Web-based Supplementary Materials for Marginal Hazards Regression for Retrospective Studies within Cohort with Possibly Correlated Failure Time Data by Sangwook Kang and Jianwen Cai

1. Outline of the Proofs of Theorems 1 and 2

We assume the following conditions hold : $(\boldsymbol{T}_i, \boldsymbol{C}_i, \boldsymbol{Z}_i), i = 1, \ldots, n$ are independent and identically distributed; $\Pr(Y(\tau) > 0) > 0$; $|Z_{ijk}(0)| + \int_0^\tau |dZ_{ijk}(u)| < C_z < \infty$ almost surely for some constant C_z; The matrix $\boldsymbol{A}(\boldsymbol{\beta}_0)$ is positive definite; $\int_0^\tau \lambda_0(t)dt < \infty$; For $d = 0, 1, 2$, there exists a neighborhood $\mathcal{B}$ of $\boldsymbol{\beta}_0$ where $\boldsymbol{s}^{(d)}(\boldsymbol{\beta}, t)$ are continuous functions of $\boldsymbol{\beta} \in \mathcal{B}$, bounded on $\mathcal{B} \times [0, \tau]$, and $s^{(0)}$ is bounded away from zero on $\mathcal{B} \times [0, \tau]$.

The following additional conditions are also needed to ensure the desired asymptotic convergence of case-control samples: For $s = 0, 1$ as $n \to \infty$, $\frac{\tilde{n}_s}{n_s}$ converges to a constant $\alpha_s \in (0, 1)$ where α_s is the realization of a function $\alpha(W)$ of a random variable W evaluated at $W = s$, i.e. $\alpha(W)|_{W=s} = \alpha_s$; $\frac{\tilde{n}_{sh}}{n_s}$ converges to a constant $w_{sh} \in (0, 1)$ for all $h = 1, \ldots, H_s$ where H_s is the number of post-stratified groups in sth stratum; $\frac{n_s}{n}$ converges to a constant $p_s \in [0, 1]$ for $s = 0, 1$ as $n \to \infty$ where $p_1 + p_0 = 1$.

Here and in what follows $\| \cdot \|$ is the Euclidean norm for vectors or matrices.

The following lemmas will be frequently used in proving the theorems.

LEMMA 1: *Let $\boldsymbol{f}_n(t)$ and $g_n(t)$ be two sequences of bounded functions. For some constant τ, assume that the following conditions (a) - (c) hold where*

(a) $\sup_{0 \le t \le \tau} \|\boldsymbol{f}_n(t) - \boldsymbol{f}(t)\| \longrightarrow 0$, *for some bounded function* $\boldsymbol{f}(t)$,

(b) $\{\boldsymbol{f}_n(t)\}$ *are monotone on* $[0, \tau]$ *and*

(c) $\sup_{0 \le t \le \tau} |g_n(t) - g(t)| \longrightarrow 0$ *where* $g(t)$ *is continuous on* $[0, \tau]$. *Then*

$$\sup_{0 \le t \le \tau} \| \int_0^t \boldsymbol{f}_n(s) dg_n(s) - \int_0^t \boldsymbol{f}(s) dg(s) \| \longrightarrow 0, \quad \sup_{0 \le t \le \tau} \| \int_0^t g_n(s) d\boldsymbol{f}_n(s) - \int_0^t g(s) d\boldsymbol{f}(s) \| \longrightarrow 0.$$

LEMMA 2: *Let $\boldsymbol{W}_n(t)$ and $G_n(t)$ be two sequences of bounded processes. For some constant τ, assume that the following conditions (a) - (c) hold where*

(a) $\sup_{0\le t\le\tau}\|\boldsymbol{W}_n(t)-\boldsymbol{W}(t)\|\xrightarrow{p}0$ *for some bounded process* $\boldsymbol{W}(t)$,

(b) $\boldsymbol{W}_n(t)$ *is monotone on* $[0,\tau]$ *and*

(c) $G_n(t)$ *converges to a zero-mean process with continuous sample paths. Then*

$$\sup_{0\le t\le\tau}\left\|\int_0^t\{\boldsymbol{W}_n(s)-\boldsymbol{W}(t)\}dG_n(s)\right\|\xrightarrow{p}0,\ \sup_{0\le t\le\tau}\left\|\int_0^t G_n(s)d\{\boldsymbol{W}_n(s)-\boldsymbol{W}(s)\}\right\|\xrightarrow{p}0.$$

LEMMA 3: *Suppose a cohort of size n can be divided into S mutually exclusive strata and this stratification is based on a discrete random variable W whose information is available for all the cohort members. Let n_s denote the size of the sth stratum ($s=1,\ldots,S$). Let X_{sj}'s be independent and identically distributed random variables and $\boldsymbol{\xi}_{sj}=(\xi_{s1},\ldots,\xi_{sn_s})$ be a random vector of $\tilde{n}_s$ ones and $n_s-\tilde{n}_s$ zeros with each permutation equally likely. Let $\tilde{n}_s=\sum_{j=1}^{n_s}\xi_{sj}$ denote the sample size drawn from the sth stratum. Then*

$$U_n=n^{-1/2}\sum_{s=1}^{S}\sum_{j=1}^{n_s}\left(\frac{\xi_{sj}}{\tilde{n}_s/n_s}-1\right)X_{sj}$$

converges to a zero-mean normal random variable with the following covariance function

$$\mathrm{E}\left\{\left(\frac{1}{\alpha(W)}-1\right)\mathrm{Var}(X_{W1}|W)\right\}$$

provided that

(a) $\dfrac{n_s}{n}\xrightarrow{p}p_s\equiv P(W=s)\in(0,1)$ *and* $\dfrac{\tilde{n}_s}{n_s}\xrightarrow{p}\alpha_s\in(0,1)$ *as* $n\to\infty$, *where* α_s *is the realization of a function* $\alpha(W)$ *of a random variable* W *evaluated at* $W=s$, *i.e.* $\alpha(W)|_{W=s}=\alpha_s$,

(b) $S_s^2 = \dfrac{1}{n_s - 1}\sum_{j=1}^{n_s}(X_{sj} - \bar{X}_s)^2 \xrightarrow{p} \sigma_s^2 = \mathrm{Var}(X_{W1}|W = s) \neq 0$ *where*

$\bar{X}_s = \dfrac{1}{n_s}\sum_{j=1}^{n_s} X_{sj}$, *and*

(c) $\dfrac{\max(X_{sj} - \bar{X}_s)^2}{\sum_{j=1}^{n_s}(X_{sj} - \bar{X}_s)^2} \longrightarrow 0$ *as* $n \to \infty$ *for* $s = 1, \ldots, S$.

