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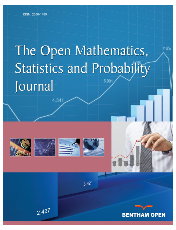

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RESEARCH ARTICLE

Consistency of the Semi-parametric MLE under the Cox Model with Right-Censored Data

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Abstract:

Objective:

We studied the consistency of the semi-parametric maximum likelihood estimator (SMLE) under the Cox regression model with right-censored (RC) data.

Methods:

Consistency proofs of the MLE are often based on the Shannon-Kolmogorov inequality, which requires finite E(lnL), where L is the likelihood function.

Results:

The results of this study show that one property of the semi-parametric MLE (SMLE) is established.

Conclusion:

Under the Cox model with RC data, E(lnL) may not exist. We used the Kullback-Leibler information inequality in our proof.

Keywords: Cox model, Maximum likelihood estimator, Consistency, Kullback-Leibler Inequality, Shannon-Kolmogorov inequality, Without loss of generality (WLOG).

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1. INTRODUCTION

We studied the consistency of the semi-parametric maximum likelihood estimator (SMLE) under the Cox model with right-censored (RC) data.

Let Y be a random survival time, $\mathbf{X}$ a p-dimensional random covariate. Conditional on $\mathbf{X} = \mathbf{x}$, Y satisfies the Cox model if its hazard function satisfies

$$h(y|\mathbf{x}) = h_o(y)\, e^{\beta'\mathbf{x}}, \quad y < \tau_Y, \qquad \textbf{(1.1)}$$

where h_o is the baseline hazard function, *i.e.*, $h_o(y) = f_o(y) / S_o(y\text{-})$, f_o is a density function, S_o (y) = $S(y|0) \stackrel{\text{def}}{=} P(Y > y\,|\mathbf{X} =$), $F_o = 1 - S_o$, $\tau_Y = sup\{t{:}S_Y(t) > 0\}$, $h(y|\mathbf{x}) = \frac{f\,(y|\mathbf{x})}{S(y-|\mathbf{x})}$, $S(\cdot|\cdot)$ $f(\cdot|\cdot)$ **or**$F(\cdot|\cdot)$) is the conditional survival function (density function (df) or cumulative distribution function (cdf)) of Y given $\mathbf{X} = \mathbf{x}$. The restriction $y<\tau_Y$ is not in the original definition of the PH model, but is necessary if S_o is discontinuous at τ_Y (see Remark 1 [1])

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2. METHODS

In this paper, we shall make use of the assumptions as follows:

AS1. Suppose that C is a random variable with the df $f_C(t)$ and the survival function $S_C(t)$, $\mathbf{X}$ takes at least p +1 values, say $\mathbf{0}$, $\mathbf{x}_1$, ..., $\mathbf{x}_p$, where $\mathbf{x}_1$, ..., $\mathbf{x}_p$ are linearly independent, (Y,$\mathbf{X}$) and C are independent. Let (Y_1,$\mathbf{X}_1$,C_1), ..., (Y_n,$\mathbf{X}_n$,C_n) be i.i.d. random vectors from (Y,$\mathbf{X}$,C). $M = min(Y,C)$ and $\delta = \mathbf{1}(Y \le C)$, where $\mathbf{1}(A)$ is the indicator function of the event A. Let (M_1, $\delta_1\mathbf{X}_1$), ..., (M_n, δ_n, $\mathbf{X}_n$) be i.i.d. RC observations from (M, δ, $\mathbf{X}$) with the df are as follows:

$$f_{M,\delta,X}(m,\delta,\mathbf{x}) = \big(S(m|\mathbf{x})\mathrm{f_c(m)}\big)^{1-\delta}\big(f(m|\mathbf{x})\mathrm{S_c(m)}\big)^{\delta} f_{\mathbf{X}}(\mathbf{x}), \quad \text{where } m \in \mathrm{D} \qquad \textbf{(1.2)}$$

$$\mathrm{D} = \begin{cases} (-\infty,\tau_M] & if\ P(Y=\tau_M|X=0)=0\ or\ P(C\ge\tau_M)>0 \\ (-\infty,\tau_M) & \text{otherwise,} \end{cases}$$

$$\tau_M = \sup\{x{:}\ S_M(x) > 0\}, S_0(\tau_M) < 1,$$

and $S(t|\mathbf{x})$ is a function of (S_o, β) (see Eq. (1.1)), but not $f_{\mathbf{x}}$ and f_C (the df's of $\mathbf{X}$ and C).

