Asymptotic Properties and Empirical Evaluation of the NPMLE in the Proportional Hazards Mixed-effects Model

Anthony Gamst, Michael Donohue, Ronghui Xu

University of California, San Diego

Supplementary Material

PROOF OF THEOREM 1.

First we prove $\hat{\Lambda}_n(\cdot)$ is bounded on $[0,\tau]$. We then invoke the compactness of the parameter space and Helly's selection theorem to conclude the existence of a convergent subsequence of $\{\theta_n\}$. Finally we show the limit of this subsequence must be θ_0 .

First, we let

$$\bar{\Lambda}_{n}(t) = \sum_{ij} \frac{\delta_{ij}(1 - Y_{ij}(t))}{\sum_{kl} Y_{kl}(X_{ij}) e^{\beta'_{0} \mathbf{Z}_{kl}} \mathcal{E}_{\theta}(e^{\mathbf{b}'_{k} \mathbf{W}_{kl}} | \mathbf{y}_{k})},$$

$$a_{i}(t) = n_{i}^{-1} \sum_{j=1}^{n_{i}} \int_{u=0}^{t} \{dN_{ij}(u) - Y_{ij}(u) e^{\beta'_{0} \mathbf{Z}_{ij}} \mathcal{E}_{\theta}(e^{\mathbf{b}'_{i} \mathbf{W}_{ij}} | \mathbf{y}_{i}) d\Lambda_{0}(u)\},$$

$$f_{n}(u) = n^{-1} \sum_{i=1}^{n} n_{i}^{-1} \sum_{j=1}^{n_{i}} Y_{ij}(u) e^{\beta'_{0} \mathbf{Z}_{ij}} \mathcal{E}_{\theta}(e^{\mathbf{b}'_{i} \mathbf{W}_{ij}} | \mathbf{y}_{i}).$$

We show $\sup_{t\in[0,\tau]} |\bar{\Lambda}_n(t) - \Lambda_0(t)| \to 0$ almost surely. Note that $\{a_i(t): i=1,2,\ldots\}$ is a mean zero independent sequence for fixed t, and by the strong law of large numbers $(SLLN) \ n^{-1} \sum_i a_i(t) \to 0$ almost surely. Also, by the boundedness assumption on \mathbf{W}_{ij} and \mathbf{Z}_{ij} , $\mathbf{E}_{\theta}(e^{\mathbf{b}_i'\mathbf{W}_{ij}}|\mathbf{y}_i)$ and $e^{\beta_0'\mathbf{Z}_{ij}}$ are both bounded. Again by SLLN, $f_n(u) \to E[Y_{ij}(u)e^{\beta_0'\mathbf{Z}_{ij}}\mathbf{E}_{\theta}(e^{\mathbf{b}_i'\mathbf{W}_{ij}}|\mathbf{y}_i)]$ almost surely.

Now consider

$$\sum_{ij} \int_{u=0}^{t} \left\{ dN_{ij}(u) - Y_{ij}(u)e^{\beta'_{0}\mathbf{Z}_{ij}} \mathbf{E}_{\theta}(e^{\mathbf{b}'_{i}\mathbf{W}_{ij}}|\mathbf{y}_{i}) d\bar{\Lambda}_{n}(u) \right\}$$

$$= \sum_{ij} \left\{ \delta_{ij}(1 - Y_{ij}(t)) - \sum_{kl} \frac{Y_{ij}(X_{kl})e^{\beta'_{0}\mathbf{Z}_{ij}} \mathbf{E}_{\theta}(e^{\mathbf{b}'_{i}\mathbf{W}_{ij}}|\mathbf{y}_{i}) \delta_{kl}(1 - Y_{kl}(t))}{\sum_{rs} Y_{rs}(X_{kl})e^{\beta'_{0}\mathbf{Z}_{rs}} \mathbf{E}_{\theta}(e^{\mathbf{b}'_{r}\mathbf{W}_{rs}}|\mathbf{y}_{r})} \right\}$$

$$= \sum_{ij} \delta_{ij}(1 - Y_{ij}(t)) - \sum_{kl} \left\{ \frac{\sum_{ij} Y_{ij}(X_{kl})e^{\beta'_{0}\mathbf{Z}_{ij}} \mathbf{E}_{\theta}(e^{\mathbf{b}'_{i}\mathbf{W}_{ij}}|\mathbf{y}_{i}) \delta_{kl}(1 - Y_{kl}(t))}{\sum_{rs} Y_{rs}(X_{kl})e^{\beta'_{0}\mathbf{Z}_{rs}} \mathbf{E}_{\theta}(e^{\mathbf{b}'_{r}\mathbf{W}_{rs}}|\mathbf{y}_{r})} \right\}$$

$$= 0.$$

By the above, for fixed t, we have:

$$\int_{u=0}^{t} f_{n}(u) d(\bar{\Lambda}_{n} - \Lambda_{0})(u) = n^{-1} \sum_{ij} n_{i}^{-1} \int_{u=0}^{t} \{dN_{ij}(u) - Y_{ij}(u)e^{\beta'_{0}\mathbf{Z}_{ij}} \mathbf{E}_{\theta}(e^{\mathbf{b}'_{i}\mathbf{W}_{ij}}|\mathbf{y}_{i}) d\Lambda_{0}(u)\}
- n^{-1} \sum_{ij} n_{i}^{-1} \int_{u=0}^{t} \{dN_{ij}(u) - Y_{ij}(u)e^{\beta'_{0}\mathbf{Z}_{ij}} \mathbf{E}_{\theta}(e^{\mathbf{b}'_{i}\mathbf{W}_{ij}}|\mathbf{y}_{i}) d\bar{\Lambda}_{n}(u)\}
= n^{-1} \sum_{i=1}^{n} a_{i}(t)
\rightarrow 0 \text{ a.s.,}$$

by SLLN.

Since $\lim f_n(u) = \mathbb{E}[Y_{ij}(u)e^{\beta'_0\mathbf{Z}_{ij}}\mathbb{E}_{\theta}(e^{\mathbf{b}'_i\mathbf{W}_{ij}}|\mathbf{y}_i)]$ is bounded away from zero, there exists some $c_1(u) > 0$ such that eventually $f_n(u) \geq c_1(u)$ almost surely. Let $c_1 = \sup_{u \in [0,\tau]} c_1(u)$. For sufficiently large n, we can write

$$0 \le c_1 \int_{u=0}^t d(\bar{\Lambda}_n - \Lambda_0)(u) \le \int_{u=0}^t f_n(u) d(\bar{\Lambda}_n - \Lambda_0)(u) \to 0 \text{ a.s.},$$

and by the squeeze theorem, we have

$$\int_{u=0}^{t} d(\bar{\Lambda}_n - \Lambda_0)(u) \to 0 \text{ a.s.}.$$

It follows that $\bar{\Lambda}_n(t) \to \Lambda_0(t)$ a.s. for all $t \in [0, \tau]$. Pointwise convergence of non-decreasing functions to a continuous limit implies local (on $[0, \tau]$ in particular) uniform continuity.

