Web-based Supplementary Materials for "Distribution-free Inference of Zero-inflated Binomial Data forLongitudinal Studies" by

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Web Appendix A: Proof of Lemma 1

Let S_i and D_i are defined in (2.5), that is

$$S_i = (s_{1i}, s_{2i})^{\intercal} = \left(I(\mathbf{y}_i = 0) - E\left[I(\mathbf{y}_i = 0) \mid \mathbf{x}_i\right],\ I(\mathbf{y}_i > 0)(\mathbf{y}_i - E\left[\mathbf{y}_i \mid \mathbf{y}_i > 0, \mathbf{x}_i\right])\right)^{\top},$$

$$D_i = \frac{\partial}{\partial \beta}\mathbf{s}_i = \begin{pmatrix} \frac{\partial}{\partial \beta_u} s_{1i} & \frac{\partial}{\partial \beta_u} s_{2i} \\ \frac{\partial}{\partial \beta_v} s_{1i} & \frac{\partial}{\partial \beta_v} s_{2i} \end{pmatrix}.$$

So we have

$$\frac{\partial s_{1i}}{\partial \beta_u} = -\left(1 - (1 - p_i)^{m_i}\right)\frac{\partial \rho_i}{\partial \beta_\mu}, \quad \frac{\partial s_{2i}}{\partial \beta_u} = \mathbf{0},$$

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and

$$\frac{\partial s_{1i}}{\partial \beta_\nu} = (1-\rho_i)\, m_i\, (1-p_i)^{m_i-1} \frac{\partial p_i}{\partial \beta_\nu},$$

$$\frac{\partial s_{2i}}{\partial \beta_\nu} = -I(\mathbf{y}_i > 0)\, \frac{1-(1-p_i)^{m_i} - p_i m_i (1-p_i)^{m_i-1}}{\left(1-(1-p_i)^{m_i}\right)^2} m_i \frac{\partial p_i}{\partial \beta_\nu}.$$

By simple algebraic computation, we have

$$Var\left[s_{1i}|\mathbf{x}_i\right] = \left[\rho_i + (1-\rho_i)(1-p_i)^{m_i}\right]\left[(1-\rho_i)\left(1-(1-p_i)^{m_i}\right)\right],$$

$$E\left[s_{2i}|\mathbf{x}_i\right] = \Pr(\mathbf{y}_i > 0|\mathbf{x}_i)\, E\left[(\mathbf{y}_i - E\left[\mathbf{y}_i|\mathbf{y}_i > 0, \mathbf{x}_i\right])\,|\mathbf{y}_i > 0, \mathbf{x}_i\right] = 0,$$

and

$$\begin{aligned} &Var\left(s_{2i} \mid \mathbf{x}_i\right) = E\left[s_{2i}^2 \mid \mathbf{x}_i\right] - \left(E\left[s_{2i}|\mathbf{x}_i\right]\right)^2 \\ &= \Pr(\mathbf{y}_i > 0 \mid \mathbf{x}_i)\left(E\left[\left[\mathbf{y}_i - E\left[\mathbf{y}_i|\mathbf{y}_i > 0, \mathbf{x}_i\right]\right]^2 |\mathbf{y}_i > 0, \mathbf{x}_i\right]\right) \\ &= \Pr(\mathbf{y}_i > 0 \mid \mathbf{x}_i)\left(E\left[\mathbf{y}_i^2|\mathbf{y}_i > 0, \mathbf{x}_i\right] - \left(E\left[\mathbf{y}_i|\mathbf{y}_i > 0, \mathbf{x}_i\right]\right)^2\right) \\ &= (1-\rho_i)(1-(1-p_i)^{m_i})\left[\frac{m_i p_i + m_i (m_i - 1) p_i^2}{1-(1-p_i)^{m_i}} - \left(\frac{m_i p_i}{1-(1-p_i)^{m_i}}\right)^2\right]. \end{aligned}$$

Hence

$$\begin{aligned} Cov(s_{1i}, s_{2i} \mid \mathbf{x}_i) &= E\left[\left(s_{1i} - E(s_{1i} \mid \mathbf{x}_i)\right)\left(s_{2i} - E(s_{2i} \mid \mathbf{x}_i)\right) \mid \mathbf{x}_i\right] \\ &= E\left(I(\mathbf{y}_i = 0) - E\left[I(\mathbf{y}_i = 0) \mid \mathbf{x}_i\right]\right) E\left[I(\mathbf{y}_i > 0)\left(\mathbf{y}_i - E\left(\mathbf{y}_i \mid \mathbf{y}_i > 0, \mathbf{x}_i\right)\right) \mid \mathbf{x}_i\right] \\ &= \Pr(\mathbf{y}_i > 0 \mid \mathbf{x}_i)\, E\left[I(\mathbf{y}_i = 0) - E\left[I(\mathbf{y}_i = 0) \mid \mathbf{x}_i\right]\right] E\left[\left(\mathbf{y}_i - E\left(\mathbf{y}_i \mid \mathbf{y}_i > 0, \mathbf{x}_i\right)\right) \mid \mathbf{y}_i > 0, \mathbf{x}_i\right] \\ &= 0. \end{aligned}$$

