

Web-based Supplementary Materials for “Additive Mixed Effect Model for Clustered Failure Time Data” by Jianwen Cai and Donglin Zeng

Web Appendix

Technical conditions for Theorems 1 and 2 To establish the asymptotic distributions of $(\widehat{\beta}, \widehat{\theta})$ and $\widehat{\Lambda}$, we need the following conditions, where any subscript 0 means the true values.

(C.1) For any constant α and a deterministic function $\mu(t)$ satisfying $\alpha \neq 0$ or $\mu(t) \neq 0$, $P(\alpha^T \mathbf{X}_{ij}(t) + \mu(t) = 0, j = 1, \dots, n_i) < 1$.

(C.2) The true parameter $H_0(t) = \Lambda_0(t) + G(t; \theta_0)$ is a right-continuous increasing function and satisfies $H_0(\tau) < \infty$ and $P(C_{ij} \geq \tau, \text{ for some } j = 1, \dots, n_i) > 0$.

(C.3) The true parameter θ_0 belongs to a known bounded set Θ . Moreover,

$$E \left\{ \sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \nabla_\theta Q(t, s; \theta) dt ds \right\}$$

is non-singular in a neighborhood of θ_0 , where $\nabla_\theta Q(t, s; \theta)$ denotes the derivative of $Q(t, s; \theta)$ with respect to θ .

(C.4) The cluster size, n_i , is bounded and independent of Y_{ij} , \mathbf{X}_{ij} and Δ_{ij} . Additionally, the censoring time is assumed to be independent of T_{ij} and ξ_i given \mathbf{X}_{ij} .

Conditions (C.1) and (C.2) imply that the matrix $n^{-1} \sum_{i=1}^n \sum_{j=1}^{n_i} \int_0^\tau Y_{ij}(t) \{\mathbf{X}_{ij}(t) - \bar{\mathbf{X}}(t)\}^{\otimes 2} dt$ is positive definite when n is large enough. Thus, $\widehat{\beta}$ is well defined. This also implies that Σ is invertible. Otherwise, suppose $\alpha^T \Sigma \alpha = 0$ for some constant vector α . Then with probability one, $\alpha^T \{\mathbf{X}_{ij}(t) - \mu(t)\} = 0$ for any t and $j = 1, \dots, n_k$. However, from condition (C.3) this implies $\alpha = 0$. Thus, Σ is positive definite. Additionally, condition (C.2) gives

$n^{-1} \sum_{i=1}^n \sum_{j=1}^{n_i} Y_{ij}(t)$ is bounded away from zero. On the other hand, condition (C.3) ensures that the estimating equation for θ has a solution which is a consistent estimator for θ_0 .

Asymptotic expansion of $\hat{\theta}$

To obtain the asymptotic distribution for $\hat{\theta}$, we perform the first-order Taylor expansion at $\theta = \theta_0$ on the left-hand side of (7). It yields

$$\begin{aligned} & \mathbf{P}_n \left[\sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \{d\hat{\epsilon}_{ij}(t) d\hat{\epsilon}_{il}(s) - Q(t, s; \theta_0) dt ds\} \right] \\ & - \left[E \left\{ \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \nabla_\theta Q(t, s; \theta_0) dt ds \right\} + o_p(1) \right] (\hat{\theta} - \theta_0) = 0. \end{aligned}$$

Note

$$\begin{aligned} & \mathbf{P}_n \left[\sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \{d\hat{\epsilon}_{ij}(t) d\hat{\epsilon}_{il}(s) - Q(t, s; \theta_0) dt ds\} \right] \\ & = (\mathbf{P}_n - \mathbf{P}) \left[\sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \{d\epsilon_{ij0}(t) d\epsilon_{il0}(s) - Q(t, s; \theta_0) dt ds\} \right] \\ & - E \left[\sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \left\{ d\hat{H}(t) - dH_0(t) + \mathbf{X}_{ij}(t)^T (\hat{\boldsymbol{\beta}} - \boldsymbol{\beta}_0) dt \right\} d\epsilon_{il0}(s) \right] \\ & - E \left[\sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) d\epsilon_{ij0}(t) \left\{ d\hat{H}(s) - dH_0(s) + \mathbf{X}_{il}(t)^T (\hat{\boldsymbol{\beta}} - \boldsymbol{\beta}_0) ds \right\} \right]. \end{aligned}$$