Since $\hat{\beta}_n$, $\hat{\Sigma}_n$, \mathbf{Z}_{kl} , and \mathbf{W}_{kl} are in compact sets, there exists some finite, possibly negative c_2 such that

$$\hat{\boldsymbol{\beta}}_n' \mathbf{Z}_{kl} + \log \mathrm{E}_{\hat{\theta}_n} [e^{\mathbf{b}_k' \mathbf{W}_{kl}} | \mathbf{y}_k] \ge \boldsymbol{\beta}_0' \mathbf{Z}_{kl} + \log \mathrm{E}_{\theta_0} [e^{\mathbf{b}_k' \mathbf{W}_{kl}} | \mathbf{y}_k] + c_2.$$

Therefore

$$\hat{\Lambda}_{n}(\tau) = \sum_{ij} \frac{\delta_{ij}(1 - Y_{ij}(\tau))}{\sum_{kl} Y_{kl}(X_{ij}) \exp\{\hat{\boldsymbol{\beta}}_{n}' \mathbf{Z}_{kl} + \log \mathbf{E}_{\hat{\boldsymbol{\theta}}_{n}}[e^{\mathbf{b}_{k}' \mathbf{W}_{kl}} | \mathbf{y}_{k}]\}}$$

$$\leq \sum_{ij} \frac{\delta_{ij}(1 - Y_{ij}(\tau))}{\sum_{kl} Y_{kl}(X_{ij}) \exp\{\boldsymbol{\beta}_{0}' \mathbf{Z}_{kl} + \log \mathbf{E}_{\theta_{0}}[e^{\mathbf{b}_{k}' \mathbf{W}_{kl}} | \mathbf{y}_{k}] + c_{2}\}}$$

$$= e^{-c_{2}} \bar{\Lambda}_{n}(\tau) \to e^{-c_{2}} \Lambda_{0}(\tau).$$

Now that we have established $\hat{\Lambda}$ has an upper bound almost surely, and $\hat{\beta}_n$ and $\hat{\Sigma}_n$ are in compact sets; we can apply Helly's selection theorem to infer the existence of a convergent subsequence which we now denote by $\hat{\theta}_n = (\hat{\Lambda}_n, \hat{\beta}_n, \hat{\Sigma}_n)$ with limit θ^* . Next we show $\theta^* = \theta_0$.

Since

$$\hat{\Lambda}_n(t) = \int_0^t \frac{\sum_{kl} Y_{kl}(u) \exp\{\boldsymbol{\beta}_0' \mathbf{Z}_{kl} + \log \mathbf{E}_{\theta_0}[e^{\mathbf{b}_k' \mathbf{W}_{kl}} | \mathbf{y}_k]\}}{\sum_{kl} Y_{kl}(u) \exp\{\hat{\boldsymbol{\beta}}_n' \mathbf{Z}_{kl} + \log \mathbf{E}_{\hat{\boldsymbol{\theta}}_n}[e^{\mathbf{b}_k' \mathbf{W}_{kl}} | \mathbf{y}_k]\}} d\bar{\Lambda}_n(u) \to \Lambda^*(t), \quad (12)$$

we see that Λ^* is absolutely continuous with respect to Λ_0 . Furthermore, $\Lambda^*(t)$ is differentiable with respect to t and $d\hat{\Lambda}_n(t)/d\bar{\Lambda}_n(t)$ converges to $d\Lambda^*(t)/d\Lambda_0(t)$.

Note that the finite sample likelihood as expressed via (4) has no finite maximum, since λ is free to go to infinity at any X_{ij} . We restrict Λ to be right continuous with jumps at X_{ij} ; and for cluster i, conditional on the random effect \mathbf{b}_i , we let the log-likelihood be (6), where $\Lambda\{t\}$ is the size of the jump in Λ at t. The likelihood of the observed data, $L_n(\theta)$, is still as defined in (4) and we let $l_n(\theta) = \log L_n(\theta)$. In place of Λ_0 , which is continuous at X_{ij} , we use $\bar{\Lambda}_n$. In particular we have:

$$0 \leq n^{-1} \{ l_{n}(\hat{\boldsymbol{\beta}}_{n}, \hat{\boldsymbol{\Sigma}}_{n}, \hat{\boldsymbol{\Lambda}}_{n}) - l_{n}(\boldsymbol{\beta}_{0}, \boldsymbol{\Sigma}_{0}, \bar{\boldsymbol{\Lambda}}_{n}) \}$$

$$= n^{-1} \sum_{i=1}^{n} \log \left\{ \int_{\mathbf{b}} R_{1i}(\hat{\boldsymbol{\beta}}_{n}, \hat{\boldsymbol{\Lambda}}_{n}, \mathbf{b}) \phi(\mathbf{b}, \hat{\boldsymbol{\Sigma}}_{n}) d\mathbf{b} \right\}$$

$$- n^{-1} \sum_{i=1}^{n} \log \left\{ \int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}_{0}, \bar{\boldsymbol{\Lambda}}_{n}, \mathbf{b}) \phi(\mathbf{b}, \boldsymbol{\Sigma}_{0}) d\mathbf{b} \right\}$$

$$+ n^{-1} \sum_{i=1}^{n} \sum_{j=1}^{n_{i}} \delta_{ij} \log(\hat{\boldsymbol{\Lambda}}_{n} \{X_{ij}\} / \bar{\boldsymbol{\Lambda}}_{n} \{X_{ij}\})$$

$$\rightarrow \mathbb{E} \log \left\{ \int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}^{*}, \boldsymbol{\Lambda}^{*}, \mathbf{b}) \phi(\mathbf{b}, \boldsymbol{\Sigma}^{*}) d\mathbf{b} \prod_{j=1}^{n_{i}} \lambda^{*} (X_{ij})^{\delta_{ij}} \right.$$

$$\times \left(\int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}_{0}, \boldsymbol{\Lambda}_{0}, \mathbf{b}) \phi(\mathbf{b}, \boldsymbol{\Sigma}_{0}) d\mathbf{b} \prod_{j=1}^{n_{i}} \lambda_{0} (X_{ij})^{\delta_{ij}} \right)^{-1} \right\},$$

where

$$R_{1i}(\boldsymbol{\beta}, \Lambda, \mathbf{b}) = \prod_{j=1}^{n_i} \exp[\delta_{ij}(\boldsymbol{\beta}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}) - \Lambda(X_{ij}) \exp(\boldsymbol{\beta}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})],$$

and ϕ is the multivariate normal distribution. The limit above is negative the Kullback-Leibler information, so almost surely

$$\int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}^{*}, \Lambda^{*}, \mathbf{b}) \phi(\mathbf{b}, \boldsymbol{\Sigma}^{*}) d\mathbf{b} \prod_{j=1}^{n_{i}} \lambda^{*}(X_{ij})^{\delta_{ij}} = \int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}_{0}, \Lambda_{0}, \mathbf{b}) \phi(\mathbf{b}, \boldsymbol{\Sigma}_{0}) d\mathbf{b} \prod_{j=1}^{n_{i}} \lambda_{0}(X_{ij})^{\delta_{ij}},$$
or
$$\int_{\mathbf{b}} \prod_{j=1}^{n_{i}} \lambda^{*}(X_{ij})^{\delta_{ij}} \exp[\delta_{ij}(\boldsymbol{\beta}^{*'}\mathbf{Z}_{ij} + \mathbf{b}'\mathbf{W}_{ij}) - \Lambda^{*}(X_{ij}) \exp(\boldsymbol{\beta}^{*'}\mathbf{Z}_{ij} + \mathbf{b}'\mathbf{W}_{ij})] \phi(\mathbf{b}, \boldsymbol{\Sigma}^{*}) d\mathbf{b}$$

$$= \int_{\mathbf{b}} \prod_{j=1}^{n_{i}} \lambda_{0}(X_{ij})^{\delta_{ij}} \exp[\delta_{ij}(\boldsymbol{\beta}_{0}'\mathbf{Z}_{ij} + \mathbf{b}'\mathbf{W}_{ij}) - \Lambda_{0}(X_{ij}) \exp(\boldsymbol{\beta}_{0}'\mathbf{Z}_{ij} + \mathbf{b}'\mathbf{W}_{ij})] \phi(\mathbf{b}, \boldsymbol{\Sigma}_{0}) d\mathbf{b}.$$
(13)

