

Confidence Bands for Survival Curve under the Additive Risk Model †

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Abstract

We consider the problem of obtaining several types of simultaneous confidence bands for the survival curve under the additive risk model. The derivation uses the weak convergence of normalized cumulative hazard estimator to a mean zero Gaussian process whose distribution can be easily approximated through simulation. The bands are illustrated by applying them from two well-known clinical studies. Finally, simulation studies are carried out to compare the performance of the proposed bands for the survival function under the additive risk model.

Key Words : Counting process; Additive risk model; Simultaneous confidence band; Hall-Wellner band; Equal-precision band.

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1. INTRODUCTION

The additive risk model(Lin and Ying, 1994) specifies that the hazard function $\lambda(t)$ for the life time T under $Z(t) = z(t)$ has the following form

$$\lambda(t; z) = \lambda_0(t) + \beta_0' z(t), \quad (1.1)$$

where $Z(\cdot)$ is a p -vector of possibly time-varying covariates, β_0 is a p -vector of unknown regression parameters and $\lambda_0(\cdot)$ is an unspecified baseline hazard function. One of the basic problems of practical interest in this model is the construction of confidence bands for the survival function as a function of covariates.

Let T and C denote the failure time and censoring time, respectively. Assume that covariates $Z(\cdot)$ is bounded and T and C are conditionally independent given $Z(\cdot)$. Suppose that the data consists of n independent replicates of $(X, \Delta, Z(\cdot))$, where $X = \min(T, C)$, $\Delta = I(T \leq C)$, and $1 - \Delta$ is the censoring indicator function. Let $N_i(t) = \Delta_i I(X_i \leq t)$ ($i = 1, 2, \dots, n$), be a counting process for the i -th subject, which indicates that the true failure time of the i -th subject is observed up to time t . Under model (1.1), the intensity function for $N_i(t)$ is given by

$$Y_i(t)d\Lambda(t; Z_i) = Y_i(t)\{d\Lambda_0(t) + \beta_0' Z_i(t)dt\},$$

where $Y_i(t)$ is a predictable indicator process indicating whether or not the i -th subject is at risk just before time t , and Λ_0 is the baseline cumulative hazard function.

The counting process $N_i(\cdot)$ can be uniquely decomposed so that for every i and t ,

$$N_i(t) = M_i(t) + \int_0^t Y_i(s)d\Lambda(s; Z_i),$$

where $M_i(\cdot)$ is a local square integrable martingale. Therefore, the natural estimator of Λ_0 is given by

$$\hat{\Lambda}_0(\hat{\beta}, t) = \int_0^t \frac{\sum_{i=1}^n \{dN_i(s) - Y_i(s)\hat{\beta}' Z_i(s)ds\}}{\sum_{j=1}^n Y_j(s)},$$

where $\hat{\beta}$ is a consistent estimator of β_0 . Lin and Ying(1994) proposed the following estimating function

$$U(\beta) = \sum_{i=1}^n \int_0^\infty Z_i(t)\{dN_i(t) - Y_i(t)d\hat{\Lambda}_0(\beta, t) - Y_i(t)\beta' Z_i(t)dt\}$$

and estimated the regression coefficients by solving the equation $U(\hat{\beta}) = 0$.

For predicting survival experience for future subjects under the model (1.1), we are interested in estimating the cumulative hazard function

$$\Lambda(t; z_0) = \int_0^t \lambda(s; z_0) ds$$

and the survival function $S(t; z_0) = e^{-\Lambda(t; z_0)}$ for a subject with a particular set of covariate values $z_0(\cdot)$. By plugging the estimators of $\Lambda_0(t)$ and β_0 , $\Lambda(t; z_0)$ is estimated by

$$\hat{\Lambda}(t; z_0) = \sum_{i=1}^n \int_0^t \frac{\{dN_i(s) - Y_i(s) \hat{\beta}' Z_i(s) ds\}}{\sum_{j=1}^n Y_j(s)} + \hat{\beta}' \int_0^t z_0(s) ds$$

and $S(t; z_0)$ by $\hat{S}(t; z_0) = e^{-\hat{\Lambda}(t; z_0)}$.

In the one sample case without covariates, simultaneous confidence bands for the cumulative hazard function and the survival function have been extensively studied by Hall and Wellner (1980), Nair (1984), Bie, Borgan and Liestøl (1987) and Borgan and Liestøl (1990), and described at great length in the text of Andersen *et al.* (1993). These bands depend on the fact that the normalized Nelson–Aalen estimator or Kaplan–Meier estimator converges weakly to a mean zero Gaussian process which can be transformed to the standard Brownian bridge.

