

## Setting

**Remark 1.1.1.** Generalized estimating equations (GEEs) model dependence of the outcome mean on covariates, while treating correlation among clustered observations as a nuisance. GEEs are indicated when there are many clusters, with few observations per cluster, and population averaged, rather than individual-level, inference is of interest.  $\blacklozenge$

Let  $\mathbf{y}_k = (y_{1,k}, \dots, y_{n_k,k})'$  denote the outcome for the  $k$ th cluster. Rather than specifying the complete distribution of  $y_{i,k}$ , adopt models for the first two moments:

$$\begin{aligned} E(y_{i,k}) &= \mu_{i,k}, \\ \text{Var}(y_{i,k}) &= \phi w_{ki} \nu(\mu_{i,k}). \end{aligned}$$

Here  $\phi$  is the dispersion parameter,  $w_{ki}$  is a known weight, and  $\nu(\cdot)$  is the variance function. Recall that for linear exponential families,  $\nu(\mu_{ki}) = \ddot{b} \circ \dot{b}^{-1}(\mu_{ki})$ , where  $b(\cdot)$  is the cumulant function.

**Definition 1.1.1.** The **quasi-log likelihood** is:

$$\ell(y_{i,k}) = \int_{y_{i,k}}^{\mu_{i,k}} \frac{y_{i,k} - u}{\phi w_{i,k} \nu(u)} du.$$

■

**Definition 1.1.2.** Suppose the following mean model:

$$g(\mu_{i,k}) = \mathbf{x}'_{i,k} \boldsymbol{\beta},$$

where  $\mathbf{x}_{i,k}$  is a  $J \times 1$ . The **generalized estimating equations** for  $\boldsymbol{\beta}$  are:

$$\mathcal{U}_{\boldsymbol{\beta}} = \sum_{k=1}^K \mathbf{D}'_k \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k).$$

Here  $\mathbf{D}_k$  is the  $n_k \times J$  defined by:

$$\mathbf{D}_k = \frac{\partial \boldsymbol{\mu}_k}{\partial \boldsymbol{\beta}'},$$

$\mathbf{V}_k$  is the  $n_k \times n_k$  working covariance structure, and  $(\mathbf{y}_k - \boldsymbol{\mu}_k)$  is the  $n_k \times 1$  residual.  $\blacksquare$

**Definition 1.1.3.** Define the *marginal covariance structure* for cluster  $k$  as:

$$\boldsymbol{\Sigma}_k = \text{diag}\{\text{Var}(y_{i,k})\} = \text{diag}\{\phi w_{i,k} \nu(\mu_{i,k})\}.$$

Let  $\mathbf{R}_k(\boldsymbol{\alpha})$  denote the cluster-specific working correlation matrix, parameterized by  $\boldsymbol{\alpha}$ . The cluster-specific **working covariance matrix** is:

$$\mathbf{V}_k = \boldsymbol{\Sigma}_k^{1/2}(\boldsymbol{\beta}) \mathbf{R}_k(\boldsymbol{\alpha}) \boldsymbol{\Sigma}_k^{1/2}(\boldsymbol{\beta}).$$

■

**Theorem 1.1.1.** Suppose that 1.  $\hat{\alpha}$  and  $\hat{\phi}$  are  $\sqrt{K}$ -consistent estimators for the correlation and dispersion parameters, and 2.  $\partial_{\beta'} \mathcal{U}_{\beta}$  converges uniformly in probability to an invertible matrix  $\mathbf{A}$  in an open neighborhood of the true  $\beta_0$ :

$$\mathbf{A} \equiv \text{plim}_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \mathbf{D}_k' \mathbf{V}_k^{-1} \mathbf{D}_k.$$

Now  $\hat{\beta}$  obtained by solving  $\mathcal{U}_{\beta}(\beta; \hat{\phi}, \hat{\alpha}) \stackrel{\text{Set}}{=} 0$  is consistent and asymptotically normal:

$$\sqrt{K}(\hat{\beta} - \beta_0) \xrightarrow{\mathcal{L}} N(\mathbf{0}, \mathbf{\Omega}),$$

where  $\mathbf{\Omega} = \mathbf{A}^{-1} \mathbf{B} \mathbf{A}^{-T}$ , with:

$$\mathbf{B} \equiv \text{plim}_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \mathbf{D}_k' \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k)(\mathbf{y}_k - \boldsymbol{\mu}_k)' \mathbf{V}_k^{-1} \mathbf{D}_k.$$

