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Empirical Likelihood Confidence Intervals for ROC Curves Under Right Censorship

Hanfang Yang

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Empirical likelihood confidence intervals for ROC curves under right censorship

A Thesis

Presented in Partial Fulfillment of Requirements for the Degree of Master of Science in the College of Arts and Sciences Georgia State University

2010

by

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EMPIRICAL LIKELIHOOD CONFIDENCE INTERVALS FOR ROC CURVES WITH RIGHT CENSORING

by

HANFANG YANG

Under the Direction of Dr. Yichuan Zhao

ABSTRACT

In this thesis, we apply smoothed empirical likelihood method to investigate confidence intervals for the receiver operating characteristic (ROC) curve with right censoring. As a particular application of comparison of distributions from two populations, the ROC curve is constructed by the combination of cumulative distribution function and quantile function. Under mild conditions, the smoothed empirical likelihood ratio converges to chi-square distribution, which is the well-known Wilks's theorem. Furthermore, the performances of the empirical likelihood method are also illustrated by simulation studies in terms of coverage probability and average length of confidence intervals. Finally, a primary biliary cirrhosis data is used to illustrate the proposed empirical likelihood procedure.

INDEX WORDS: Confidence interval, Smoothed empirical likelihood, Right censored data, ROC curves.

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Chapter 1

INTRODUCTION

1.1 ROC curve

In the field of modern medicine, diagnostic tests are used to distinguish diseased group from non-diseased group. In the statistical study, the accuracy of a binary diagnostic test can be measured by its specificity and sensitivity.

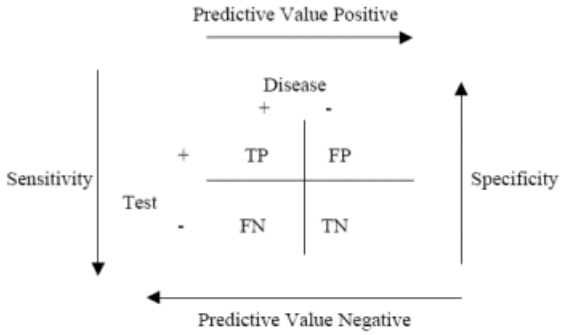

Figure 1: Operating characteristics of diagnostic tests: sensitivity, specificity.

The sensitivity or true positive rate (TPR) of the test is a proportion between diseased patients who are correctly identified and whole diseased patients. The specificity or true negative rate (TNR) of the test refers a proportion that non-diseased patients who are correctly identified and the whole non-diseased patients. The false positive rate (FPR) and false negative rate (FNR) are defined as 1-specificity and 1-sensitivity, respectively. As Figure 1 shows, specificity increases at the expense of sensitivity. The compromise between sensitivity and specificity is accounted for assessing discriminatory accuracy. In general, the receiver op-

erating characteristic (ROC) curve is a plot of sensitivity (TPR) against 1-specificity (FPR), which is a graphical summary of the discriminatory accuracy of a diagnostic test.

To be specific, suppose a continuous statistics $T(X)$ generated from two samples, i.e., diseased patients and non-diseased patients. Let c denote the criterion value of a binary test to be evaluated by the ROC curve.

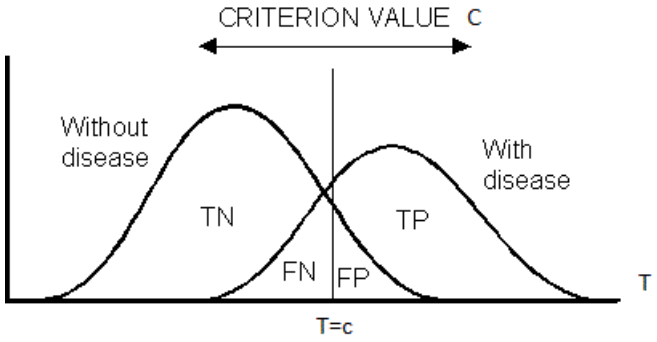

Figure 2: The distributions of the test results overlap.

In Figure 2, the sensitivity is indicated by the area (TP) overlapped by the diseased region and the positive region, where $T \geq c$, and, correspondingly, specificity is defined at the area of non-diseased region and positive region, where $T \leq c$. People are interested in the modification of sensitivity and specificity along criterion value c. Consider true positive function $TPF(c) = Pr(T \geq c \mid Diseased)$ and false positive function $FPF(c) = Pr(T \geq c \mid Non - diseased)$ as the extensions of TPR and FPR. Thus, TPF and FPF are absolutely monotonically increasing when criterion value c increases and have the same ranges within $[0, 1]$. Thus, the ROC curve as a point set can be present by

$$ROC = \{(p, \theta) : FPF(c) = p, TPF(c) = \theta, c \in (-\infty, \infty)\}.$$

Furthermore, due to the absolute monotone property of TPF and FPF, the ROC curve can be revised as a curve of function, from $[0, 1]$ to $[0, 1]$,

$$ROC(p) = \{\theta : FPF(c) = p, TPF(c) = \theta, c \in (-\infty, \infty)\}.$$

Due to the increasing monotone property by sensitivity p, the ROC curve always starts from the left bottom point $(0, 0)$ and ends up at right top point $(1, 1)$, lying on the upper half of diagonal line generally. For instance, Figure 3 demonstrates the typical shape of ROC curve.

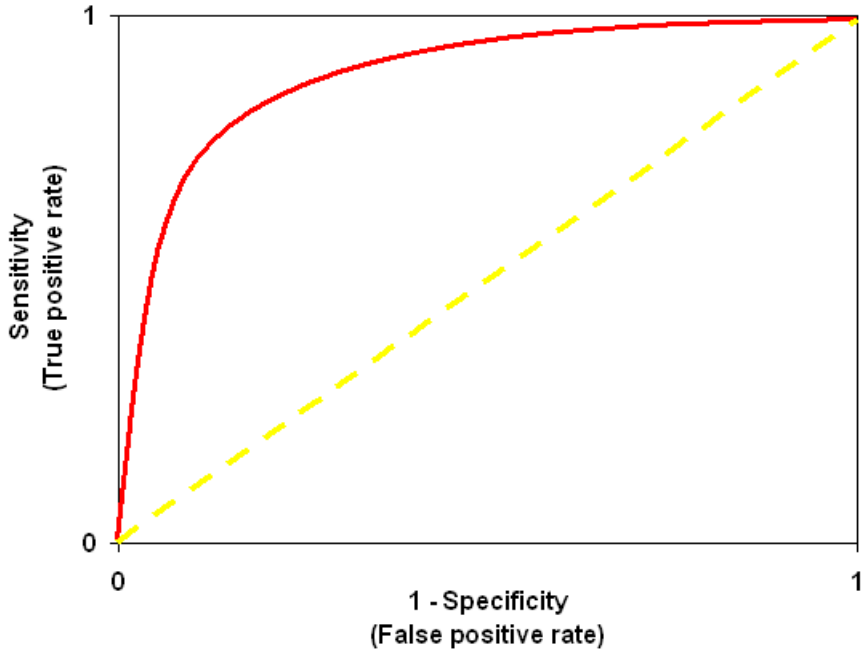

Figure 3: ROC curve: a plot of the true positive rate against the false positive rate.

In addition, the ROC curve of one perfect binary diagnostic test should pass through the left top point $(0, 1)$ since this shape of ROC curve indicates that type 1 error (false positive) and type 2 error (false negative) could not happen absolutely. Thus, the higher the ROC curve, the better efficiency a diagnostic test. This property of the ROC curve addresses a

criterion to evaluate performances of diagnostic tests. At the same time, area under ROC curve (AUC) extends to the maximum value 1, when ROC curve goes through the left top point. Alternatively, the value of AUC is one of popular criteria to compare binary diagnostic tests.

Assuming that cumulative distribution functions of diseased group and non-diseased can be estimated, the ROC curve function can be represented by

$$ROC(p) = 1 - F_D(F_{\bar{D}}^{-1}(1-p)),$$

where F_D and $F_{\bar{D}}$ are cumulative distribution functions of diseased population and non-diseased population, respectively. $F_{\bar{D}}^{-1}$ is the quantile function of non-diseased population, i.e., $F_{\bar{D}}^{-1}(a) = \inf\{c : F_{\bar{D}}(c) \geq a\}$. In this thesis, we develop our procedure based on this pattern of the ROC curve.