Lemma 4: *Suppose that within each stratum S we have further classified the sample into H_s mutually exclusive groups based on a discrete random variable V and the sizes of strata, n_{sh}, for $h = 1, \ldots, H_s$, $s = 1, \ldots, S$, are known. Let $\tilde{n}_{sh} = \sum_{j=1}^{n_{sh}} \xi_{shj}$ denote the sample size drawn from the hth stratum in the sth stratum. Then*

$$U_n = n^{-1/2}\sum_{s=1}^{S}\sum_{h=1}^{H_s}\sum_{j=1}^{n_{sh}}\left(\frac{\xi_{shj}}{\tilde{n}_{sh}/n_{sh}} - 1\right)X_{shj}$$

converges to a zero-mean normal random variable with the following covariance function

$$\mathrm{E}\left\{\left(\frac{1}{\alpha(W)} - 1\right)\mathrm{Var}(X_{WV1}|W, V)\right\}$$

provided that

(a) $\dfrac{n_s}{n} \xrightarrow{p} p_s \equiv P(W = s) \in (0,1), \dfrac{n_{sh}}{n_s} \xrightarrow{p} q_{sh} \equiv P(V = h|W = S) \in (0,1)$, *and*
$\dfrac{\tilde{n}_s}{n_s} \xrightarrow{p} \alpha_s \in (0,1)$ *as* $n \to \infty$, *where α_s is the realization of a function $\alpha(W)$ of a random variable W evaluated at $W = s$, i.e. $\alpha(W)|_{W=s} = \alpha_s$,*

(b) $S_{sh}^2 = \dfrac{1}{n_{sh} - 1}\sum_{j=1}^{n_{sh}}(X_{shj} - \bar{X}_{sh})^2 \xrightarrow{p} \sigma_{sh}^2 = \mathrm{Var}(X_{WV1}|W = s, V = h) \neq 0$
where $\bar{X}_{sh} = \dfrac{1}{n_{sh}}\sum_{j=1}^{n_{sh}} X_{shj}$, *and*

(c) $\dfrac{\max(X_{shj} - \bar{X}_{sh})^2}{\sum_{j=1}^{n_{sh}}(X_{shj} - \bar{X}_{sh})^2} \longrightarrow 0$ *as* $n \to \infty$ *for* $s = 1, \ldots, S$ *and* $h = 1, \ldots, H_s$.

Proof of Theorem 1 We first consider the proof of the consistency of $\hat{\boldsymbol{U}}(\boldsymbol{\beta}_0)$. Denote n^{-1} times $\hat{\boldsymbol{U}}(\boldsymbol{\beta})$ by $\boldsymbol{U}_n(\boldsymbol{\beta})$. Based on a straightforward extension of Foutz (1977), one can show $\hat{\boldsymbol{\beta}}$ to be consistent for $\boldsymbol{\beta}_0$ provided: (i) $\partial \boldsymbol{U}_n(\boldsymbol{\beta})/\partial \boldsymbol{\beta}^T$ exists and is continuous in an open neighborhood $\mathcal{B}$ of $\boldsymbol{\beta}_0$, (ii)$\partial \boldsymbol{U}_n(\boldsymbol{\beta}_0)/\partial \boldsymbol{\beta}_0^T$ is negative definite with probability going to one as $n \to \infty$, (iii) $\partial \boldsymbol{U}_n(\boldsymbol{\beta})/\partial \boldsymbol{\beta}^T$ converges to $\boldsymbol{A}(\boldsymbol{\beta}_0)$ in probability uniformly for $\boldsymbol{\beta}$ in an open neighborhood about $\boldsymbol{\beta}_0$, and (iv) $\boldsymbol{U}_n(\boldsymbol{\beta}) \to 0$ in probability.

One can write

$$\frac{\partial \boldsymbol{U}_n(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}^T} = -n^{-1} \int_0^\tau \hat{\boldsymbol{V}}(\boldsymbol{\beta}, t) d\hat{N}(t) \text{ where } \hat{N}(t) = \sum_{i=1}^n \sum_{k=1}^K w_i N_{ik}(t),$$

$$w_i = \frac{\xi_i}{\pi_i} \text{ and } \hat{\boldsymbol{V}}(\boldsymbol{\beta}, t) = \left\{ \frac{\hat{\boldsymbol{S}}^{(2)}(\boldsymbol{\beta}, t)\hat{S}^{(0)}(\boldsymbol{\beta}, t) - \hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta}, t)^{\otimes 2}}{\hat{S}^{(0)}(\boldsymbol{\beta}, t)^2} \right\}. \tag{1}$$

Then, (i) is clearly satisfied on the basis of (1) and by the continuity of each component. Now, following Andersen and Gill (1982),

$$\begin{aligned}
\left\| \left(-\frac{\partial \boldsymbol{U}_n(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}^T} \right) - \boldsymbol{A}(\boldsymbol{\beta}) \right\| \; &\leq \; \left\| \sum_{k=1}^K \int_0^\tau \{\hat{\boldsymbol{V}}(\boldsymbol{\beta}, t) - \boldsymbol{v}(\boldsymbol{\beta}, t)\} n^{-1} d\bar{N}_k(t) \right\| \\
&+ \left\| \sum_{k=1}^K \int_0^\tau \{\hat{\boldsymbol{V}}(\boldsymbol{\beta}, t) - \boldsymbol{v}(\boldsymbol{\beta}, t)\} d n^{-1} \sum_{i=1}^n (w_i - 1) N_{ik}(t) \right\| \\
&+ \left\| \sum_{k=1}^K \int_0^\tau \boldsymbol{v}(\boldsymbol{\beta}, t) n^{-1} d\bar{M}_k(t) \right\| + \left\| \sum_{k=1}^K n^{-1} \sum_{i=1}^n (w_i - 1) \int_0^\tau \boldsymbol{v}(\boldsymbol{\beta}, t) dM_{ik}(t) \right\| \\
&+ \left\| \int_0^\tau \boldsymbol{v}(\boldsymbol{\beta}, t) \{\hat{S}^{(0)}(\boldsymbol{\beta}, t) - s^{(0)}(\boldsymbol{\beta}, t)\} \lambda_0(t) dt \right\|
\end{aligned} \tag{2}$$

where $\bar{N}_k(t) = \sum_{i=1}^n N_{ik}(t)$ and $\bar{M}_k(t) = \sum_{i=1}^n M_{ik}(t)$.

