum_{i=1}^{m} g_{ij}^1(y_i, b) \right\} \right\rvert \tag{S7.7}
\]

\[
+ \sup_{b \in \mathbb{B}} \left\lvert E_{\beta_m} \left\{ m^{-1} \sum_{i=1}^{m} g_{ij}^1(y_i, b) \right\} \right\rvert. \tag{S7.8}
\]

For \( \delta^* = (\delta - 1)/2 > 0 \), we have by the Cauchy–Schwarz inequality

\[
E_{\beta_m} \left\{ \sup_{b \in \mathbb{B}} |g_{ij}^1(y_i, b)| \right\}^{1+\delta^*} \leq E_{\beta_m} \left\{ \sup_{b \in \mathbb{B}} |\varphi_{ij}(y_i, b)| \right\} \sup_{b \in \mathbb{B}} |\psi_{ij}(y_i, b)|^{1+\delta^*}
\]

\[
\leq \left\{ E_{\beta_m} \left\{ \sup_{b \in \mathbb{B}} |\varphi_{ij}(y_i, b)| \right\}^{1+\delta^*} \right\} \left\{ E_{\beta_m} \left\{ \sup_{b \in \mathbb{B}} |\psi_{ij}(y_i, b)| \right\}^{1+\delta^*} \right\}^{1/2},
\]

so using conditions (C2) and (C6) we have (S7.8) = \( O(1) \). The term (S7.7) can be shown to be of order \( o_{P_m}(1) \) using Lemma 1 with \( g_{ij}^1 \) playing the role of \( \psi_i \). To that end we need to check that condition (C3) holds for \( g_{ij}^1 \), i.e., that for any \( c > 0 \) and sequence \( \{y_i\} \) satisfying \( |y_i| \leq c \), the sequence of functions \( \{g_{ij}^1(y_i, b)\}_{i=1}^{\infty} \) is equicontinuous on \( \mathbb{B} \). This follows from (C3) and (C6) using the inequality

\[
|g_{ij}^1(y_i, t) - g_{ij}^1(y_i, s)| \leq |\varphi_{ij}(y_i, t)||\psi_{ij}(y_i, t) - \psi_{ij}(y_i, s)| + |\varphi_{ij}(y_i, t) - \varphi_{ij}(y_i, s)||\psi_{ij}(y_i, s)|.
\]

We have now shown that (S7.3) = \( o_{P_m}(1) \), so (S7.2) holds. Then using the second part of condition (C8) combined with (S7.2) and (S7.1), we have \( \Sigma \) converges in probability under \( H_{1m} \) to \( \Sigma_{\beta_0} \). Thus \( B\Sigma B^T \) converges in probability under \( H_{1m} \) to \( B\Sigma_{\beta_0} B^T \). From Theorem 1, \( \sqrt{m}(\hat{\psi} - \psi_0) \) converges in distribution under \( H_{1m} \) to \( N(h, B\Sigma_{\beta_0} B^T) \). Therefore, by Slutsky’s lemma and the continuous mapping theorem, \( W_m \) converges in distribution under \( H_{1m} \) to non-central \( \chi^2_m \) with non-centrality parameter \( \nu = h^T (B\Sigma_{\beta_0} B^T)^{-1} h \). Next we derive the asymptotic distribution for \( T_m \).
Asymptotic distribution of $T_m$

An estimate $\hat{\lambda}$ of the nuisance parameter vector $\lambda$ under $H_0$ is needed to calculate the quasi-score statistic. For this purpose it suffices to use the first $k - p$ estimating equations, so $\hat{\lambda}$ can be taken as a solution of $Cs_m(\lambda, \psi_0) = 0$, where $C = (I_{(k - p)}, 0_{(k - p) \times p})$. Write the quasi-score statistic as

$$ T_m = \left\{ m^{-1/2}Bs_m(\tilde{\beta}) \right\}^T (m^{-1}V_T)^{-1} \left\{ m^{-1/2}Bs_m(\tilde{\beta}) \right\}, $$