In addition to the diagnostic tests, receiver operating characteristic (ROC) curves are widely used in epidemiology and medical research, industrial quality control and signal detection. Furthermore, the ROC curve can be utilized in model optimization and adjustment.

1.2 Empirical Likelihood

In the parametric statistical approach, one assumes the data set follows certain distribution with parameters to be determined. However, in many situations, without enough prior information, there is no reason to suppose that the data follows a certain distribution family. To avoid such a problem, statisticians prefer nonparametric methods rather than parametric

methods. And, empirical likelihood (EL) is one kind of nonparametric method for statistical inference, which employs the maximum likelihood method without having to assume a known distribution family for the data. Empirical likelihood combines the advantages of nonparametric methods and the likelihood methods. Let a sample $X_1, \ldots, X_n \in \mathbb{R}, n \geq 1$ from a cumulative distribution function F_0, empirical cumulative distribution function of $X_1, \ldots, X_n$ is

$$F_n(x) = \frac{1}{n} \sum_{i=1}^{n} 1_{X_i \leq x}, \quad -\infty < x < \infty,$$

and

$$F_n(x-) = \frac{1}{n} \sum_{i=1}^{n} 1_{X_i < x}, \quad -\infty < x < \infty.$$

Generally, given any cumulative distribution function F, the nonparametric likelihood can be defined as

$$L(F) = \prod_{i=1}^{n} \{F(X_i) - F(X_i-)\}.$$

Empirical cumulative distribution function is the maximum nonparametric likelihood estimator of F (Owen 2001), i.e.,

$$L(F_n) = \sup\{L(F) : F \in \mathcal{F}\},$$

where $\mathcal{F}$ is nonparametric cumulative distribution function space. Furthermore, for every nonparametric distribution function F, the likelihood ratio can be defined as

$$R(F) = \frac{L(F)}{L(F_n)},$$

and

$$R(F) = \prod_{i=1}^{n} np_i,$$

where p_i denote the probability of X_i happens. In addition, considering the subspace of $\mathcal{F}$ generated by $\ell = T(F)$, where T is functional mapping from CDF $F \in \mathcal{F}$ to real number ℓ, the profile of the likelihood ratio equation is adjusted as,

$$\mathcal{R}(\ell) = \sup\{R(F) : T(F) = \ell, F \in \mathcal{F}\},$$

where the likelihood ratio $R(F) = L(F)/L(F_n)$. Then, $T(F)$ is normally considered as a statistics method, such as mean or variance. Once a statistics is required to satisfy a certain restriction, like $T(F) = \ell$, we can built up a hypothesis test. In this thesis, two population restriction $T(F_1, F_2) = \ell$ can be specified by $\{1 - F_D(F_{\bar{D}}^{-1}(1-p)) = \theta\}$ or $\{F_1(\eta) = 1 - \theta(p), F_2(\eta) = 1 - p, \eta \in \mathcal{R}\}$, which are introduced in the previous section of ROC curve. Then, a well-known asymptotic theorem, Empirical Likelihood Theorem (ELT) proposed by Owen(1990), i.e.,

$$-2\log(\mathcal{R}(\ell)) \to \chi^2_{(1)}.$$

Relying on this theorem, an empirical likelihood hypothesis test can be established. The null hypothesis, $H_0 : T(F_0) = \ell_0$, should be rejected, when $-2\log(\mathcal{R}(\ell)) > \chi_1^2(\alpha)$. Also, empirical likelihood confidence regions are of the form

$$\{\ell : -2\log(\mathcal{R}(\ell)) \leq \chi_1^2(\alpha)\},$$

where α is confidence level.

1.3 Structure

The thesis is organized as follows. In Chapter 2, we review literatures about ROC curve, empirical likelihood and survival data with right censoring. In Chapter 3, major procedures for empirical likelihood ratio are proposed, including the introduction of data with right censoring, methods to develop smoothed empirical likelihood and asymptotic results of empirical likelihood likelihood ratio. In Chapter 4, simulation studies and analysis are conducted to evaluate empirical likelihood confidence intervals for ROC curves in small and moderate samples in terms of coverage probability and average length of confidence intervals. In Chapter 5, an application of the empirical likelihood procedure is proposed by investigating primary biliary cirrhosis data. General conclusions are summarized in Chapter 6. The list of tables, Splus/R codes and proofs of Empirical Likelihood Theorem are attached in the Appendix.

Chapter 2

LITERATURE REVIEW

Empirical likelihood enables us to make develop the inference without the assumption of a known distribution. Based on this data-driven likelihood, Thomas and Grunkemeier (1975) introduced the EL method to derive point-wise confidence intervals for complete survival data. However, during next 10 years, the EL method was not close to the mainstream research as it was supposed to be, until Owen (1988), (1990) largely extended empirical likelihood method to wide varieties of statistical aspects, especially for the mean of population. Also, empirical likelihood (EL) was recognized by many researchers DiCiccio (1991), DiCiccio and Romano (1989, 1990) as a powerful method, holding lots of unique features, such as range respecting, transformation-preserving, asymmetric confidence interval, Bartlett correctability and the accuracy of coverage probability from Hall (1990) for small sample. Afterward, Li (1995) and Murphy (1995) proposed the EL point-wise confidence intervals for empirical likelihood method with a rigorous proof. As a milestone of EL methods, Owen (2001) has comprehensively and systematically illustrated the theory and application of empirical likelihood methods.

Afterwards, due to great adaption and flexibility, researches on empirical likelihood methods continue to be very active in statistical communities, especially for incomplete data problems. Particularly, according to studies about sample comparison , lots of researchers

employed the empirical likelihood method to compare two samples from a variety of uncomplete data sets, recently. For censored data, the empirical likelihood based Q-Q plot method for comparing two or more censored distribution is developed by Einmahl and McKeague (1999). McKeague and Zhao (2002) obtained simultaneous confidence bands for the ratios of two survival functions; also, McKeague and Zhao (2005) derived empirical likelihood simultaneous confidence band for the ratio and difference of distribution functions, and then Shen and He (2006) derived empirical likelihood confidence intervals for the difference of two survival functions. In the following year, Shen and He (2007) introduced EL method for the difference of quantiles for one sample censored data.

Receiver operating characteristic (ROC) curve originated from signal processing during World War II, and then was utilized in medical diagnostic test. Right now, it plays a critical role in many other areas, such as epidemiology, econometrics, industrial quality control and signal detection. Under the assumption of parametric methods, ROC curve is proposed with strong convergence by Tosteston and Begg (1988). However, due to problems of parametric methods, such as unreasonable assumptions, impractical computation cost, especially, poor covariance estimator from small and moderate sample sizes, more and more researchers concerned the feasibility and efficiency of non-parametric methods dealing with ROC curve problem. Hsieh and Turnbull (1996) started to estimate ROC curve in empirical methods, contributing the foundation of asymptotic properties. Later, statisticians derive smoothing methodologies for ROC curves. Zou, Hall and Shapiro (1997) and Lloyd (1998) constructed a smooth version, a kernel distribution estimator of ROC curve. Then, Lloyd and Yong (1999)

show that the kernel estimator is better than empirical estimator because of smaller mean squared error. Claeskens, Jing, Peng and Zhou (2003) proposed the empirical likelihood confidence intervals for ROC curves, showing that the bandwidth of kernal function needs to be determined. Additionally, Swets and Pickett (1982), Pepe (1997) and Metz, Herman and Shen (1998) illustrate ROC curves and their applications.

However, to the best of my knowledge, few literature has ever proposed empirical likelihood (EL) confidence intervals for the ROC curve with right censoring. In this thesis, we are interested in investigating the formation and asymptotic properties of empirical likelihood ratio related to the ROC curve with right censoring. Also, we investigate this performance of the proposed EL method by simulation studies.