Web Appendix B: Proof of Theorem 1

Based on (2.5), the GEE $\mathbf{w}_n(\beta) = \frac{1}{n}\sum_{i=1}^n D_i V_i^{-1} S_i$. Since $E\left(D_i V_i^{-1} S_i\right) = 0$, the GEE (2.5) is unbiased and the estimate $\widehat{\beta}$, i.e., the solution to the equations, is also consistent.

By applying a Taylor expansion to (2.5), we have

$$\sqrt{n}\mathbf{w}_n = -\left(\frac{\partial}{\partial \beta}\mathbf{w}_n\right)^\top \sqrt{n}\left(\widehat{\beta} - \beta\right) + \mathbf{o}_p(1). \quad (1)$$

It follows from (1) that

$$\sqrt{n}\left(\widehat{\beta}-\beta\right)=\left(-\frac{\partial}{\partial\beta}\mathbf{w}_n\right)^{-\top}\frac{\sqrt{n}}{n}\sum_{i=1}^{n}\mathbf{w}_{ni}+\mathbf{o}_p\left(1\right). \tag{2}$$

Since

$$\frac{\partial}{\partial\beta}\mathbf{w}_n=\frac{1}{n}\sum_{i=1}^{n}\left(\frac{\partial}{\partial\beta}S_i\right)\left(D_iV_i^{-1}\right)^T=\frac{1}{n}\sum_{i=1}^{n}D_i\left(D_iV_i^{-1}\right)^T+\mathbf{o}_p\left(1\right)\to_p B. \tag{3}$$

where $\to_p$ denotes convergence in probability, it follows from (2) and (3) that

$$\sqrt{n}\left(\widehat{\beta}-\beta\right)=-B^{-\top}\frac{\sqrt{n}}{n}\sum_{i=1}^{n}\mathbf{w}_{ni}+\mathbf{o}_p\left(1\right). \tag{4}$$

By applying the central limit theorem and Slutsky's theorem, $\widehat{\beta}$ is asymptotically normal with the asymptotic variance given by Σ in Theorem 1.

Web Appendix C: Proof of Theorem 3

Based on (4.3), the weighted GEE $\mathbf{w}_n\left(\beta\right)=\frac{1}{n}\sum_{i=1}^{n}D_iV_i^{-1}\mathbf{\Delta}_iS_i$. By definition, $\mathbf{\Delta}_i$ is a $m\times m$ block diagonal matrix with the tth block diagonal matrix given by $\frac{r_{it}}{\pi_{it}}\mathbf{I}_2$ $(1\leq t\leq m)$, with $\mathbf{I}_m$ denoting the $m\times m$ identify matrix. Since $E\left(\frac{r_{it}}{\pi_{it}}\mathbf{I}_2\mid\mathbf{r}_i,\mathbf{y}_i,\mathbf{x}_i\right)=\mathbf{I}_2$, we have $E\left(D_iV_i^{-1}\mathbf{\Delta}_iS_i\right)=E\left[D_iV_i^{-1}S_iE\left(\mathbf{\Delta}_i\mid\mathbf{r}_i,\mathbf{y}_i,\mathbf{x}_i\right)\right]$. It follows that $E\left(D_iV_i^{-1}\mathbf{\Delta}_iS_i\right)=E\left(D_iV_i^{-1}S_i\right)=0$. Thus, the WGEE (4.6) is unbiased and the estimate $\widehat{\beta}$ obtained as the solution to the equations is consistent.

Let $\widehat{\gamma}$ be the solution to the (4.5). By a Taylor expansion of the estimating equations in (4.5) and solving for $\widehat{\gamma}-\gamma$, we obtain

$$\sqrt{n}\left(\widehat{\gamma}-\gamma\right)=-H^{-1}\frac{\sqrt{n}}{n}\sum_{i=1}^{n}\mathbf{Q}_{ni}+\mathbf{o}_p\left(1\right), \tag{5}$$

where $\mathbf{o}_p\left(1\right)$ denotes the stochastic $\mathbf{o}\left(1\right)$[1] and H is defined as in Theorem (3). Also, by applying a Taylor series expansion to (4.6), we have

$$\sqrt{n}\mathbf{w}_n=-\left(\frac{\partial}{\partial\beta}\mathbf{w}_n\right)^{\top}\sqrt{n}\left(\widehat{\beta}-\beta\right)-\left(\frac{\partial}{\partial\alpha}\mathbf{w}_n\right)^{\top}\sqrt{n}\left(\widehat{\alpha}-\alpha\right)- \tag{6}$$
$$-\left(\frac{\partial}{\partial\gamma}\mathbf{w}_n\right)^{\top}\sqrt{n}\left(\widehat{\gamma}-\gamma\right)+\mathbf{o}_p\left(1\right).$$