In the additive risk model or the proportional hazards model, where covariates are involved, $n^{\frac{1}{2}} \{\hat{\Lambda}(t; z_0) - \Lambda(t; z_0)\}$ also converges weakly to a mean zero Gaussian process. But in these cases, we cannot construct the simultaneous confidence band for the survival function directly since the limiting distributions cannot be transformed to the standard Brownian bridge. In the proportional hazards model, Burr and Doss (1993) developed simulated–process bands and bootstrap bands for the p th quantile of the distribution of the lifetime of an individual as a function of covariates. Recently, Lin, Fleming and Wei (1994) constructed simultaneous confidence bands for the survival curves by simulating a Gaussian process.

In this paper, we construct simultaneous confidence bands for the survival function under the model (1.1), by using the idea of Lin, Fleming and Wei (1994) in the proportional hazard model. In Section 2, we derive the weak convergence result of the process $n^{\frac{1}{2}} \{\hat{\Lambda}(t; z_0) - \Lambda(t; z_0)\}$. In Section 3, we construct the Hall–Wellner type bands and Equal-Precision type bands for

the survival function. In Section 4, two real data sets are applied to construct the proposed simultaneous confidence bands for the survival function for illustrations. And we compare the coverage probabilities and band widths of the proposed confidence bands through simulation studies.

2. LIMITING DISTRIBUTION

In order to construct simultaneous confidence bands for the survival function under the additive risk model, we, in this section, derive the limiting distribution of the cumulative hazard estimator.

Let

$$L_n(t; z_0) = n^{\frac{1}{2}} \{ \hat{\Lambda}(t; z_0) - \Lambda(t; z_0) \},$$

and

$$\tau = \inf \{ t \geq 0 ; H(t) = 1 \},$$

where $H(\cdot)$ is the distribution function of the observed failure time X_i .

Theorem 1. Let

$$G(t; z_0) = \int_0^t \{ z_0(s) - \bar{Z}(s) \} ds, \quad \bar{Y}(t) = \frac{1}{n} \sum_{j=1}^n Y_j(t)$$

and

$$C^{-1} = \frac{1}{n} \sum_{i=1}^n \int_0^\infty \{ Z_i(s) - \bar{Z}(s) \} Y_i(s) Z_i'(s) ds,$$

where

$$\bar{Z}(t) = \frac{\sum_{i=1}^n Y_i(t) Z_i(t)}{\sum_{j=1}^n Y_j(t)}.$$

Then $L_n(t; z_0)$, $0 \leq t < \tau$, is equivalent to the process $\tilde{L}_n(t; z_0)$, where

$$\begin{aligned} \tilde{L}_n(t; z_0) &= \frac{1}{\sqrt{n}} \sum_{i=1}^n \int_0^t \frac{1}{\bar{Y}(s)} dM_i(s) \\ &\quad + \frac{G'(t; z_0) C'}{\sqrt{n}} \sum_{i=1}^n \int_0^\infty \{ Z_i(s) - \bar{Z}(s) \} dM_i(s). \end{aligned} \quad (2.1)$$

Proof. By the estimator of $\Lambda(t; z_0)$, $L_n(t; z_0)$ can be rewritten as follows;

$$\frac{1}{\sqrt{n}} \sum_{i=1}^n \int_0^t \frac{1}{\bar{Y}(s)} dM_i(s) + \sqrt{n} (\hat{\beta} - \beta_0)' \int_0^t \{z_0(s) - \bar{Z}(s)\} ds.$$

Also, by the Taylor series expansion of $U(\hat{\beta})$ at β_0 , $(\hat{\beta} - \beta_0)$ is of the form

$$(\hat{\beta} - \beta_0) = \frac{C}{n} \sum_{i=1}^n \int_0^\infty \{Z_i(s) - \bar{Z}(s)\} dM_i(s).$$

Hence this completes the proof. \square

In order to derive the limiting distribution of $L_n(t; z_0)$, let us consider the limiting distribution of $\tilde{L}_n(t; z_0)$ in Theorem 2.

Theorem 2. Assume that there exists a function $\bar{y}(t)$ such that, as $n \rightarrow \infty$, $\sup_{0 \leq t < \tau} |\bar{Y}(t) - \bar{y}(t)| \xrightarrow{P} 0$. Then the process $\tilde{L}_n(t; z_0)$ converges weakly to a mean zero Gaussian process on $[0, \tau)$.