Due to (AS1) and Eq. (1.2), the generalized likelihood function can be written as:

$$L(S_0, \beta) = \prod_{i=1}^{n}[(S(M_i|X_i))^{(1-\delta_i)}(S(M_i-|X_i) - S(M_i|X_i))^{\delta_i}], \quad \textbf{(1.3)}$$

which coincides with the standard form of the generalized likelihood [2]. Eq. (1.3) is identical to the next expression:

$$L(S_0, \beta) = \prod_{i=1}^{n}[(S(M_i|X_i))^{1-\delta_i}(S(M_i-\eta_n|X_i) - S(M_i|X_i))^{\delta_i}] \quad \textbf{(1.4)}$$

where $\eta_n = \min\{|M_i-M_j|: M_i \neq M_j, i, j \in \{1,2, ..., n\}\}$. This form allows S_o to be arbitrary (discrete or continuous, or others), thus is more convenient in the later proofs. If Y is continuous then $S(t|\mathbf{x}) = (S(t|0))^{\exp(\mathbf{X}'\beta)} = (S_o(t))^{\exp(\mathbf{X}'\beta)}$, but

$S(t|\mathbf{x}) \neq (S(t|0))^{\exp(\mathbf{x}'\beta)}$ under the discrete Cox model ([3]). **(1.5)**

If Y is discrete then $S(t|\mathbf{x}) = \prod_{s\leq t}(1 - h(s|\mathbf{x})) = \prod_{s\leq t}(1 - h_0(s)e^{\mathbf{X}'\beta})$ If Y has a mixture distribution, then $S(t|\mathbf{x}) = p(S_{01}(t))^{\exp(\mathbf{X}'\beta)} + (1-p)\prod_{s\leq t}(1 - h_{02}(s)e^{\mathbf{X}'\beta}$ where $p \in (0,1)$, h_{01} and h_{02} are two hazard functions. $h_0(t) = ph_{01} + (1-p)h_{02}$ and $S_0(t) = pS_{01} + (1-p)S_{02}$

The SMLE of (S_o, β) maximizes L $(S, \mathbf{b})$ overall possible survival function S and $\mathbf{b} \in \boldsymbol{R}^p$, denoted by $(\hat{S}_o, \hat{\beta})$. The SMLE of $S(t|\mathbf{x})$ is denoted by $\hat{S}$ $(t|\mathbf{x})$, which is a function of $(\hat{S}_o, \hat{\beta})$. The computation issue of the SMLE under the Cox model has been studied, but its consistency has not been established under the model [3]. Their simulation results suggest that the SMLE is more efficient than the partial likelihood estimator under the Cox model.

The partial likelihood estimator is a common estimator under the Cox model, which maximizes the partial likelihood:

$L_0 = \prod_{i\in D}\frac{\exp(\beta'\mathbf{X}_i)}{\sum_{k\in\boldsymbol{R}_i}\exp(\beta'\mathbf{X}_k)}$, where D is the collection of indices of the exact observations and $\boldsymbol{R}_i$ is the risk set {j: $M_j \geq Y_j$}. The asymptotic properties of the estimator are well understood [4].

The consistency of the SMLE under the continuous Cox model with interval-censored (IC) data has been established, making use of the following result [5]:

The Shannon-Kolmogorov (S-K) inequality. *Let f_o and f be two densities with respect to (w.r.t.)* a measure μ and $\int f_0(t)\ln f_0(t)d\mu(t)$ is finite. Then, $\int f_0(t)\ln f_0(t)d\mu(t) \geq \int f_0(t)\ln f(t)d\mu(t)$, with equality *iff* $f = f_o$ a.e. w.r.t. μ.

Under the Cox model with IC data, the S-K inequality becomes $E(\ln L(S_o, \beta)) \geq E(\ln L(S, \mathbf{b}))$ $\forall$ $(S, \mathbf{b})$, where $L(\cdot,\cdot)$ is the likelihood function of the Cox model with IC data, which is different from L $(\cdot,\cdot)$ in Eq. (1.3) and S is a baseline survival function and $\mathbf{b} \in \boldsymbol{R}^p$. Their approach cannot be extended to the Cox model with RC data as the key assumption (in the S-K inequality) [3].

That is, finite $E(\ln L(S_o, \beta))$, may not hold. Indeed, if Y has a df $f_0(t) \propto \frac{\mathbf{1}(x\in\{2,3,4...\})}{x(\ln x)^2}$, $\delta_i \equiv 1$ and $\beta = 0$, then L

$$(S_0, \beta) = \prod_{i=1}^{n}(f_0(Y_i) \text{ and } E(\ln L)) = \sum_x f_0(x)\ln f_0(x) \propto \int_{x\geq 2}\frac{\ln x + 2\ln\ln x}{x(\ln x)^2} = -\infty.$$

A related inequality is as follows.

The Kullback-Leibler (K-L) information inequality. *Let f_o and f be two densities w.r.t. a measure μ. Then $\int f_0(t)\ln(f_0/f)(t)d\mu(t) \geq 0$, with equality iff $f = f_o$ a.e. w.r.t. μ.*

The K-L inequality says that $\int f_0(t)\ln(f_0/f)(t)d\mu(t)$ exists, though it maybe ∞. The two inequalities are not equivalent. In fact,

$$\int f_0(t)\ln f_0(t)d\mu(t) \geq 0 \text{ if } \int f_0(t)\ln f_0(t)d\mu(t) \geq \int f_0(t)\ln f(t)d\mu(t).$$

In this note, we show that the SMLE under the Cox model is consistent, making use of the Kullback-Leibler information inequality [6]

2. The Main Results. Notice that under the assumption that h_o exists, S_o, f_o, F_o and h_o are equivalent, in the sense that given one of them, the other 3 functions can be derived. Thus, the Cox model is applicable only to the distributions that the density functions exist, that is, Y is either continuous, or discrete, or the mixture of the previous two. Since the expression of $S(t|\mathbf{x})$ varies in these three cases, for simplicity, we only prove the consistency of the SMLE under the Cox model in the first two cases.