If $\widehat{\alpha}$ is $\sqrt{n}$-consistent, it follows that

$$\left(\frac{\partial}{\partial\alpha}\mathbf{w}_n\left(\beta,\alpha\right)\right)^{\top}\sqrt{n}\left(\widehat{\alpha}-\alpha\right)=\mathbf{o}_p\left(1\right)\sqrt{n}\left(\widehat{\alpha}-\alpha\right)=\mathbf{o}_p\left(1\right).$$

By substituting $\mathbf{o}_p\left(1\right)$ for $\left(\frac{\partial}{\partial\alpha}\mathbf{w}_n\left(\beta,\alpha\right)\right)^{\top}\sqrt{n}\left(\widehat{\alpha}-\alpha\right)$ in (6) and solving for $\sqrt{n}\left(\widehat{\beta}-\beta\right)$, we obtain

$$\sqrt{n}\left(\widehat{\beta}-\beta\right)=\left(-\frac{\partial}{\partial\beta}\mathbf{w}_n\right)^{-\top}\sqrt{n}\left[\mathbf{w}_n+C\left(\widehat{\gamma}-\gamma\right)\right]+\mathbf{o}_p\left(1\right). \tag{7}$$

It follows from (5) and (7) that

$$\sqrt{n}\left(\widehat{\beta}-\beta\right)=\left(-\frac{\partial}{\partial\beta}\mathbf{w}_n\right)^{-\top}\frac{\sqrt{n}}{n}\sum_{i=1}^{n}\left(\mathbf{w}_{ni}-CH^{-1}\mathbf{Q}_{ni}\right)+\mathbf{o}_p\left(1\right). \tag{8}$$

Since

$$\frac{\partial}{\partial\beta}\mathbf{w}_n=\frac{1}{n}\sum_{i=1}^{n}\left(\frac{\partial}{\partial\beta}\mathbf{\Delta}_i S_i\right)\left(D_iV_i^{-1}\right)^{T}+\mathbf{o}_p\left(1\right)=\frac{1}{n}\sum_{i=1}^{n}D_i\mathbf{\Delta}_i\left(D_iV_i^{-1}\right)^{T}+\mathbf{o}_p\left(1\right)\rightarrow_p B. \tag{9}$$

where $\rightarrow_p$ denotes convergence in probability, it follows from (8) and (9) that

$$\sqrt{n}\left(\widehat{\beta}-\beta\right)=-B^{-\top}\frac{\sqrt{n}}{n}\sum_{i=1}^{n}\left(\mathbf{w}_{ni}-CH^{-1}\mathbf{Q}_{ni}\right)+\mathbf{o}_p\left(1\right). \tag{10}$$

By applying the central limit theorem and Slutsky's theorem to (10)[1], $\widehat{\beta}$ is asymptotically normal with the asymptotic variance given by Σ_β in Theorem 3.

Web Appendix D: Derivative of $Corr(y_{i1}, y_{i2} \mid x_i)$

For ith subject in the at-risk group, the $Cov(y_{i1}, y_{i2} \mid x_i)$ and $Var(y_{i1} \mid x_i)$ can be computed as

$$\begin{aligned}Cov(y_{i1}, y_{i2} \mid x_i) &= E(y_{i1}y_{i2} \mid x_i) - E(y_{i1} \mid x_i)E(y_{i2} \mid x_i)\\ &= (1-\rho_i)(\lambda_i mp_i - \lambda_i mp_i^2 + (mp_i)^2) - [(1-\rho_i)mp_i]^2\\ &= (1-\rho_i)mp_i(\lambda_i - \lambda_i p_i + \rho_i mp_i),\end{aligned}$$

and

$$\begin{aligned} Var(y_{i1} \mid x_i) &= E(y_{i1}^2 \mid x_i) - [E(y_{i1} \mid x_i)]^2 \\ &= (1-\rho_i)mp_i(1-p_i+mp_i) - [(1-\rho_i)mp_i]^2 \\ &= (1-\rho_i)mp_i(1-p_i+m\rho_i p_i), \end{aligned}$$

hence we have

$$corr(y_{i1}, y_{i2}|x_i) = \frac{\lambda_i - p_i(\lambda_i - m\rho_i)}{1 - p_i(1-m\rho_i)}.$$

References

[1] Jeanne Kowalski, Xin M. Tu. *Modern applied U-statistics.* Wiley Series in Probability and Statistics. Wiley-Interscience, Hoboken, NJ, 2008.