Now we adapt techniques used in the identifiability step of the proportional odds case (Zeng et al., 2005) to conclude $\theta^* = \theta_0$. Note that $P[(X_{ij}, \delta_{ij}) = (x, \delta)] > 0$ for any (x, δ) in $[0, \tau] \times \{1\} \cup \{\tau\} \times \{0\}$. This allows us to manipulate (X_{ij}, δ_{ij}) within that set and maintain the almost sure equality (13). A particular manipulation, which we now demonstrate, will allow us to conclude $\theta^* = \theta_0$.

Fix some k in $1, \ldots, n_i$. For $j \leq k$, let $\delta_{ij} = 1, X_{ij} = 0$ in (13) and note that we assume $\Lambda^*(0) = \Lambda_0(0) = 0$. If j > k and $\delta_{ij} = 0$, we replace X_{ij} with τ . Otherwise, if $j = k + 1, \ldots, n_i$ and $\delta_{ij} = 1$, we integrate X_{ij} from 0 to τ . We get:

$$\int_{\mathbf{b}} \prod_{j=1}^{k} \lambda^{*}(0) \exp[\beta^{*'} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}] \\
\times \prod_{j=k+1}^{n_{i}} \left\{ \exp[-\Lambda^{*}(\tau) \exp(\beta^{*'} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \right\}^{1-\delta_{ij}} \\
\times \prod_{j=k+1}^{n_{i}} \left\{ \int_{y=0}^{\tau} \lambda^{*}(y) \exp[\beta^{*'} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij} - \Lambda^{*}(y) \exp(\beta^{*'} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] dy \right\}^{\delta_{ij}} \phi(\mathbf{b}, \mathbf{\Sigma}^{*}) d\mathbf{b} \\
= \int_{\mathbf{b}} \prod_{j=1}^{k} \lambda_{0}(0) \exp[\beta'_{0} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}] \\
\times \prod_{j=k+1}^{n_{i}} \left\{ \exp[-\Lambda_{0}(\tau) \exp(\beta_{0}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \right\}^{1-\delta_{ij}} \\
\times \prod_{j=k+1}^{n_{i}} \left\{ \int_{y=0}^{\tau} \lambda_{0}(y) \exp[\beta_{0}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij} - \Lambda_{0}(y) \exp[\beta_{0}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] dy \right\}^{\delta_{ij}} \phi(\mathbf{b}, \mathbf{\Sigma}_{0}) d\mathbf{b}$$

$$\int_{\mathbf{b}} \prod_{j=1}^{k} \lambda^{*}(0) \exp[\boldsymbol{\beta}^{*'} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}]
\times \prod_{j=k+1}^{n_{i}} \left\{ \exp[-\Lambda^{*}(\tau) \exp(\boldsymbol{\beta}^{*'} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \right\}^{1-\delta_{ij}}
\times \prod_{j=k+1}^{n_{i}} \left\{ 1 - \exp[-\Lambda^{*}(\tau) \exp(\boldsymbol{\beta}^{*'} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \right\}^{\delta_{ij}} \phi(\mathbf{b}, \boldsymbol{\Sigma}^{*}) d\mathbf{b}
= \int_{\mathbf{b}} \prod_{j=1}^{k} \lambda_{0}(0) \exp[\boldsymbol{\beta}'_{0} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}]
\times \prod_{j=k+1}^{n_{i}} \left\{ \exp[-\Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \right\}^{1-\delta_{ij}}
\times \prod_{j=k+1}^{n_{i}} \left\{ 1 - \exp[-\Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \right\}^{\delta_{ij}} \phi(\mathbf{b}, \boldsymbol{\Sigma}_{0}) d\mathbf{b}. \tag{14}$$

For j > k, we can choose δ_{ij} to be 0 or 1. If we sum (14) over all possible combinations of δ_{ij} , the j > k factors sum to one and we are left with:

$$\int_{\mathbf{b}} \prod_{j=1}^{k} \lambda^{*}(0) \exp[\boldsymbol{\beta}^{*'} \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}] \phi(\mathbf{b}, \boldsymbol{\Sigma}^{*}) d\mathbf{b} = \int_{\mathbf{b}} \prod_{j=1}^{k} \lambda_{0}(0) \exp[\boldsymbol{\beta}_{0}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}] \phi(\mathbf{b}, \boldsymbol{\Sigma}_{0}) d\mathbf{b}$$

and

$$\exp\left\{\sum_{j=1}^{k} \boldsymbol{\beta}^{*'} \mathbf{Z}_{ij} + \frac{(\sum_{j=1}^{k} \mathbf{W}_{ij})' \boldsymbol{\Sigma}^{*} (\sum_{j=1}^{k} \mathbf{W}_{ij})}{2}\right\} \lambda^{*}(0)^{k}$$

$$= \exp\left\{\sum_{j=1}^{k} \boldsymbol{\beta}_{0}' \mathbf{Z}_{ij} + \frac{(\sum_{j=1}^{k} \mathbf{W}_{ij})' \boldsymbol{\Sigma}_{0} (\sum_{j=1}^{k} \mathbf{W}_{ij})}{2}\right\} \lambda_{0}(0)^{k}$$

We assume $\lambda^*(0) > 0$. Since k is arbitrarily chosen, the index set of the above summations can be replaced by any subset of $\{1, \ldots, n_i\}$. In particular, if we choose an index set $\{j, j'\}$, $j \neq j'$, we get

$$\beta^{*'}(\mathbf{Z}_{ij} + \mathbf{Z}_{ij'}) + \frac{(\mathbf{W}_{ij} + \mathbf{W}_{ij'})'\Sigma^{*}(\mathbf{W}_{ij} + \mathbf{W}_{ij'})}{2} + 2\log\lambda^{*}(0)$$

$$= \beta_{0}'(\mathbf{Z}_{ij} + \mathbf{Z}_{ij'}) + \frac{(\mathbf{W}_{ij} + \mathbf{W}_{ij'})'\Sigma_{0}(\mathbf{W}_{ij} + \mathbf{W}_{ij'})}{2} + 2\log\lambda_{0}(0).$$

If we subtract from this equality the resulting equalities with the singleton index sets $\{j\}$ and $\{j'\}$, we have:

$$\mathbf{W}'_{ij}(\mathbf{\Sigma}^* - \mathbf{\Sigma}_0)\mathbf{W}_{ij'} = 0, j \neq j' : j, j' = 1, \dots, n_i.$$

