Supporting information for "Improving the efficiency of estimation in the additive hazards model for stratified case-cohort design with multiple diseases" by Soyoung Kim, Jianwen Cai, and David Couper

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1 Proofs of Theorems

We will outline the proofs for the main theorems. We make the following assumptions:

(a) $\{T_{li}, C_{li}, Z_{li}\}$, $i = 1, \ldots, n$ and $l = 1, \ldots, L$ are independent and identically distributed where $T_{li} = (T_{li1}, \ldots, T_{liK})^T$, $C_{li} = (C_{li1}, \ldots, C_{liK})^T$, and $Z_{li} = (Z_{li1}, \ldots, Z_{liK})^T$;

(b) P$\{Y_{lik}(t) = 1\} > 0$ for $t \in [0, \tau]$, $i = 1, \ldots, n_l$, $k = 1, 2$, and $l = 1, \ldots, L$;

(c) $|Z_{lik}(0)| + \int_0^\tau |dZ_{lik}(t)| < D_z < \infty$, $i = 1, \ldots, n_l$, $k = 1, 2$, and $l = 1, \ldots, L$ almost surely and D_z is a constant;

(d) The matrix A_k is positive definite for $k = 1, 2$ where $A_k = \Sigma_{l=1}^{L} q_l E_l (\int_0^\tau Y_{l1k}(t)\{Z_{l1k}(t)^{\otimes 2} - [E\{Y_{l1k}(t)Z_{l1k}(t)\}/E\{Y_{l1k}(t)\}]^{\otimes 2}\}dt)$ where $q_l = \lim_{n\to\infty} n_l/n$;

(e) For all $k = 1, 2$, $\int_0^\tau \lambda_{0k}(t)dt < \infty$;

To show the desired asymptotic properties for generalized case-cohort samples, the following conditions are also needed:

(f) For all $l = 1, \ldots, L$, $\lim_{n\to\infty} \tilde{\alpha}_l = \alpha_l$, where $\tilde{\alpha}_l = \tilde{n}_l/n_l$ and α_l is a positive constant.

(g) $\lim_{n\to\infty} n_{lk}/n_l = p_{lk}$, where p_{lk} is a positive constant on [0,1] for all $k = 1, 2$ and $l = 1, \ldots, L$.

(h) $\lim_{n\to\infty} n_l/n = q_l$, where q_l is a positive constant on [0,1] for all $l = 1, \ldots, L$.

The following lemmas are used in order to prove the theorems. The proof of Lemma 1.1 is in Lin [1] and Lemma 1.2 is in Lemma A1 in Kang and Cai [2].

Lemma 1.1 *Let $\mathcal{H}_n(t)$ and $\mathcal{W}_n(t)$ be two sequences of bounded process. If we assume that the following conditions: (1) $\sup_{0\le t\le\tau} \parallel \mathcal{H}_n(t) - \mathcal{H}(t) \parallel \to_p 0$ for some bounded process $\mathcal{H}(t)$,(2) $\mathcal{H}_n(t)$ is monotone on $[0,\tau]$ and (3) $\mathcal{W}_n(t)$ converges to zero-mean process with continuous sample paths, hold for some constant τ, then*

$\sup_{0\le t\le\tau} \parallel \int_0^t \{\mathcal{H}_n(s) - \mathcal{H}(s)\} d\mathcal{W}_n(s) \parallel \to_p 0$,$\sup_{0\le t\le\tau} \parallel \int_0^t \mathcal{W}_n(s) d\{\mathcal{H}_n(s) - \mathcal{H}(s)\} \parallel \to_p 0$

Lemma 1.2 *Let $B_i(t)$, $i = 1,\dots,n$ be independent and identically distributed real-valued random process on $[0,\tau]$ and denote random process vector, $\mathbf{B}(t) = [B_1(t),\dots,B_n(t)]$ with $EB_i(t) \equiv \mu_B(t)$, var $B_i(0) < \infty$, and var $B_i(\tau) < \infty$. Let $\xi = [\xi_1,\dots,\xi_n]$ be random vector containing $\tilde{n}$ ones and $n-\tilde{n}$ zeros with each permutation equally likely. Let ξ be independent of $\mathbf{B}(t)$. Suppose that almost all paths of $B_i(t)$ have finite variation. Then $n^{-1/2}\sum_{i=1}^n \xi_i\{B_i(t) - \mu_B(t)\}$ converges weakly in $l^\infty[0,\tau]$ to a zero-mean Gaussian process, and $n^{-1}\sum_{i=1}^n \xi_i\{B_i(t) - \mu_B(t)\}$ converges in probability to zero uniformly in t.*