□

**Proof.** See section on Inference. ■

**Remark 1.1.2.** If the working covariance matrix is correctly specified, then:

$$\begin{aligned} \mathbf{B} &= \lim_{n \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K E \{ \mathbf{D}_k' \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k)(\mathbf{y}_k - \boldsymbol{\mu}_k)' \mathbf{V}_k^{-1} \mathbf{D}_k \} \\ &= \lim_{n \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \mathbf{D}_k' \mathbf{V}_k^{-1} E \{ (\mathbf{y}_k - \boldsymbol{\mu}_k)(\mathbf{y}_k - \boldsymbol{\mu}_k)' \} \mathbf{V}_k^{-1} \mathbf{D}_k \\ &= \lim_{n \rightarrow \infty} \frac{1}{m} \sum_{k=1}^m \mathbf{D}_k' \mathbf{V}_k^{-1} \mathbf{V}_k \mathbf{V}_k^{-1} \mathbf{D}_k = \lim_{n \rightarrow \infty} \frac{1}{m} \sum_{k=1}^m \mathbf{D}_k' \mathbf{V}_k^{-1} \mathbf{D}_k = \mathbf{A}. \end{aligned}$$

Thus, under correct specification of the working covariance matrix, the limiting covariance  $\mathbf{\Omega}$  reduces to  $\mathbf{\Omega} = \mathbf{A}^{-1}$ . ◆

## Estimation

### 2.1 Fisher-Scoring Algorithm

**Definition 1.2.1.** Define the following  $n_k \times n_k$  matrices:

$$\Delta_k = \left\{ \frac{\partial g(\mu_{ki})}{\partial \mu_{ki}} \right\} = \text{diag} \{ \dot{g}(\mu_{i,k}) \}, \quad \mathbf{W}_k^{-1} = \Delta_k \mathbf{V}_k \Delta_k.$$

■

**Proposition 1.2.1.** Let  $g(\mu_{i,k}) = \eta_{i,k} = \mathbf{x}'_{i,k}\boldsymbol{\beta}$  and  $\mu_{i,k} = h(\eta_{i,k})$  s.t.  $h = g^{-1}$ . The first derivatives of  $g(\mu_{i,k})$  and  $h(\eta_{i,k})$  are related via:

$$\dot{h}(\eta_{i,k}) = \frac{1}{\dot{g}(\mu_{i,k})}.$$

◆

**Proof.**

$$1 = \frac{d}{dt}t = \frac{d}{dt}g\{h(t)\} = \dot{g}\{h(t)\}\dot{h}(t) \implies \dot{h}(\eta_{i,k}) = \frac{1}{\dot{g}\{h(\eta_{i,k})\}} = \frac{1}{\dot{g}(\mu_{i,k})}.$$

■

**Proposition 1.2.2.** The matrix  $\mathbf{D}_k$  is expressible as:

$$\mathbf{D}_k = \frac{\partial \boldsymbol{\mu}_k}{\partial \boldsymbol{\beta}'_k} = \boldsymbol{\Delta}_k^{-1} \mathbf{X}_k$$

◆

**Proof.**

$$\frac{\partial \mu_{i,k}}{\partial \boldsymbol{\beta}'} = \frac{\partial}{\partial \boldsymbol{\beta}'} h(\eta_{i,k}) = \dot{h}(\eta_{i,k}) \mathbf{x}'_{i,k} = \frac{1}{\dot{g}(\mu_{i,k})} \mathbf{x}'_{i,k}$$

■

**Corollary 1.2.1.** The GEEs for  $\boldsymbol{\beta}$  are expressible as:

$$\mathcal{U}_{\boldsymbol{\beta}} = \sum_{k=1}^K \mathbf{X}'_k \boldsymbol{\Delta}_k^{-1} \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k).$$

♣

**Definition 1.2.2.** Define the  $n_k \times 1$  working vector  $\mathbf{z}_k$ :

$$\mathbf{z}_k = \boldsymbol{\eta}_k + \boldsymbol{\Delta}_k (\mathbf{y}_k - \boldsymbol{\mu}_k).$$