Theorem 1. *Under the Cox model with RC data, if Y is either continuous or discrete, and if $S_o(\tau_M) < 1$, then the SMLE* ($(\hat{S}_o(t), \hat{\beta})$) is consistent $\forall$ $t \in$ D (see Eq. (1.2)).

The proof of Theorem 1 makes use of a modified K-L inequality. K-L inequality requires that f_0 and f are both densities w.r.t. the measure μ. That is $\int f(t)d\mu(t) = 1$. However, in our case, we encounter the case that $\int f(t)d\mu(t) \in [0,1]$.

Lemma 1 (the modified K-L inequality). If $f_i \geq 0$, μ_1 is a measure, $\int f_1(t)d\mu_1(t) = 1$ and $\int f_2(t)d\mu_1(t) \leq 1$, then $\int f_1(t)\ln\frac{f_1(t)}{f_2(t)}d\mu_1(t) \geq 0$, with equality iff $f_1 = f_2$ a.e. w.r.t. μ_1.

Proof. In view of the K-L inequality, it suffices to prove the inequality $\int f_1(t)\ln\frac{f_1(t)}{f_2(t)}d\mu_1(t) \geq 0$ under the additional assumptions that $\int f_2(t)d\mu_1(t) < 1$, $\int f_1(t)d\mu_2(t) = 0$ and $\int f_2(t)d\mu(t) < 1$, where μ_2 is a measure and $\mu = \mu_1 + \mu_2$ Since $\int f_2(t)d\mu(t) = 1$, f_1 and f_2 are df's w.r.t. μ.

$$0 \leq \int f_1(t)\ln\frac{f_1(t)}{f_2(t)}d(\mu_1(t) + \mu_2(t)) \quad \text{(by the K-L inequality)}$$

$$= \int f_1(t)\ln\frac{f_1(t)}{f_2(t)}d\mu_1(t) + \int f_1(t)\ln\frac{f_1(t)}{f_2(t)}d\mu_2(t) = \int f_1(t)\ln\frac{f_1(t)}{f_2(t)}d\mu_1(t).$$

Proof of Theorem 1. Let Ω_0 be the subset of the sample space Ω such that the empirical distribution function (edf) $\hat{F}_n$, $(t, s, \boldsymbol{x})$ based on $(M_i, \delta_i, \boldsymbol{X}_i)$ converges to $F(t,s,\mathbf{x})$, the cdf of $(M, \delta, \mathbf{X})$. It is well-known that $P(\Omega,)$ =1. Notice that the SMLE ($\hat{S}_o, \hat{\beta}$) is a function of (ω, n), say ($\hat{S}_{o,n}(t)(\omega)$, $\hat{\beta}_{o,n}(t_n)(\omega)$, where $\omega \in \Omega$ and n is the sample size. Hereafter, fix an $\omega \in \Omega_0$, since $\hat{\beta}(=\hat{\beta}_n(\omega))$ is a sequence of vectors in $\boldsymbol{R}^p$, there is a convergent subsequence with the limit β^*, where the components of β_* can be $\pm\infty$. Moreover, S_o (= $S_{o,n}(\cdot)(\omega)$) is a sequence of bounded non-increasing functions, Helly's selection theorem ensures that given any subsequence of $\hat{S}_o$, there exists a further subsequence which is convergent. Without loss of generality (WLOG), we assume that $\hat{S}_o \to S_*$ and $\hat{\beta} \to \beta_*$. Of course, (β_*, S_*) depends on $\omega(\in \Omega_0)$. We prove in Theorem 2 for the discrete case and in Theorem 3 for the continuous case that:

$$(S_*(t), \beta_*) = (S_*(t), \beta_*)\ (\omega) = (S_0(t), \beta)\ \forall\ t \in \mathrm{D} \quad \textbf{(2.1)}$$

Since ω can be arbitrary in Ω_0 and $\mathrm{P}(\Omega_0) = 1$, the SMLE is consistent.

Before we prove Theorems 2 and 3, we present a preliminary result.

Lemma 2 (Proposition 17 in Royden (1968), page 231). *Suppose that* μ_n *is a sequence of measures on the measurable space* $(J, \mathscr{B})$ *such that* $\mu_n(B)\ \mu(B), \to B \in \mathscr{B}$, g_n and f_n *are non-negative* measurable functions, and $\lim_{n\to\infty} (f_n, g_n)(x) = (f, g)(x)$ *Then*,

(1) $\int f d\mu \leq \underline{lim}_{n\to\infty} \int f_n\, d\mu_n$;

(2) *if* $g_n \geq f_n\ (\geq 0)$ *and* $\lim_{n\to\infty} \int g_n d\mu_n = \int g d\mu$, *then* $\int f d\mu = \lim_{n\to\infty} \int f_n d\mu_n$.

Corollary 1. *Suppose that* μ_n *is a sequence of measures on the measurable space (J , B) such that* $\lim_{n\to\infty} \mu_n(B) \to \mu(B), \forall B \in \mathscr{B}$, f *and* f_n $(n \geq 1)$ *are integrable functions that are bounded below and* $f(x)_{n\to\infty} = \lim f_n(x)$. *Then* $\int f\, d\mu \leq \underline{\lim}_{n\to\infty} \int f_n\, d\mu_n$.