The proof of Theorem 1

We first show the consistency of $\tilde{\beta}$. Denote $\widetilde{U}_n = n^{-1}\widetilde{U}$. Based on the extension of Fourtz [3], if the following conditions are satisfied (i) $\frac{\partial \widetilde{U}_n(\beta)}{\partial \beta^T}$ exists and is continuous in an open neighborhood $\mathcal{B}$ of β_0, (ii) $\frac{\partial \widetilde{U}_n(\beta)}{\partial \beta^T}$ is negative definite with probability going to one as n $\to\infty$, (iii) -$\frac{\partial \widetilde{U}_n(\beta)}{\partial \beta^T}$ converges to $A(\beta_0)$ in probability uniformly for β in an open neighborhood about β_0, (iv) $\widetilde{U}_n(\beta)$ converges to 0 in probability, then, we can show that $\tilde{\beta}$ converges to β_0 in probability. Note that $-\frac{\partial \widetilde{U}_n(\beta)}{\partial \beta^T} = \frac{1}{n}\sum_{l=1}^L\sum_{i=1}^{n_l}\sum_{k=1}^2\int_0^\tau \pi_{lik}(t)Y_{lik}(t)\{Z_{lik}(t)^{\otimes 2} - \tilde{Z}_k(t)^{\otimes 2}\}dt$

Definitely, condition (i) is satisfied. Conditions (ii) and (iii) also are satisfied due to uniform convergence of $\tilde{Z}_k(t)$ to $e_k(t)$ for $k = 1,2$, uniform convergence of $\tilde{\alpha}_{lk}(t)^{-1} - \tilde{\alpha}_l^{-1}$, $\tilde{\gamma}_{l1k}(t)^{-1} - \tilde{\gamma}_{l1k}$, and $\tilde{\gamma}_{l2k}(t)^{-1} - \tilde{\gamma}_{l2k}$ to zero, condition (c), and Lemma 1.2. $n^{1/2}\widetilde{U}_n(\beta)$ can be decomposed into four parts:

$$\begin{aligned} n^{1/2}\widetilde{U}_n(\beta) &= n^{-1/2}\sum_{l=1}^L\sum_{i=1}^{n_l}\sum_{k=1}^2\int_0^\tau\{Z_{lik}(t) - e_k(t)\}dM_{lik}(t) \\ &+ n^{-1/2}\sum_{l=1}^L\sum_{i=1}^{n_l}\sum_{k=1}^2\int_0^\tau\{\pi_{lik}(t) - 1\}\{Z_{lik}(t) - e_k(t)\}dM_{lik}(t) \\ &+ n^{-1/2}\sum_{l=1}^L\sum_{i=1}^{n_l}\sum_{k=1}^2\int_0^\tau\{e_k(t) - \tilde{Z}_k(t)\}dM_{lik}(t) \\ &+ n^{-1/2}\sum_{l=1}^L\sum_{i=1}^{n_l}\sum_{k=1}^2\int_0^\tau\{\pi_{lik}(t) - 1\}\{e_k(t) - \tilde{Z}_k(t)\}dM_{lik}(t) \qquad (1) \end{aligned}$$

Since the first term on the right-hand side of (1) is the pseudo partial likelihood score function for the full likelihood, it is asymptotically zero-mean normal with covariance $V_{lI}^a(\beta_0) = n^{-1/2}\sum_{l=1}^L q_l E_l[\sum_{k=1}^2 Q_{l1k}(\beta_0)]^{\otimes 2}$ where $Q_{lik}(t,\beta) = \int_0^t\{Z_{lik}(t) - e_k(t)\}dM_{lik}(t)$ Yin and Cai[4].