■

**Result 1.2.1.** The iteratively reweighted least squares (IRLS) update for  $\boldsymbol{\beta}$  is:

$$\boldsymbol{\beta}^{(r+1)} \leftarrow \left( \sum_{k=1}^K \mathbf{X}'_k \mathbf{W}_k^{(r)} \mathbf{X}_k \right)^{-1} \sum_{k=1}^K \mathbf{X}'_k \mathbf{W}_k^{(r)} \mathbf{z}_k^{(r)}.$$

This is WLS of the  $r$ th working vector  $\mathbf{z}^{(r)}$  on  $\mathbf{X}$  using working weights  $\mathbf{W}^{(r)}$ .

♣

**Proof.** Let  $\beta^{(r)}$  denote the current state of  $\beta$ . Take the first order Taylor expansion of the score  $\mathcal{U}(\beta)$  about  $\beta^{(r)}$ :

$$\mathcal{U}(\beta) = \mathcal{U}(\beta^{(r)}) + \dot{\mathcal{U}}(\beta^{(r)})(\beta - \beta^{(r)}) + \mathcal{O}_p(K^{-1})$$

At the solution  $\mathcal{U}(\hat{\beta}) = \mathbf{0}$ . Make the approximation:

$$\mathbf{0} = \mathcal{U}(\hat{\beta}) \approx \mathcal{U}(\beta^{(r+1)}) = \mathcal{U}(\beta^{(r)}) + \dot{\mathcal{U}}(\beta^{(r)})(\beta^{(r+1)} - \beta^{(r)}) + \mathcal{O}_p(K^{-1}).$$

Solving for  $\beta^{(r+1)}$ :

$$-\dot{\mathcal{U}}(\beta^{(r)})\beta^{(r+1)} = -\dot{\mathcal{U}}(\beta^{(r)})\beta^{(r)} + \mathcal{U}(\beta^{(r)}) + \mathcal{O}_p(K^{-1}).$$

Consider the gradient of  $\mathcal{U}$  w.r.t.  $\beta$ :

$$\frac{\partial \mathcal{U}}{\partial \beta'} = \sum_{k=1}^K \left\{ \frac{\partial}{\partial \beta'} D'_k V_k^{-1} \right\} (\mathbf{y}_k - \boldsymbol{\mu}_k) - D'_k V_k^{-1} D_k.$$

The first term is eliminated upon taking the expectation:

$$E \left( \frac{\partial \mathcal{U}}{\partial \beta'} \right) = E(\dot{\mathcal{U}}_\beta) = - \sum_{k=1}^K D'_k V_k^{-1} D_k$$

As in Fisher scoring, adopt the following update equation for  $\beta^{(r)}$ :

$$\begin{aligned} -E(\dot{\mathcal{U}}_\beta)\beta^{(r+1)} &= -E(\dot{\mathcal{U}}_\beta)\beta^{(r)} + \mathcal{U}(\beta^{(r)}), \\ \sum_{k=1}^K D'_k V_k^{-1} D_k \beta^{(r+1)} &= \sum_{k=1}^K D'_k V_k^{-1} D_k \beta^{(r)} + \sum_{k=1}^K D'_k V_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k). \end{aligned}$$

Re-expressing  $D'_k V_k^{-1} D_k$ :

$$D'_k V_k^{-1} D_k = \mathbf{X}'_k \boldsymbol{\Delta}_k^{-1} V_k^{-1} \boldsymbol{\Delta}_k^{-1} \mathbf{X}_k = \mathbf{X}'_k \mathbf{W}_k \mathbf{X}_k$$

The system of equations becomes:

$$\left( \sum_{k=1}^K \mathbf{X}'_k \mathbf{W}_k \mathbf{X}_k \right) \beta^{(r+1)} = \left( \sum_{k=1}^K \mathbf{X}'_k \mathbf{W}_k \mathbf{X}_k \right) \beta^{(r)} + \sum_{k=1}^K \mathbf{X}'_k \mathbf{W}_k \boldsymbol{\Delta}_k (\mathbf{y}_k - \boldsymbol{\mu}_k).$$