Each of the terms on the right side of the above inequality can be shown to converge to zero, uniformly in $\boldsymbol{\beta} \in \mathcal{B}$. The first and the third terms can be shown to converge to 0 by the Lenglart inequality for $n^{-1}\bar{N}_k(\tau)$ and $n^{-1} \sum_{i=1}^n \int_0^\tau \boldsymbol{v}(\boldsymbol{\beta}, t) dM_{ik}(t)$, respectively (Andersen and Gill, 1982, p1115). The second and the fourth terms can be shown to converge to 0 by applying lemma 3.

The last term on the right side of (2) can be shown to converge to zero in probability, uniformly in $\boldsymbol{\beta} \in \mathcal{B}$ as $n \to \infty$. Therefore,

$$-\frac{\partial \boldsymbol{U}_n(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}^T} \xrightarrow{p} \boldsymbol{A}(\boldsymbol{\beta}) \text{ as } n \to \infty \text{ uniformly in } \boldsymbol{\beta} \in \mathcal{B}$$

and, thus, (ii) and (iii) are satisfied.

For (iv), we can show that $n^{-1/2}\hat{\boldsymbol{U}}(\boldsymbol{\beta})$ is asymptotically equivalent to $n^{-1/2}\sum_{i=1}^{n}\sum_{k=1}^{K}\boldsymbol{M}_{\tilde{\boldsymbol{z}},ik}$. Specifically, write

$$
\begin{aligned}
n^{1/2}\boldsymbol{U}_n(\boldsymbol{\beta}) &= n^{-1/2}\sum_{i=1}^{n}\sum_{k=1}^{K}\int_0^{\tau} w_i\left\{\boldsymbol{Z}_{ik}(t)-\frac{\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta},t)}{\hat{S}^{(0)}(\boldsymbol{\beta},t)}\right\}dM_{ik}(t)\\
&= n^{-1/2}\sum_{i=1}^{n}\sum_{k=1}^{K}\int_0^{\tau} w_i\tilde{\boldsymbol{Z}}_{ik}(\boldsymbol{\beta},t)dM_{ik}(t)\\
&+ n^{-1/2}\sum_{i=1}^{n}\sum_{k=1}^{K}\int_0^{\tau} w_i\left\{\boldsymbol{e}(\boldsymbol{\beta},t)-\frac{\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta},t)}{\hat{S}^{(0)}(\boldsymbol{\beta},t)}\right\}dM_{ik}(t)\\
&= U_1 \;+\; U_2
\end{aligned}
$$

Now, we can show that U_2 converges to zero in probability as $n\to\infty$. Write $U_2 = U_{21}+U_{22}$ where

$$
\begin{aligned}
U_{21} &= n^{-1/2}\sum_{i=1}^{n}\sum_{k=1}^{K}\int_0^{\tau}\left\{\boldsymbol{e}(\boldsymbol{\beta},t)-\frac{\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta},t)}{\hat{S}^{(0)}(\boldsymbol{\beta},t)}\right\}dM_{ik}(t) \text{ and}\\
U_{22} &= \sum_{k=1}^{K}\int_0^{\tau}\left\{\boldsymbol{e}(\boldsymbol{\beta},t)-\frac{\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta},t)}{\hat{S}^{(0)}(\boldsymbol{\beta},t)}\right\}d\left\{n^{-1/2}\sum_{i=1}^{n}(w_i-1)M_{ik}(t)\right\}
\end{aligned}
$$

Note that, for fixed t, $n^{-1/2}\sum_{i=1}^{n}M_{ik}(t)$ is a sum of i.i.d. zero-mean random variables. $M_{ik}(t)$ can be shown to be of bounded variation and therefore can be written as a difference of two monotone functions in t. It then follows from the example of 2.11.16 of van der Vaart and Wellner (1996, p215) that $n^{-1/2}\sum_{i=1}^{n}M_{ik}(t)$ converges weakly to a zero-mean Gaussian process, say $\mathcal{W}_M(t)$. It can be shown that $\mathrm{E}\{\mathcal{W}_M(t)-\mathcal{W}_M(s)\}^4 \le C\{\Lambda_0(t)-\Lambda_0(s)\}^2$ for some constant $C>0$. Thus, by the conditions on $\Lambda_0(t)$, $\exists$ a constant M, such that $\Lambda_0(t)-\Lambda_0(s)\le M(t-s)$. Then, by the Kolmogorov-Centsov Theorem (Karatzas and Shereve, 1988, p53), $\mathcal{W}_M(t)$ has continuous sample paths.

In addition, $\hat{S}^{(0)}(\boldsymbol{\beta},t)$ and $\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta},t)$ can be written as a sum of two monotone functions in t, respectively. By applying lemma 2 twice, we have

$$
U_{21} = \sum_{k=1}^{K}\int_0^{\tau}\left\{\frac{\boldsymbol{s}^{(1)}(\boldsymbol{\beta},t)}{s^{(0)}(\boldsymbol{\beta},t)}-\frac{\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta},t)}{\hat{S}^{(0)}(\boldsymbol{\beta},t)}\right\}n^{-1/2}\sum_{i=1}^{n}dM_{ik}(t)\xrightarrow{p} 0 \text{ as } n\to\infty.
$$

In similar manners, U_{22} can be shown to converge to zero in probability as $n\to\infty$.