The third term can be written as $\sum_{l=1}^L n_l^{1/2} n^{-1/2}\sum_{k=1}^2\int_0^\tau\{e_k(t) - \tilde{Z}_k(t)\}\{n_l^{-1/2}\sum_{i=1}^{n_l} dM_{lik}(t)\}$ and $M_{l1k}(t)$, $\dots, M_{lnk}(t)$ is identically and independently distributed zero-mean random variable for fixed t. Since $M_{lik}^2(0) < \infty$ and $M_{lik}^2(\tau) < \infty$ are satisfied based on conditions (c) and (e), $M_{lik}(t)$ is of bounded variation and therefore it can be written as a difference of two monotone functions in t. From the example of 2.11.16 of van der Vaart and Wellner [5](p215), $n_l^{-1/2}\sum_{i=1}^{n_l} M_{lik}(t)$ converges weakly to a zero-mean Gaussian process, say $\mathcal{P}_{M,lk}(t)$.

Since $\tilde{Z}_k(t)$ is of bounded variation and can be written as sum of two monotone functions in t, the third and fourth terms on the right-hand side of (1) converge to zero in probability uniformly in t as $n \to \infty$ by Lemma 1.1 and boundness of $\pi_{lik}(t) - 1$.

By using the asymptotic property of $n_l^{1/2}\{\tilde{\alpha}_{lk}^{-1}(t) - \tilde{\alpha}_l^{-1}\}$, $n_l^{1/2}\{\tilde{\gamma}_{lmk}^{-1}(t) - \tilde{\gamma}_{lmk}^{-1}\}(m = 1, 2, 3, 4)$, Glivenko-Cantelli lemma and Lemma 1.2, the second term on the right-hand side of (1) is asymptotically equivalent to

$$
\begin{aligned}
& n^{-1/2}\sum_{l=1}^{L}\sum_{i=1}^{n_l}\sum_{k=1}^{2}\prod_{j=1}^{2}(1-\Delta_{lij})(\frac{\xi_{li}}{\tilde{\alpha}_l}-1)\int_0^{\tau}\left[B_{lik}(\beta_0,t) - Y_{lik}(t)\frac{E_l\{\prod_{j=1}^{2}(1-\Delta_{lij})B_{1k}(\beta_0,t)\}}{E_l\{\prod_{j=1}^{2}(1-\Delta_{lij})Y_{l1k}(t)\}}\right]dt \\
+ \; & n^{-1/2}\sum_{l=1}^{L}\sum_{i=1}^{n_l}\sum_{k=1}^{2}\Delta_{li1}(1-\Delta_{li2})(\frac{\eta_{li1}}{\tilde{\gamma}_{l1k}}-1)\left[Q_{lik}(\beta) - \int_0^{\tau} Y_{lik}(t)\frac{E_l\{dQ_{lik}(t,\beta)|\theta_{l10},\xi_{l1}=0\}}{E_l\{Y_{l1k}(t)|\theta_{l10}\}}\right] \\
+ \; & n^{-1/2}\sum_{l=1}^{L}\sum_{i=1}^{n_l}\sum_{k=1}^{2}(1-\Delta_{li1})\Delta_{li2}(\frac{\eta_{li2}}{\tilde{\gamma}_{l2k}}-1)\left[Q_{lik}(\beta) - \int_0^{\tau} Y_{lik}(t)\frac{E_l\{dQ_{lik}(t,\beta)|\theta_{l01},\xi_{l1}=0\}}{E_l\{Y_{l1k}(t)|\theta_{l01}\}}\right] \\
+ \; & n^{-1/2}\sum_{l=1}^{L}\sum_{i=1}^{n_l}\sum_{k=1}^{2}\Delta_{li1}\Delta_{li2}(\frac{\eta_{li1}+\eta_{li2}-\eta_{li1}\eta_{li2}}{\tilde{\gamma}_{l1k}+\tilde{\gamma}_{l2k}-\tilde{\gamma}_{l1k}\tilde{\gamma}_{l2k}}-1) \\
\times \; & [Q_{lik}(\beta) - \int_0^{\tau} Y_{lik}(t)\frac{E_l\{dQ_{lik}(t,\beta)|\theta_{l11},\xi_{l1}=0\}}{E_l\{Y_{l1k}(t)|\theta_{l11}\}}] \qquad (2)
\end{aligned}
$$

where $B_{lik}(t,\beta) = \{Z_{lik}(t) - e_k(t)\}Y_{lik}(t)\{\lambda_{0k}(t) + \beta_0^T Z_{lik}(t)\}$.