Proof. Let $k = \inf_n \inf f_n(x)$. If $k \geq 0$ then the corollary follows from Lemma 2. Otherwise, let $f_n^-(x) = 0 \wedge f_n(x)$, $f_n^+(x) = 0 \vee f_n(x)$, $f^-(x) = 0 \wedge f(x)$ and $f^+(x) = 0 \vee f(x)$. Then, $f_n^+ \to f^+$ and $f_n^- \to f^-$ point wisely, as, $f_n \to f$

$\underline{\lim}_{n\to\infty} \int f_n\, d\mu_n = \underline{\lim}_{n\to\infty} \int (f_n^+ + f_n^-) d\mu_n = \underline{\lim}_{n\to\infty} [\int f_n^+\, d\mu_n + f_n^-\, d\mu_n] \geq \int \underline{\lim}_{n\to\infty} f_n^+\, d\mu + \int \underline{\lim}_{n\to\infty} f_n^-\, d\mu$ (by Lemma2, as $f_n^+(x)$ is nonnegative and $|f^-(x)| \leq k$) $= \int f^+\, d\mu + \int f^-\, d\mu = \int (f^+ + f^-) d\mu = \int f\, d\mu$.

Theorem 2. Under the discrete Cox model with RC data, Eq. (2.1) holds.

Proof. For the given $\omega \in \Omega_0$ and (S_*, β_*) in the proof of Theorem 1, as assumed, $(\hat{S}_o, \hat{\beta})(\omega) \to (S_*, \beta_*)$. Defining $h_*(t) = \frac{S_*(t-) - S_*(t)}{S_*(t-)}$ and $h_*(t|\boldsymbol{x}) = h_*(t)^{e^{\beta_* x}}$ (for $S_*(t-) > 0$) yeilds $S_*(t|\boldsymbol{x})$ and $f_*(t|\boldsymbol{x})$, which are continuous functions of S_* and β_*. Consequently, $\hat{S}(\cdot|\cdot) \to S_*(\cdot|\cdot)$.

Let $G_n(S_0, \beta) = \ln L(S_0, \beta)/n$ (see Eq.(1.3)). Then, the SMLE $(\hat{S}_o, \hat{\beta})$ satisfies

$$\begin{aligned} G_n(\hat{S}o, \hat{\beta}) &= \frac{1}{n}\sum_{i=1}^{n}(1-\delta_i) ln\hat{S}(M_i|\mathbf{X}_i) + \frac{1}{n}\sum_{i=1}^{n}\delta_i \ln(\hat{S}(M_i - |\mathbf{X}_i) - \hat{S}(M_i|\mathbf{X}_i)) \\ &= \int ln\hat{S}(t|\mathbf{x}) d\hat{F}_n(t,0,\mathbf{x}) + \int \ln(\hat{S}(t-|\mathbf{x}) - \hat{S}(t|\mathbf{x})) d\hat{F}_n(t,1,\mathbf{x}) \geq G_n(\mathrm{S}_0, \beta). \end{aligned} \quad \textbf{(2.2)}$$

$$=> 0 \geq \int ln \frac{s(t|\mathbf{X})}{\hat{s}(t|\mathbf{X})}\, d\hat{F}_n(t,0,\mathbf{x}) + \int ln \frac{s(t-|\mathbf{X}) - s(t|\mathbf{X})}{\hat{s}(t-|\mathbf{X}) - \hat{s}(t|\mathbf{X})}\, d\hat{F}_n(t,1,\mathbf{x}).$$

Let $\mu_n(B) = \int_B \frac{\hat{s}(t|\mathbf{X})}{s(t|\mathbf{X})} d\hat{F}_n(t,0,\mathbf{x})$, .

where B is a measurable set in $\boldsymbol{R}^{p+1}$. To apply Lemma 2,

$$\text{Let } K(t,0,\mathbf{x}) \stackrel{\text{def}}{=} \frac{1}{s(t|\mathbf{X})} \left(\geq \frac{\hat{s}(t|\mathbf{X})}{s(t|\mathbf{X})}\right), \text{ then} \quad \textbf{(2.3)}$$

$$\begin{aligned} \int K(t,0,\mathbf{x}) d\hat{F}_n(t,0,\mathbf{x}) &= \int \frac{1}{s(t|\mathbf{X})} d\hat{F}_n(t,0,\mathbf{x}) \\ &\to \int \frac{1}{s(t|\mathbf{X})} dF(t,0,\mathbf{x}) \quad (\text{as } \omega \in \Omega_0) \\ &= \int \frac{1}{s(t|\mathbf{X})} S(t|\mathbf{x}) dF_C(t)\, dF_{\mathbf{X}}(\mathbf{x}) \quad (by(1.2)); \end{aligned} \quad \textbf{(2.4)}$$

$$\underline{lim}_{n\to\infty}\mu_n(B) = \underline{lim}_{n\to\infty}\int_B \frac{\hat{S}(t|\mathbf{X})}{S(t|\mathbf{X})} d\hat{F}_n(t,0,\mathbf{x}) \quad \textbf{(2.5)}$$

$$= \int_B \underline{lim}_{n\to\infty}\frac{\hat{S}(t|\mathbf{X})}{S(t|\mathbf{X})} dF(t,0,\mathbf{x}) \text{ (by statement (2) of Lemma 2, (2.3)and (2.4))}$$

$$= \int_B \frac{S_*(t|\mathbf{X})}{S(t|\mathbf{X})} dF(t,0,\mathbf{x}) \ \left(= \int_B \frac{S_*(t|\mathbf{X})}{S(t|\mathbf{X})} S(t|\mathbf{x})dF_C(t)dF_{\mathbf{X}}(\mathbf{x}) \quad (see\ Eq.(1.2))\right)$$

$$= \int_B dF_*(t,0,\mathbf{x}) \overset{\text{def}}{=} \mu(B). \quad \textbf{(2.6)}$$