Proof. The first term of the right hand side of the equality in equation (2.1) is tight because the two moment inequalities hold in Lemma 1 (Lin *et al.* (1993)). Also, by the law of large numbers, C and $G(t; z_0)$ converge to some nonrandom functions and

$$\frac{1}{\sqrt{n}} \sum_{i=1}^n \int_0^\infty \{Z_i(s) - \bar{Z}(s)\} dM_i(s)$$

converges in distribution, so $\tilde{L}_n(t; z_0)$ is tight. Let

$$H(t, s) = \frac{1}{\sqrt{n}} \left[\frac{I(s \leq t)}{\bar{Y}(s)} + G'(t; z_0) C' \{Z_i(s) - \bar{Z}(s)\} \right],$$

$\tilde{L}_n(t; z_0)$ can be rewritten as

$$\tilde{L}_n(t; z_0) = \sum_{i=1}^n \int_0^\infty H(t, s) dM_i(s). \quad (2.2)$$

Since $\tilde{L}_n(t; z_0)$ is essentially the sum of independent mean zero random variables, it follows from the Lindeberg-Feller theorem and the above tightness result that the process $\tilde{L}_n(\cdot; \cdot)$ converges weakly to a mean zero Gaussian process on $[0, \tau)$. Furthermore, the covariance function of $\tilde{L}_n(t; z_0)$ is given

by

$$\begin{aligned} & \text{Cov} \left[\tilde{L}_n(t_1; z_0), \tilde{L}_n(t_2; z_0) \right] \\ &= \text{E} \left[\int_0^{t_1 \wedge t_2} \frac{\{d\Lambda_0(s) + \beta_0' \bar{Z}(s) ds\}}{\bar{Y}(s)} + G'(t_2; z_0) C' D_1(t_1, \beta_0) \right. \\ & \quad \left. + G'(t_1; z_0) C' D_1(t_2, \beta_0) + G'(t_1; z_0) C' D_2 C G(t_2; z_0) \right], \quad (2.3) \end{aligned}$$

where $t_1 \wedge t_2 = \min(t_1, t_2)$, and

$$D_1(t, \beta) = \sum_{i=1}^n \int_0^t \frac{\{Z_i(s) - \bar{Z}(s)\} Y_i(s) \beta' Z_i(s) ds}{\sum_{j=1}^n Y_j(s)}$$

and

$$D_2 = \frac{1}{n} \sum_{i=1}^n \int_0^\infty \{Z_i(s) - \bar{Z}(s)\}^{\otimes 2} Y_i(s) \{d\Lambda_0(s) + \beta_0' Z_i(s) ds\},$$

where for column vector a , $a^{\otimes 2}$ denotes the outer product aa' . The variance of $\tilde{L}_n(t_1; z_0)$ can be consistently estimated by

$$\begin{aligned} \tilde{\sigma}^2(t; z_0) &= n \int_0^t \frac{d\hat{\Lambda}_0(\hat{\beta}, s) + \hat{\beta}' \bar{Z}(s) ds}{\sum_{j=1}^n Y_j(s)} \\ & \quad + 2 G'(t; z_0) C' D_1(t, \hat{\beta}) + G'(t; z_0) C' \hat{D}_2 C G(t, z_0), \end{aligned}$$

where

$$\hat{D}_2 = \frac{1}{n} \sum_{i=1}^n \int_0^\infty \{Z_i(s) - \bar{Z}(s)\}^{\otimes 2} Y_i(s) \{d\hat{\Lambda}_0(\hat{\beta}, s) + \hat{\beta}' Z_i(s) ds\}.$$

□

By the covariance function of $\tilde{L}_n(t; z_0)$, the process $\tilde{L}_n(\cdot; z_0)$ does not have an independent increment structure asymptotically even if covariates are time invariant. Therefore, the limiting distribution cannot be transformed to the standard Brownian bridge for construction of the confidence band.

We now need to show how to approximate the limiting distribution of the process $n^{-\frac{1}{2}} \tilde{L}_n(\cdot; z_0)$. If we know the stochastic structure of the martingale process $M_l(s)$, we could easily simulate $\tilde{L}_n(\cdot; z_0)$. But the distributional form of $M_l(s)$ is unknown, so one way is to replace $M_l(s)$ with one which has a known distribution (Lin *et al.*(1993)). Since for any t ,