By Hájek [6]'s central limit theorem and conditions (c) and (f), the first term in (2) is asymptotically zero-mean normal random variable with covariance matrix $\sum_{l=1}^{L} q_l \frac{1-\alpha_l}{\alpha_l} V_{II,l}^a(\beta_0)$ where $V_{II,l}^a(\beta_0)$ is defined in Theorem 1.

It follows from Lemma 1.2 and Hájek [6]'s central limit theorem that the second, third, fourth, and fifth terms are asymptotically zero-mean normal with covariance matrix $\sum_{l=1}^{L} q_l(1-\alpha_l)\sum_{k=1}^{2} V_{III,lk}^a(\beta_0)$ where $V_{III,lk}^a(\beta_0)$ is defined in Theorem 1.

Since all five terms in (2)are mutually independent from conditional expectation arguments, $n^{1/2}\tilde{U}_n(\beta)$ is asymptotically normally distributed with mean zero and variance Σ. Therefore, $\tilde{U}_n(\beta)$ converges to zero in probability and condition (iv) is satisfied.

Since all conditions (i), (ii), (iii) and (iv) by an extension of Fourtz [3] are satisfied, $\tilde{\beta}$ is a consistent estimator of β_0. By consistency of $\tilde{\beta}$ and Taylor expansion of $\tilde{U}(\beta)$, $n^{1/2}(\tilde{\beta} - \beta_0)$ is asymptotically normally distributed with mean zero and with variance matrix $A^{-1}\Sigma(\beta_0)A^{-1}$ where $A = \sum_{k=1}^{2} A_k$.

The proof of Theorem 2

$n^{1/2}\{\tilde{\Lambda}_{0k}(\tilde{\beta}, t) - \Lambda_{0k}(t)\}$ can be decomposed into three parts:

$$
n^{1/2}\{\int_0^t \frac{\sum_{l=1}^{L}\sum_{i=1}^{n_l}\pi_{lik}(u)(\beta_0-\tilde{\beta})^T Z_{lik}(u)du}{\sum_{l=1}^{L}\sum_{i=1}^{n_l}\pi_{lik}(u)Y_{lik}(u)} + \int_0^t \frac{\sum_{l=1}^{L}\sum_{i=1}^{n_l} dM_{lik}(u)}{\sum_{l=1}^{L}\sum_{i=1}^{n_l}\pi_{lik}(u)Y_{lik}(u)}
$$

$$+\int_0^t \frac{\sum_{l=1}^L \sum_{i=1}^{n_l} (\pi_{lik}(u)-1) dM_{lik}(u)}{\sum_{l=1}^L \sum_{i=1}^{n_l} \pi_{lik}(u) Y_{lik}(u)}\}. \tag{3}$$

Due to the uniform convergence of $\tilde{Z}_k(t)$ to $e_k(t)$, the first term in (3) is asymptotically equivalent to $n^{1/2}(\tilde{\beta}-\beta_0) l_k(t)$ where $l_k(t) = \int_0^\tau \{-e_k(u)\} du$.

The term $\{n^{-1}\sum_{l=1}^L \sum_{i=1}^{n_l} \pi_{lik}(t) Y_{lik}(t)\}^{-1}$ can be written as the sum of two monotone functions in u and converges to $[\sum_{l=1}^L q_l E_l\{Y_{l1k}(t)\}]^{-1}$ where $\sum_{l=1}^L q_l E_l\{Y_{l1k}(u)\}$ is bounded away from zero and $n^{-1/2}\sum_{l=1}^L \sum_{i=1}^{n_l} M_{lik}(u)$ converges to a zero-mean Gaussian process with continuous sample paths. Therefore, it follows from Lemma 1.1 that the second term in (3) is asymptotically equivalent to $\int_0^t \frac{1}{\sum_{l=1}^L q_l E_l\{Y_{l1k}(t)\}} d\{n^{1/2}\sum_{l=1}^L \sum_{i=1}^{n_l} M_{lik}(u)\}$.