Verify that $\int ln\frac{S(t|\boldsymbol{X})}{\hat{S}(t|\boldsymbol{X})} d\hat{F}_n(t,0,\mathbf{x}) = \int H(\frac{S(t|\boldsymbol{X})}{\hat{S}(t|\boldsymbol{X})})\frac{\hat{S}(t|\boldsymbol{X})}{S(t|\boldsymbol{X})} d\hat{F}_n(t,0,\mathbf{x}),\ \ where$

$$H(t) = tlogt \geq -1/e \text{ for } t > 0 \text{ and } H\left(S(t|\boldsymbol{X})/\hat{S}(t|\boldsymbol{X})\right) \geq -1/e \quad \textbf{(2.7)}$$

$$\underline{lim}_{n\to\infty}\int \frac{S(t|\mathbf{x})}{\hat{S}(t|\mathbf{x})} d\hat{F}_n(t,0,\mathbf{x}) = \underline{lim}_{n\to\infty}\int H(\frac{S(t|\mathbf{x})}{\hat{S}(t|\mathbf{x})})\frac{\hat{S}(t|\mathbf{x})}{S(t|\mathbf{x})} d\hat{F}_n(t,0,\mathbf{x})$$

$$= \underline{lim}_{n\to\infty}\int H(\frac{S(t|\mathbf{X})}{\hat{S}(t|\mathbf{X})})d\mu_n(t,\mathbf{x}) \qquad \text{(see (2.5))}$$

$$\geq \int \underline{lim}_{n\to\infty}H(\frac{S(t|\mathbf{X})}{\hat{S}(t|\mathbf{X})})d\mu(t,\mathbf{x}) \qquad \text{(by (2.6), (2.7) and Corollary 1)}$$

$$= \int \underline{lim}_{n\to\infty}H(\frac{S(t|\mathbf{X})}{\hat{S}(t|\mathbf{X})})\, dF_*(t,0,\mathbf{x}) \qquad \text{(see (2.6))}$$

$$= \int \frac{S(t|\mathbf{X})}{S_*(t|\mathbf{X})} ln\frac{S(t|\mathbf{X})}{S_*(t|\mathbf{X})} dF_*(t,0,\mathbf{x}) \quad \textbf{(2.8)}$$

$$= \int\int \frac{S(t|\mathbf{X})}{S_*(t|\mathbf{X})} ln\frac{S(t|\mathbf{X})}{S_*(t|\mathbf{X})} S_*(t|\mathbf{x})dF_C(t)dF_{\mathbf{x}}(\mathbf{x}) \qquad \text{(by Eq. (1.2))}$$

$$= \int ln\frac{S(t|\mathbf{X})}{S_*(t|\mathbf{X})} dF(t,0,\mathbf{x})$$

Similarly, since $\frac{\hat{S}(t-|\mathbf{X})-\hat{S}(t|\mathbf{X})}{S(t-|\mathbf{X})-S(t|\mathbf{X})} \leq \frac{1}{S(t-|\mathbf{X})-S(t|\mathbf{X})} \overset{\text{def}}{=} K(y,1,\mathbf{x})$ and

$$\int_B K(t,1,\mathbf{x})d\hat{F}_n(t,1,\mathbf{x}) = \int_B \frac{1}{S(t-|\mathbf{X})-S(t|\mathbf{X})} d\hat{F}_n(t,1,\mathbf{x})$$

$$\to \int_B \frac{1}{S(t-|\mathbf{X})-S(t|\mathbf{X})} S_C(t)dF(t|\mathbf{x})dF_X(\mathbf{x}),$$

letting $v_n(B) \overset{\text{def}}{=} \int_B \frac{\hat{S}(t-|\mathbf{X})-\hat{S}(t|\mathbf{X})}{S(t-|\mathbf{X})-S(t|\mathbf{X})} d\hat{F}_n(t,1,\mathbf{x}),$

$$\underline{lim}_{n\to\infty}v_n(B) = \int_B \underline{lim}_{n\to\infty}\frac{\hat{S}(t-|\mathbf{X})-\hat{S}(t|\mathbf{X})}{S(t-|\mathbf{X})-S(t|\mathbf{X})} dF(t,1,\mathbf{x}) \qquad \text{(by statement (2)of Lemma 2)}$$

$$= \int_B \frac{S_*(t-|\mathbf{x})-S_*(t|\mathbf{x})}{S(t-|\mathbf{x})-S(t|\mathbf{x})} dF(t,1,\mathbf{x})$$