Specifically, the finite dimensional convergence of the $n^{-1/2}\sum_{i=1}^{n}(w_i-1)M_{ik}(t)$ to a zero-mean normal random variable follows from lemma 3. The tightness follows from the example 3.6.14 of van der Vaart and Wellner (1996, p356). The limiting process can be shown to have continuous sample paths via the Kolmogorov-Centsov Theorem (Karatzas and Shereve, 1988, p53). It then follows from lemma 2 that U_{22} converges to zero in probability as $n\to\infty$. Hence, U_2 converges to zero in probability as $n\to\infty$.

Now, one can write $U_1 = U_{11}+U_{12}$ where

$$U_{11} = n^{-1/2}\sum_{i=1}^{n}\sum_{k=1}^{K}\mathbf{M}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta}) \;\text{ and }\; U_{12} = n^{-1/2}\sum_{i=1}^{n}\sum_{k=1}^{K}(w_i-1)\mathbf{M}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta})$$

Then, under the regularity conditions, the first term is asymptotically zero-mean normal with covariance matrix $\boldsymbol{Q}(\boldsymbol{\beta}_0)$ by Spiekerman and Lin (1998). The second term can be shown to be asymptotically zero-mean normal with covariance matrix $\boldsymbol{V}(\boldsymbol{\beta}_0)$ by lemma 3. Note that U_{11} and U_{12} are independent since $\mathrm{Cov}(U_{11},U_{12}) = \mathrm{E}(U_{11}U_{12}) = \mathrm{E}(\mathrm{E}(U_{11}U_{12}|\mathcal{F}(\tau))) = \mathrm{E}(U_{11}\,\mathrm{E}(U_{12}|\mathcal{F}(\tau))) = 0$.

Therefore, $n^{1/2}\boldsymbol{U}_n(\boldsymbol{\beta})$ is asymptotically normally distributed with mean zero and with finite variance $\boldsymbol{Q}(\boldsymbol{\beta}_0)+\boldsymbol{V}(\boldsymbol{\beta}_0)$. Hence $\boldsymbol{U}_n(\boldsymbol{\beta})$ converges to zero in probability. Thus, (iv) is satisfied. By (i),(ii),(iii) and (iv), it follows that there is a unique sequence $\hat{\boldsymbol{\beta}}$ *s.t.* $\boldsymbol{U}(\hat{\boldsymbol{\beta}}) = 0$ with probability converging to one as $n\to 0$ and with $\hat{\boldsymbol{\beta}}$ converging in probability to $\boldsymbol{\beta}_0$ by extension of Foutz (1977, Thm.2).

The asymptotic normality of $\hat{\boldsymbol{\beta}}$ follows from the consistency of $\hat{\boldsymbol{\beta}}$ and a Taylor series expansion of $\hat{\boldsymbol{U}}(\boldsymbol{\beta})$.

Proof of Theorem 2 One can make decomposition

$$\begin{aligned} &n^{1/2}\{\hat{\Lambda}_0(\hat{\boldsymbol{\beta}},t)-\Lambda_0(t)\} \\ &= n^{1/2}\left\{\hat{\Lambda}_0(\hat{\boldsymbol{\beta}},t)-\int_0^t\frac{d\hat{N}(u)}{n\hat{S}^{(0)}(\boldsymbol{\beta}_0,u)}\right\} + n^{1/2}\left\{\int_0^t\frac{d\hat{N}(u)}{n\hat{S}^{(0)}(\boldsymbol{\beta}_0,u)}-\Lambda_0(t)\right\}\end{aligned}$$

$$
\begin{aligned}
&= n^{1/2}\int_0^t \left(\frac{1}{n\hat{S}^{(0)}(\hat{\boldsymbol\beta},u)} - \frac{1}{n\hat{S}^{(0)}(\boldsymbol\beta_0,u)}\right) d\hat{M}(u) \\
&+ n^{1/2}\int_0^t \left(\frac{1}{n\hat{S}^{(0)}(\hat{\boldsymbol\beta},u)} - \frac{1}{n\hat{S}^{(0)}(\boldsymbol\beta_0,u)}\right) n\hat{S}^{(0)}(\boldsymbol\beta_0,u) d\Lambda_0(u) \\
&+ n^{1/2}\int_0^t \frac{1}{n\hat{S}^{(0)}(\boldsymbol\beta_0,u)} d\hat{M}(u) \quad \text{where} \qquad (3) \\
&\hat{M}(t) = \sum_{k=1}^K\sum_{i=1}^n \left(w_i N_{ik}(t) - \int_0^t w_i Y_{ik}(t) e^{\boldsymbol\beta^T \boldsymbol{Z}_{ik}(u)} d\Lambda_0(u)\right)
\end{aligned}
$$

One can write the first term of (3) as

$$
\begin{aligned}
&\sum_{k=1}^K \int_0^t \left(\frac{1}{\hat{S}^{(0)}(\hat{\boldsymbol\beta},u)} - \frac{1}{\hat{S}^{(0)}(\boldsymbol\beta_0,u)}\right) dn^{-1/2}\bar{M}_k(u) \\
&+ \sum_{k=1}^K \int_0^t \left(\frac{1}{\hat{S}^{(0)}(\hat{\boldsymbol\beta},u)} - \frac{1}{\hat{S}^{(0)}(\boldsymbol\beta_0,u)}\right) d\left\{n^{-1/2}\sum_{i=1}^n (w_i-1)M_{ik}(u)\right\} \qquad (4)
\end{aligned}
$$

By the Taylor expansion of $\hat{S}^{(0)}(\hat{\boldsymbol\beta},u)^{-1}$ around $\boldsymbol\beta_0$, together with the consistency of $\hat{\boldsymbol\beta}$, $\hat{S}^{(0)}(\boldsymbol\beta^*,u)$, $\hat{\boldsymbol{S}}^{(1)}(\boldsymbol\beta^*,u)$ and the weak convergence of $n^{-1/2}\sum_{i=1}^n M_{ik}(t)$ with continuous sample paths, the first term of (4) converges to 0 uniformly in t in probability by applying lemma 2. By the same argument, together with the weak convergence of $n^{-1/2}\sum_{i=1}^n (w_i-1)M_{ik}(t)$ with continuous sample paths, it follows from lemma 2 that the second term of (4) converges to 0 uniformly in t in probability. Combining these results, the first term of (3) converges to 0 uniformly in t in probability.