Chapter 3

THEORY AND PROCEDURE

3.1 Right censoring data

Suppose that non-negative failure times T_{ji}, $j = 1, 2$, $i = 1, \ldots, n_j$ are i.i.d. samples with independent two populations, together with corresponding i.i.d. non-negative censoring times, C_{ji}, $j = 1, 2$, $i = 1, \ldots, n_j$. Distribution functions of T_{ji} and C_{ji} are denoted as K_j and G_j, $j = 1, 2$, respectively. Under right censoring, we have the observations for each sample recorded in the form (X_{ji}, δ_{ji}), where $X_{ji} = \min(T_{ji}, C_{ji})$ and $\delta_{ji} = I(T_{ji} \leq C_{ji})$, the indicator of $T_{ji} \leq C_{ji}$. We denote the distribution function of i.i.d random variables T_{ji}, $j = 1, 2$, $i = 1, \ldots, n_j$ by F_j, $j = 1, 2$ throughout the thesis. Then, we suppose that sequences $X_{(j1)} \leq X_{(j2)} \leq \cdots X_{(jn_j)}$ are the ordered statistics of each sample j, and $\delta_{(ji)}$ are consequences accompanying $X_{(ji)}$, and denote $r_{ji} = \sum_{i=1}^{n_j} I(X_{ji} \geq X_{(ji)}) = n_j - i + 1$, $j = 1, 2, i = 1, ..., n_j$.

3.2 Smoothed empirical likelihood ratio

Then, we wish to obtain interval estimator for the ROC curve $\theta(p) = 1 - F_1(F_2^{-1}(1-p))$, where $0 \leq p \leq 1$. The empirical likelihood function is defined by

$$L(F_1, F_2) = \prod_{j=1}^{2} \prod_{i=1}^{n_j} \left[F_j(x_{ji}) - F_j(x_{ji}-)\right]^{\delta_{ji}} \left[1 - F_j(x_{ji})\right]^{1-\delta_{ji}}.$$

From Li (1995), the empirical likelihood function $L(F_1, F_2)$ can be changed as

$$L(F_1, F_2) = \prod_{j=1}^{2} \prod_{i=1}^{n_j} \varphi_{ji}^{\delta_{ji}} (1 - \varphi_{ji})^{(r_{ji} - \delta_{ji})}.$$

where $\varphi_{j1}, \varphi_{j2}, \ldots, \varphi_{jn_j}$ are the hazard values at $X_{(j1)}, X_{(j2)}, \ldots, X_{(jn_j)}$ given by

$$\varphi_{ji} = \frac{F_j(X_{(ji)}) - F_j(X_{(ji)}-)}{1 - F_j(X_{(ji)}-)}.$$

We define the empirical likelihood ratio for $\theta(p)$ as follows

$$R(\theta(p), \eta, p) = \frac{\sup\limits_{\varphi_{ji} \in \Phi} \{L(F_1, F_2) : F_1(\eta) = 1 - \theta(p), F_2(\eta) = 1 - p\}}{\sup\limits_{\varphi_{ji} \in \Phi} L(F_1, F_2)}. \tag{3.1}$$

Without the restriction $F_1(\eta) = 1 - \theta(p), F_2(\eta) = 1 - p$, the supremum of likelihood function is re-expressed as

$$\sup_{\varphi_{ji} \in \Phi} L(F_1, F_2) = \prod_{j=1}^{2} \prod_{i=1}^{n_j} (\varphi_{ji}/r_{ji})^{\varphi_{ji}} (1 - \varphi_{ji}/r_{ji})^{(r_{ji} - \varphi_{ji})}.$$

We rewrite the likelihood function

$$R(\theta(t), \eta, t) = \frac{\sup\limits_{\varphi_{ji} \in \Phi_1} L(F_1, F_2)}{\sup\limits_{\varphi_{ji} \in \Phi} L(F_1, F_2)},$$

where

$$\Phi_1 = \{\varphi \in \Phi : \prod_{X_{1i} \le \eta} (1 - \varphi_{1i}) = \theta, \prod_{X_{2i} \le \eta} (1 - \varphi_{2i}) = p\}.$$

Since it is not easy to maximize $L(F_1, F_2)$ under discrete restriction, we consider the smoothed empirical likelihood ratio version. Noted that $G(t)$ is the smooth distribution function chosen as

$$G(t) = \int_{u \le t} K(u) \mathtt{d}u.$$

Define $G_h(t) = G(t/h)$, where h is a bandwidth. The value of bandwidth and the type of the kernel function need to be specified by statisticians.

After kernel functions involved in the discrete restriction, the restricted condition can be adjusted as

$$\Phi_2 = \{\varphi \in \Phi : \Sigma_{i=1}^{n_1} G_{h_1}(\eta - X_{1i}) \ln(1 - \varphi_{1i}) = \ln \theta, \Sigma_{i=1}^{n_2} G_{h_2}(\eta - X_{2i}) \ln(1 - \varphi_{2i}) = \ln p\}.$$

Then, the empirical likelihood ratio is updated to the smoothed empirical likelihood ratio,

$$\tilde{R}(\theta(p), \eta, p) = \frac{\sup\limits_{\varphi_{ji} \in \Phi_2} L(F_1, F_2)}{\sup\limits_{\varphi_{ji} \in \Phi} L(F_1, F_2)}.$$

For the fixed p, using Lagrange multiplier's method, we are able to obtain the log-likelihood

function,

$$\ln \tilde{R}(\theta, \eta, \lambda_1, \lambda_2) = \sum_{j=1}^{2} \sum_{i=1}^{n_j} (r_{ji} - \delta_{(ji)}) \ln \left(1 + \frac{\lambda_j G_{h_j}(\eta - X_{(ji)})}{r_{ji} - \delta_{(ji)}} \right) - r_{ji} \ln \left(1 + \frac{\lambda_j G_{h_j}(\eta - X_{(ji)})}{r_{ji}} \right), \tag{3.2}$$

where the Lagrange multiplier $\lambda = (\lambda_1, \lambda_2)$ and η have to satisfy,

$$Q_{1n_1} = \sum_{i=1}^{n_1} G_{h_1}(\eta - X_{(1i)}) \ln \left(1 - \frac{\delta_{(1i)}}{r_{1i} + \lambda_1 G_{h_1}(\eta - X_{(1i)})} \right) - \ln \theta = 0, \tag{3.3}$$

$$Q_{1n_2} = \sum_{i=1}^{n_2} G_{h_2}(\eta - X_{(2i)}) \ln \left(1 - \frac{\delta_{(2i)}}{r_{2i} + \lambda_2 G_{h_2}(\eta - X_{(2i)})} \right) - \ln p = 0, \tag{3.4}$$

$$Q_{3n_1n_2} = \sum_{j=1}^{2} \sum_{i=1}^{n_j} \lambda_j G'_{h_j}(\eta - X_{(ji)}) \ln \left(1 - \frac{\delta_{(ji)}}{r_{ji} + \lambda_j G_{h_j}(\eta - X_{(ji)})} \right) = 0. \tag{3.5}$$

Denote the left sides of equations (3.3),(3.4) and (3.5) as Q_{1n_1}, Q_{2n_2} and $Q_{3n_1n_2}$, respectively. These equations are deducted from the procedure that maximizes the log-likelihood function for the Lagrange multiplier $\lambda = (\lambda_1, \lambda_2)$ and intermediate variable η.

3.3 Asymptotic Studies

With the following two conditions $(C1) - (C3)$,

$(C1)$ Let $0 < h_1(\eta), h_2(\eta) < \infty$, here $h_j(\eta) = F'_j(\eta)/(1 - F_j(\eta))$, the $h'_j(x)$ exists and is continuous in neighborhoods of η, respectively, $j = 1, 2$.

$(C2)$ As $n_j \to \infty$, we have $h_j \to 0, n_j h_j \to \infty, n_j h_j^4 \to 0$, $\ln h_j^{-1}/(n_j h_j) \to 0$ and $\ln h_j^{-1} / \ln \ln n_j \to \infty$, $j = 1, 2$.