We also clearly have

$$\mathbf{c}'[1,\mathbf{Z}'_{ij}]' + \mathbf{W}'_{ij}(\mathbf{\Sigma}^* - \mathbf{\Sigma}_0)\mathbf{W}_{ij} = 0, \ j = 1,\dots, n_i$$

where $\mathbf{c} = 2[\log \lambda^*(0) - \log \lambda_0(0), \boldsymbol{\beta}^{*'} - \boldsymbol{\beta}_0']'$. Therefore under C7 $\mathbf{c} = \mathbf{0}$ and it follows $\boldsymbol{\Sigma}^* = \boldsymbol{\Sigma}_0, \, \boldsymbol{\beta}^* = \boldsymbol{\beta}_0, \, \text{and} \, \lambda^*(0) = \lambda_0(0).$

To show $\Lambda^* = \Lambda_0$, we manipulate the terms of (13) again. Let $\delta_{i1} = 1$ and integrate X_{i1} from 0 to t. Also for $j = 2, \ldots, n_i$, if $\delta_{ij} = 0$, replace X_{ij} with τ and if $\delta_{ij} = 1$ integrate X_{ij} from 0 to τ . Summing the result over all possible values of δ_{ij} , j > 1, this time we get

$$\int_{\mathbf{b}} 1 - \exp[-\Lambda^*(t) \exp(\boldsymbol{\beta}_0' Z_{i1} + \mathbf{b}' \mathbf{W}_{i1})] \phi(\mathbf{b}, \boldsymbol{\Sigma}_0) d\mathbf{b}$$

$$= \int_{\mathbf{b}} 1 - \exp[-\Lambda_0(t) \exp(\boldsymbol{\beta}_0' Z_{i1} + \mathbf{b}' \mathbf{W}_{i1})] \phi(\mathbf{b}, \boldsymbol{\Sigma}_0) d\mathbf{b}. \tag{15}$$

Because both sides of (15) are strictly monotone in $\Lambda^*(t)$ and $\Lambda_0(t)$, we have $\Lambda^*(t) = \Lambda_0(t)$. Since Λ_0 is non-decreasing and continuous, the pointwise convergence can be extended to uniform convergence on $[0, \tau]$.

PROOF OF THEOREM 2.

First let

$$\mathcal{H} = \{ (\mathbf{h}_1, \mathbf{h}_2, h_3) : \mathbf{h}_1 \in \mathbf{R}^{d_1}, \mathbf{h}_2 \in \mathbf{R}^{d_2(d_2+1)/2}, \\ h_3(\cdot) \text{ is a function on } [0, \tau]; \|\mathbf{h}_1\|, \|\mathbf{h}_2\|, \|h_3\|_V \le 1 \}$$

where $||h_3||_V$ denotes the total variation of $h_3(\cdot)$ in $[0,\tau]$. Let S_n be a sequence of maps from \mathcal{U} , a neighborhood of $(\beta_0, \Sigma_0, \Lambda_0)$, into $l^{\infty}(\mathcal{H})$:

$$S_{n}(\boldsymbol{\beta}, \boldsymbol{\Sigma}, \boldsymbol{\Lambda})[\mathbf{h}_{1}, \mathbf{h}_{2}, h_{3}]$$

$$\equiv n^{-1} \frac{d}{d\epsilon} l_{n} \left(\boldsymbol{\beta} + \epsilon \mathbf{h}_{1}, \boldsymbol{\Sigma} + \epsilon \mathbf{h}_{2}, \boldsymbol{\Lambda}(t) + \epsilon \int_{0}^{t} h_{3}(s) d\boldsymbol{\Lambda}(s) \right) \Big|_{\epsilon=0}$$

$$\equiv A_{n1}[\mathbf{h}_{1}] + A_{n2}[\mathbf{h}_{2}] + A_{n3}[h_{3}].$$

Here we treat Σ as an extended column vector consisting of the upper triangle elements of the covariance matrix. The terms A_{np} , p=1,2,3, are linear functionals on \mathbf{R}^{d_1} , $\mathbf{R}^{d_2(d_2+1)/2}$ and $BV[0,\tau]$ (the space of functions with finite total variation in $[0,\tau]$). Let l_{β} , l_{Σ} and l_{Λ} be the score functions for β, Σ , and Λ (along $\int_0^t 1 + \epsilon h_3(s) d\Lambda(s)$) for a single cluster, then

$$A_{n1}[\mathbf{h}_1] = \mathcal{P}_n[\mathbf{h}_1'l_{\boldsymbol{\beta}}], A_{n2}[\mathbf{h}_2] = \mathcal{P}_n[\mathbf{h}_2'l_{\boldsymbol{\Sigma}}], \text{ and } A_{n3}[h_3] = \mathcal{P}_n[l_{\Lambda}[h_3]]$$

where \mathcal{P}_n denotes the empirical measure based on n independent clusters. We now seek explicit expressions for A_{np} . Recall the log-likelihood

$$n^{-1}l_n(\theta) = n^{-1}\sum_{i=1}^n \log \left\{ \int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}, \boldsymbol{\Lambda}, \mathbf{b}) \phi(\mathbf{b}, \boldsymbol{\Sigma}) d\mathbf{b} \right\} + n^{-1}\sum_{i=1}^n \sum_{j=1}^{n_i} \delta_{ij} \log \Lambda \{X_{ij}\}$$

where

$$R_{1i}(\boldsymbol{\beta}, \boldsymbol{\Lambda}, \mathbf{b}) = \exp \left\{ \sum_{j=1}^{n_i} \delta_{ij} (\boldsymbol{\beta}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}) - \Lambda(X_{ij}) \exp(\boldsymbol{\beta}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}) \right\}.$$

Note that

$$\frac{\partial}{\partial \epsilon} R_{1i}(\boldsymbol{\beta} + \epsilon \mathbf{h}_1, \Lambda, \mathbf{b}) \Big|_{\epsilon=0} = R_{1i}(\boldsymbol{\beta}, \Lambda, \mathbf{b}) \sum_{j=1}^{n_i} \mathbf{h}_1' \mathbf{Z}_{ij} \left(\delta_{ij} - \Lambda(X_{ij}) \exp(\boldsymbol{\beta}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}) \right).$$

Furthermore let $\Lambda_{\epsilon}(t) = \int_0^t 1 + \epsilon h_3 d\Lambda$, then $\frac{\partial}{\partial \epsilon} \Lambda_{\epsilon}(t) = \int_0^t h_3(s) d\Lambda(s)$ and

$$\frac{\partial}{\partial \epsilon} R_{1i} \left(\boldsymbol{\beta}, \Lambda_{\epsilon}, \mathbf{b} \right) \Big|_{\epsilon=0} = -R_{1i} \left(\boldsymbol{\beta}, \Lambda, \mathbf{b} \right) \sum_{j=1}^{n_i} \int_0^{X_{ij}} h_3(s) \, d\Lambda(s) \exp(\boldsymbol{\beta}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}).$$