where

$$ V_T = \left\{ BM_m(\tilde{\beta})^{-1}B^T \right\}^{-1} \times BM_m(\tilde{\beta})^{-1} \left\{ \sum_{i=1}^m \psi_i(\tilde{y}_i, \tilde{\beta})\psi_i(\tilde{y}_i, \tilde{\beta})^T \right\} BM_m(\tilde{\beta})^{-1}B^T \times \left\{ BM_m(\tilde{\beta})^{-1}B^T \right\}^{-1}, $$

and $\tilde{\beta} = (\tilde{\lambda}^T, \psi_0^T)^T$. We first establish a connection between $\hat{\psi} - \psi_0$ and $s_m(\tilde{\beta})$:

$$ \sqrt{m}(\hat{\psi} - \psi_0) = \sqrt{m}B\{M_m(\beta_0)\}^{-1}B^T Bs_m(\tilde{\beta}) + o_{P_m}(1). \quad (S7.9) $$

According to (S6.7),

$$ (1 + o_{P_m}(1))\sqrt{m}(\hat{\beta} - \beta_0) = \sqrt{m}\{M_m(\beta_0)\}^{-1}s_m(\beta_0) = \sqrt{m}\{M_m(\beta_0)\}^{-1}s_m(\tilde{\beta}) + \sqrt{m}\{M_m(\beta_0)\}^{-1}\{s_m(\beta_0) - s_m(\tilde{\beta})\}. $$

Under conditions (C1)–(C9), it can be shown that $\sqrt{m}(\hat{\lambda} - \lambda_0) = O_{P_m}(1)$ using a similar proof as Theorem 1. Following the steps between (S6.2) and (S6.7) with $s_m(\tilde{\beta})$ in place of $s_m(\tilde{\beta})$, we have

$$ \sqrt{m}\{M_m(\beta_0)\}^{-1}\{s_m(\beta_0) - s_m(\tilde{\beta})\} = (1 + o_{P_m}(1))\sqrt{m}(\beta_0 - \tilde{\beta}) = (1 + o_{P_m}(1))\sqrt{m}C^T(\lambda_0 - \tilde{\lambda}) = O_{P_m}(1)C + o_{P_m}(1). $$

Combining the results of the above two displays, we have

$$ (1 + o_{P_m}(1))\sqrt{m}(\hat{\psi} - \psi_0) = \sqrt{m}B\{M_m(\beta_0)\}^{-1}s_m(\tilde{\beta}) + B\{C^T O_{P_m}(1) + o_{P_m}(1)\} $$

$$ = \sqrt{m}B\{M_m(\beta_0)\}^{-1}s_m(\tilde{\beta}) + o_{P_m}(1) $$

$$ = \sqrt{m}B\{M_m(\beta_0)\}^{-1}B^T Bs_m(\tilde{\beta}) + o_{P_m}(1) $$

$$ = B\{m^{-1/2} M_m(\beta_0)\}^{-1}B^T m^{-1/2} Bs_m(\tilde{\beta}) + o_{P_m}(1). $$

The above display implies equation (S7.9), which together with Theorem 1 and Slutsky’s lemma shows that $m^{-1/2}Bs_m(\tilde{\beta})$ converges under $P_m$ in distribution to a normal distribution with mean $\{BM(\beta_0)^{-1}B^T\}^{-1}h$ and variance

$$ \{BM(\beta_0)^{-1}B^T\}^{-1}(BS_{\beta_0}B^T)\{BM(\beta_0)^{-1}B^T\}^{-1}. $$
We have that \( m^{-1} \sum_{i=1}^{m} \Psi_i(y_i, \tilde{\beta}) \Psi_i(y_i, \tilde{\beta})^T \) and \( m^{-1} M_m(\tilde{\beta}) \) converge in probability under \( P_m \) to \( \lim_{m \to \infty} \left[ m^{-1} \sum_{i=1}^{m} \text{Var}_{\beta_0} \{ \Psi_i(y_i, \beta_0) \} \right] \) and \( M(\beta_0) \) respectively using the same argument for (S7.1) and (S7.2) in Theorem 2. Therefore, \( m^{-1} V_T \) converges in probability under \( P_m \) to the asymptotic variance of \( m^{-1/2} B_{s_m}(\tilde{\beta}) \).