Again, by the Taylor expansion of $\hat{S}^{(0)}(\hat{\boldsymbol\beta},u)^{-1}$ around $\boldsymbol\beta_0$, the asymptotic expansion of $n^{1/2}(\hat{\boldsymbol\beta}-\boldsymbol\beta_0)$ along with the consistency of $\hat{S}^{(0)}(\boldsymbol\beta_0,u)$, $\hat{S}^{(0)}(\boldsymbol\beta^*,u)$, $\hat{\boldsymbol{S}}^{(1)}(\boldsymbol\beta^*,u)$, $\hat{\boldsymbol\beta}$ and the boundedness condition on $\Lambda_0(\tau)$, it follows that the second term of (3) is

$$
\left(-\int_0^t \frac{\boldsymbol{s}^{(1)}(\boldsymbol\beta_0,u)^T}{s^{(0)}(\boldsymbol\beta_0,u)} d\Lambda_0(u)\right) \boldsymbol{A}^{-1}(\boldsymbol\beta_0) n^{-1/2}\sum_{k=1}^K\sum_{i=1}^n w_i \mathbf{M}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol\beta_0) + o_p(1)
$$

One can write the third term of (3) as

$$
\sum_{k=1}^K \int_0^t \frac{1}{\hat{S}^{(0)}(\boldsymbol\beta_0,u)} dn^{-1/2}\sum_{i=1}^n M_{ik}(u) + \sum_{k=1}^K \int_0^t \frac{1}{\hat{S}^{(0)}(\boldsymbol\beta_0,u)} d\left\{n^{-1/2}\sum_{i=1}^n (w_i-1)M_{ik}(u)\right\} \quad (5)
$$

By applying lemma 2, each of these two terms can be shown to be asymptotically equivalent to $\sum_{k=1}^K \int_0^t \frac{1}{s^{(0)}(\boldsymbol{\beta}_0,u)} d\left\{n^{-1/2}\sum_{i=1}^n M_{ik}(u)\right\}$ and $\sum_{k=1}^K \int_0^t \frac{1}{s^{(0)}(\boldsymbol{\beta}_0,u)} d\left\{n^{-1/2}\sum_{i=1}^n (w_i-1) M_{ik}(u)\right\}$, respectively.

By combining the results, we have

$$\begin{aligned} n^{1/2}(\hat{\Lambda}_0(\hat{\boldsymbol{\beta}},t)-\Lambda_0(t)) &= n^{-1/2}\sum_{k=1}^K\sum_{i=1}^n \left\{\int_0^t \frac{dM_{ik}(u)}{s^{(0)}(\boldsymbol{\beta}_0,u)} + \boldsymbol{r}(\boldsymbol{\beta}_0,t)^T \boldsymbol{A}^{-1}(\boldsymbol{\beta}_0)\mathbf{M}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta}_0)\right\} \\ &+ n^{-1/2}\sum_{k=1}^K\sum_{i=1}^n (w_i-1)\left\{\int_0^t \frac{dM_{ik}(u)}{s^{(0)}(\boldsymbol{\beta}_0,u)} + \boldsymbol{r}(\boldsymbol{\beta}_0,t)^T \boldsymbol{A}^{-1}(\boldsymbol{\beta}_0)\mathbf{M}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta}_0)\right\} \\ &= U_1^{\Lambda}(\boldsymbol{\beta}_0,t) \;+\; U_2^{\Lambda}(\boldsymbol{\beta}_0,t) \end{aligned}$$

The first term converges weakly to a zero-mean Gaussian process with covariance function $\phi(t_1,t_2)$ at (t_1,t_2) (Spiekerman and Lin, 1998). The weak convergence of the second term to a zero-mean Gaussian process with covariance function $\sigma(t_1,t_2)$ at (t_1,t_2) follows from lemma 3 and the example 3.6.14 of van der Vaart and Wellner (1996, p356). Note that these two terms are independent since $\mathrm{Cov}(U_1^{\Lambda},U_2^{\Lambda}) = \mathrm{E}(U_1^{\Lambda}U_2^{\Lambda}) = \mathrm{E}(\mathrm{E}(U_1^{\Lambda}U_2^{\Lambda}|\mathcal{F}(\tau))) = \mathrm{E}(U_1^{\Lambda}\,\mathrm{E}(U_2^{\Lambda}|\mathcal{F}(\tau))) = 0$. This completes the proof.

2. Consistent estimators for the asymptotic variances

In Theorem 1, $\boldsymbol{A}(\boldsymbol{\beta}_0)$, $\boldsymbol{Q}(\boldsymbol{\beta}_0)$ and $\boldsymbol{V}(\boldsymbol{\beta}_0)$ can be consistently estimated by $\hat{\boldsymbol{A}}(\hat{\boldsymbol{\beta}}), \hat{\boldsymbol{Q}}(\hat{\boldsymbol{\beta}})$ and $\hat{\boldsymbol{V}}(\hat{\boldsymbol{\beta}})$ where

$$\begin{aligned} \hat{\boldsymbol{A}}(\boldsymbol{\beta}) &= -n^{-1}\frac{\partial \hat{\boldsymbol{U}}(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}},\ \hat{\boldsymbol{Q}}(\boldsymbol{\beta}) = n^{-1}\sum_{i=1}^n w_i\left(\sum_{k=1}^K \hat{\mathbf{M}}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta})\right)^{\otimes 2}, \\ \hat{\boldsymbol{V}}(\boldsymbol{\beta}) &= \sum_{s=0}^1 \hat{p}_s \frac{1-\hat{\alpha}_s}{\hat{\alpha}_s}\widehat{\mathrm{Var}}\left(\sum_{k=1}^K \mathbf{M}_{\tilde{\boldsymbol{z}},1k}(\boldsymbol{\beta})\middle|\, \Delta_{11}=s\right), \\ \hat{\mathbf{M}}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta}) &= \Delta_{ik}\left\{\boldsymbol{Z}_{ik}(X_{ik}) - \frac{\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta};X_{ik})}{\hat{S}^{(0)}(\boldsymbol{\beta};X_{ik})}\right\} \\ &\quad - n^{-1}\sum_{j=1}^n w_j \sum_{l=1}^K \frac{\Delta_{jl}Y_{ik}(X_{jl})e^{\boldsymbol{\beta}^T\boldsymbol{Z}_{ik}(X_{jl})}}{\hat{S}^{(0)}(\boldsymbol{\beta};X_{jl})}\left\{\boldsymbol{Z}_{ik}(X_{jl}) - \frac{\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta};X_{jl})}{\hat{S}^{(0)}(\boldsymbol{\beta};X_{jl})}\right\}, \\ \hat{p}_s &= \frac{n_s}{n},\ \hat{\alpha}_s = \frac{\tilde{n}_s}{n_s},\ w_i = \frac{\xi_i}{\pi_i} \ \text{ and} \end{aligned}$$