$E[M_l(t)] = 0$, $\text{Var}[M_l(t)] = E[N_l(t)]$, a natural candidate for $M_l(s)$ is $N_l(s)G_l$, with the same first and second moments, where $N_l(s)$ is the observed counting process and $\{G_l ; l = 1, \dots, n\}$ denotes a random sample of standard normal variables. Then we have the representation for $\widehat{L}_n(t; z_0)$ by the definition of counting process $N_i(\cdot)$ as follows;

$$\frac{1}{\sqrt{n}} \sum_{i=1}^n \int_0^\infty \left[\frac{I(s \leq t)}{Y(s)} + G'(t; z_0) C' \{Z_i(s) - \bar{Z}(s)\} \right] dN_i(s) G_i.$$

We regard $\{G_l\}$ ($l = 1, 2, \dots, n$) as random and $\{X_i, \Delta_i, Z_i(\cdot)\}$ ($i = 1, 2, \dots, n$) as fixed in $\widehat{L}_n(\cdot; z_0)$. Therefore we obtain the following Theorem 3.

Theorem 3. The conditional distribution of $\widehat{L}_n(t; z_0)$ given the observed data $\{X_i, \Delta_i, Z_i(\cdot)\}$ ($i = 1, 2, \dots, n$) is the same in the limit as the unconditional distribution of $\widetilde{L}_n(t; z_0)$.

Proof. $\widehat{L}_n(t; z_0)$ can be rewritten as

$$\begin{aligned} \widehat{L}_n(t; z_0) &= \frac{1}{\sqrt{n}} \sum_{i=1}^n \Delta_i \frac{I(X_i \leq t)}{Y(X_i)} G_i \\ &\quad + \frac{1}{\sqrt{n}} \sum_{i=1}^n G'(t; z_0) C' \{Z_i(X_i) - \bar{Z}(X_i)\} \Delta_i G_i, \end{aligned}$$

and the only random components in $\widehat{L}(t, z_0)$ given $\{X_i, \Delta_i, Z_i\}$ are the independent standard normal variables $\{G_i\}$. Thus the proof of the tightness of $\widehat{L}(t, z_0)$ is analogous to that of Theorem 2. Also, by description of $\widetilde{L}_n(t; z_0)$ in (2.2), $\widehat{L}_n(t; z_0)$ can be rewritten as

$$\widehat{L}_n(t; z_0) = \sum_{i=1}^n \int_0^\infty H(t, s) dN_i(s) G_i.$$

Since $\widehat{L}_n(\cdot; z_0)$ is simply the sum of n independent mean zero random variables at each fixed time point, it follows by applying the Lindeberg-Feller theorem and the above tightness result that the process $\widehat{L}_n(\cdot; z_0)$ converges to a mean zero Gaussian process.

Also, the covariance function of $\widehat{L}_n(t; z_0)$ is given by

$$\begin{aligned} &\text{Cov} \left[\widehat{L}_n(t_1; z_0), \widehat{L}_n(t_2; z_0) \mid \{X_i, \Delta_i, Z_i(\cdot)\}, i = 1, 2, \dots, n \right] \\ &= n \sum_{i=1}^n \frac{I(X_i \leq t_1 \wedge t_2) \Delta_i}{(\sum_{j=1}^n Y_j(X_i))^2} \end{aligned}$$

$$\begin{aligned}
& +G'(t_1; z_0) C' \sum_{i=1}^n \frac{I(X_i \leq t_2) \Delta_i}{\sum_{j=1}^n Y_j(X_i)} \{Z_i(X_i) - \bar{Z}(X_i)\} \\
& +G'(t_2; z_0) C' \sum_{i=1}^n \frac{I(X_i \leq t_1) \Delta_i}{\sum_{j=1}^n Y_j(X_i)} \{Z_i(X_i) - \bar{Z}(X_i)\} \\
& +\frac{1}{n} G'(t_2; z_0) C' \sum_{i=1}^n \Delta_i \{Z_i(X_i) - \bar{Z}(X_i)\}^{\otimes 2} C G(t_1, z_0).
\end{aligned}$$

And the covariance function of $\hat{L}_n(t; z_0)$ converges to (2.3) with probability one by the fact that $Y_i(s) \{d\Lambda_0(s) + \beta'_0 Z_i(s) ds\}$ is the intensity function of $N_i(s)$. Furthermore, the variance of $\hat{L}_n(t; z_0)$ is given by

$$\begin{aligned}
\hat{\sigma}^2(t; z_0) &= n \sum_{i=1}^n \frac{I(X_i \leq t) \Delta_i}{(\sum_{j=1}^n Y_j(X_i))^2} \\
& +2G'(t; z_0) C' \sum_{i=1}^n \frac{I(X_i \leq t) \Delta_i}{\sum_{j=1}^n Y_j(X_i)} \{Z_i(X_i) - \bar{Z}(X_i)\} \\
& +\frac{1}{n} G'(t; z_0) C' \sum_{i=1}^n \Delta_i \{Z_i(X_i) - \bar{Z}(X_i)\}^{\otimes 2} C G(t, z_0)
\end{aligned}$$

and this is asymptotically equivalent of $\tilde{\sigma}^2(t; z_0)$. This completes the proof. \square