By Slutsky’s lemma and the continuous mapping theorem, it follows that \( T_m \) converges in distribution under \( P_m \) to noncentral chi-squared with non-centrality parameter

\[
\begin{bmatrix}
(BM(\beta_0)^{-1}B^T)^{-1} & \{BM(\beta_0)^{-1}B^T\}^{-1}(B\Sigma_{\beta_0}B^T)\{BM(\beta_0)^{-1}B^T\}^{-1}
\end{bmatrix}
\]

concluding the proof.

**S8 Derivation of (4.1)**

In Example 4.1, the matrix \( \tilde{B} \) becomes the vector \((0, 1)\) since \( \kappa \) and \( \psi \) are both univariate, \( \theta_A = (\kappa_0, \psi_A)^T, \theta_0 = (\kappa_0, \psi_0)^T, \beta_A = (\sigma, \alpha^T, \kappa_0, \psi_A)^T \) and \( \mu_1 = 1_n(\kappa + \psi x_i) \), where \( 1_n \) is the \( n \times 1 \) vector with all elements being 1. Following the sample size calculation procedure given near the end of Section 3 in the manuscript, we first choose type I error rate \((\zeta)\) and desired power \((1 - \eta)\) in step 1. The cluster sizes are the same \((n)\) and the covariate \( x_i \)'s could have any arbitrary distribution in step 2. We give values of \( \psi_0, \psi_A, \kappa_0, \alpha \) and \( \sigma \) and calculate \( \tilde{D}_1 \) and \( V_1 \) in step 3. The \( n \times 2 \) matrix \( D_j = \partial \mu_1 / \partial \theta \) evaluated under \( H_0 \) is \( D_j = 1_n(1, x_i) \). The \( n \times n \) variance matrices evaluated under \( H_0 \) are \( V_j = \sigma^2 \mathbf{R} \), where \( \mathbf{R} \) is a \( n \times n \) correlation matrix.

Then we calculate \( \text{Var}_{\beta_A}(y_1 | z_1, x_1, n_1) \) in step 4. In this example, that conditional variance is equal to \( V_j \) obtained in the previous step. We calculate the following quantities in step 5:

\[
E(D_1^T V_1^{-1} D_1) = \frac{1_n^T R^{-1} 1_n}{\sigma^2} \begin{pmatrix}
1 & E(x_1) \\
E(x_1) & E(x_1^2)
\end{pmatrix},
\]

\[
E(D_1^T V_1^{-1}(\mu_1(\theta_A) - \mu_1(\theta_0))) = \frac{(1_n^T R^{-1} 1_n)(\psi_A - \psi_0)}{\sigma^2} \begin{pmatrix}
E(x_1) \\
E(x_1^2)
\end{pmatrix},
\]

and

\[
E[D_1^T V_1^{-1} \text{cov}_{\beta_A}(y_1 | x_1)V_1^{-1} D_1] = E(D_1^T V_1^{-1} D_1) = \frac{1_n^T R^{-1} 1_n}{\sigma^2} \begin{pmatrix}
1 & E(x_1) \\
E(x_1) & E(x_1^2)
\end{pmatrix}.
\]

In step 6, we calculate

\[
\tilde{\xi}_\psi = B(E[D_1^T V_1^{-1} D_1])^{-1} E\{D_1^T V_1^{-1}[\mu_1(\theta_A) - \mu_1(\theta_0)]\} = \psi_A - \psi_0,
\]

where \( \psi_A \) and \( \psi_0 \) are the limiting values of \( \psi \) and \( \psi_0 \) respectively.
\[ \tilde{\Sigma}_\psi = \tilde{B}[E(D_i^T V_1^{-1} D_1)]^{-1} E[D_i^T V_1^{-1} \text{cov}_{\beta_A}(y_1|x_1)V_1^{-1} D_1][E(D_i^T V_1^{-1} D_1)]^{-1} \tilde{B}^T \]

\[ = \frac{\sigma^2}{(1_n^T R^{-1} 1_n) \text{var}(x_1)}, \]

and \( \tilde{\nu} = (z_{1-\zeta/2} + z_{1-\eta})^2 \). Formula (4.1) is obtained by (3.7).