Combining terms on the right:

$$\left( \sum_{k=1}^K \mathbf{X}'_k \mathbf{W}_k \mathbf{X}_k \right) \beta^{(r+1)} = \sum_{k=1}^K \mathbf{X}'_k \mathbf{W}_k \{ \mathbf{X}_k \beta^{(r)} + \boldsymbol{\Delta}_k (\mathbf{y}_k - \boldsymbol{\mu}_k) \}.$$

Identify  $\mathbf{z}_k = \mathbf{X}_k \beta^{(r)} + \boldsymbol{\Delta}_k (\mathbf{y}_k - \boldsymbol{\mu}_k)$ . ■

## 2.2 Missingness

**Remark 1.2.1.** The GEE estimator  $\beta$  is consistent if data are missing completely at random. However, if the data are missing at random, consistency is not guaranteed. In this case, weighted estimating equations are needed, where the weighting is inversely proportional to the probability of dropout at a given time.  $\blacklozenge$

## Inference

### 3.1 Asymptotics

**Result 1.3.1.** Under the regularity conditions for M-estimation,  $\hat{\beta}$  solving  $\mathcal{U}_{\beta} \stackrel{\text{Set}}{=} \mathbf{0}$  converges in distribution as:

$$\sqrt{K}(\hat{\beta} - \beta_0) \xrightarrow{\mathcal{L}} N(\mathbf{0}, \Omega), \quad (1.3.1)$$

where  $\Omega = \mathbf{A}^{-1} \mathbf{B} \mathbf{A}^{-T}$ , and:

$$\begin{aligned} \mathbf{A} &= \text{plim}_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \mathbf{D}'_k \mathbf{V}_k^{-1} \mathbf{D}_k \\ \mathbf{B} &= \text{plim}_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \mathbf{D}'_k \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k) (\mathbf{y}_k - \boldsymbol{\mu}_k)' \mathbf{V}_k^{-1} \mathbf{D}_k \end{aligned}$$

$\clubsuit$

**Proof.** Take the Taylor expansion of  $\mathcal{U}(\beta)$  about  $\beta_0$ :

$$\mathcal{U}(\beta) = \mathcal{U}(\beta_0) + \dot{\mathcal{U}}(\beta_0)(\beta - \beta_0) + \mathcal{O}_p(K^{-1})$$

Evaluating the Taylor expansion at  $\hat{\beta}$ :

$$\mathbf{0} = \mathcal{U}(\hat{\beta}) = \mathcal{U}(\beta_0) + \dot{\mathcal{U}}(\beta_0)(\hat{\beta} - \beta_0) + \mathcal{O}_p(K^{-1})$$

Solving for  $(\hat{\beta} - \beta_0)$ :

$$\begin{aligned} \sqrt{K}(\hat{\beta} - \beta_0) &= \sqrt{K}\{-\dot{\mathcal{U}}^{-1}(\beta_0)\}\mathcal{U}(\beta_0) + \mathcal{O}_p(K^{-1/2}) \\ &= \{-K^{-1}\dot{\mathcal{U}}(\beta_0)\}^{-1} K^{-1/2} \mathcal{U}(\beta_0) + \mathcal{O}_p(K^{-1/2}). \end{aligned}$$

The term under the inverse converges in probability as:

$$\begin{aligned} -K^{-1}\dot{\mathcal{U}}(\beta_0) &= -\frac{1}{K} \frac{\partial \mathcal{U}}{\partial \beta'}(\beta_0) = -\frac{1}{K} \sum_{k=1}^K \left\{ \frac{\partial}{\partial \beta'} \mathbf{D}'_k \mathbf{V}_k^{-1} \right\} (\mathbf{y}_k - \boldsymbol{\mu}_k) + \mathbf{D}'_k \mathbf{V}_k^{-1} \mathbf{D}_k \\ &\xrightarrow{p} -\text{plim}_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \mathbf{D}'_k \mathbf{V}_k^{-1} \mathbf{D}_k = -\mathbf{A} \end{aligned}$$