$(C3)$ The derivative K(t) of $G(t)$ is a bounded nonnegative function having compact support $[-c, c]$, such that

$$\int_{-\infty}^{\infty} u^i K(u)\mathtt{d}u = \begin{cases} 1 & i = 0 \\ 0 & i = 1 \\ C_0 & i = 2, \end{cases}$$

where C_0 is a nonzero constant. The second derivative of $G(t)$ exists.

Theorem 1. *Assuming satisfying* $(C_1) - (C_3)$ *and* $\max\{a_{F_1}, a_{F_2}\} < \eta < min\{b_{F_1}, b_{F_2}\}$ *for every fixed* p*, such that* $\tilde{R}(\theta, \eta)$ *attains maximum value at* (θ_0, η_0)*, and as* $n_j \to \infty$*,* $j = 1, 2$*,* $n_1/(n_1 + n_2) \to \rho_1, 0 < \rho_1 < 1$*,*

$$-2 \ln \tilde{R}(\theta_0(p), \eta_0, p) \xrightarrow{\mathfrak{D}} \chi_1^2.$$

Thus, the asymptotic $100(1 - \alpha)\%$ EL confidence interval for $\theta(p) = ROC(p)$ is

$$I_{n,\alpha}(p) = \left\{\theta(p) : -2 \log R(\theta(p), \eta_0, p) \leqslant \chi_1^2(\alpha)\right\}, \tag{3.6}$$

where $\chi_1^2(\alpha)$ is the upper α-quantile of χ_1^2.

Chapter 4

SIMULATION

4.1 Setting

After proposing the asymptotic theory, we conduct a simulation study to investigate the performance of empirical likelihood confidence interval for the ROC curve with right censoring in terms of coverage accuracy and average length of confidence intervals.

With the objective of investigating ROC curve, we need to generate independent data with right censoring from two distinguished populations. First, we consider two data sets as failure times, which are generated by same distribution family but different parameters. In order to investigate broad patterns of data, we arrange six distributions which are chi-square family with parameter 1 and 2, exponential family with parameter 1 and 1.5 and Weibull family with parameter $(1, 1)$ and $(1, 1.5)$. All of them are widely utilized in survival analysis. In addition, the exponential family is selected to produce censoring time data. Then, combining three failure times data with censoring data respectively, we can obtain three survival data with right censoring, (X_{ji}, δ_{ji}), where $X_{ji} = \min(T_{ji}, C_{ji})$ and $\delta_{ji} = I(T_{ji} \leq C_{ji}), i = 1, ..., n_j, j = 1, 2$. In order to observe the performance of empirical likelihood method under different censoring rates, censoring rates are specified at 10% and 40%. Then, we hold parameters of failure times and carefully calibrate parameters of censoring times. The selected parameters of censoring distribution are represented in Appendix B. In details,

they are located under the survival distributions, such as chi-square, exponential and Weibull distribution. Then, we are ready to explore the simulation with 10% and 40% censoring rates, respectively.

Before further specifying simulation settings, we need to determine the kernel function. Following Shen and He (2006), the Epanechnikov kernel

$$K(u) = \begin{cases} \frac{3}{4}(1-u^2) & \text{if } |u| \leq 1 \\ 0 & \text{otherwise} \end{cases}$$

is utilized, and the smoothing parameter is chosen to be $h = cn^{-1/3}$ which be called bandwidth. The constant c would determine the bandwidth entirely when the sample size is fixed. In order to make the EL method work efficiently, the bandwidth should be selected appropriately. After the calibration, the constant c is selected within the range $[0.1, 10]$ for those three distribution families. The selected parameters of c are shown in Appendix B.

In this simulation, it is unnecessary to demonstrate empirical likelihood ratio asymptotically converges to chi-square at every fixed point from $[0, 1]$. Our simulation only presents the performance of empirical likelihood method at the two specified points $p = 0.2$ and $p = 0.7$. Also, in order to see the performance trend associated with sample sizes, we consider three different small sample sizes, $n = 30, 50$ and 100. Additionally, I need to investigate the condition that two samples sizes differ from each other but are still proportional with each other. Therefore, we arrange all possible combination of data pairs according to three sample sizes, which are totally nine outcomes in Appendix B.

Coverage probabilities are generated by 1000 repetitions. If EL method works well in small sample, the proportion that negative twice log-likelihood ratio fall within 95% confidence interval of chi-square should be close to 0.95, since the coverage probability converges to chi-square asymptotically. Also, ideally, the proportion about 90% confidence interval should be close to 0.90. Finally, results of coverage probability are illustrated from Table 1 to Table 8 in Appendix B.

Furthermore, we need to show the simulation results are reliable by checking their average length. In details, 95% confidence interval for ROC curves can be determined by bisection method, employing Kaplan Meier estimator of θ as initial true positive value (sensitivity). Then, after 1000 repetitions, we can get the average of 1000 differences between every two boundary points of confidence interval, i.e., average length. In addition, when we search the two boundary points by bisection methods, we pick the condition that the initial ROC values are placed within 95% confidence interval since computational costs were saved greatly and the average length does not be influenced. We follow the same settings as coverage probability, where failure time follows Chi-square distribution and censoring time follows exponential distribution. We also need consider simulation results with different sample sizes (30, 50, 100) in order to investigate the effect of sample size to average length. Table 9 and Table 10 in Appendix B demonstrate the simulated average length with different censoring rates 10% and 40%.

4.2 Analysis

The Appendix B includes ten tables about simulation results. The first eight tables illustrate the coverage accuracy at different settings. The last two tables show the result of the average length of 95% confidence intervals under 10% and 40% censoring rates. For instance, Table 1 shows coverage probability of 90% confidence intervals for the ROC curve at $p = 0.2$ with 10% censoring rate. After carefully calibrating the proper bandwidth, we can observe that coverage probability of Table 1 in large samples are placed at the ideal region, which is around 0.90. If we compare the results with distributions of failure times, we can realize the Weibull and exponential family's results are more precise than chi-square family's. It shows that in the small samples the EL methods was influenced by data patterns, more specifically, distribution functions. Then, concerning the impacts of sample sizes, we need compare coverage probabilities at one certain column at Table 1. From Table 1 according to different sample sizes, the performance of EL with large sample size are better than that with the small sample size generally. In summary, from every individual table, we can get a similar result as Table 1, such as acceptable accuracy of coverage probability, slight influence from local data pattern and predictable data trend according to sample size changing.

After investigating within one single Table, we would consider the information cross tables. At first, for example, we set up a comparison between Table 1 and Table 2. Table 2 demonstrates coverage probability of 95% confidence interval for the ROC curve at $p = 0.2$ with 10% censoring rate. In Table 2, we can obtain that coverage probabilities with large sample are around 95% and other similar conclusions as Table 1. It indicates that the

simulated coverage probability does not influenced too much if the confidence level is modified only. Also, it is same as Table 1 that results of Weibull and exponential distributions in Table 2 perform better than that in chi-square distribution.

In addition, if we attempt to investigate the effect of negative false value p, we can carefully compare Table 1 and Table 3. In Table 3, settings were adjusted to 90% confidence level, 10% censoring rate and $p = 0.2$. Even though all coverage probability in Table 3 are close enough to 0.9, chi-square and Weibull distribution operate better. This result varies from Table 1. Also, we find the selected bandwidth in Table 3 is widely different from Table 1. Hence, we can say that the bandwidth has to be selected for every settings individually.

Then, we are interested in the analysis of Table 1 and Table 5 for the effect of censoring rate. With the censoring rate 40%, the performance of chi-square and exponential distribution declines slightly; Weibull distribution's performance maintained at the same level as Table 1. When the censoring rate becomes heavy, accuracies of coverage probabilities are reduced by strong impacts from the censoring time distribution. Finally, we can arrange other similar cross-tables comparisons with varied settings, such as Table 2 versus Table 6 or Table 5 versus Table 7. No matter which two tables are selected, we can obtain similar conclusions as before.

At the end, we investigate simulation results of the average length, showed by Table 9 and Table 10. From either of the two tables, we can clearly obtain the reasonable conclusion that the larger sample size has the narrower average length, even if two sample sizes may be different. Besides, comparing average length with $(n_1, n_2) = (30, 100)$ and the other with

$(n_1, n_2) = (50, 50)$, it could not be determined intuitively whose average length is narrower or wider. Also, there is no general relation between average length and negative false value p. However, comparing Table 9 and Table 10, we can realize performances with 10% censoring rate are constantly better than that with 40% censoring rate. Hence, it shows that 40% censoring rate loses much more information than 10% censoring rate does.