**S9 Derivation of the sample size formula in Example 4.2**

In this example, again the matrix \( \tilde{B} \) becomes the vector \((0, 1)\) since \( \kappa \) and \( \psi \) are both univariate, \( \theta_A = (\kappa_0, \psi_0)^T, \theta_0 = (\kappa_0, \psi_0)^T, \beta_A = (\alpha^T_0, \kappa, \psi A)^T \) and \( \mu_i = 1_n \expit(\kappa + \psi x_i) \) where \( 1_n \) is the \( n \times 1 \) vector with all elements being 1. As in the previous derivation, we similarly follow the steps in the sample size calculation procedure. The \( 2 \times n \) matrix \( D_i = \partial \mu_i / \partial \theta \) evaluated under \( H_0 \) is \( D_i = 1_n(x_1, v_{0x_1}) \), where \( v_{0x_1} = p_{0x_1}(1 - p_{0x_1}) \) and \( p_{0x_1} = \expit(\kappa_0 + \psi_0 x_1) \). The \( n \times n \) variance matrices evaluated under \( H_0 \) are \( V_i = v_{0x_1} \bar{R} \), where \( \bar{R} \) is a \( n \times n \) correlation matrix. Therefore,

\[ E(D_i^T V_1^{-1} D_1) = (1_n^T R^{-1} 1_n) \begin{pmatrix} E(v_{0x_1}) & E(x_1 v_{0x_1}) \\ E(x_1 v_{0x_1}) & E(x_1^2 v_{0x_1}) \end{pmatrix}, \]

\[ E(D_i^T V_1^{-1} | \mu_i(\theta_A) - \mu_i(\theta_0)) = (1_n^T R^{-1} 1_n) \begin{pmatrix} E(p_{1x_1}) - E(p_{0x_1}) \\ E(x_1 p_{1x_1}) - E(x_1 p_{0x_1}) \end{pmatrix}, \]

and

\[ E[D_i^T V_1^{-1} \text{cov}_{\beta_A}(y_1|x_1)V_1^{-1} D_1] = (1_n^T R^{-1} 1_n) \begin{pmatrix} E(v_{1x_1}) & E(x_1 v_{1x_1}) \\ E(x_1 v_{1x_1}) & E(x_1^2 v_{1x_1}) \end{pmatrix}, \]

where \( v_{1x_1} = p_{1x_1}(1 - p_{1x_1}) \) and \( p_{1x_1} = \expit(\kappa_0 + \psi_A x_1) \). Then

\[ \tilde{\xi}_\psi = \frac{\tilde{B}[E(D_i^T V_1^{-1} D_1)]^{-1} E[D_i^T V_1^{-1} | \mu_i(\theta_A) - \mu_i(\theta_0)]}{E(v_{0x_1}) (E(x_1 p_{1x_1}) - E(x_1 p_{0x_1})) - E(x_1 v_{0x_1}) (E(p_{1x_1}) - E(p_{0x_1}))}, \]

and

\[ \tilde{\Sigma}_\psi = \frac{\tilde{B}[E(D_i^T V_1^{-1} D_1)]^{-1} E[D_i^T V_1^{-1} \text{cov}_{\beta}(y_1|x_1)V_1^{-1} D_1][E(D_i^T V_1^{-1} D_1)]^{-1} \tilde{B}^T}{E(v_{0x_1}) (E(x_1 v_{0x_1})^2 + E(x_1^2 v_{0x_1}) | E(v_{0x_1})|^2 - 2E(x_1 v_{0x_1}) E(x_1 v_{0x_1}) E(v_{0x_1}))}, \]