By the central limit theorem:

$$K^{-1/2}\mathcal{U}(\beta_0) = \frac{1}{\sqrt{K}} \sum_{k=1}^K \mathbf{D}'_k \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k) \xrightarrow{\mathcal{L}} N(\mathbf{0}, \mathbf{B}),$$

where:

$$\mathbf{B} \equiv \lim_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \mathbf{D}'_k \mathbf{V}_k^{-1} E\{(\mathbf{y}_k - \boldsymbol{\mu}_k)(\mathbf{y}_k - \boldsymbol{\mu}_k)'\} \mathbf{V}_k^{-1} \mathbf{D}_k.$$

The remainder term  $\mathcal{O}_p(K^{-1/2}) = o_p(1)$ . Overall:

$$\sqrt{K}(\hat{\beta} - \beta_0) \xrightarrow{\mathcal{L}} N(\mathbf{0}, \mathbf{A}^{-1} \mathbf{B} \mathbf{A}^{-1})$$

■

**Corollary 1.3.1.** The influence function expansion for  $\beta$  is:

$$\sqrt{K}(\hat{\beta} - \beta_0) = \frac{1}{\sqrt{K}} \sum_{k=1}^K \mathbf{A}^{-1} \mathbf{D}'_k \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k) + o_p(1).$$

♣

**Remark 1.3.1.** The empirical estimators of  $\mathbf{A}$  and  $\mathbf{B}$  are:

$$\begin{aligned} \hat{\mathbf{A}} &= \frac{1}{K} \sum_{k=1}^K \mathbf{D}'_k \mathbf{V}_k^{-1} \mathbf{D}_k \\ \hat{\mathbf{B}} &= \frac{1}{K} \sum_{k=1}^K \mathbf{D}'_k \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k)(\mathbf{y}_k - \boldsymbol{\mu}_k)' \mathbf{V}_k^{-1} \mathbf{D}_k. \end{aligned}$$

♦

## 3.2 Hypothesis Testing

Partition the regression coefficient  $\beta = (\beta_1, \beta_2)'$ . Let

$$\boldsymbol{\Omega} = \begin{pmatrix} \boldsymbol{\Omega}_{11} & \boldsymbol{\Omega}_{12} \\ \boldsymbol{\Omega}'_{12} & \boldsymbol{\Omega}_{22} \end{pmatrix}$$

denote the corresponding partition of the asymptotic covariance matrix. Suppose  $\beta_1$  is the target parameter,  $\beta_2$  is a nuisance parameter, and consider evaluating  $H_0 : \beta_1 = \mathbf{0}$ .

**Result 1.3.2.** The Wald statistic for assessing  $H_0 : \beta_1 = \mathbf{0}$  is:

$$T_W = K \cdot \hat{\beta}'_1 \boldsymbol{\Omega}_{11}^{-1} \hat{\beta}_1 \xrightarrow{\mathcal{L}} \chi^2_{\dim(\beta_1)}$$

♣

**Proof.** Follows from (1.3.1). ■

**Result 1.3.3.** Let  $\tilde{\beta}_2$  denote the M-estimator of  $\beta_2$  under  $H_0 : \beta_1 = \mathbf{0}$ , i.e.  $\tilde{\beta}_2$  is a solution to the equation  $\mathcal{U}_2(\beta_1 = \mathbf{0}, \beta_2) \stackrel{\text{Set}}{=} \mathbf{0}$ . Let  $\tilde{\mathcal{U}}_1$  denote the score for  $\beta_1$  evaluated at  $\mathcal{U}_1(\beta_1 = \mathbf{0}, \beta_2 = \tilde{\beta}_2)$ . The score test of  $H_0 : \beta_1 = \mathbf{0}$  is:

$$T_S = \frac{1}{K} \tilde{\mathcal{U}}_1' \Omega_{11|2} \tilde{\mathcal{U}}_1,$$

where:

$$\Omega_{11|2} = \mathbf{B}_{11} - \mathbf{B}_{12} \mathbf{A}_{22}^{-1} \mathbf{A}_{21} - \mathbf{A}_{12} \mathbf{A}_{22}^{-1} \mathbf{B}_{21} + \mathbf{A}_{12} \mathbf{A}_{22}^{-1} \mathbf{B}_{22} \mathbf{A}_{22}^{-1} \mathbf{A}_{21}.$$