Since $\{n^{-1}\sum_{l=1}^L \sum_{i=1}^{n_l} \pi_{lik}(t) Y_{lik}(t)\}^{-1}$ converges to $\sum_{l=1}^L q_l E_l\{Y_{l1k}(u)\}^{-1}$, where $\sum_{l=1}^L q_l\ E_l\{Y_{l1k}(u)\}$ is bounded away from zero in probability uniformly and $n^{-1}\sum_{l=1}^L \sum_{i=1}^{n_l} \frac{\xi_{li}}{\tilde{\alpha}_l} \times \prod_{j=1}^2 (1-\Delta_{lij}) Y_{lik}(u)$ converges to $\sum_{l=1}^L q_l E_l\{\prod_{j=1}^2 (1-\Delta_{l1j})\ Y_{l1k}(u) \beta_0^T Z_{l1k}(u)\}$ from Lemma 1.2, the third term in (3) is asymptotically equivalent to

$$\begin{aligned}
& n^{-1/2}\sum_{l=1}^L \sum_{i=1}^{n_l} (1-\frac{\xi_{li}}{\tilde{\alpha}_l}) \prod_{j=1}^2 (1-\Delta_{lij}) \int_0^t Y_{lik}(u) \\
\times\ & \left[\beta_0^T Z_{lik}(u) - \frac{E_l\{\prod_{j=1}^2(1-\Delta_{l1j}) Y_{l1k}(u)\beta_0^T Z_{lik}(u)\}}{E_l\{\prod_{j=1}^2(1-\Delta_{l1j}) Y_{l1k}(u)\}}\right] \frac{du}{\sum_{l=1}^L q_l E_l\{Y_{l1k}(u)\}} \\
+\ & n^{-1/2}\sum_{l=1}^L \sum_{i=1}^{n_l} (1-\xi_{li})[\\
+\ & (\frac{\eta_{li1}}{\tilde{\gamma}_{l1k}}-1)\Delta_{li1}(1-\Delta_{li2}) \int_0^t \frac{1}{\sum_{l=1}^L q_l E_l\{Y_{11k}(t)\}} \left[dM_{lik}(u) - Y_{lik}(u)\frac{E_l\{dM_{l1k}(\beta_0,u)|\theta_{l10}, \xi_{li}=0\}}{E_l\{Y_{l1k}(u)|\theta_{l10}\}}\right] \\
+\ & (\frac{\eta_{li2}}{\tilde{\gamma}_{l2k}}-1)(1-\Delta_{li1})\Delta_{li2} \int_0^t \frac{1}{\sum_{l=1}^L q_l E_l\{Y_{11k}(t)\}} \left[dM_{lik}(u) - Y_{lik}(u)\frac{E_l\{dM_{l1k}(\beta_0,u)|\theta_{l01}, \xi_{li}=0\}}{E_l\{Y_{l1k}(u)|\theta_{l01}\}}\right] \\
+\ & (\frac{\eta_{li1}+\eta_{li1}-\eta_{li2}\eta_{li2}}{\tilde{\gamma}_{l1k}+\tilde{\gamma}_{l2k}-\tilde{\gamma}_{l2k}\tilde{\gamma}_{l2k}}-1)\Delta_{li1}\Delta_{li2} \int_0^t \frac{1}{\sum_{l=1}^L q_l E_l\{Y_{11k}(t)\}} \\
\times\ & \left[dM_{lik}(u) - Y_{lik}(u)\frac{E_l\{dM_{l1k}(\beta_0,u)|\theta_{l11}, \xi_{li}=0\}}{E_l\{Y_{l1k}(u)|\theta_{l11}\}}\right]],
\end{aligned}$$

Combining all results, we get

$$\begin{aligned}
& n^{1/2}\{\tilde{\Lambda}_{0k}(\tilde{\beta},t) - \Lambda_{0k}(t)\} \\
&= n^{-1/2}\sum_{l=1}^L \sum_{i=1}^{n_l} \mu_{lik}(\beta_0,t) + n^{-1/2}\sum_{l=1}^L \sum_{i=1}^{n_l} (1-\frac{\xi_{li}}{\tilde{\alpha}_l}) w_{lik}(\beta_0,t) + n^{-1/2}\sum_{l=1}^L \sum_{i=1}^{n_l} \nu_{lik}(\beta_0,t) + o_p(1),
\end{aligned}$$

where

$$\mu_{lik}(\beta,t) = l_k(t)^T A^{-1} \sum_{m=1}^2 Q_{lim}(\beta) + \int_0^t \frac{1}{\sum_{l=1}^L q_l E_l\{Y_{l1k}(u)\}} dM_{lik}(u),$$