Thus, from equations (A.1) and (A.2), we obtain

$$\hat{\theta} - \theta_0 = (\mathbf{P}_n - \mathbf{P}) S_\theta(\mathbf{O}_i) + o_p(n^{-1/2}),$$

where

$$\begin{aligned} S_\theta(\mathbf{O}_i) & = \left[E \left\{ \sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \nabla_\theta Q(t, s; \theta_0) dt ds \right\} \right]^{-1} \\ & \times \left\{ \sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \{d\epsilon_{ij0}(t) d\epsilon_{il0}(s) - Q(t, s; \theta_0) dt ds\} \right. \\ & - E \left[\sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) \left\{ dS_H(\mathbf{O}_i; t) + \mathbf{X}_{ij}(t)^T S_\beta(\mathbf{O}_i) dt \right\} d\epsilon_{il0}(s) \right] \\ & \left. - E \left[\sum_{j \neq l, j, l=1}^{n_i} \int_0^\tau \int_0^\tau Y_{ij}(t) Y_{il}(s) d\epsilon_{ij0}(t) \left\{ dS_H(\mathbf{O}_i; s) + \mathbf{X}_{il}(t)^T S_\beta(\mathbf{O}_i) ds \right\} \right] \right\}. \end{aligned}$$

Consistent estimation of asymptotic variance. Clearly, the asymptotic covariance of $(\widehat{\boldsymbol{\beta}}, \widehat{H}, \widehat{\theta})$ is given by the covariance of the corresponding influence function $(\mathbf{S}_{\boldsymbol{\beta}}, S_H, S_{\theta})$. Thus, a consistent estimator of the asymptotic covariance can be obtained from the empirical covariance of $(\widehat{\mathbf{S}}_{\boldsymbol{\beta}}, \widehat{S}_H, \widehat{S}_{\theta})$, where the latter are the consistent estimators of $(\mathbf{S}_{\boldsymbol{\beta}}, S_H, S_{\theta})$. Particularly, we can choose

$$\widehat{\mathbf{S}}_{\boldsymbol{\beta}}(\mathbf{O}_i) = \left[n^{-1} \sum_{i=1}^n \sum_{j=1}^{n_i} \int_0^{\tau} Y_{ij}(t) \{ \mathbf{X}_{ij}(t) - \overline{\mathbf{X}}(t) \}^{\otimes 2} dt \right]^{-1} \sum_{j=1}^{n_i} \int_0^{\tau} Y_{ij}(t) \{ \mathbf{X}_{ij}(t) - \overline{\mathbf{X}}(t) \} d\widehat{\epsilon}_{ij}(t),$$

$$\widehat{S}_H(\mathbf{O}_i; s) = \int_0^s \frac{\sum_{j=1}^{n_i} Y_{ij}(t) d\widehat{\epsilon}_{ij}(t)}{n^{-1} \sum_{i=1}^n \sum_{j=1}^{n_i} Y_{ij}(t)} - \int_0^s \overline{\mathbf{X}}(t)^T dt \widehat{\mathbf{S}}_{\boldsymbol{\beta}}(\mathbf{O}_i),$$

and

$$\begin{aligned} \widehat{S}_{\theta}(\mathbf{O}_i) &= \left\{ n^{-1} \sum_{i=1}^n \sum_{j \neq l, j, l=1}^{n_i} \int_0^{\tau} \int_0^{\tau} Y_{ij}(t) Y_{il}(s) \nabla_{\theta} Q(t, s; \widehat{\theta}) dt ds \right\}^{-1} \\ &\times \left\{ \sum_{j \neq l, j, l=1}^{n_i} \int_0^{\tau} \int_0^{\tau} Y_{ij}(t) Y_{il}(s) \left\{ d\widehat{\epsilon}_{ij}(t) d\widehat{\epsilon}_{il}(s) - Q(t, s; \widehat{\theta}) dt ds \right\} \right. \\ &\quad \left. - n^{-1} \sum_{k=1}^n \left[\sum_{j \neq l, j, l=1}^{n_k} \int_0^{\tau} \int_0^{\tau} Y_{kj}(t) Y_{kl}(s) \left\{ d\widehat{S}_H(\mathbf{O}_i; t) + \mathbf{X}_{kj}(t)^T \widehat{\mathbf{S}}_{\boldsymbol{\beta}}(\mathbf{O}_i) dt \right\} d\widehat{\epsilon}_{kl}(s) \right] \right. \\ &\quad \left. - n^{-1} \sum_{k=1}^n \left[\sum_{j \neq l, j, l=1}^{n_k} \int_0^{\tau} \int_0^{\tau} Y_{kj}(t) Y_{kl}(s) d\widehat{\epsilon}_{kj}(t) \left\{ d\widehat{S}_H(\mathbf{O}_i; s) + \mathbf{X}_{kl}(t)^T \widehat{\mathbf{S}}_{\boldsymbol{\beta}}(\mathbf{O}_i) ds \right\} \right] \right\}. \end{aligned}$$