♣

**Proof.** Partition the estimating equations  $\mathcal{U} = (\mathcal{U}_1, \mathcal{U}_2)'$ , where:

$$\mathcal{U}_l = \frac{1}{K} \sum_{k=1}^K \mathbf{D}_{k,l}' \mathbf{V}_k^{-1} (\mathbf{y}_k - \boldsymbol{\mu}_k), \quad \mathbf{D}_{l,k} = \frac{\partial \boldsymbol{\mu}_k}{\partial \beta_l'}.$$

Similarly, partition  $\mathbf{A}$  and  $\mathbf{B}$  as:

$$\mathbf{A} = \begin{pmatrix} \mathbf{A}_{11} & \mathbf{A}_{12} \\ \mathbf{A}_{21} & \mathbf{A}_{22} \end{pmatrix}, \quad \mathbf{B} = \begin{pmatrix} \mathbf{B}_{11} & \mathbf{B}_{12} \\ \mathbf{B}_{21} & \mathbf{B}_{22} \end{pmatrix}.$$

Here, the component matrices are defined as:

$$\begin{aligned} \mathbf{A}_{l,l'} &= \text{plim}_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^K \mathbf{D}_{l,k}' \mathbf{V}_k^{-1} \mathbf{D}_{l',k}, \\ \mathbf{B}_{l,l'} &= \text{plim}_{K \rightarrow \infty} \frac{1}{K} \sum_{k=1}^m \mathbf{D}_{l,k}' \mathbf{V}_k^{-1} (\mathbf{y} - \boldsymbol{\mu}_k) (\mathbf{y} - \boldsymbol{\mu}_k)' \mathbf{V}_k^{-1} \mathbf{D}_{l',k}. \end{aligned}$$

Let  $\tilde{\beta}_2$  denote the solution to  $\mathcal{U}_2 \stackrel{\text{Set}}{=} \mathbf{0}$  under  $H_0 : \beta_1 = \mathbf{0}$ :

$$\mathbf{0} = \mathcal{U}_2(\beta_1 = \mathbf{0}, \beta_2 = \tilde{\beta}_2).$$

Take the Taylor expansion of  $\mathcal{U}_2$  about  $(\beta_1 = \mathbf{0}, \beta_{2,0})$ :

$$\mathcal{U}_2(\beta_2) = \mathcal{U}_2(\beta_{2,0}) + \left\{ \frac{\partial \mathcal{U}_2}{\partial \beta_2'}(\beta_{2,0}) \right\} (\beta_2 - \beta_{2,0}) + \mathcal{O}_p(K^{-1})$$

Evaluating at  $\tilde{\beta}_2$ :

$$\mathbf{0} = \mathcal{U}_2(\tilde{\beta}_{2,0}) = \mathcal{U}_2(\beta_{2,0}) + \left\{ \dot{\mathcal{U}}_2(\beta_{2,0}) \right\} (\tilde{\beta}_2 - \beta_{2,0}) + \mathcal{O}_p(K^{-1})$$

Re-arranging:

$$\sqrt{K}(\tilde{\beta}_2 - \beta_{2,0}) = \{ -K^{-1}\dot{\mathcal{U}}_2(\beta_{2,0}) \}^{-1} K^{-1/2} \mathcal{U}_2(\beta_{2,0}) + \mathcal{O}_p(K^{-1/2}) \quad (1.3.2)$$

The term under the inverse converges as:

$$\begin{aligned} -K^{-1}\dot{\mathcal{U}}_2(\beta_{2,0}) &= -\frac{1}{K} \sum_{k=1}^K \left\{ \frac{\partial}{\partial \beta'} D'_{2,k} V_k^{-1} \right\} (\mathbf{y}_k - \boldsymbol{\mu}_k) + D'_{2,k} V_k^{-1} D_{2,k} \\ &\xrightarrow[p]{K \rightarrow \infty} -\text{plim} \frac{1}{K} \sum_{k=1}^K D'_{2,k} V_k^{-1} D_{2,k} = \mathbf{A}_{22}, \end{aligned}$$

or in order notation  $-K^{-1}\dot{\mathcal{U}}_2(\beta_{2,0}) = \mathbf{A}_{22} + o_p(1)$ . Re-expressing (1.3.2):

$$\sqrt{K}(\tilde{\beta}_2 - \beta_2) = K^{-1/2} \mathbf{A}_{22}^{-1} \mathcal{U}_2(\beta_2 = \beta_{2,0}) + o_p(1) \quad (1.3.3)$$