$\widehat{\mathrm{Var}}\left(\sum_{k=1}^{K}\hat{\mathbf{M}}_{\tilde{\boldsymbol{z}},1k}(\boldsymbol{\beta})\middle|\Delta_{11}=s\right)$ is a sample variance of $\left\{\sum_{k=1}^{K}\hat{\mathbf{M}}_{\tilde{\boldsymbol{z}},1k}(\hat{\boldsymbol{\beta}})\middle|\Delta_{11}=s\right\}$ for $s=0,1$.

In Theorem 2, $\phi(t_1,t_2)(\boldsymbol{\beta}_0)$ and $\sigma(t_1,t_2)(\boldsymbol{\beta}_0)$ can be consistently estimated by $\hat{\phi}(t_1,t_2)(\hat{\boldsymbol{\beta}})$ and $\hat{\sigma}(t_1,t_2)(\hat{\boldsymbol{\beta}})$ where

$$\hat{\phi}(t_1,t_2)(\boldsymbol{\beta})=n^{-1}\sum_{i=1}^{n}w_i\left(\sum_{k=1}^{K}\hat{\phi}_{ik}(\boldsymbol{\beta},t_1)\right)\left(\sum_{m=1}^{K}\hat{\phi}_{im}(\boldsymbol{\beta},t_2)\right),$$

$$\hat{\sigma}(t_1,t_2)(\boldsymbol{\beta})=\sum_{s=0}^{1}\hat{p}_s\frac{1-\hat{\alpha}_s}{\hat{\alpha}_s}\widehat{\mathrm{Cov}}\left(\sum_{k=1}^{K}\phi_{1k}(\boldsymbol{\beta},t_1),\sum_{m=1}^{K}\phi_{1m}(\boldsymbol{\beta},t_2)\middle|\Delta_{11}=s\right),$$

$$\hat{\phi}_{ik}(\boldsymbol{\beta},t)=\int_0^t\frac{d\hat{M}_{ik}(u)}{\hat{S}^{(0)}(\boldsymbol{\beta},u)}+\boldsymbol{R}(\boldsymbol{\beta},t)^T\hat{\boldsymbol{A}}^{-1}(\boldsymbol{\beta})\hat{\mathbf{M}}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta}),$$

$$\int_0^t\frac{d\hat{M}_{ik}(u)}{\hat{S}^{(0)}(\boldsymbol{\beta},u)}=\frac{\Delta_{ik}I(X_{ik}\le t)}{\hat{S}^{(0)}(\boldsymbol{\beta},X_{ik})}-n^{-1}\sum_{j=1}^{n}w_j\sum_{l=1}^{K}\frac{\Delta_{jl}I(X_{jl}\le t)Y_{ik}(X_{jl})e^{\boldsymbol{\beta}^T\boldsymbol{Z}_{ik}(X_{jl})}}{\hat{S}^{(0)}(\boldsymbol{\beta},X_{jl})^2},$$

$$\boldsymbol{R}(\boldsymbol{\beta},t)=-n^{-1}\sum_{i=1}^{n}w_i\sum_{l=1}^{K}\frac{\Delta_{il}I(X_{il}\le t)\hat{\boldsymbol{S}}^{(1)}(\boldsymbol{\beta},X_{il})}{\hat{S}^{(0)}(\boldsymbol{\beta},X_{il})^2}\quad\text{and}$$

$\widehat{\mathrm{Cov}}\left(\sum_{k=1}^{K}\phi_{1k}(\boldsymbol{\beta},t_1),\sum_{m=1}^{K}\phi_{1m}(\boldsymbol{\beta},t_2)\middle|\Delta_{11}=s\right)$ is a sample covariance for $\left\{\left(\sum_{k=1}^{K}\hat{\phi}_{1k}(\hat{\boldsymbol{\beta}},t_1),\sum_{m=1}^{K}\hat{\phi}_{1m}(\hat{\boldsymbol{\beta}},t_2)\right)\middle|\Delta_{11}=s\right\}$ for $s=0,1$.

In Theorem 3, $\boldsymbol{A}(\boldsymbol{\beta}_0),\boldsymbol{Q}(\boldsymbol{\beta}_0)$ and $\boldsymbol{V}_c(\boldsymbol{\beta}_0)$ can be consistently estimated by $\hat{\boldsymbol{A}}_c(\hat{\boldsymbol{\beta}}_c)$, $\hat{\boldsymbol{Q}}_c(\hat{\boldsymbol{\beta}}_c)$ and $\hat{\boldsymbol{V}}_c(\hat{\boldsymbol{\beta}}_c)$ where

$$\hat{\boldsymbol{A}}_c(\boldsymbol{\beta})=-n^{-1}\frac{\partial\hat{\boldsymbol{U}}_c(\boldsymbol{\beta})}{\partial\boldsymbol{\beta}},\ \hat{\boldsymbol{Q}}_c(\boldsymbol{\beta})=n^{-1}\sum_{i=1}^{n}w_i\left(\sum_{k=1}^{K}\hat{\mathbf{M}}^c_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta})\right)^{\otimes 2},$$