By (3.7), we can obtain the formula.
S10 Derivation of the sample size formula in Example 4.3

In this example, again the matrix $\bar{B} = (0, 1)$, $\theta_A = (\kappa_0, \psi_A)^T$, $\theta_0 = (\kappa_0, \psi_0)^T$ and $\beta_A = (\rho, \kappa_0, \psi_A)^T$, where the correlation $\rho$ is a scalar since the cluster size is 2. There is only one type of clusters with cluster sizes being 2. That is, $x_i = (x_{i1}, x_{i2})^T$ follows a degenerate distribution $P(x_i = (0, 1)^T) = 1$. The corresponding vector mean is $\mu_i = (\expit(\kappa_0), \expit(\kappa + \psi))^T$. As in the derivation of 4.1, we also follow the steps in the sample size calculation procedure. The matrix $D_i = \partial \mu_i / \partial \theta$ evaluated under $H_0$ equals

$$D_i = \begin{pmatrix} v_0 & 0 \\ \bar{v}_0 & \tilde{v}_0 \end{pmatrix},$$

where $\bar{v}_0 = \bar{p}_0 (1 - \bar{p}_0), v_0 = p_0 (1 - p_0), \tilde{p}_0 = \expit(\kappa_0 + \psi_0)$ and $p_0 = \expit(\kappa_0)$. Then the variance matrix $V_i$ evaluated under $H_0$ is

$$V_i = \begin{pmatrix} v_0 & \rho \sqrt{v_0 \tilde{v}_0} \\ \rho \sqrt{v_0 \tilde{v}_0} & \tilde{v}_0 \end{pmatrix}.$$

Thus

$$[E(D_i^T V_i^{-1} D_i)]^{-1} = (D_i^T V_i^{-1} D_i)^{-1} = D_i^{-1} V_i (D_i^T)^{-1}.$$

$$E\{D_i^T V_i^{-1} [\mu_1(\theta_A) - \mu_1(\theta_0)]\} = D_i^T V_i^{-1} [\mu_1(\theta_A) - \mu_1(\theta_0)]$$

$$= D_i^T V_i^{-1} \begin{pmatrix} 0 \\ 1 \end{pmatrix} (p_1 - \tilde{p}_0),$$

where $p_1 = \expit(\kappa_0 + \psi_A)$. Then

$$\hat{\xi}_\psi = \bar{B} [E(D_i^T V_i^{-1} D_i)]^{-1} E \{D_i^T V_i^{-1} [\mu_1(\theta_A) - \mu_1(\theta_0)]\}$$

$$= \bar{B} D_i^{-1} \begin{pmatrix} 0 \\ 1 \end{pmatrix} (p_1 - \tilde{p}_0)$$

$$= \frac{1}{v_0 \tilde{v}_0} \bar{B} \begin{pmatrix} \tilde{v}_0 \\ -v_0 \end{pmatrix} \begin{pmatrix} 0 \\ 1 \end{pmatrix} (p_1 - \tilde{p}_0)$$

$$= \frac{p_1 - \tilde{p}_0}{\bar{v}_0}.$$

We have

$$\text{cov}_{\beta_A}(y_i | x_i) = \begin{pmatrix} v_0 & \rho \sqrt{v_0 \tilde{v}_0} \\ \rho \sqrt{v_0 \tilde{v}_0} & \tilde{v}_0 \end{pmatrix}.$$
where \( v_1 = p_1(1 - p_1) \). Thus

\[
\tilde{\Sigma}_\psi = \bar{B} [E(D_1^T V_1^{-1} D_1)]^{-1} E(D_1^T V_1^{-1} \text{cov}_\beta(y_1|x_1) V_1^{-1} D_1) [E(D_1^T V_1^{-1} D_1)]^{-1} \bar{B}^T
\]