By the above theorems, $L_n(\cdot; z_0)$ and $\hat{L}_n(\cdot; z_0)$ have the same limiting distribution given the observed data $\{X_i, \Delta_i, Z_i(\cdot)\}$, ($i = 1, 2, \dots, n$). Therefore, we simulate a number of realizations from $\hat{L}_n(\cdot; z_0)$ by repeatedly generating normal random samples $\{G_l\}$ while holding the observed data $\{X_i, \Delta_i, Z_i(\cdot)\}$, ($i = 1, 2, \dots, n$) to approximate the distribution of $L_n(\cdot; z_0)$.

3. CONSTRUCTION OF CONFIDENCE BANDS

For constructing 100(1- α)% confidence bands for $S(\cdot; z_0)$ on $[t_1, t_2]$ ($0 \leq t_1 \leq t_2 < \tau$), it is useful to consider the following process.

$$B(t; z_0) = \sqrt{n} g(t; z_0) [\phi\{\hat{\Lambda}(t; z_0)\} - \phi\{\Lambda(t; z_0)\}],$$

where ϕ is a known function whose derivative ϕ' is continuous and nonzero in the time interval $[t_1, t_2]$ and the weight function $g(\cdot; z_0)$ converges in probability to a nonnegative bounded function uniformly on $[t_1, t_2]$. By the

functional delta-method, the process $B(t; z_0)$ is asymptotically equivalent to the process $\tilde{B}(t; z_0)$ given by

$$\tilde{B}(t; z_0) = g(t, z_0) \phi' \{ \Lambda(t; z_0) \} L_n(t; z_0).$$

And by Theorem 3 the distribution of $\tilde{B}(t; z_0)$ can be approximated by that of $\hat{B}(t; z_0)$ given by

$$\hat{B}(t; z_0) = g(t, z_0) \phi' \{ \hat{\Lambda}(t; z_0) \} \hat{L}_n(t; z_0).$$

Also, the construction of a $100(1 - \alpha)\%$ confidence band requires q_α , the approximated value of the $100(1 - \alpha)$ percentile of the distribution of $\sup \{ B(t; z_0); t_1 \leq t \leq t_2 \}$. q_α is the value satisfying $\Pr \{ \max_{t_1 \leq X_j \leq t_2} | \hat{B}(X_j; z_0) | > q_\alpha \} = \alpha$, the probability being estimated through simulation. Then an approximate $100(1 - \alpha)\%$ confidence band for $\phi \{ \Lambda(t; z_0) \}$ on $[t_1, t_2]$ is

$$\phi \{ \hat{\Lambda}(t; z_0) \} \mp \frac{1}{\sqrt{n}} q_\alpha / g(t; z_0). \tag{3.1}$$

By letting $\phi(x) = x$ and $\phi(x) = e^{-x}$, one may calculate the confidence bands for $S(\cdot, z_0)$, directly. But the resulting band for $\Lambda(\cdot, z_0)$ may include negative values, and that of $S(\cdot, z_0)$ may contain values outside $[0, 1]$. In order to avoid this problem, we choose the log transformation, $\phi(x) = \log x$, which not only restricts the bands for $\Lambda(\cdot, z_0)$ and $S(\cdot, z_0)$ to meaningful range but also improves the attained coverage probabilities in small samples.

The weight function $g(\cdot; z_0)$ affects the relative widths of the band at different time points. We shall consider the two weight functions as

$$g_1(t; z_0) = \frac{\hat{\Lambda}(t; z_0)}{1 + \hat{\sigma}^2(t; z_0)}, \quad g_2(t; z_0) = \frac{\hat{\Lambda}(t; z_0)}{\hat{\sigma}(t; z_0)},$$

which is given by Lin, Fleming and Wei(1994) in the proportional hazards model.

3.1 Hall-Wellner type bands

Let $\phi(x) = \log x$ and $g(\cdot; z_0) = g_1(\cdot; z_0)$ in (3.1), the approximate $100(1 - \alpha)\%$ confidence band for $S(\cdot; z_0)$ is of the form

$$\hat{S}(t; z_0) \exp \left[\pm n^{-\frac{1}{2}} q_{1,\alpha} \{ 1 + \hat{\sigma}^2(t; z_0) \} / \hat{\Lambda}(t; z_0) \right],$$

where $q_{1,\alpha}$ is the critical value associated with $g_1(\cdot; z_0)$. We will denote it by THW band, because the band corresponds to the one sample transformed Hall-Wellner band (Bie, Borgan and Liestøl, 1987).