Also $\Lambda_{\epsilon}\{t\} = (1 + \epsilon h_3(t)) \Lambda\{t\}$, so

$$\frac{d}{d\epsilon} \log \Lambda_{\epsilon} \{t\} \Big|_{\epsilon=0} = \frac{h_3(t)\Lambda\{t\}}{\Lambda_{\epsilon} \{t\}} \Big|_{\epsilon=0} = h_3(t).$$

If we let H_2 denote the matrix corresponding to the extended vector \mathbf{h}_2 , then

$$\begin{split} \frac{\partial}{\partial \epsilon} \phi(\mathbf{b}; \mathbf{\Sigma} + \epsilon \mathbf{h}_2) \big|_{\epsilon = 0} &= \frac{\partial}{\partial \epsilon} |\mathbf{\Sigma} + \epsilon \mathbf{h}_2|^{-1/2} e^{-\mathbf{b}'(\mathbf{\Sigma} + \epsilon \mathbf{h}_2)^{-1}\mathbf{b}/2} \big|_{\epsilon = 0} \\ &= \left\{ \mathbf{b}' \mathbf{\Sigma}^{-1} H_2 \mathbf{\Sigma}^{-1} \mathbf{b}/2 - \operatorname{trace}(\mathbf{\Sigma}^{-1} H_2)/2 \right\} e^{-\mathbf{b}' \mathbf{\Sigma}^{-1}\mathbf{b}/2}. \end{split}$$

Finally, we can explicitly write A_{np} as

$$A_{n1}[\mathbf{h}_{1}] = n^{-1} \sum_{i=1}^{n} \left(\int_{\mathbf{b}} \sum_{j=1}^{n_{i}} \mathbf{h}_{1}' \mathbf{Z}_{ij} \left(\delta_{ij} - \Lambda(X_{ij}) e^{\beta' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) \right)$$

$$\times R_{1i}(\boldsymbol{\beta}, \boldsymbol{\Lambda}, \mathbf{b}) e^{-\mathbf{b}' \boldsymbol{\Sigma}^{-1} \mathbf{b}/2} d\mathbf{b}$$

$$\times \left(\int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}, \boldsymbol{\Lambda}, \mathbf{b}) e^{-\mathbf{b}' \boldsymbol{\Sigma}^{-1} \mathbf{b}/2} d\mathbf{b} \right)^{-1}$$

$$A_{n2}[\mathbf{h}_{2}] = n^{-1} \sum_{i=1}^{n} \left(\int_{\mathbf{b}} \left\{ \mathbf{b}' \boldsymbol{\Sigma}^{-1} H_{2} \boldsymbol{\Sigma}^{-1} \mathbf{b}/2 - \operatorname{trace}(\boldsymbol{\Sigma}^{-1} H_{2})/2 \right\} \right)$$

$$\times R_{1i}(\boldsymbol{\beta}, \boldsymbol{\Lambda}, \mathbf{b}) e^{-\mathbf{b}' \boldsymbol{\Sigma}^{-1} \mathbf{b}/2} d\mathbf{b}$$

$$\times \left(\int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}, \boldsymbol{\Lambda}, \mathbf{b}) e^{-\mathbf{b}' \boldsymbol{\Sigma}^{-1} \mathbf{b}/2} d\mathbf{b} \right)^{-1}$$

$$A_{n3}[h_{3}] = n^{-1} \sum_{i=1}^{n} \sum_{j=1}^{n_{i}} \delta_{ij} h_{3}(X_{ij}) - \int_{0}^{X_{ij}} h_{3}(s) d\boldsymbol{\Lambda}(s)$$

$$\times \int_{\mathbf{b}} e^{\beta' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} R_{1i}(\boldsymbol{\beta}, \boldsymbol{\Lambda}, \mathbf{b}) e^{-\mathbf{b}' \boldsymbol{\Sigma}^{-1} \mathbf{b}/2} d\mathbf{b}$$

$$\times \left(\int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}, \boldsymbol{\Lambda}, \mathbf{b}) e^{-\mathbf{b}' \boldsymbol{\Sigma}^{-1} \mathbf{b}/2} d\mathbf{b} \right)^{-1}$$

or

$$A_{n1}[\mathbf{h}_{1}] = n^{-1} \sum_{i=1}^{n} \int_{\mathbf{b}} \sum_{j=1}^{n_{i}} \mathbf{h}_{1}' \mathbf{Z}_{ij} \left(\delta_{ij} - \Lambda(X_{ij}) e^{\beta' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) d\mu_{i}(\mathbf{b})$$

$$A_{n2}[\mathbf{h}_{2}] = n^{-1} \sum_{i=1}^{n} \int_{\mathbf{b}} \left\{ \mathbf{b}' \mathbf{\Sigma}^{-1} H_{2} \mathbf{\Sigma}^{-1} \mathbf{b} / 2 - \operatorname{trace}(\mathbf{\Sigma}^{-1} H_{2}) / 2 \right\} d\mu_{i}(\mathbf{b})$$

$$A_{n3}[h_{3}] = n^{-1} \sum_{i=1}^{n} \sum_{j=1}^{n_{i}} \delta_{ij} h_{3}(X_{ij}) - \int_{0}^{X_{ij}} h_{3}(s) d\Lambda(s) \int_{\mathbf{b}} e^{\beta' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} d\mu_{i}(\mathbf{b})$$

where

$$d\mu_i(\mathbf{b}) = \frac{R_{1i}(\boldsymbol{\beta}, \Lambda, \mathbf{b})e^{-\mathbf{b}'\boldsymbol{\Sigma}^{-1}\mathbf{b}/2}d\mathbf{b}}{\int_{\mathbf{b}} R_{1i}(\boldsymbol{\beta}, \Lambda, \mathbf{b})e^{-\mathbf{b}'\boldsymbol{\Sigma}^{-1}\mathbf{b}/2}d\mathbf{b}}$$

We define the limit map $S: (\boldsymbol{\beta}, \boldsymbol{\Sigma}, \Lambda)[\mathbf{h}_1, \mathbf{h}_2, h_3] \to l^{\infty}(\mathcal{H})$ as

$$S(\boldsymbol{\beta}, \boldsymbol{\Sigma}, \Lambda)[\mathbf{h}_1, \mathbf{h}_2, h_3] = A_1[\mathbf{h}_1] + A_2[\mathbf{h}_2] + A_3[h_3]$$

where the linear functionals A_p are obtained by replacing the empirical sum in A_{np} by the expectation. By construction, $S_n(\hat{\beta}_n, \hat{\Sigma}_n, \hat{\Lambda}_n) = 0$ and $S(\beta_0, \Sigma_0, \Lambda_0) = 0$.

