Relationship and Interpretation Difference of Regression Coefficients in GEE and GLMM in Clustered Data

GEEs

Recall GEE:

$$\begin{aligned} E(Y_{ij}) &= \mu_{ij} \\ var(Y_{ij}) &= \phi a_{ij}^{-1} v(\mu_{ij}) \end{aligned}$$

Marginal Model:

$$g(\mu_{ij}) = \mathbf{X}_{ij}^T \beta$$

Estimation using GEE:

$$\sum_{i=1}^{m} \mathbf{D}_i^T \mathbf{V}_i^{-1} (\mathbf{Y}_i - \boldsymbol{\mu}_i) = 0$$

GLMMs

Recall GLMM:

Conditional on cluster specific random effects $\boldsymbol{b}_i$,

$$\begin{aligned} E(Y_{ij}|b_i) &= \mu_{ij}^{\mathbf{b}} \\ var(Y_{ij}|b_i) &= \phi a_{ij}^{-1} v(\mu_{ij}^{\mathbf{b}}) \end{aligned}$$

Random Effects Model :

$$g(\mu_{ij}^{\mathbf{b}}) = \mathbf{X}_{ij}^T \beta + \mathbf{Z}_{ij}^T \mathbf{b}_i$$

where

$$\mathbf{b}_i \sim N\{0, \mathbf{D}_0(\boldsymbol{\theta})\}$$

Estimation using MLE

$$e^{\ell(\beta,\boldsymbol{\theta})} \propto |\mathbf{D}|^{-\frac{1}{2}} \int exp^{\{\sum_{i=1}^{n} \ell_i(Y_i|\mathbf{b};\beta) - \frac{1}{2}\mathbf{b}^{\mathbf{T}}\mathbf{D}^{-1}\mathbf{b}\}} d\mathbf{b}$$

Some Questions

Question 1: How is β in the GEE model related β in the GLMM? Are they the same?

Question 2: Do they have the same interpretation?

References

- Zeger, Liang and Albert (1988). Biometrics, 1049-60.
- Neuhaus, Kalbfleisch and Hauck (1991). Int. Stat. Rev, 25-35.
- Zeger and Liang (1992) Stat. in Med,1825-39.

Relationship between β in GLMM and GEE

Under the GLMM,

$$\mu_{ij} = E(Y_{ij}) = E\{g^{-1}(\mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i)\}$$

$\Rightarrow$ Question 1 is identical to asking

$$\mu_{ij} \quad = \quad E\{g^{-1}(\mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i)\} \stackrel{?}{=} g^{-1}(\mathbf{X}_{ij}^T\beta)$$

or

$$g[E\{g^{-1}(\mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i)\}] \stackrel{?}{=} \mathbf{X}_{ij}^T\beta$$

Answer 1: Often no. βs from GEE and GLMM are typically not the same.

When do the βs coincide?

Recall GEE:

$$g(\mu_{ij}) = \mathbf{X}_{ij}^T \beta$$

Recall GLMM:

$$g(\mu_{ij}^{\mathbf{b}}) = \mathbf{X}_{ij}^T \beta + \mathbf{Z}_{ij}^T \mathbf{b}_i$$

We need to check whether the marginal mean of Y_{ij} in GLMM $\mu_{ij} = E[g^{-1}(\mathbf{X}_{ij}^T \beta + \mathbf{Z}_{ij}^T \mathbf{b}_i)]$ satisfies $g(\mu_{ij}) = \mathbf{X}_{ij}^T \beta$.

Let's see some examples.

Linear (Identity) Link (e.g. Normal data)

$$\mu_{ij}^{\mathbf{b}} = \mathbf{X}_{ij}^T \beta + \mathbf{Z}_{ij}^T \mathbf{b}_i$$

$$\Downarrow$$

$$\begin{aligned} \mu_{ij} &= E(Y_{ij}) = E[E(Y_{ij}|b_i)] \\ &= E(\mu_{ij}^{\mathbf{b}}) = E(\mathbf{X}_{ij}^T \beta + \mathbf{Z}_{ij}^T \mathbf{b}_i) \\ &= \mathbf{X}_{ij}^T \beta \end{aligned}$$

Thus, β in the GEE and the GLMM are the same!

Probit Link (Binary data)

$$\Phi^{-1}(\mu_{ij}^{\mathbf{b}}) = \mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i$$

Then

$$\begin{aligned}\mu_{ij} &= E(\mu_{ij}^{\mathbf{b}}) = E[\Phi(\mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i)] \\ &= \Phi\{(\mathbf{1} + \mathbf{Z_{ij}^T D Z_{ij}})^{-\frac{1}{2}}\mathbf{X}_{ij}^{T}\beta\}\end{aligned}$$

$$\Downarrow$$

$$\begin{aligned}\Phi^{-1}(\mu_{ij}) &= \frac{1}{(1+\mathbf{Z}_{ij}^T\mathbf{D}\mathbf{Z}_{ij})^{\frac{1}{2}}}\mathbf{X}_{ij}^T\beta \\ &\neq \mathbf{X}_{ij}^T\beta \qquad\qquad \text{if } \mathbf{D} \neq \mathbf{0}\end{aligned}$$

Hence β_{GEE} is often attenuated compared to the β_{GLMM}.

Logit Link (Binary data)

$$logit(\mu_{ij}^{\mathbf{b}}) = \mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i$$

Note

$$\begin{aligned}
\mu_{ij} &= E(\mu_{ij}^{\mathbf{b}}) = E[\frac{e^{\mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i}}{1 + e^{\mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i}}] \\
&\approx F(\frac{1}{(1 + c^2\mathbf{Z}_{ij}^T\mathbf{D}\mathbf{Z}_{ij})^{\frac{1}{2}}}\mathbf{X}_{ij}^T\beta)
\end{aligned}$$

where F is the logistic cdf, $c = 16 \times \sqrt{3}/15\pi = 0.58$, and $c^2 = 0.35$.

$$\Downarrow$$

$$\begin{aligned}
logit(\mu_{ij}) &\approx \frac{1}{(1 + c^2\mathbf{Z}_{ij}^T\mathbf{D}\mathbf{Z}_{ij})^{\frac{1}{2}}}\mathbf{X}_{ij}^T\beta \\
&\neq \mathbf{X}_{ij}^T\beta \qquad \text{if } \mathbf{D} \neq \mathbf{0}
\end{aligned}$$

Hence β_{GEE} is often attenuated compared to the β_{GLMM}.

Log Link (Count, Poisson data)

$$ln(\mu_{ij}^{\mathbf{b}}) = \mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i$$

Note

$$\begin{aligned}\mu_{ij} &= E(\mu_{ij}^{\mathbf{b}}) = E[e^{\mathbf{X}_{ij}^T\beta + \mathbf{Z}_{ij}^T\mathbf{b}_i}] \\ &= e^{\mathbf{X}_{ij}^T\beta + \frac{1}{2}\mathbf{Z}_{ij}^T\mathbf{D}\mathbf{Z}_{ij}}\end{aligned}$$

$$\Downarrow$$

$$ln(\mu_{ij}) = \mathbf{X}_{ij}^T\beta + \underbrace{\frac{1}{2}\mathbf{Z}_{ij}^T\mathbf{D}\mathbf{Z}_{ij}}_{\downarrow\ \textit{offset}}$$

So β_{GEE} and β_{GLMM} differ by an intercept if **X** and **Z** do not overlap except for the intercept.

Some MORE Questions

Outstanding Questions:

Question 2: Do they have the same interpretation?

Question 3: Which is correct?

Question 4: Which should I use?