$$= \int \sum_t \mathbf{1}((t,\mathbf{x}) \in B) \frac{f_*(t|\mathbf{x})}{f(t|\mathbf{x})} f(t|\mathbf{x}) S_C(t) dF_X(\mathbf{x}) \qquad \text{(see Eq. (1.2))}$$

$$= \int_B 1 dF_*(t,1,\mathbf{x}) \stackrel{\text{def}}{=} v(B). \tag{2.9}$$

Since $\int ln \frac{S(t-|\mathbf{x})-S(t|\mathbf{x})}{\hat{S}(t-|\mathbf{x})-\hat{S}(t|\mathbf{x})} d\hat{F}_n(t,1,\mathbf{x})$

$$= \int H\left(\frac{S(t-|\mathbf{x})-S(t|\mathbf{x})}{\hat{S}(t-|\mathbf{x})-\hat{S}(t|\mathbf{x})}\right) \frac{\hat{S}(t-|\mathbf{x})-\hat{S}(t|\mathbf{x})}{S(t-|\mathbf{x})-S(t|\mathbf{x})} d\hat{F}_n(t,1,\mathbf{x}),$$

$H\left(\frac{S(t-|\mathbf{x})-S(t|\mathbf{x})}{\hat{S}(t-|\mathbf{x})-\hat{S}(t|\mathbf{x})}\right) \geq -\frac{1}{e}$ and v_n converges set wisely to a finite measure v (see (2.9)), by a similar argument as in (2.4), (2.6), (2.7) and (2.8), we have:

$$\underline{lim}_{n\to\infty} \int ln \frac{S(t-|\mathbf{x})-S(t|\mathbf{x})}{\hat{S}(t-|\mathbf{x})-\hat{S}(t|\mathbf{x})} d\hat{F}_n(t,1,\mathbf{x})$$

$$= \underline{lim}_{n\to\infty} \int H\left(\frac{S(t-|\mathbf{x})-S(t|\mathbf{x})}{\hat{S}(t-|\mathbf{x})-\hat{S}(t|\mathbf{x})}\right) \frac{\hat{S}(t-|\mathbf{x})-\hat{S}(t|\mathbf{x})}{S(t-|\mathbf{x})-S(t|\mathbf{x})} d\hat{F}_n(t,1,\mathbf{x})$$

$$\geq \int \underline{lim}_{n\to\infty} H\left(\frac{S(t-|\mathbf{x})-S(t|\mathbf{x})}{\hat{S}(t-|\mathbf{x})-\hat{S}(t|\mathbf{x})}\right) dF_*(t,1,\mathbf{x})$$

$$= \int \ln \frac{f(t|\mathbf{x})}{f_*(t|\mathbf{x})} dF(t,1,\mathbf{x}) \quad \text{(as } Y \text{ is discrete).} \tag{2.10}$$

$$0 \geq \int ln \frac{S(t|\mathbf{x})}{S_*(t|\mathbf{x})} dF(t,0,\mathbf{x}) + \int ln \frac{S(t-|\mathbf{x})-S(t|\mathbf{x})}{S_*(t-|\mathbf{x})-S_*(t|\mathbf{x})} dF(t,1,\mathbf{x}) \text{ (by Eq. (2.2))}$$

$$= \int ln \frac{S(t|\mathbf{x})}{S_*(t|\mathbf{x})} dF(t,0,\mathbf{x}) + \int ln \frac{f(t|\mathbf{x})}{f_*(t|\mathbf{x})} dF(t,1,\mathbf{x}) \quad \text{(by 2.8)and (2.10))}$$

$$\geq 0 \qquad \text{(by Lemma 1, the modified K-L inequality).}$$

Thus, $\int ln \frac{S(t|\mathbf{x})}{S_*(t|\mathbf{x})} dF(t,0,\mathbf{x}) + \int ln \frac{f_*(t|\mathbf{x})}{f(t|\mathbf{x})} dF(t,1,\mathbf{x}) = 0$. Hence, $(S_0(t),\beta) = (S_*(t),\beta) \forall t \in D$ by the 2nd statement of the K-L inequality.

Theorem 3. *Under the Cox model with RC data, if Y is continuous then Eq. (2.1) holds.*

Proof. For the given $\omega \in \Omega$ and (S_*,β_*) in the proof of Theorem 1, as well as $\hat{\beta}(\omega)$ and $\hat{S}(t|\mathbf{x})(\omega)$, we have $S_*(t|\mathbf{x}) = (S_*(t))^{\exp(\beta'\mathbf{x})}$. By a similar argument as in proving Eq. (2.8), we can show:

$$\underline{lim}_{n\to\infty} \int ln \frac{S(t|\mathbf{x})}{\hat{S}(t|\mathbf{x})} d\hat{F}_n(t,0,\mathbf{x}) = \underline{lim}_{n\to\infty} \int H\left(\frac{S(t|\mathbf{x})}{\hat{S}(t|\mathbf{x})}\right) \frac{\hat{S}(t|\mathbf{x})}{S(t|\mathbf{x})} d\hat{F}_n(t,0,\mathbf{x}) \geq \int ln \frac{S(t|\mathbf{x})}{S_*(t|\mathbf{x})} dF(t,0,\mathbf{x}) \tag{2.11}$$