Next, take the Taylor expansion of  $\mathcal{U}_1$  about  $(\beta_1 = \mathbf{0}, \beta_{2,0})$ :

$$\mathcal{U}_1(\beta_2) = \mathcal{U}_1(\beta_{2,0}) + \left\{ \frac{\partial \mathcal{U}_1}{\partial \beta'_2}(\beta_{2,0}) \right\} (\beta_2 - \beta_{2,0}) + \mathcal{O}_p(K^{-1})$$

Evaluating at  $\tilde{\beta}_2$ :

$$\mathcal{U}_1(\tilde{\beta}_2) = \mathcal{U}_1(\beta_{2,0}) + \{ \dot{\mathcal{U}}_1(\beta_{2,0}) \} (\tilde{\beta}_2 - \beta_{2,0}) + \mathcal{O}_p(K^{-1})$$

Re-scaling:

$$K^{-1/2} \mathcal{U}_1(\tilde{\beta}_2) = K^{-1/2} \mathcal{U}_1(\beta_{2,0}) + \{ K^{-1} \dot{\mathcal{U}}_1(\beta_{2,0}) \} K^{1/2} (\tilde{\beta}_2 - \beta_{2,0}) + \mathcal{O}_p(K^{-3/2}).$$

By the law of large numbers  $K^{-1} \dot{\mathcal{U}}_1(\beta_{2,0}) = \mathbf{A}_{12} + o_p(1)$ . Now:

$$K^{-1/2} \mathcal{U}_1(\tilde{\beta}_2) = K^{-1/2} \mathcal{U}_1(\beta_{2,0}) - \mathbf{A}_{12} K^{1/2} (\tilde{\beta}_2 - \beta_{2,0}) + \mathcal{O}_p(K^{-3/2}). \quad (1.3.4)$$

Substituting (1.3.3) into (1.3.4):

$$K^{-1/2} \mathcal{U}_1(\tilde{\beta}_2) = K^{-1/2} \mathcal{U}_1(\beta_{2,0}) - K^{-1/2} \mathbf{A}_{12} \mathbf{A}_{22}^{-1} \mathcal{U}_2(\beta_{2,0}) + o_p(1). \quad (1.3.5)$$

Re-expressing the Taylor expansion of  $\mathcal{U}_1$  in terms of the total score  $\mathcal{U} = (\mathcal{U}_1, \mathcal{U}_2)'$ :

$$\frac{1}{\sqrt{K}} \mathcal{U}_1(\tilde{\beta}_2) = \left( \mathbf{I}, -\mathbf{A}_{12} \mathbf{A}_{22}^{-1} \right) \cdot \frac{1}{\sqrt{K}} \begin{pmatrix} \mathcal{U}_{1,0} \\ \mathcal{U}_{2,0} \end{pmatrix} + o_p(1).$$

By the central limit theorem:

$$\frac{1}{\sqrt{K}} \mathcal{U}_1(\beta_1 = \mathbf{0}, \beta_2 = \tilde{\beta}_2) \xrightarrow{\mathcal{L}} N(\mathbf{0}, \boldsymbol{\Omega}_{11|2})$$

The limiting variance of the score for  $\beta_1$  under  $H_0$  is:

$$\begin{aligned} \boldsymbol{\Omega}_{11|2} &\equiv \left( \mathbf{I}, -\mathbf{A}_{12} \mathbf{A}_{22}^{-1} \right) \begin{pmatrix} \mathbf{B}_{11} & \mathbf{B}_{12} \\ \mathbf{B}_{21} & \mathbf{B}_{22} \end{pmatrix} \begin{pmatrix} \mathbf{I} \\ -\mathbf{A}_{22}^{-1} \mathbf{A}_{21} \end{pmatrix} \\ &= \mathbf{B}_{11} - \mathbf{B}_{12} \mathbf{A}_{22}^{-1} \mathbf{A}_{21} - \mathbf{A}_{12} \mathbf{A}_{22}^{-1} \mathbf{B}_{21} + \mathbf{A}_{12} \mathbf{A}_{22}^{-1} \mathbf{B}_{22} \mathbf{A}_{22}^{-1} \mathbf{A}_{21} \end{aligned}$$

■