$$w_{lik}(\beta,t)=l_k(t)^TA^{-1}\sum_{m=1}^{2}\prod_{j=1}^{2}(1-\Delta_{lij})$$
$$\times\int_0^{\tau}[B_{lim}(\beta,u)-\frac{Y_{lim}(u)E_l\{\prod_{j=1}^2(1-\Delta_{l1j})B_{l1m}(\beta,u)\}}{E_l\{\prod_{j=1}^2(1-\Delta_{l1j})Y_{l1m}(u)\}}]du+\prod_{j=1}^{2}(1-\Delta_{lij})$$
$$\times\int_0^{t}Y_{lik}(u)\{\beta_0^TZ_{lik}(u)-\frac{E\{\prod_{j=1}^2(1-\Delta_{l1j})Y_{l1k}(u)\beta_0^TZ_{l1k}(u)\}}{E\{\prod_{j=1}^2(1-\Delta_{l1j})Y_{l1k}(u)\}}\cdot\frac{du}{\sum_{l=1}^L q_lE_l\{Y_{l1k}(u)\}}\},$$

$$\nu_{lik}(\beta,t)=l_k(t)^TA^{-1}\sum_{m=1}^{2}\nu_{lim}^{(1)}(\beta,t)+\nu_{lim}^{(2)}(\beta,t),$$
$$\nu_{lik}^{(1)}(\beta,t)=\Delta_{li1}(1-\Delta_{li2})(1-\xi_{li})(\frac{\eta_{li1}}{\tilde{\gamma}_{l1k}}-1)\nu_{lik,1}^{(1)}(\beta,t)$$
$$+(1-\Delta_{li1})\Delta_{li2}(1-\xi_{li})(\frac{\eta_{li2}}{\tilde{\gamma}_{l2k}}-1)\nu_{lik,2}^{(1)}(\beta,t),$$
$$+\Delta_{li1}\Delta_{li2}(1-\xi_{li})\{(\frac{\eta_{li1}+\eta_{li2}-\eta_{li1}\eta_{li2}}{\tilde{\gamma}_{l1k}+\tilde{\gamma}_{l2k}-\tilde{\gamma}_{l1k}\tilde{\gamma}_{l2k}}-1)+(\frac{\eta_{li2}}{\tilde{\gamma}_{l4k}}-1)\}\nu_{lim,3}^{(1)}(\beta,t),$$
$$\nu_{lik,1}^{(1)}(\beta,t)=Q_{lik}(\beta,t)-\int_0^{\tau}Y_{lik}(t)\frac{E_l\{dQ_{l1k}(\beta,t)|\theta_{l10},\xi_{l1}=1\}}{E_l\{Y_{l1k}(t)|\theta_{l10}\}},$$
$$\nu_{lik,2}^{(1)}(\beta,t)=Q_{lik}(\beta,t)-\int_0^{\tau}Y_{ik}(t)\frac{E_l\{dQ_{l1k}(\beta,t)|\theta_{l01},\xi_{l1}=1\}}{E_l\{Y_{l1k}(t)|\theta_{l01}\}},$$
$$\nu_{lik,3}^{(1)}(\beta,t)=Q_{lik}(\beta,t)-\int_0^{\tau}Y_{lik}(t)\frac{E_l\{dQ_{l1k}(\beta,t)|\theta_{l11},\xi_{l1}=1\}}{E_l\{Y_{l1k}(t)|\theta_{l11}\}},$$
$$\nu_{lik}^{(2)}(\beta,t)=(1-\xi_{li})\{\Delta_{li1}(1-\Delta_{li2})(\frac{\eta_{li1}}{\tilde{\gamma}_{1k}}-1)\nu_{lik,1}^{(2)}(\beta,t)+(1-\Delta_{li1})\Delta_{li2}(\frac{\eta_{li2}}{\tilde{\gamma}_{2k}}-1)\nu_{lik,2}^{(2)}(\beta,t),$$
$$+\Delta_{li1}\Delta_{li2}\{(\frac{\eta_{li1}+\eta_{li2}-\eta_{li1}\eta_{li2}}{\tilde{\gamma}_{1k}+\tilde{\gamma}_{2k}-\tilde{\gamma}_{1k}\tilde{\gamma}_{2k}}-1)+(\frac{\eta_{li2}}{\tilde{\gamma}_{4k}}-1)\}\nu_{lik,3}^{(2)}(\beta,t)\},$$
$$\nu_{lik,1}^{(2)}(\beta,t)=\int_0^{t}\frac{1}{\sum_{l=1}^L q_lE_l\{Y_{l1k}(u)\}}[dM_{lik}(\beta,u)-Y_{lik}(u)\frac{E_l\{dM_{l1k}(\beta,u)|\theta_{l10},\xi_{l1}=0\}}{E_l\{Y_{l1k}(u)|\theta_{l10}\}}],$$
$$\nu_{lik,2}^{(2)}(\beta,t)=\int_0^{t}\frac{1}{\sum_{l=1}^L q_lE_l\{Y_{l1k}(u)\}}[dM_{lik}(\beta,u)-Y_{lik}(u)\frac{E_l\{dM_{l1k}(\beta,u)|\theta_{l01},\xi_{l1}=0\}}{E_l\{Y_{l1k}(u)|\theta_{l01}\}}],$$
$$\nu_{lik,3}^{(2)}(\beta,t)=\int_0^{t}\frac{1}{\sum_{l=1}^L q_lE_l\{Y_{l1k}(u)\}}[dM_{lik}(\beta,u)-Y_{lik}(u)\frac{E_l\{dM_{l1k}(\beta,u)|\theta_{l11},\xi_{l1}=0\}}{E_l\{Y_{l1k}(u)|\theta_{l11}\}}]$$