In view of Eq. (1.4) due to Y is continuous, we denote:

$$G(t,\mathbf{x},n) = \frac{\hat{S}(t-\eta_n|\mathbf{x})-\hat{S}(t|\mathbf{x})}{S(t-\eta_n|\mathbf{x})-S(t|\mathbf{x})}, \quad A_k = \{G(t,\mathbf{x},n) \leq k, \forall n\} \text{ and } B_k = A_k \backslash A_{k-1} \tag{2.12}$$

$$G(t,\mathbf{x},n) = \frac{\hat{S}(t-\eta_n|\mathbf{x})-\hat{S}(t|\mathbf{x})}{S(t-\eta_n|\mathbf{x})-S(t|\mathbf{x})} = \frac{\hat{S}(t-\eta_n|\mathbf{x})-\hat{S}(t|\mathbf{x})/\eta_n}{S(t-\eta_n|\mathbf{x})-S(t|\mathbf{x})/\eta_n} \to \frac{F'_*(t|\mathbf{x})}{F'(t|\mathbf{x})} \text{ a.e.,} \tag{2.13}$$

as S_* is a monotone function, S_*' exists a.e., and so do $S_*'(t|\mathbf{x})$ and $F_*'(t|\mathbf{x})$. We have

$$\int \mathbf{1}(\cup_{k\geq 1} B_k)\, dF(t,s,\mathbf{x}) = 1. \qquad \textbf{(2.14)}$$

The reason is as follows. For each $(t, \mathbf{x})$ such that $F'(t|\mathbf{x}) > 0$ and Eq. (2.13) holds, $F_*'(t|\mathbf{x}) / F'(t|\mathbf{x})$ $(= f_*(t|\mathbf{x}) / f(t|\mathbf{x}))$ is finite. Then, there exists n_o such that $G(t, \mathbf{x}, n) < 1 + F_*'(t|\mathbf{x}) / F'(t|\mathbf{x})$ for $n \geq n_o$. On the other hand, $G(t, \mathbf{x}, n)$ is finite for $n = 1, ..., n_o$. Thus, $G(t, \mathbf{x}, n) < k$ for some k. Since Eq. (2.1) holds a.e. and $\int 1 dF(t, s, \mathbf{x}) = 1$, Eq. (2.14) holds.

We shall prove in Lemma 3 that

$$\underline{lim}_{n\to\infty} \int_{B_k} ln \frac{s(t-\eta_n|\mathbf{x}) - s(t|\mathbf{x})}{\hat{s}(t-\eta_n|\mathbf{x}) - \hat{s}(t|\mathbf{x})} d\hat{F}_n(t,1,\mathbf{x}) \geq \int_{B_k} ln \frac{f(t|\mathbf{x})}{f_*(t|\mathbf{x})} dF(t,1,\mathbf{x}) \quad \text{for } k \geq 1. \qquad \textbf{(2.15)}$$

Then,

$$\begin{aligned}
&\underline{lim}_{n\to\infty} \int ln \frac{S(t-\eta_n|\mathbf{x}) - S(t|\mathbf{x})}{\hat{S}(t-\eta_n|\mathbf{x}) - \hat{S}(t|\mathbf{x})}\, d\hat{F}_n(t,1,\mathbf{x}) \\
&= \underline{lim}_{n\to\infty} \int -lnG(t,\mathbf{x},n) d\hat{F}_n(t,1,\mathbf{x}) \\
&= \underline{lim}_{n\to\infty} \textstyle\sum_{k\geq 1} \int_{B_k} -lnG(t,\mathbf{x},n) d\hat{F}_n(t,1,\mathbf{x}) \qquad \text{(by (2.14))} \\
&= \underline{lim}_{n\to\infty} \int_{k\geq 1}\int_{B_k} -lnG(t,\mathbf{x},n) d\hat{F}_n(t,1,\mathbf{x})\, dv(k) \qquad (dv \text{ is a counting measure}) \\
&= \underline{lim}_{n\to\infty} \int_{k\geq 1}\int_{B_k} H((G(t,\mathbf{x},n))^{-1}) G(t,\mathbf{x},n) d\hat{F}_n(t,1,\mathbf{x})\, dv(k) \qquad (H(t) = tlnt) \\
&\geq \int_{k\geq 1} \underline{lim}_{n\to\infty} \int_{B_k} H((G(t,\mathbf{x},n))^{-1}) G(t,\mathbf{x},n) d\hat{F}_n(t,1,\mathbf{x}) dv(k) \qquad (\text{by Corollary 1, as} \\
&\qquad\qquad H(t) \geq -\frac{1}{e} \text{ and } \int_{B_k} \ln(G(t,\boldsymbol{x},n))^{-1} d\hat{F}_n(t,1,\boldsymbol{x}) \quad \text{is bounded below by} - 1/\mathrm{e} \\
&\geq \textstyle\sum_{k\geq 1} \underline{lim}_{n\to\infty} \int_{B_k} -lnG(t,\mathbf{x},n) d\hat{F}_n(t,1,\mathbf{x}) \qquad (\text{ by (2.15)}) \qquad \textbf{(2.16)} \\
&= \sum_{k\geq 1} \int_{B_k} ln \frac{f(t|\mathbf{x})}{f_*(t|\mathbf{x})} dF(t,1,\mathbf{x}) \\
&= \int ln \frac{f(t|\mathbf{x})}{f_*(t|\mathbf{x})} dF(t,1,\mathbf{x})
\end{aligned}$$