Chapter 5

THE PRIMARY BILIARY CIRRHOSIS (PBC) DATA

The primary biliary cirrhosis (PBC) data was gained from the Mayo Clinic trial between 1974 and 1984. A amount of 424 patients of (PBC) data fulfilled qualification standards in terms of randomized placebo controlled the treatment trial, drug D-penicillamine. The 112 cases did not involve in the clinical trial, but those 112 patients accepted to entered basic measurements and to be followed for survival. Six of them were lost to follow-up after diagnosis shortly. Additional 312 cases in the data set participated in the randomized trial and contain main data. To be conservative, the data selected in the thesis only comprises 312 randomized participants with complete information. 158 patients of those 312 cases obtained D-penicillamine, and other 154 patients were assembled as the placebo. The right censoring rate is extremely high, 187 out of 312. More details and extended discussions can be found in Fleming and Harrington (1991), Dickson, et al., (1989) and Markus, et al., (1989).

We construct the 95% confidence interval of ROC curves in terms of treatment (D-penicillamine) and placebo. To investigate the test of these two sample data with heavy right censoring rate, we implement the procedure introduced previously by empirical likelihood methods with smoothing kernel function. In order to plot the piecewise ROC curve avoiding extreme boundary point, we sperate the interval $[0.1, 0.9]$ to 50 parts equally as all sensitivities. For those levels of sensitivity, we can determine the Kaplan Meier estimator

firstly. Without the known true sensitivity, we use the Kaplan Meier estimator of θ as initial true positive value to set up bisection methods. The bandwidths of kernal functions are selected according to $h = cn^{-1/3}$, which is same as settings in Chapter 4. Then, the bisection method is used to search two numerical roots of the following equation as confidence interval,

$$-2\ln \tilde{R}(\theta, \eta, \lambda_1, \lambda_2) = 1.96^2,$$

under three restrictions $Q_{1n_1} = 0$, $Q_{1n_2} = 0$ and $Q_{3n_1n_2} = 0$. After we obtain the empirical likelihood confidence interval regarding each specificity p, respectively, we can plot point-wise ROC curve.

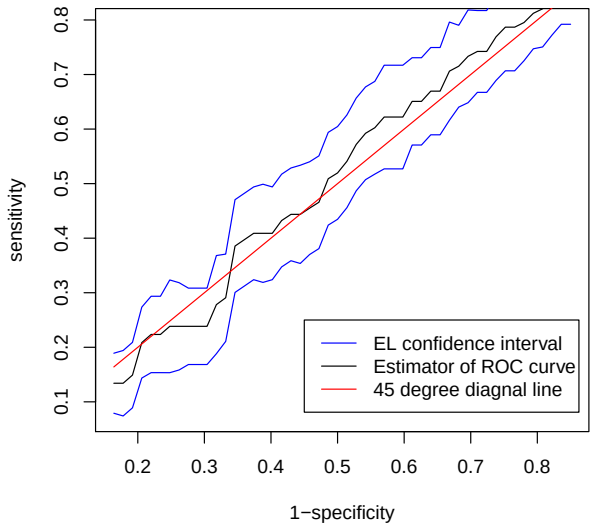

Figure 4: 95% Empirical likelihood confidence interval for ROC curves

Hence, 95% empirical likelihood confidence intervals for the ROC curves are illustrated in Figure 4 above. It can be observed that the green line indicates the upper bound of confidence

interval and blue line shows the lower bound of confidence interval.

Chapter 6

CONCLUSION

The theoretical proof provides the asymptotic property of the empirical likelihood method for the ROC curve under right censoring data. Also, the simulation results demonstrate that coverage probability of EL confidence interval can be very close to ideal results regardless of distribution, location of the ROC curve for even moderate censoring rate. Thus, the smoothing empirical likelihood method can be recognized a feasible procedure for the ROC curve with right censoring.

Because the normal approximation confidence interval for ROC curves with right censoring still needs to be established in the future, our simulation results are lack of enough comparison with alternative methods. Additionally, the optimal selection of bandwidth are still disputable. Without the appropriate calibration, we can not guarantee the selection of bandwidth is the optimal one. Besides, researchers should keep seeking more efficient and precise algorithm to replace bisection method, which costs a number amount of computation resource. Also, a few strange results in the simulation study about coverage probability of different censoring rates maybe enlighten some advanced thinking about the performance in small samples.

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Appendix A

PROOF OF WILKS' THEROM

Lemma A.1. *Assume* $\max\{a_{F_1}, a_{F_2}\} < \eta < min\{b_{F_1}, b_{F_2}\}$ *and the density* $G^{'}(t)$ *of* $G(t)$ *has compact support* $[-c, c]$. $\sup\{L(F_1, F_2)\}$ *subject to restriction* Φ_2 *attained at a unique* φ *with probability one for large n, where*

$$\Phi_2 = \{\varphi \in \Phi : \Sigma_{i=1}^{n_1} G_{h_1}(\eta - X_{(1i)}) \ln(1 - \varphi_{1i}) = \ln\theta, \Sigma_{i=1}^{n_2} G_{h_2}(\eta - X_{(2i)}) \ln(1 - \varphi_{2i}) = \ln p\}.$$

.

Proof. The full version of restrictionj, functions were demonstrated as followings,

$$\begin{cases} \Sigma_{i=1}^{n_1} G_{h_1}(\eta - X_{(1i)}) \ln(1 - \varphi_{1i}) = \ln\theta \\ \Sigma_{i=1}^{n_2} G_{h_2}(\eta - X_{(2i)}) \ln(1 - \varphi_{2i}) = \ln p \\ 0 < \varphi_{1j} < 1, i = 1, ...n_1 \\ 0 < \varphi_{2j} < 1, i = 1, ...n_2 \end{cases} \tag{A.1}$$

Since the equations system can be decomposed as two independent equations, we only show the procedure for one of them,

$$\begin{cases} \Sigma_{i=1}^{n_1} G_{h_1}(\eta - X_{(1i)}) \ln(1 - \varphi_{1i}) = \ln\theta \\ 0 < \varphi_{1i} < 1, i = 1, ...n_1 \end{cases}$$

It is easy to see that $\varphi_1 = (\varphi_{11}, ..., \varphi_{1n_1})$, the solution of restriction functions, exists. Then, define that

$$\omega_i = \frac{G_{h_1}(\eta - X_{(1i)}) \ln(1 - \varphi_{1i})}{\ln \theta}, i = 1, ..., n_1.$$

Due to $0 < \theta < 1$ and $0 < \varphi_{1i} < 1, i = 1, ..., n_1$, ω_i must fall into the interval $[0, 1]$ for $i = 1, ...n_1$. After the transformation based on the definition of ω_i, we can get a compact solution set $\varphi_1 = (\varphi_{11}, ..., \varphi_{1n_1})$,

$$\varphi_{1i} = 1 - \exp\{\frac{\omega_i \ln(\theta)}{G_{h_1}(\eta - X_{(1i)})}\},$$

and

$$0 \leq \varphi_{1i} \leq 1 - \exp\{\frac{\omega_i \ln(\theta)}{G_{h_1}(\eta - X_{(1i)})}\} \leq 1, i = 1, ..., n_1,$$

since $0 \leq \omega_i \leq 1$. Similar results of $\varphi_2 = (\varphi_{21}, ..., \varphi_{2n_2})$ can be obtained also. Then, the subject function,

$$L(F_1, F_2) = \prod_{j=1}^{2} \prod_{i=1}^{n_j} \varphi_{ji}^{\delta_{ji}} (1 - \varphi_{ji})^{(r_{ji} - \delta_{ji})},$$

is a continuous function of $\varphi = (\varphi_1, \varphi_2)$ on closed and compact domain. Therefore, the supremum of likelihood function can be achieved. Then, we investigate the uniqueness of solutions. Assume that two distinct solutions $\varphi^1 = (\varphi_1^1, \varphi_2^1)$ and $\varphi^2 = (\varphi_1^2, \varphi_2^2)$. Then, we construct a set of solutions of equations (A.1) generated by φ^1 and φ^2,