As in Murphy (1995), asymptotic normality follows by verifying four conditions on the score function: convergence to a tight Gaussian process, Fréchet differentiability, invertibility, and the approximation condition. First, $\sqrt{n}(S_n(\beta_0, \Sigma_0, \Lambda_0)) - S(\beta_0, \Sigma_0, \Lambda_0)$ weakly converges to a tight Gaussian process on $l^{\infty}(\mathcal{H})$, because \mathcal{H} is a Donsker class and the functionals A_{np} are bounded Lipschitz functionals with respect to \mathcal{H} . The approximation condition that

$$\sup_{(\mathbf{h}_1, \mathbf{h}_2, h_3) \in \mathcal{H}} |(S_n - S)(\hat{\boldsymbol{\beta}}_n, \hat{\boldsymbol{\Sigma}}_n, \hat{\boldsymbol{\Lambda}}_n) - (S_n - S)(\boldsymbol{\beta}_0, \boldsymbol{\Sigma}_0, \boldsymbol{\Lambda}_0)|$$

$$= o_p \left(n^{-1/2} \vee \left\{ ||\hat{\boldsymbol{\beta}}_n - \boldsymbol{\beta}_0|| + ||\hat{\boldsymbol{\Sigma}}_n - \boldsymbol{\Sigma}_0|| + \sup_{t \in [0, \tau]} |\hat{\boldsymbol{\Lambda}}_n(t) - \boldsymbol{\Lambda}_0(t)| \right\} \right)$$

can be proved in a manner similar to Lemma 1 in the appendix of Murphy (1995). Fréchet differentiability holds by the smoothness of $S(\beta, \Sigma, \Lambda)$. We consider the derivative, denoted $\dot{S}(\beta_0, \Sigma_0, \Lambda_0)$, to be a linear map, T, from the space

$$\{(\boldsymbol{\beta}-\boldsymbol{\beta}_0,\boldsymbol{\Sigma}-\boldsymbol{\Sigma}_0,\boldsymbol{\Lambda}-\boldsymbol{\Lambda}_0):(\boldsymbol{\beta},\boldsymbol{\Sigma},\boldsymbol{\Lambda}) \text{ is in the neighborhood } \mathcal{U} \text{ of } (\boldsymbol{\beta}_0,\boldsymbol{\Sigma}_0,\boldsymbol{\Lambda}_0)\}$$

to $l^{\infty}(\mathcal{H})$. Lastly, we need to show T is continuously invertible on its range. We write

$$T(\boldsymbol{\beta} - \boldsymbol{\beta}_0, \boldsymbol{\Sigma} - \boldsymbol{\Sigma}_0, \boldsymbol{\Lambda} - \boldsymbol{\Lambda}_0) = (\boldsymbol{\beta} - \boldsymbol{\beta}_0)' \mathcal{Q}_1(\mathbf{h}_1, \mathbf{h}_2, h_3) + (\boldsymbol{\Sigma} - \boldsymbol{\Sigma}_0)' \mathcal{Q}_2(\mathbf{h}_1, \mathbf{h}_2, h_3) + \int_0^{\tau} \mathcal{Q}_3(\mathbf{h}_1, \mathbf{h}_2, h_3) d(\boldsymbol{\Lambda} - \boldsymbol{\Lambda}_0)$$

where the Q_i are the respective partial derivatives of S with respect to β , Σ , and Λ . The Q_i are of the form

$$Q_1(\mathbf{h}_1, \mathbf{h}_2, h_3) = B_1 \begin{pmatrix} \mathbf{h}_1 \\ \mathbf{h}_2 \end{pmatrix} + \int_0^{\tau} h_3(t) D_1(t) dt,$$

$$Q_2(\mathbf{h}_1, \mathbf{h}_2, h_3) = B_2 \begin{pmatrix} \mathbf{h}_1 \\ \mathbf{h}_2 \end{pmatrix} + \int_0^{\tau} h_3(t) D_2(t) dt,$$

and

$$Q_3(\mathbf{h}_1, \mathbf{h}_2, h_3) = B_3 \begin{pmatrix} \mathbf{h}_1 \\ \mathbf{h}_2 \end{pmatrix} + b_4 h_3(t) + \int_0^{\tau} h_3(t) D_3(t) dt;$$

where B_1 , B_2 , and B_3 are constant matrices; $D_1(t)$, $D_2(t)$, $D_3(t)$ are continuously differentiable functions; and $b_4 > 0$; each of which depends on θ_0 . The operator $\mathcal{Q} = (\mathcal{Q}_1, \mathcal{Q}_2, \mathcal{Q}_3)'$ is the sum of a continuously invertible operator and a compact operator from \mathcal{H} to itself and to prove T is invertible it suffices to show the invertibility of the linear operator $\mathcal{Q}(\mathbf{h}_1, \mathbf{h}_2, h_3)$ (Rudin, 1973). Suppose $\mathcal{Q}(\mathbf{h}_1, \mathbf{h}_2, h_3) = \mathbf{0}$, then $T(\boldsymbol{\beta} - \boldsymbol{\beta}_0, \boldsymbol{\Sigma} - \boldsymbol{\Sigma}_0, \boldsymbol{\Lambda} - \boldsymbol{\Lambda}_0)[\mathbf{h}_1, \mathbf{h}_2, h_3] = \mathbf{0}$ for any $(\boldsymbol{\beta}, \boldsymbol{\Sigma}, \boldsymbol{\Lambda})$ in the neighborhood \mathcal{U} .

For a small constant ϵ , let

$$oldsymbol{eta} = oldsymbol{eta}_0 + \epsilon \mathbf{h}_1, \quad oldsymbol{\Sigma} = oldsymbol{\Sigma}_0 + \epsilon \mathbf{h}_2, \ \Lambda(t) = \Lambda_0(t) + \epsilon \int_0^t h_3(t) \, d\Lambda_0(t).$$

It follows, by the definition of T, that

$$0 = T(\boldsymbol{\beta} - \boldsymbol{\beta}_0, \boldsymbol{\Sigma} - \boldsymbol{\Sigma}_0, \boldsymbol{\Lambda} - \boldsymbol{\Lambda}_0)[\mathbf{h}_1, \mathbf{h}_2, h_3]$$
$$= \epsilon \mathbb{E}\{(l_{\boldsymbol{\beta}_0}[\mathbf{h}_1] + l_{\boldsymbol{\Sigma}_0}[\mathbf{h}_2] + l_{\boldsymbol{\Lambda}_0}[h_3])^2\},$$

so that $l_{\beta_0}[\mathbf{h}_1] + l_{\Sigma_0}[\mathbf{h}_2] + l_{\Lambda_0}[h_3] = 0$ almost surely. Expanding this expression we get

$$0 = \sum_{j=1}^{n_i} \int_{\mathbf{b}} \mathbf{h}_1' \mathbf{Z}_{ij} \left(\delta_{ij} - \Lambda_0(X_{ij}) e^{\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0)$$

$$+ \int_{\mathbf{b}} \left\{ \mathbf{b}' \boldsymbol{\Sigma}_0^{-1} H_2 \boldsymbol{\Sigma}_0^{-1} \mathbf{b} / 2 - \operatorname{trace}(\boldsymbol{\Sigma}_0^{-1} H_2) / 2 \right\} R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0)$$

$$+ \sum_{j=1}^{n_i} \int_{\mathbf{b}} \left(\delta_{ij} h_3(X_{ij}) - \int_0^{X_{ij}} h_3(s) d\Lambda_0(s) e^{\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0)$$

$$(16)$$

where

$$R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) = R_{1i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) \prod_{j=1}^{n_i} \{\lambda_0(X_{ij})\}^{\delta_{ij}}$$

$$= \prod_{j=1}^{n_i} \exp[\delta_{ij}(\boldsymbol{\beta}_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}) - \Lambda_0(X_{ij}) \exp(\boldsymbol{\beta}_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \{\lambda_0(X_{ij})\}^{\delta_{ij}}.$$