$$\hat{\boldsymbol{V}}_c(\boldsymbol{\beta})=\sum_{s=0}^{1}\sum_{h=1}^{H_s}\hat{w}_{sh}\frac{1-\hat{\alpha}_s}{\hat{\alpha}_s}\widehat{\mathrm{Var}}\left(\sum_{k=1}^{K}\mathbf{M}_{\tilde{\boldsymbol{z}},1k}(\boldsymbol{\beta})\middle|X_{11}=h,\Delta_{11}=s\right),$$

$$\widehat{\mathrm{Var}}\left(\sum_{k=1}^{K}\mathbf{M}_{\tilde{\boldsymbol{z}},1k}(\boldsymbol{\beta})\middle|X_{11}=h,\Delta_{11}=s\right)=n^{-1}\sum_{i=1}^{n}w_i\times\left[\sum_{k=1}^{K}\hat{\mathbf{M}}^c_{\tilde{\boldsymbol{z}},ik}(\hat{\boldsymbol{\beta}}_c)-\hat{\mathrm{E}}\left(\sum_{k=1}^{K}\mathbf{M}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta}_0)\middle|X_{i1}=h,\Delta_{i1}=s\right)\right]^{\otimes 2},$$

$$\hat{\mathrm{M}}^c_{\tilde{\boldsymbol{z}},il}(\boldsymbol{\beta}) = \Delta_{il}\left\{\boldsymbol{Z}_{il}(X_{il}) - \frac{\hat{\boldsymbol{S}}^{(1)}_c(\boldsymbol{\beta}, X_{il})}{\hat{S}^{(0)}_c(\boldsymbol{\beta}, X_{il})}\right\} - n^{-1}\sum_{j=1}^n w_j$$
$$\times \sum_{k=1}^K \frac{\Delta_{jk} Y_{il}(X_{jk}) e^{\boldsymbol{\beta}^T \boldsymbol{Z}_{il(X_{jk})}}}{\hat{S}^{(0)}_c(\boldsymbol{\beta}, X_{jk})}\left\{\boldsymbol{Z}_{il}(X_{jk}) - \frac{\hat{\boldsymbol{S}}^{(1)}_c(\boldsymbol{\beta}, X_{jk})}{\hat{S}^{(0)}_c(\boldsymbol{\beta}, X_{jk})}\right\}, \ w_i = \frac{\xi_i}{r_n(X_{i1}, \Delta_{i1})} \quad \text{and}$$

$\hat{\mathrm{E}}\left[\left(\sum_{k=1}^K \mathbf{M}_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta}_0)\middle| X_{i1} = h, \Delta_{i1} = s\right)\right]$ is a local average of $\left(\sum_{k=1}^K \hat{\mathbf{M}}^c_{\tilde{\boldsymbol{z}},ik}(\hat{\boldsymbol{\beta}}_c)\middle| X_{i1} = h, \Delta_{i1} = s\right)$, $i = 1, \ldots, n$ using the partitions.

In Theorem 4, $\phi(t_1, t_2)(\boldsymbol{\beta}_0)$ and $\sigma_c(t_1, t_2)(\boldsymbol{\beta}_0)$ can be consistently estimated by $\hat{\phi}_c(t_1, t_2)(\hat{\boldsymbol{\beta}}_c)$ and $\hat{\sigma}_c(t_1, t_2)(\hat{\boldsymbol{\beta}}_c)$ where

$$\hat{\phi}_c(t_1, t_2)(\boldsymbol{\beta}) = n^{-1}\sum_{i=1}^n w_i \left(\sum_{k=1}^K \hat{\phi}^c_{ik}(\boldsymbol{\beta}, t_1)\right)\left(\sum_{l=1}^K \hat{\phi}^c_{il}(\boldsymbol{\beta}, t_2)\right),$$
$$\hat{\sigma}_c(t_1, t_2)(\boldsymbol{\beta}) = \sum_{s=0}^1 \sum_{h=1}^{H_s} \hat{w}_{sh}\frac{1-\hat{\alpha}_s}{\hat{\alpha}_s}\widehat{\mathrm{Cov}}\left(\sum_{k=1}^K \phi_{1k}(\boldsymbol{\beta}, t_1), \sum_{m=1}^K \phi_{1m}(\boldsymbol{\beta}, t_2)\middle| X_{11} = h, \Delta_{11} = s\right),$$
$$\hat{\phi}^c_{ik}(\boldsymbol{\beta}, t) = \int_0^t \frac{d\hat{M}^c_{ik}(u)}{\hat{S}^{(0)}_c(\boldsymbol{\beta}, u)} + \boldsymbol{R}_c(\boldsymbol{\beta}, t)^T \hat{\boldsymbol{A}}_c^{-1}(\boldsymbol{\beta})\hat{\mathrm{M}}^c_{\tilde{\boldsymbol{z}},ik}(\boldsymbol{\beta}),$$
$$\int_0^t \frac{d\hat{M}^c_{ik}(u)}{\hat{S}^{(0)}_c(\boldsymbol{\beta}, u)} = \frac{\Delta_{ik} I(X_{ik} \leq t)}{\hat{S}^{(0)}_c(\boldsymbol{\beta}, X_{ik})} - n^{-1}\sum_{j=1}^n w_j \sum_{l=1}^K \frac{\Delta_{jl} I(X_{jl} \leq t) Y_{ik}(X_{jl}) e^{\boldsymbol{\beta}^T \boldsymbol{Z}_{ik(X_{jl})}}}{\hat{S}^{(0)}_c(\boldsymbol{\beta}, X_{jl})^2},$$
$$\boldsymbol{R}_c(\boldsymbol{\beta}, t) = -n^{-1}\sum_{i=1}^n w_i \sum_{l=1}^K \frac{\Delta_{il} I(X_{il} \leq t)\hat{\boldsymbol{S}}^{(1)}_c(\boldsymbol{\beta}, X_{il})}{\hat{S}^{(0)}_c(\boldsymbol{\beta}, X_{il})^2} \quad \text{and}$$

$$\widehat{\mathrm{Cov}}\left(\sum_{k=1}^K \phi_{1k}(\boldsymbol{\beta}, t_1), \sum_{m=1}^K \phi_{1m}(\boldsymbol{\beta}, t_2)\middle| X_{11} = h, \Delta_{11} = s\right) = n^{-1}\sum_{i=1}^n w_i$$
$$\times \left[\sum_{k=1}^K \hat{\phi}^c_{ik}(\hat{\boldsymbol{\beta}}, t_1) - \hat{\mathrm{E}}\left(\sum_{k=1}^K \phi_{ik}(\boldsymbol{\beta}, t_1)\middle| X_{i1} = h, \Delta_{i1} = s\right)\right]$$
$$\times \left[\sum_{m=1}^K \hat{\phi}^c_{im}(\hat{\boldsymbol{\beta}}, t_2) - \hat{\mathrm{E}}\left(\sum_{m=1}^K \phi_{im}(\boldsymbol{\beta}, t_2)\middle| X_{i1} = h, \Delta_{i1} = s\right)\right].$$