$$\varphi_{ji} = 1 - (1 - \varphi_{ji}^1)^{\lambda} (1 - \varphi_{ji}^2)^{1-\lambda}, \quad i = 1, ..., n_j, \quad j = 1, 2,$$

where $0 < \lambda < 1$. By the inequality

$$1 - x^{\lambda} y^{1-\lambda} > (1-x)^{\lambda}(1-y)^{1-\lambda}, \quad 0 \le x, y \le 1, x \ne y,$$

we can obtain that

$$\varphi_{ji} > (\varphi_{ji}^1)^{\lambda}(\varphi_{ji}^2)^{1-\lambda}.$$

Since we know that

$$1 - \varphi_{ji} = (1-\varphi_{ji}^1)^{\lambda}(1-\varphi_{ji}^2)^{1-\lambda},$$

$$\prod_{j=1}^{2}\prod_{i=1}^{n_j} \varphi_{ji}^{\delta_{ji}}(1-\varphi_{ji})^{(r_{ji}-\delta_{ji})} > (\prod_{j=1}^{2}\prod_{i=1}^{n_j}(\varphi_{ji}^1)^{\delta_{ji}}(1-\varphi_{ji}^1)^{(r_{ji}-\delta_{ji})})^{\lambda}(\prod_{j=1}^{2}\prod_{i=1}^{n_j}(\varphi_{ji}^2)^{\delta_{ji}}(1-\varphi_{ji}^2)^{(r_{ji}-\delta_{ji})})^{1-\lambda},$$

which is

$$L(\varphi) > L(\varphi^1)^{\lambda} L(\varphi^2)^{1-\lambda} = L(\varphi^1)$$

However, this inequality contradict with assumption that $L(\varphi^1)$ achieved the supremum of likelihood function. Hence, the solution is unique.

□

Lemma A.2. *Assume* $\max\{a_{F_1}, a_{F_2}\} < \eta_0 < \min\{b_{F_1}, b_{F_2}\}$ *and conditions* $(C_1) - (C_3)$. *If* $|\eta - \eta_0| \le \varepsilon_n = \min\{\varepsilon_{n_1}, \varepsilon_{n_2}\}$, *where* $\varepsilon_{n_1} = n_1^{-s}$ *and* $\varepsilon_{n_2} = n_2^{-s}, 1/3 < s < 1/2$, $n = n_1 + n_2$ *and* n_1 *and* n_2 *proportional, i.e* $n_1/n_2 \to p > 0$, *then the solution* $\lambda = (\lambda_1(\eta), \lambda_2(\eta))$ *of equations (3.3) and (3.4) satisfy*

$$\lambda_j(\eta)/n_j = O(\epsilon_{n_j}), j = 1, 2.$$

Proof. Let us consider first equation (3.3), $Q_{1n_1}(\eta, \lambda_1) = 0$, where λ_1, λ_2 are the solution of equations (3.3) and (3.4) for every fixed η. By the inequality $|\ln(1-x)-ln(1-y)| \geq |x-y|$, $0 < x, y < 1$, and $\lambda_1(\ln(1 - \frac{\delta_{(1i)}}{\gamma_{1i}+\lambda_1 G_{h_1}(\eta - X_{(1i)})}) - \ln(1 - \delta_{(1i)}/\gamma_{1i})) > 0$,

$$
\begin{aligned}
&\lambda_1(Q_{1n_1}(\eta, \lambda_1) - Q_{1n_1}(\eta, 0)) \\
&= \sum_{i=1}^{n_1} \lambda_1 G_{h_1}(\eta - X_{(1i)})(\ln(1 - \frac{\delta_{(1i)}}{\gamma_{1i} + \lambda_1 G_{h_1}(\eta - X_{(1i)})}) - \ln(1 - \delta_{(1i)}/\gamma_{1i})) \\
&\geq \sum_{i=1}^{n_1} \lambda_1 G_{h_1}(\eta - X_{(1i)})|\frac{\delta_{(1i)}}{\gamma_{1i} + \lambda_1 G_{h_1}(\eta - X_{(1i)})} - \frac{\delta_{(1i)}}{\gamma_{1i}}| \\
&= \lambda_1/n_1 \sum_{i=1}^{n_1} \frac{\lambda_1 n_1 \delta_{(1i)} G_{h_1}^2(\eta - X_{(1i)})}{\gamma_{1i}^2(1 + \frac{\lambda_1}{\gamma_{1i}} G_{h_1}(\eta - X_{(1i)}))} \\
&> \frac{\lambda_1}{n_1} \frac{\lambda_1}{1 + \lambda_1 \max \gamma_{1i}^{-1}} \sum_{i=1}^{n_1} \frac{n_1 \delta_{(1i)} G_{h_1}^2(\eta - X_{(1i)})}{\gamma_{1i}^2} \\
&> \frac{\lambda_1}{n_1} \frac{\lambda_1}{1 + \lambda_1 \max \gamma_{1i}^{-1}} \int_0^\infty G_{h_1}^2(\eta - X_{(1i)}) \mathtt{d}\hat{\sigma_1^2}(\eta) \\
&= \frac{\lambda_1}{n_1} \frac{\lambda_1(\sigma^2(\eta_0) + o(1))}{1 + \lambda_1 \max \gamma_{1i}^{-1}},
\end{aligned} \tag{A.2}
$$

where

$$
\hat{\sigma_1}^2(\eta) = n_1 \sum_{i=1}^{n_1} \frac{\delta_{(i)}}{\gamma_{1i}^2} I(X_{(1i)} \leq \eta),
$$

and

$$
\int_0^\infty G_{h_j}^2(\eta - s) \mathtt{d}\hat{\sigma_j^2}(s) = \sigma^2(\eta_0) + o(1), \quad a.s.
$$

which is represented by Theorem 1 (Csörgo and Horvath, 1983) and Lemma 4.1 (Shen and He, 2007).

Then, considering the Taylor expansion of Q_{1n_1}, we get

$$
\begin{aligned}
& Q_{1n_1}(\eta, 0) \\
&= \sum_{i=1}^{n_1} G_{h_1}(\eta - X_{(1i)}) \ln(1 - \frac{\delta_{(1i)}}{\gamma_{1i}}) - ln(\theta) \\
&= -\sum_{i=1}^{n_1} G_{h_1}(\eta - X_{(1i)}) \frac{\delta_{(1i)}}{\gamma_{1i}} - ln(\theta) + O(n_1^{-1}) \\
&= -\int_0^{\infty} G_{h_1}(\eta - u) \frac{\mathtt{d}H_{1n}(u)}{1 - H_n(u-)} + \int_0^{\eta} \frac{\mathtt{d}F_1(u)}{S_1(u-)} + O(n_1^{-1}) \\
&= -\tilde{\Lambda}_{n_1}(\eta) + \Lambda(\eta_0) + O(n_1^{-1}) \quad a.s. \\
&= O(\varepsilon_{n1}) \quad a.s., \qquad \text{(A.3)}
\end{aligned}
$$

where

$$\tilde{\Lambda}_{n_1}(\eta) = \int_0^{\infty} G_{h_1}^2(\eta - s) \frac{\mathtt{d}H_{1n_1}(s)}{\bar{H}_n(s-)},$$

$$\Lambda(\eta) = \int_0^{\eta} \frac{\mathtt{d}F_1(u)}{S_1(u-)},$$

$$H_{1n}(x) = n^{-1} \sum_{i=1}^{n_1} I\{X_i \leq x, \delta_i = 1\},$$

$$H_n(x) = n^{-1} \sum_{i=1}^{n_1} I\{X_i \leq x\}$$

and

$$\tilde{\Lambda}_{n_1}(\eta) = \Lambda(\eta_0) + O(\varepsilon_{n1})$$

from Lemma 4.1 (Shen and He, 2007). Then, combining the the previous inequalities (A.2)

and (A.3), we can obtain easily

$$\frac{\lambda_1}{n_1} \leq \frac{1+\lambda_1 \max \gamma_{1i}^{-1}}{\lambda_1(\sigma^2(\eta_0)+o(1))}\lambda_1(Q_{1n_1}(\eta,\lambda_1)-Q_{1n_1}(\eta,0)) = \frac{1+\lambda_1 \max \gamma_{1i}^{-1}}{(\sigma^2(\eta_0)+o(1))}O(\varepsilon_{n_1}) = O(\varepsilon_{n_1}). \quad a.s.$$