Let $G^{(1)}(t)=\{G_1^{(1)}(t),G_2^{(1)}(t)\}$ where $G_k^{(1)}(t)=n^{-1/2}\sum_{l=1}^L\sum_{i=1}^{n_l}\mu_{lik}(\beta,t)$, $G^{(2)}(t)=\{G_1^{(2)}(t),G_2^{(2)}(t)\}$ where $G_k^{(2)}(t)=n^{-1/2}\sum_{l=1}^L\sum_{i=1}^{n_l}(1-\frac{\xi_{li}}{\tilde{\alpha}_l})w_{lik}(\beta,t)$, and $G^{(3)}(t)=\{G_1^{(3)}(t),G_2^{(3)}(t)\}$ where $G_k^{(3)}(t)=n^{-1/2}\sum_{l=1}^L\sum_{i=1}^{n_l}\nu_{lik}(\beta,t)$. Then $G^{(1)}(t)$ converges weakly to a zero-mean Gaussian process, $\mathcal{G}^{(1)}(t)=\{\mathcal{G}_1^{(1)}(t),\mathcal{G}_2^{(1)}(t)\}$ in $D[0,\tau]^k$ where the covariance function between $\mathcal{G}_j^{(1)}(t)$ and $\mathcal{G}_k^{(1)}(s)$ is $E\{\mu_{1j}(\beta_0,t),\mu_{1k}(\beta,s)\}$ by theorem 2 of Yin and Cai[4].

It can be shown that $G^{(2)}(t)$ converges weakly to a zero-mean Gaussian process $\mathcal{G}^{(2)}(t)=\{\mathcal{G}_1^{(2)}(t),\mathcal{G}_2^{(2)}(t)\}$ where covariance function $\mathcal{G}_j^{(2)}(t)$ and $\mathcal{G}_k^{(2)}(s)$ is $\frac{1-\alpha_l}{\alpha_l}E_l\{w_{l1j}(\beta_0,t),w_{l1k}(\beta_0,s)\}$

by Lemma 1.2, Cramer-Wold device and the marginal tightness of $G_k^{(2)}(t)$ for each k.

Similarly, $G^{(3)}(t)$ converges weakly to a zero-mean Gaussian process. By the conditional expectation arguments, the three terms $(G^{(1)}(t), G^{(2)}(t), G^{(3)}(t))$ are mutually independent. Therefore, $G(t) = G^{(1)}(t) + G^{(2)}(t) + G^{(3)}(t)$ converges to a zero-mean Gaussian process $\mathcal{G}(t) = \mathcal{G}^{(1)}(t) + \mathcal{G}^{(2)}(t) + \mathcal{G}^{(3)}(t)$.

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