In the processes $B(t; z_0)$ and $\tilde{B}(t; z_0)$, let

$$\phi(x) = e^{-x} \text{ and } g(t; z_0) = \frac{1}{1 + \hat{\sigma}^2(t; z_0)},$$

then the process $B(t; z_0)$ is rewritten as

$$B_1(t; z_0) \equiv \sqrt{n} \frac{1}{1 + \hat{\sigma}^2(t; z_0)} \left[\hat{S}(t; z_0) - S(t; z_0) \right]$$

and $\tilde{B}(t; z_0)$ is

$$\tilde{B}_1(t; z_0) \equiv -g_1(t; z_0) \log' \{ \Lambda(t; z_0) \} L_n(t; z_0) S(t; z_0).$$

The distribution of $B_1(t; z_0)/S(t; z_0)$ can be approximated by that of $\tilde{B}(t; z_0)$ associated with $\phi(x) = \log x$ and $g(t; z_0) = g_1(t; z_0)$. Thus the resulting $100(1 - \alpha)\%$ confidence band for $S(\cdot; z_0)$ is of the form

$$\hat{S}(t; z_0) \mp n^{-\frac{1}{2}} q_{1,\alpha} \hat{S}(t; z_0) \{1 + \hat{\sigma}^2(t; z_0)\}.$$

We shall call it as HW band, because the band is equivalent to the original one sample Hall-Wellner band (Hall and Wellner, 1980).

3.2 Equal-precision type bands

Let $\phi(x) = \log x$ and $g(\cdot; z_0) = g_2(\cdot; z_0)$ in (3.1), the approximate $100(1 - \alpha)\%$ confidence band for $S(\cdot; z_0)$ is of the form

$$\hat{S}(t; z_0) \exp \left[\pm n^{-\frac{1}{2}} q_{2,\alpha} \hat{\sigma}(t; z_0) / \hat{\Lambda}(t; z_0) \right]$$

where $q_{2,\alpha}$ is the critical value associated with $g_2(\cdot; z_0)$. We will denote it by TEP band, because the band corresponds to the one sample transformed Equal-Precision band (Bie, Borgan and Liestøl, 1987).

In the processes $B(t; z_0)$ and $\tilde{B}(t; z_0)$, let

$$\phi(x) = e^{-x} \text{ and } g(t; z_0) = \frac{1}{\hat{\sigma}^2(t; z_0)},$$

then the process $B(t; z_0)$ is rewritten as

$$B_2(t; z_0) \equiv \sqrt{n} \frac{1}{\hat{\sigma}^2(t; z_0)} \left[\hat{S}(t; z_0) - S(t; z_0) \right]$$

and $\tilde{B}(t; z_0)$ is

$$\tilde{B}_2(t; z_0) \equiv -g_2(t; z_0) \log' \{ \Lambda(t; z_0) \} L_n(t; z_0) S(t; z_0).$$

The distribution of $B_2(t; z_0)/S(t; z_0)$ can be approximated by that of $\hat{B}(t; z_0)$ associated with $\phi(x) = \log x$ and $g(t; z_0) = g_2(t; z_0)$. Thus the resulting $100(1 - \alpha)\%$ confidence band for $S(\cdot; z_0)$ is of the form

$$\hat{S}(t; z_0) \mp n^{-\frac{1}{2}} q_{2, \alpha} \hat{S}(t; z_0) \hat{\sigma}(t; z_0).$$

We shall call it as EP band, because the band is equivalent to the original one sample equal-precision band (Nair, 1984).

Because the approximations tend to be poor for t close to 0 or τ , we shall confine HW type bands between the first and last failure time points. Also, according to the recommendations of Nair (1984) and Bie, Borgan and Liestøl (1987) for the one sample case, we shall restrict the EP type bands to the time interval $[t_1^*, t_2^*]$ such that $\hat{c}_1 = 1 - \hat{c}_2 = 0.05$, where

$$\hat{c}_k = \frac{\hat{\sigma}^2(t_k^*; z_0)}{1 + \hat{\sigma}^2(t_k^*; z_0)} \quad (k = 1, 2).$$

4. NUMERICAL RESULTS

Two data sets are illustrated to construct the proposed confidence bands, which are HW, EP, THW and TEP band.