That is

$$\frac{\lambda_1}{n_1} = O(\varepsilon_{n_1}). \quad a.s.$$

Similarly, from the equation (3.4), $Q_{2n_2}(\eta,\lambda_2)=0$, we can get

$$\frac{\lambda_2}{n_2} = O(\varepsilon_{n_2}). \quad a.s.$$

□

Lemma A.3. *Assume* $\max\{a_{F_1}, a_{F_2}\} < \eta < \min\{b_{F_1}, b_{F_2}\}$ *and conditions* $(C_1)-(C_3)$. *Then, there exists* η_E *to equation (3.5) such that* $R(\theta,\eta)$ *attains its maximum value.*

Proof. Firstly, using Taylor expansion with respect to $\lambda_j, j=1,2$, we consider equation

$$\begin{aligned}
&\ln(1-\frac{\delta_{(ji)}}{\gamma_{ji}+\lambda_j G_{n_j}(\eta-X_{(ji)})}) \\
&= \ln(1-\frac{\delta_{(ji)}}{\gamma_{ji}}(1-\frac{\lambda_j G_{n_j}(\eta-X_{(ji)})}{\gamma_{ji}}+O(\frac{\lambda_j^2\delta_{(ji)}G_{nj}^2(\eta-X_{(ji)})}{\gamma_{ji}^2}))) \\
&= \ln(1-\frac{\delta_{(ji)}}{\gamma_{ji}})+\frac{\delta_{(ji)}}{\gamma_{ji}(\gamma_{ji}-\delta_{(ji)})}\lambda_j G_{nj}(\eta-X_{(ji)})+O(\varepsilon_{n_j}^2/n_j), \quad j=1,2. \qquad (A.4)
\end{aligned}$$

Hence, the equation (3.3) and (3.4), $Q_{1n_1}(\eta,\lambda_1)=0$ and $Q_{2n_2}(\eta,\lambda_2)=0$ can be transformed

by (3) as the following procedures,

$$
\begin{aligned}
&(Q_{1n_1}(\eta,\lambda_1), Q_{2n_2}(\eta,\lambda_2)) \\
&= (Q_{1n_1}(\eta,0), Q_{2n_2}(\eta,0)) + (\lambda_1/n_1, \lambda_2/n_2)\check{\Sigma} + O(\varepsilon_{n_1}^2) + O(\varepsilon_{n_2}^2) \quad a.s. \\
&= (Q_{1n_1}(\eta,0), Q_{2n_2}(\eta,0)) + (\lambda_1/n_1, \lambda_2/n_2)\Sigma + O(\varepsilon_n^2), \quad a.s. \qquad \text{(A.5)}
\end{aligned}
$$

where

$$
\check{\Sigma}(\eta) = \begin{pmatrix} n_1 \sum_{i=1}^{n_1} \frac{\delta_{(1i)}}{\gamma_{1i}(\gamma_{1i}-\delta_{(1i)})} G_{n1}^2(\eta - X_{(1i)}) & 0 \\ 0 & n_2 \sum_{i=1}^{n_2} \frac{\delta_{(2i)}}{\gamma_{2i}(\gamma_{2i}-\delta_{(2i)})} G_{n2}^2(\eta - X_{(2i)}) \end{pmatrix},
$$

and

$$
\Sigma(\eta) = \begin{pmatrix} \int_0^\eta \frac{\mathtt{d}F_1(u)}{1-F_1(u)(1-H_1(u-))} & 0 \\ 0 & \int_0^\eta \frac{\mathtt{d}F_2(u)}{1-F_2(u)(1-H_2(u-))} \end{pmatrix}.
$$

It is also relied on the Greenwood estimate from Andersen et al. (1993). Define that

$$
\check{\sigma}_1^2(\eta) = n_1 \sum_{i=1}^{n_1} \frac{\delta_{(1i)}}{\gamma_{1i}(\gamma_{1i} - \delta_{(1i)})} G_{n1}^2(\eta - X_{(1i)})
$$

and

$$
\sigma_1^2(\eta) = \int_0^\eta \frac{\mathtt{d}F_1(u)}{1 - F_1(u)(1 - H_1(u-))}.
$$

When $|\eta - \eta_0| \leq \epsilon_n = \min\{\epsilon_{n_1}, \epsilon_{n_2}\}$, the smoothed $\sigma_1^2(\eta)$, $\check{\sigma}_1^2(\eta)$, can be represented as

following procedures,

$$
\begin{aligned}
& n_1 \sum_{i=1}^{n_1} \frac{\delta_{(1i)}}{\gamma_{1i}(\gamma_{1i} - \delta_{(1i)})} G_{n1}^2(\eta - X_{(1i)}) \\
&= \int_0^{\infty} G_{h_1}^2(\eta - u) \mathtt{d}\hat{\sigma}_n^2(s) \\
&= \int_0^{\eta} \frac{\mathtt{d}F_1(u)}{1 - F_1(u)(1 - H_1(u-))} + o(1) \quad a.s. \\
&= \sigma_1^2 + o(1) \quad a.s.
\end{aligned}
$$

where

$$
\hat{\sigma}_n^2(s) = n_1 \sum_{i=1}^{n_1} \frac{\delta_{1i}}{\gamma_{1i}(\gamma_{1i} - \delta_{1i})} I(X_{(1i)} \leq s).
$$

Then, we transform the previous equation (A.5) as

$$
(\lambda_1/n_1, \lambda_2/n_2) = -(Q_{1n_1}(\eta, 0), Q_{2n_2}(\eta, 0))\Sigma^{-1} + O(\varepsilon_n^2). \tag{A.6}
$$

Then, we focus on the empirical log likelihood ratio.

$$
\begin{aligned}
&-2\ln R(\eta)\\
&=-\sum_{j=1}^{2}\sum_{i=1}^{n_j}\left((r_{ji}-\delta_{ji})\ln\left(1+\frac{\lambda_j G_{h_j}(\eta-X_{(ji)})}{r_{ji}-\delta_{ji}}\right)-r_{ji}\ln\left(1+\frac{\lambda_j G_{h_j}(\eta-X_{(ji)})}{r_{ji}}\right)\right)\\
&=-\sum_{j=1}^{2}\sum_{i=1}^{n_j}\frac{\delta_{(ji)}}{\gamma_{ji}(\gamma_{ji}-\delta_{(ji)})}G_{nj}^{2}(\eta-X_{(ji)})\lambda_j^2+O(n_1\varepsilon_{n_1}^3)+O(n_2\varepsilon_{n_2}^3)\\
&=(n_1\lambda_1/n_1,n_2\lambda_2/n_2)\check{\Sigma}(\lambda_1/n_1,\lambda_2/n_2)^T+O(n\varepsilon_n^3)\\
&=(n_1Q_{1n_1}(\eta,0),n_2Q_{2n_2}(\eta,0))\check{\Sigma}^{-1}(Q_{1n_1}(\eta,0),Q_{2n_2}(\eta,0))^T+O(n\varepsilon_n^3)\\
&=(n_1Q_{1n_1}(\eta_0,0)+n_1\check{\tau}_1(\eta')\varepsilon_{n_1},n_2Q_{2n_2}(\eta_0,0)+n_2\check{\tau}_2(\eta')\varepsilon_{n_2})\check{\Sigma}^{-1}(Q_{1n_1}(\eta_0,0)\\
&\quad+\check{\tau}_1(\eta')\varepsilon_{n_1},Q_{2n_2}(\eta_0,0)+\check{\tau}_2(\eta')\varepsilon_{n_2})^T+O(n\varepsilon_n^3),
\end{aligned}
$$

where $\eta' \in (\eta_0,\eta)$

$$\check{\tau}_j(\eta)=-\sum_{i=1}^{n_j}\ln(1-\delta_{ji}/\gamma_{ji})G_{h_j}'(\eta-X_{(ji)}),$$

and we know $|\check{\tau}_j(\eta')-\tau(\eta_0)|\longrightarrow 0$ a.s. by (Diehl and Stute, 1988).