\[
= \bar{B} D_1^{-1} \text{cov}_\beta(y_1|x_1)(D_1^T)^{-1} \bar{B}^T
\]

\[
= \frac{1}{v_0 \tilde{v}_0} \bar{B} \begin{pmatrix} \tilde{v}_0 & 0 \\ -\tilde{v}_0 & v_0 \end{pmatrix} \begin{pmatrix} v_0 & \rho \sqrt{v_0 v_1} \\ \rho \sqrt{v_0 v_1} & v_1 \end{pmatrix} \frac{1}{v_0 \tilde{v}_0} \begin{pmatrix} \tilde{v}_0 & 0 \\ 0 & -\tilde{v}_0 \end{pmatrix} \bar{B}^T
\]

\[
= \frac{1}{(v_0 \tilde{v}_0)^2} \bar{B} \begin{pmatrix} v_0 \tilde{v}_0^2 & \rho v_0 \tilde{v}_0 \sqrt{v_0 v_1} - v_0 \tilde{v}_0^2 \\ \rho v_0 \tilde{v}_0 \sqrt{v_0 v_1} - v_0 \tilde{v}_0^2 & v_0^2 v_1 - 2 \rho v_0 \tilde{v}_0 \sqrt{v_0 v_1} + v_0 \tilde{v}_0^2 \end{pmatrix} \bar{B}^T
\]

\[
= \frac{v_0^2 v_1 - 2 \rho v_0 \tilde{v}_0 \sqrt{v_0 v_1} + v_0 \tilde{v}_0^2}{(v_0 \tilde{v}_0)^2}.
\]

Then the formula is obtained by (3.7).
SAS code of sample size calculation for the Arsenic study;

alpha: type I error rate;
eta: type II error rate;
lambda: intercept in the logistic regression;
psi: coefficient of the Arsenic exposure in the logistic regression;
rho: correlation in exchangeable correlation structure or correlation between adjacent measurements in AR1 structure;
a1: mean of the natural log transformed exposure;
b1: standard deviation of the natural log transformed exposure;
n: number of iterations of Monte Carlo integral;
cluster: cluster size;

/***************************************************************;
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between adjacent measurements in AR1 structure;
a1: mean of the natural log transformed exposure;
b1: standard deviation of the natural log transformed exposure;
n: number of iterations of Monte Carlo integral;
cluster: cluster size;
****************************************************************/;
%macro sample(alpha, eta, lambda, psi, rho, a1, b1, n, cluster);
proc iml;
*************************************************read the design
parameters from prespecification or pilot data;
lambda=&lambda; psi=&psi; a1=&a1; b1=&b1; rho=&rho; n=&n;
**************************************************create the correlation
structure;
R=J(&cluster, &cluster, .);
do t=1 to &cluster;
do s=1 to &cluster;
***AR1 structure;
*R[t,s]=rho**abs(t-s);
***Exchangeable structure;
if t=s then R[t,s]=1;
end;
end;
****************Monte Carlo integration for the expectations in the
sample size formulae in Example 4.2;
seed=100;
umex=0;
denoxpx=0;
mx=a1;***mean value of the log-arsenic;
do i=1 to n;
x=a1+b1*rannor(seed);
px=exp(lambda+psi*x)/(1+exp(lambda+psi*x));
vx=px*(1-px);
umex=numex+mx*m x vx+x*x vx-2*mx*x vx;
denoxpx=denoxpx+(x-mx)*px;
end;
mnumex=numex/n;
ddenoxpx=denoxpx/n;

********************************************************************

NUTILDE=(probit(1-alpha/2)+probit(1-eta))**2;
numer=NUTILDE*mnumex;
deno=J(1, &cluster, 1)*inv(R)*J(&cluster, 1, 1)*mdenoxpx*mdenoxpx;
m=numer/deno;
print m;
quit;
%mend;

%sample(alpha=0.05, eta=0.1, lambda=-2.71662, psi=0.4055, rho=0.2, a1=0.653, b1=2.00, n=10000000, cluster=4);