The first one is a clinical trial to evaluate the efficacy of maintenance chemotherapy for acute myelogenous leukemia (AML). The control (non-maintained) group has 12 remission times with one censored case and the treatment (maintained) group has 11 remission times with four censored case. The only covariate is the group indicator which is denoted as control group or treatment group. In this data, Song *et al.* (1996) showed that the additive risk assumption holds (p -value = 0.627).

Figure 1 shows the proposed 95% confidence bands for the survival function in control group. From Figure 1, it is observed that the lower bound of HW and EP bands are negative after around 30 weeks, but the THW and TEP bands remedy this problem.

For the second example, let us consider Stanford heart transplant data taken from Crowely and Hu (1977). In this data, we only regard age as

covariate and we know that the additive risk model assumption holds by the results of Song *et al.* (1996) (p -value = 0.238).

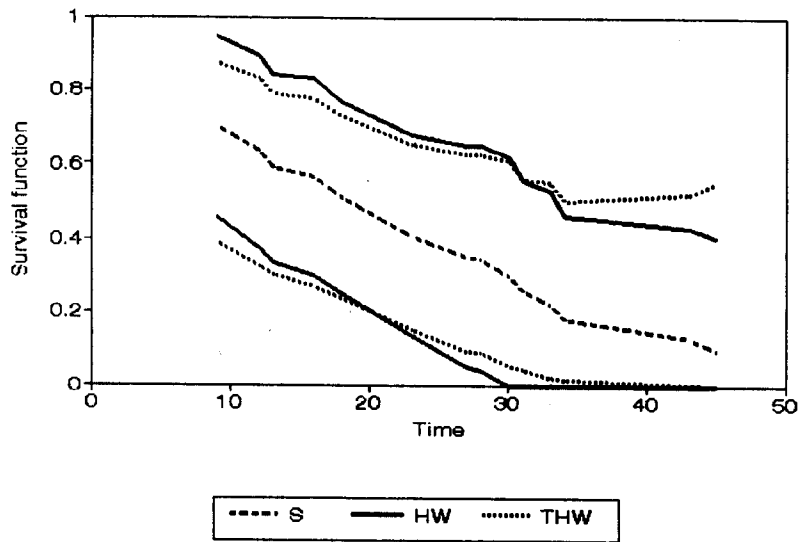
Figure 2 displays the proposed 95% confidence bands for survival function for a patient with 30 years of age. From Figure 2, we can observe that the EP type bands are narrower than HW type bands and the transformed bands narrower than the nontransformed bands for large time. It implies that the EP type bands are more precise than the HW type bands and the transformed bands are more precise than the nontransformed band.

Now, we consider the performances of the proposed confidence bands through the Monte Carlo simulation. The simulation scheme is designed to compare coverage probabilities with a time invariant 0 – 1 covariate Z . The simulated coverage probabilities are estimated from 1000 replications and for each replication, the boundary values $q_{1,\alpha}$ and $q_{2,\alpha}$ are calculated from 1000 realizations of $\hat{B}(\cdot; z_0)$. And, as a censoring distribution, exponential distribution with parameters having censoring rates approximately 10% and 30%, respectively are considered. The results of these simulations are given in Table 1. From Table 1, we can see that all bands tend to achieve the true confidence level as n increase and the coverage probabilities of all bands tend to decrease as the censoring rates increase. In the case of $z = 0$, the performances of the nontransformed bands are better than those of the other bands in the aspect of the coverage probabilities, and in the case of $z = 1$, the performances of all the bands tend to be similar.

Table 1. Empirical coverage probabilities of confidence bands for survival function with $\alpha = 0.05$ under the model $\lambda(t; z) = 1 + 2z$

n	z_0	10% censoring				30% censoring			
		HW	THW	EP	TEP	HW	THW	EP	TEP
30	0	0.95	0.86	0.94	0.83	0.94	0.84	0.92	0.80
	1	0.88	0.91	0.93	0.91	0.84	0.85	0.86	0.83
50	0	0.95	0.88	0.93	0.84	0.94	0.87	0.93	0.83
	1	0.89	0.93	0.91	0.93	0.92	0.93	0.93	0.92
100	0	0.96	0.92	0.96	0.88	0.94	0.90	0.94	0.85
	1	0.94	0.95	0.95	0.94	0.94	0.94	0.94	0.93