3. A sample S-plus/R script for parameter and variance estimation

The regression parameter estimates and their variance estimates can be obtained using any standard statistical software which supports the incorporation of `weights` option (or an `offset` option) and the calculation of `dfbeta` residuals (Therneau and Li, 1999). S-plus/R support all these necessary options. Here we provide a sample script of S-plus/R for the calculation of the parameter estimates and their variance estimates below.

```
coxfit <- coxph(Surv(time,delta)~z,weights=w)
dfb.coxfit <- resid(coxfit,type='dfbeta',collapse=id)
var.full <- matrix(rep(0,p^2),nrow=p)
var.samp <- matrix(rep(0,p^2),nrow=p)
for (strt in 1:no.strt){
    var.full <- var.full + inc.prob.vec[strt]*t(dfb.coxfit[ind.strt==strt,])
                    %*%dfb.coxfit[ind.strt==strt,]
    var.samp <- var.samp + n.tilde.vec[strt]*(1-inc.prob.vec[strt])*
                    var(dfb.coxfit[ind.strt==strt,])
}
var.new <- var.full + var.samp
```

The `coxph` function with `weights` option enables one to obtain the regression parameter estimates. Here `time` is observed failure times, `delta` is failure indicator, `z` is a covariate and `w` is the inverse of the inclusion probabilities. The `resid` function provides the so-called 'DFBETAS' which is essential in calculating the variance estimates. The `collapse` option in `resid` function performs the summation of the 'DFBETAS' within each cluster. The variable `id` is the cluster indicators. The variance estimates can then be calculated using these summed 'DFBETAS'. `var.full` is the variance due to the sampling of the cohort and `var.samp` is the variance due to the sampling of the case-controls. `strt` is the strata indicator and we have two strata(cases and controls). `no.strt` denotes this number of strata. `inc.prob.vec` contains the inclusion probabilities for each stratum and `n.tilde.vec` contains the number of samples in each strata as elements. `var.new` is the final variance estimates which is the sum of the two components.

4. Simulation results when the marginal distribution follows Weibull

Table 1 shows simulation summary statistics when the marginal distribution follows Weibull distribution with the scale parameter and the shape parameter being set to 1 and 0.5, respectively. The binary covariate which mimics our motivating dental example was considered where the value of the first member is equal to one and the value of the second member is equal to zero ($Z_{i1} = 1$ and $Z_{i2} = 0$). The findings are similar to those of Tables 1 and 2 in the main article.

[Table 1 about here.]

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Table 1

Summary of simulation results. $Z_{i1} = 1$, $Z_{i2} = 0$. Failure times are from Weibull distributions with the scale parameter and the shape parameter being equal to 1 and 0.5.

β_0	n	event proportion	$\widetilde{n}$	τ_θ	mean $\hat{\beta}$	indep. s.e.	proposed s.e.	true S.D.	95% Coverage
0	1000	10%	185	0.83	0.013	0.1410	0.2106	0.2181	0.923
			185	0.43	0.030	0.1423	0.2918	0.3052	0.934
			185	0.29	0.041	0.1425	0.3030	0.3187	0.939
			184	0.09	0.026	0.1424	0.3130	0.3183	0.951
		20%	361	0.83	0.002	0.1000	0.0853	0.0850	0.945
			361	0.43	0.005	0.1002	0.1362	0.1387	0.943
			362	0.29	0.005	0.1000	0.1435	0.1435	0.952
			360	0.09	0.003	0.1003	0.1517	0.1553	0.944
	2000	10%	371	0.83	0.002	0.0992	0.1490	0.1536	0.934
			371	0.43	0.022	0.0996	0.2048	0.2090	0.947
			371	0.29	0.022	0.0996	0.2122	0.2143	0.953
			371	0.09	0.022	0.0996	0.2182	0.2249	0.944
		20%	724	0.83	0.002	0.0706	0.0602	0.0608	0.942
			724	0.43	0.000	0.0706	0.0960	0.0953	0.952
			724	0.29	0.003	0.0706	0.1015	0.1041	0.946
			724	0.09	0.001	0.0706	0.1065	0.1051	0.953
0.693	1000	10%	184	0.83	0.729	0.1742	0.2617	0.2856	0.845
			184	0.43	0.766	0.1792	0.3990	0.4212	0.935
			185	0.29	0.773	0.1809	0.4169	0.4536	0.943
			184	0.09	0.770	0.1831	0.4373	0.4919	0.944
		20%	355	0.83	0.698	0.1215	0.1106	0.1098	0.945
			355	0.43	0.704	0.1221	0.1808	0.1811	0.946
			355	0.29	0.710	0.1221	0.1912	0.1926	0.946
			353	0.09	0.702	0.1222	0.2019	0.2043	0.950
	2000	10%	370	0.83	0.713	0.1212	0.1892	0.1976	0.920
			370	0.43	0.735	0.1230	0.2803	0.2860	0.949
			369	0.29	0.739	0.1235	0.2922	0.3075	0.941
			370	0.09	0.730	0.1230	0.3003	0.3042	0.961
		20%	711	0.83	0.697	0.0857	0.0778	0.0815	0.937
			710	0.43	0.698	0.0858	0.1275	0.1281	0.952
			711	0.29	0.700	0.0859	0.1349	0.1311	0.961
			710	0.09	0.700	0.0859	0.1415	0.1399	0.953