Since $\hat{S}(t|\mathbf{x})$ is the SMLE,

$$\begin{aligned}
0 &\geq \underline{lim}_{n\to\infty} \left[\int ln \frac{S(t|\mathbf{x})}{\hat{S}(t|\mathbf{x})} d\hat{F}_n(t,0,\mathbf{x}) + \int ln \frac{S(t-\eta_n|\mathbf{x}) - S(t|\mathbf{x})}{\hat{S}(t-\eta_n|\mathbf{x}) - \hat{S}(t|\mathbf{x})} d\hat{F}_n(t,1,\mathbf{x}) \right] \\
&\geq \int ln \frac{S(t|\mathbf{x})}{S_*(t|\mathbf{x})} dF(t,0,\mathbf{x}) + \int ln \frac{f(t|\mathbf{x})}{f_*(t|\mathbf{x})} dF(t,1,\mathbf{x}) \qquad \text{(by (2.11) and (2.16))} \\
&\geq 0 \qquad \big(\text{by Lemma 1 (the modified K} - \text{L inequality)}\big).
\end{aligned}$$

3. RESULTS

The last inequality further implies that $\int ln \frac{S(t|\mathbf{x})}{S_*(t|\mathbf{x})} d\, F(t,0,\mathbf{x})$ + $\int ln \frac{f(t|\mathbf{x})}{f_*(t|\mathbf{x})} d\, F(t,1,\mathbf{x}) = 0$. Thus, $(S_0(t),\beta) = (S_*(t),\beta_*)\ \forall t \in$ D by the 2nd statement of the K-L inequality and by the assumption ASI.

Lemma 3. Inequality (2.15) holds.

Proof. Let $k \geq 1$ and $\nu_n(B) \overset{\text{def}}{=} \int_{B \cap \mathrm{B}_n} \mathrm{G}_n(t,\mathbf{x},n) d\hat{F}_n(t,1,\mathbf{x})$, where B is a measurable set and $G(t,\mathbf{x},n) = \frac{\hat{s}(t-|\mathbf{x})-\hat{s}(t|\mathbf{x})}{s(t-|\mathbf{x})-s(t|\mathbf{x})} \in [0,k]$ on B_k,

$$\lim_{n\to\infty} \nu_n(B) = \lim_{n\to\infty} \int_{B\cap \mathrm{B}_k} \mathrm{G}_n(t,\mathbf{x},n) d\hat{F}_n(t,1,\mathbf{x})$$
$$= \int_{B\cap \mathrm{B}_k} \lim_{n\to\infty} G(t,\mathbf{x},n) dF(t,1,\mathbf{x}) \quad \text{(by Lemma 2, as } G(t,\mathbf{x},n) \in [0,k])$$
$$= \iint \mathbf{1}((t,\mathbf{x}) \in B\cap \mathrm{B}_k) \frac{f_*(t|\mathbf{x})}{f(t|\mathbf{x})} f(t|\mathbf{x}) \mathrm{S}_c(t) dt F_{\mathbf{x}}(\mathbf{x}) \quad \text{(see Eq. (1.2))}$$
$$= \int_{B\cap \mathrm{B}_k} \mathrm{dF}_*(t,1,\mathbf{x}) \overset{\text{def}}{=} d\nu(B) \quad \text{(see Eq. (1.2))}$$

CONCLUSION

Since $H((S(t\text{-}\eta_n|\mathbf{x}) - (S(t|\mathbf{x}))/((\hat{S}(t\text{-}\eta_n|\mathbf{x}) - (\hat{S}(t|\mathbf{x}))) \geq -1/e$ and v_n converges set wisely to a finite measure v by a similar argument as in (2.4), (2.6), (2.7) and (2.8), we can show that:

$$\underline{lim}_{n\to\infty} \int_{\mathrm{B}_k} ln \frac{S(t-\eta_n|\mathbf{x}) - S(t|\mathbf{x})}{\hat{S}(t-\eta_n|\mathbf{x}) - \hat{S}(t|\mathbf{x})} d\hat{F}_n(t,1,\mathbf{x})$$
$$= \underline{lim}_{n\to\infty} \int_{\mathrm{B}_k} H\left(\frac{s(t-\eta_n|\mathbf{x})-s(t|\mathbf{x})}{\hat{s}(t-\eta_n|\mathbf{x})-\hat{s}(t|\mathbf{x})}\right) \frac{\hat{s}(t-\eta_n|\mathbf{x})-\hat{s}(t|\mathbf{x})}{s(t-\eta_n|\mathbf{x})-s(t|\mathbf{x})} d\hat{F}_n(t,1,\mathbf{x})$$
$$\geq \int_{\mathrm{B}_k} \underline{lim}_{n\to\infty} H\left(\frac{s(t-\eta_n|\mathbf{x})-s(t|\mathbf{x})}{\hat{s}(t-\eta_n|\mathbf{x})-\hat{s}(t|\mathbf{x})}\right) dF_*(t,1,\mathbf{x})$$
$$= \int_{\mathrm{B}_k} ln \frac{f(t|\mathbf{x})}{f_*(t|\mathbf{x})} dF(t,1,\mathbf{x}) \quad \text{for } k \geq 1. \quad \square$$

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