(a1) Hall-Wellner type bands



(a2) Equal-precision type bands

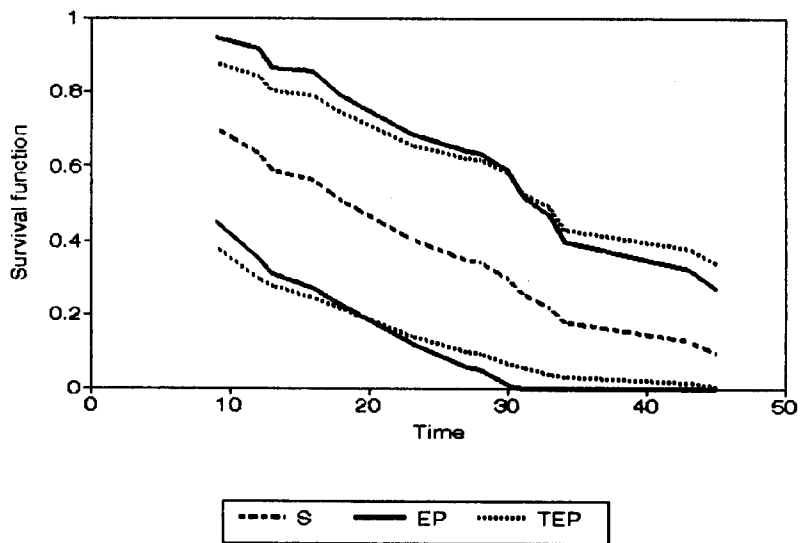
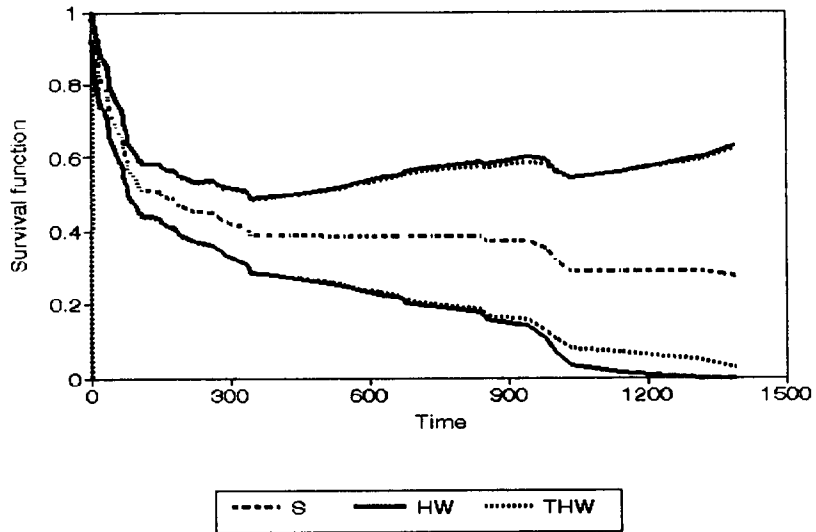


Figure 1. 95% confidence bands for survival function of patients in control group – AML data

(a1) Hall-Wellner type bands



(a2) Equal-precision type bands

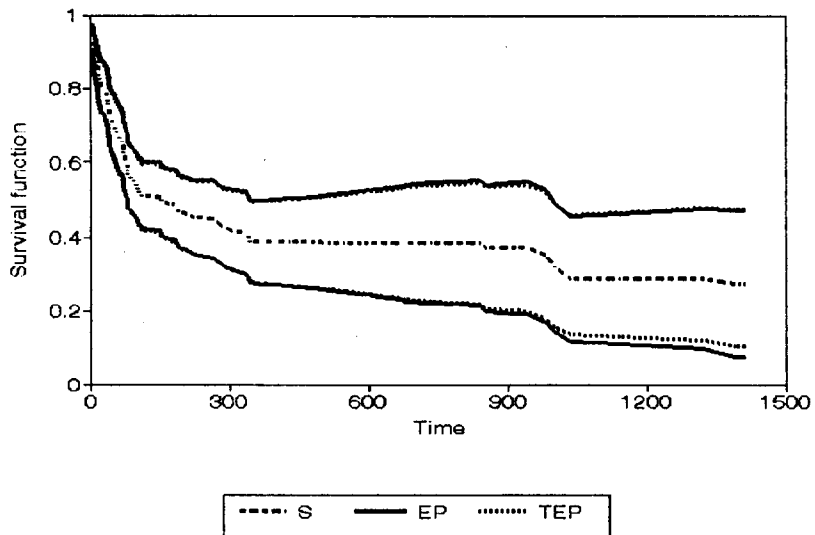


Figure 2. 95% confidence bands for survival function of patients with age 30 – Stanford Heart Transplant data

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