Similar to the identifiability step of the consistency proof, we show that (16) implies $\mathbf{h}_1 = \mathbf{0}$, $\mathbf{h}_2 = \mathbf{0}$, and $h_3 = 0$. Let \mathbf{Z}_{ij} and \mathbf{W}_{ij} be fixed. Then for fixed integer k in $1, \ldots, n_i$, we define measures μ_1, \ldots, μ_{n_i} on the set $\{0, 1\} \times [0, \tau]$ as follows:

$$\mu_m(\{0\} \times A) = 0, \quad \mu_m(\{1\} \times A) = I(0 \in A), \quad m \le k,$$

and

$$\mu_m(\{0\} \times A) = I(\tau \in A), \quad \mu_m(\{1\} \times A) = \int I_A dx, \quad m > k,$$

where A is any Borel set in $[0,\tau]$. We integrate both sides of (16) with respect to $\{(\delta_{i1}, X_{i1}), \ldots, (\delta_{in_i}, X_{in_i})\}$ and the product measure $d\mu_1 \cdots d\mu_{n_i}$. That is, we let $\delta_{im} = 1$ and $X_{im} = 0$ for all $m \leq k$. Where m > k, we choose $X_{im} = \tau$ if $\delta_{im} = 0$, integrate X_{im} from 0 to τ if $\delta_{im} = 1$, then sum over $\delta_{ij} \in \{0, 1\}$. Then we sum all of the equalities of (16) for all possible combinations of $\{\delta_{i1}, \ldots, \delta_{in_i}\} \in \{0, 1\}^{n_i - k}$.

We compute the integral of each term on the right side of (16) with respect to the product measure, $\prod_{m=1}^{n_i} \mu_m$, the sum of which must be 0. First note, for any **b**,

$$\int R_{2i}(\boldsymbol{\beta}_{0}, \Lambda_{0}, \mathbf{b}) d \left(\prod_{m=1}^{n_{i}} \mu_{m} \right)
= \prod_{m \leq k} \{\lambda_{0}(0) e^{\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im}} \}
\times \sum_{\substack{\delta_{im} \in \{0,1\} \\ m > k}} \prod_{m > k} (\exp[-\Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im})])^{1-\delta_{im}}
\times \left\{ \int_{y=0}^{\tau} \exp[\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im} - \Lambda_{0}(y) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im})] \lambda_{0}(y) dy \right\}^{\delta_{im}}
= \prod_{m \leq k} \{\lambda_{0}(0) e^{\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im}} \}
\times \sum_{\substack{\delta_{im} \in \{0,1\} \\ m > k}} \prod_{m > k} (\exp[-\Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im})])^{1-\delta_{im}}
\times (1 - \exp[-\Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im})])^{\delta_{im}}
= \prod_{m \leq k} \{\lambda_{0}(0) e^{\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im}} \}.$$

For the first term of (16), where $j \leq k$, we have for any **b**:

$$\int \mathbf{h}_{1}' \mathbf{Z}_{ij} \left(\delta_{ij} - \Lambda_{0}(X_{ij}) e^{\beta_{0}' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) R_{2i}(\boldsymbol{\beta}_{0}, \Lambda_{0}, \mathbf{b}) d \left(\prod_{m=1}^{n_{i}} \mu_{m} \right)$$

$$= \int \mathbf{h}_{1}' \mathbf{Z}_{ij} R_{2i}(\boldsymbol{\beta}_{0}, \Lambda_{0}, \mathbf{b}) d \left(\prod_{m=1}^{n_{i}} \mu_{m} \right)$$

$$= \mathbf{h}_{1}' \mathbf{Z}_{ij} \prod_{m \leq k} \{ \lambda_{0}(0) e^{\beta_{0}' \mathbf{Z}_{im} + \mathbf{b}' \mathbf{W}_{im}} \}.$$

When j > k,

$$\begin{split} &\int \mathbf{h}_{1}^{\prime} \mathbf{Z}_{ij} \left(\delta_{ij} - \Lambda_{0}(X_{ij}) e^{\beta_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij}} \right) R_{2i}(\boldsymbol{\beta}_{0}, \Lambda_{0}, \mathbf{b}) \, d \left(\prod_{m=1}^{n_{i}} \mu_{m} \right) \\ &= \mathbf{h}_{1}^{\prime} \mathbf{Z}_{ij} \prod_{m \leq k} \left\{ \lambda_{0}(0) e^{\beta_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im}} \right\} \\ &\times \sum_{\substack{\delta_{im} \in \{0,1\} \\ m > k, m \neq j}} \prod_{\substack{m \geq k \\ m \neq j}} \left(\exp[-\Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im})] \right)^{\delta_{im}} \\ &\times \left(1 - \exp[-\Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im})] \right)^{\delta_{im}} \\ &\times \sum_{\delta_{ij} \in \{0,1\}} \left(1 - \delta_{ij} \right) \left(-\Lambda_{0}(\tau) e^{\beta_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij}} \right) \exp[-\Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij})] \\ &+ \delta_{ij} \int_{y=0}^{\tau} \left(1 - \Lambda_{0}(y) e^{\beta_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij}} \right) \exp[\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij} - \Lambda_{0}(y) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij})] \lambda_{0}(y) dy \\ &= \mathbf{h}_{1}^{\prime} \mathbf{Z}_{ij} \prod_{m \leq k} \left\{ \lambda_{0}(0) e^{\beta_{0}^{\prime} \mathbf{Z}_{im} + \mathbf{b}^{\prime} \mathbf{W}_{im} \right\} \\ &\times \sum_{\delta_{ij} \in \{0,1\}} \left(1 - \delta_{ij} \right) \left(-\Lambda_{0}(\tau) \exp[\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij} - \Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij})] \right) \\ &+ \delta_{ij} \Lambda_{0}(\tau) \exp[\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij} - \Lambda_{0}(\tau) \exp(\boldsymbol{\beta}_{0}^{\prime} \mathbf{Z}_{ij} + \mathbf{b}^{\prime} \mathbf{W}_{ij})] \\ &= 0 \end{split}$$

So contributions from the first term of (16) reduce to:

$$\int \sum_{j=1}^{n_i} \int_{\mathbf{b}} \mathbf{h}_1' \mathbf{Z}_{ij} \left(\delta_{ij} - \Lambda_0(X_{ij}) e^{\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0) d \left(\prod_{m=1}^{n_i} \mu_m \right) \\
= \sum_{j \le k} \mathbf{h}_1' \mathbf{Z}_{ij} \int_{\mathbf{b}} \prod_{m \le k} \left\{ \lambda_0(0) e^{\beta_0' \mathbf{Z}_{im} + \mathbf{b}' \mathbf{W}_{im}} \right\} d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0). \tag{17}$$

Similarly, contributions from the second term of (16) reduce to:

$$\int \int_{\mathbf{b}} \left\{ \mathbf{b}' \boldsymbol{\Sigma}_{0}^{-1} H_{2} \boldsymbol{\Sigma}_{0}^{-1} \mathbf{b} / 2 - \operatorname{trace}(\boldsymbol{\Sigma}_{0}^{-1} H_{2}) / 2 \right\} R_{2i}(\boldsymbol{\beta}_{0}, \Lambda_{0}, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_{0}) d \left(\prod_{m=1}^{n_{i}} \mu_{m} \right) \\
= \int_{\mathbf{b}} \left\{ \mathbf{b}' \boldsymbol{\Sigma}_{0}^{-1} H_{2} \boldsymbol{\Sigma}_{0}^{-1} \mathbf{b} / 2 - \operatorname{trace}(\boldsymbol{\Sigma}_{0}^{-1} H_{2}) / 2 \right\} \prod_{m \leq k} \left\{ \lambda_{0}(0) e^{\boldsymbol{\beta}_{0}' \mathbf{Z}_{im} + \mathbf{b}' \mathbf{W}_{im}} \right\} d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_{0}). \tag{18}$$

From the third term of (16), if $j \leq k$ then

$$\int \left(\delta_{ij} h_3(X_{ij}) - \int_0^{X_{ij}} h_3(s) d\Lambda_0(s) e^{\beta'_0 \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d \left(\prod_{m=1}^{n_i} \mu_m \right)
= h_3(0) \prod_{m < k} \{ \lambda_0(0) e^{\beta'_0 \mathbf{Z}_{im} + \mathbf{b}' \mathbf{W}_{im}} \};$$
(19)

if j > k, then

$$\int \left(\delta_{ij} h_3(X_{ij}) - \int_0^{X_{ij}} h_3(s) d\Lambda_0(s) e^{\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d \left(\prod_{m=1}^{n_i} \mu_m \right) \\
= \prod_{m \leq k} \left\{ \lambda_0(0) e^{\beta_0' \mathbf{Z}_{im} + \mathbf{b}' \mathbf{W}_{im}} \right\} \\
\times \sum_{\delta_{ij} \in \{0,1\}} \left\{ - (1 - \delta_{ij}) \int_0^{\tau} h_3(s) d\Lambda_0(s) \\
\times \exp[\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij} - \Lambda_0(t) \exp(\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \\
+ \delta_{ij} \int_{y=0}^{\tau} \left(h_3(y) - \int_{s=0}^{y} h_3(s) d\Lambda_0(s) e^{\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) \\
\times \exp[\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij} - \Lambda_0(t) \exp(\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \lambda_0(y) dy \right\} \\
= \prod_{m \leq k} \left\{ \lambda_0(0) e^{\beta_0' \mathbf{Z}_{im} + \mathbf{b}' \mathbf{W}_{im}} \right\} \\
\times \sum_{\delta_{ij} \in \{0,1\}} \left\{ - (1 - \delta_{ij}) \int_0^{\tau} h_3(s) d\Lambda_0(s) \\
\times \exp[\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij} - \Lambda_0(t) \exp(\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] \\
+ \delta_{ij} \int_{s=0}^{\tau} h_3(s) d\Lambda_0(s) \exp[\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij} - \Lambda_0(t) \exp(\beta_0' \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij})] = 0.$$

So contributions from the third term (16) reduce to:

$$\int \sum_{j=1}^{n_i} \int_{\mathbf{b}} \left(\delta_{ij} h_3(X_{ij}) - \int_0^{X_{ij}} h_3(s) d\Lambda_0(s) e^{\beta'_0 \mathbf{Z}_{ij} + \mathbf{b}' \mathbf{W}_{ij}} \right) R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0) d \left(\prod_{m=1}^{n_i} \mu_m \right) \\
= \sum_{j \le k} h_3(0) \int_{\mathbf{b}} \prod_{m \le k} \{ \lambda_0(0) e^{\beta'_0 \mathbf{Z}_{im} + \mathbf{b}' \mathbf{W}_{im}} \} d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0) \tag{20}$$

Combining (17), (18), and (20) and integrating over \mathbf{b} , we obtain

$$\sum_{j=1}^{k} \mathbf{h}_{1}' \mathbf{Z}_{ij} + \frac{1}{2} \left(\sum_{j=1}^{k} \mathbf{W}_{ij} \right)' H_{2} \left(\sum_{j=1}^{k} \mathbf{W}_{ij} \right) + k h_{3}(0) = 0.$$

Since the choice of k is arbitrary, we conclude

$$\sum_{j=k_1+1}^{k_2} \mathbf{h}_1' \mathbf{Z}_{ij} + \frac{1}{2} \left(\sum_{j=k_1+1}^{k_2} \mathbf{W}_{ij} \right)' H_2 \left(\sum_{j=k_1+1}^{k_2} \mathbf{W}_{ij} \right) + (k_2 - k_1) h_3(0) = 0.$$

for any $1 \le k_1 < k_2 \le n_i$. Finally we have $\mathbf{W}'_{ij}H_2\mathbf{W}_{ij'} = 0$ for $j \ne j'$ and $\mathbf{Z}'_{ij}\mathbf{h}_1 + \mathbf{W}'_{ij}H_2\mathbf{W}_{ij}/2 + h_3(0) = 0$, so that applying Condition C7 yields $H_2 = \mathbf{0}$, $\mathbf{h}_1 = \mathbf{0}$, and $h_3(0) = 0$.

Setting $X_{ij} = 0$, $j = 2, \dots, n_i$, and $\delta_{ij} = 1$, $j = 1, \dots, n_i$ in (20) gives us

$$h_3(X_{i1}) = \frac{\int_0^{X_{i1}} h_3(s) d\Lambda_0(s) \int_{\mathbf{b}} e^{\beta_0' Z_{i1} + \mathbf{b}' \mathbf{W}_{i1}} R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0)}{\int_{\mathbf{b}} R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0)}.$$

Therefore $g(y) \equiv \int_0^y h_3(t) d\Lambda_0(t)$ satisfies the homogeneous equation

$$\frac{g'(y)}{\lambda_0(y)} - g(y) \frac{\int_{\mathbf{b}} e^{\beta_0' Z_{i1} + \mathbf{b}' \mathbf{W}_{i1}} R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0)}{\int_{\mathbf{b}} R_{2i}(\boldsymbol{\beta}_0, \Lambda_0, \mathbf{b}) d_{\mathbf{b}} N(\mathbf{0}, \boldsymbol{\Sigma}_0)} = 0$$

with boundary condition g(0) = 0. We conclude g(y) = 0, $h_3(y) = 0$, \mathcal{Q} is one-to-one, and $\dot{S}(\boldsymbol{\beta}_0, \boldsymbol{\Sigma}_0, \Lambda_0)$ is invertible. Asymptotic normality follows from Theorem 2 of Murphy (1995).

Asymptotic efficiency of $\hat{\theta}_n$ follows from Bickel, Klaasen, Ritov, and Wellner (1993), Chapter 5 by showing each component is asymptotically linear with efficient influence function in the tangent space of the model. The proof relies on the decomposition of $\dot{S}(\theta_0)$ in terms of the invertible \mathcal{Q} operator.

PROOF OF THEOREM 3.

The proof is analogous to that in Parner (1998). The first step is to derive the linear approximation to the Fréchet derivative, $\dot{S}(\theta_0)(\hat{\theta} - \theta_0)[\mathbf{h}_1, \mathbf{h}_2, h_3]$, in terms of \mathbf{J}_n . Then we use Theorem 2 and the invertibility of \mathbf{J}_n to conclude the result.