By (Csörgo and Horvath, 1983), note that

$$Q_{jn_j}(\eta_0,0)=\tilde{\Lambda}_{n_j}(\eta_0)-\Lambda_{n_j}(\eta_0)+O(n^{-1})=o(\varepsilon_{n_j}).$$

So we can simplify

$$-2\ln R(\eta) = O(n_1\varepsilon_{n_1}^2) + o(n_2\varepsilon_{n_2}^2) + O(n\varepsilon_n^3) = O(n\varepsilon_n^2).$$

On the other hand,

$$-2\ln R(\eta_0) = (n_1 Q_{1n_1}(\eta_0, 0), n_2 Q_{2n_2}(\eta_0, 0))\check{\Sigma}^{-1}(Q_{1n_1}(\eta_0, 0), Q_{2n_2}(\eta_0, 0))^T + O(n\varepsilon_n^3)$$

$$= o(n\varepsilon_n^2) + O(n\varepsilon_n^3) = o(n\varepsilon_n^2).$$

Hence, when n_1 and n_2 are large enough, $-2\ln R(\eta) \geq -2\ln R(\eta_0)$, where $|\eta - \eta_0| \leq \epsilon_n$. That means that $-2\ln R(\eta)$ can attain minimum value at η_E. □

Proof of Theorem 1:

Proof. Now, we are ready to demonstrate the main procedure to prove Theorem 1. Firstly, We define $\beta_1 = \lambda_1/n_1$, $\beta_2 = \lambda_2/n_2$ and Jacobian matrix of equations Q_1, Q_2 and Q_3,

$$\hat{S}_n(\eta_0) = \frac{\partial(Q_{1n_1}Q_{2n_2}Q_{3n})}{\partial(\eta, \beta_1, \beta_2)}|_{(\eta_0,0,0)}$$
$$= \begin{pmatrix} -\check{\tau}_1(\eta_0) & \check{\sigma}_1^2(\eta_0) & 0 \\ -\check{\tau}_2(\eta_0) & 0 & \check{\sigma}_2^2(\eta_0) \\ 0 & -n_1\check{\tau}_1(\eta_0) & -n_2\check{\tau}_2(\eta_0) \end{pmatrix},$$

where $\check{\tau}_j$ and $\check{\sigma}_j$, $j = 1, 2$ are defined the same as before.

By Taylor expansion, we can obtain

$$\begin{pmatrix} Q_{1n_1}(\eta_E,\lambda_1,\lambda_2) \\ Q_{2n_2}(\eta_E,\lambda_1,\lambda_2) \\ Q_{3n}(\eta_E,\lambda_1,\lambda_2) \end{pmatrix} = \begin{pmatrix} Q_{1n_1}(\eta_0,0,0) \\ Q_{2n_2}(\eta_0,0,0) \\ Q_{3n}(\eta_0,0,0) \end{pmatrix} + \hat{S}_n(\eta_0) \begin{pmatrix} \eta_E-\eta_0 \\ \beta_1 \\ \beta_2 \end{pmatrix} + O(\varepsilon_n^2), \quad a.s. \quad \text{(A.7)}$$

Then, since left side of the equation equals to zero, the equation can be rewritten as follows,

$$\begin{pmatrix} \eta_E-\eta_0 \\ \beta_1 \\ \beta_2 \end{pmatrix} = -\hat{S}_n^{-1}(\eta_0) \begin{pmatrix} Q_{1n_1}(\eta_0,0,0) \\ Q_{2n_2}(\eta_0,0,0) \\ Q_{3n}(\eta_0,0,0) \end{pmatrix} + O(\varepsilon_n^2), \quad a.s.$$

where

$$\hat{S}_n^{-1} = \frac{1}{Det(\hat{S}_n)} \begin{pmatrix} n_1\check{\tau}_1(\eta_0)\check{\sigma}_2^2(\eta_0) & n_2\check{\sigma}_1^2(\eta_0)\check{\tau}_2(\eta_0) & \check{\sigma}_1^2(\eta_0)\check{\sigma}_2^2(\eta_0) \\ -n_2\check{\tau}_2^2(\eta_0) & n_2\check{\tau}_2(\eta_0)\check{\tau}_1(\eta_0) & \check{\tau}_1(\eta_0)\check{\sigma}_2^2(\eta_0) \\ n_1\check{\tau}_2(\eta_0)\check{\tau}_1(\eta_0) & -n_1\check{\tau}_1^2(\eta_0) & \check{\sigma}_1^2(\eta_0)\check{\tau}_2(\eta_0) \end{pmatrix},$$

and

$$Det(\hat{S}_n) = -n_1\check{\tau}_1^2(\eta_0)\check{\sigma}_2^2(\eta_0) - n_2\check{\sigma}_1^2(\eta_0)\check{\tau}_2^2(\eta_0).$$

By Andersen et al. (1993), Stute (1982), Shen and He (2007), when $n_j h^4 \to 0$, we know

$$n_j^{1/2} Q_{jn_j}(\eta_0,0,0) \xrightarrow{\mathfrak{D}} N\left(0,\sigma_j^2(\eta_0)\right), \quad j=1,2.$$

Then, applying these results and $\check{\sigma}_j \xrightarrow{\mathfrak{D}} \sigma_j$, $\check{\tau}_j \xrightarrow{\mathfrak{D}} \tau_j, j = 1, 2$, on Q_{1n_1}, Q_{2n_2} , we can obtain two independent normal distributions when $n_j h^4 \to 0, j = 1, 2$ and $n_1/n_2 \to p$, as follows,

$$
\begin{aligned}
&(-\check{\tau}_2^2\sqrt{n_1}Q_{1n_1}(\eta_0,0,0) + \frac{\sqrt{n_1}\check{\tau}_2\check{\tau}_1}{\sqrt{n_2}}\sqrt{n_2}Q_{2n_2}(\eta_0,0,0))^2 \\
&\xrightarrow{\mathfrak{D}} (N\left(0,\tau_2^4\sigma_1^2\right) + \sqrt{p}N\left(0,\tau_2^2\tau_1^2\sigma_2^2\right))^2 \\
&= (N\left(0,\tau_2^4\sigma_1^2 + p\tau_2^2\tau_1^2\sigma_2^2\right))^2 \\
&= \tau_2^2(\tau_2^2\sigma_1^2 + p\tau_1^2\sigma_2^2)\chi_1^2.
\end{aligned}
$$

By the condition of Theorem 1, $\varepsilon_{n_1} = n_1^{-s}$ and $\varepsilon_{n_2} = n_2^{-s}, 1/3 < s < 1/2$, we know $O(n\varepsilon_n^4) + O(\varepsilon_n^2) = O(n\varepsilon_n^4) = o(1)$.

$$
\begin{aligned}
&\frac{\lambda_1^2}{n_1} = \frac{n_1}{Det(\hat{S}_n)^2}(-n_2\check{\tau}_2^2(\eta_0)Q_{1n_1}(\eta_0,0,0) + n_2\check{\tau}_2(\eta_0)\check{\tau}_1(\eta_0)Q_{2n_2}(\eta_0,0,0))^2 + O(n\varepsilon_n^4) + O(\varepsilon_n^2) \\
&= \frac{n_1}{(-n_1\check{\tau}_1^2\check{\sigma}_2^2 - n_2\check{\sigma}_1^2\check{\tau}_2^2)^2}(\frac{-n_2\check{\tau}_2^2}{\sqrt{n_1}}\sqrt{n_1}Q_{1n_1}(\eta_0,0,0) + \frac{n_2\check{\tau}_2\check{\tau}_1}{\sqrt{n_2}}\sqrt{n_2}Q_{2n_2}(\eta_0,0,0))^2 + O(n\varepsilon_n^4) \\
&= \frac{n_2^2}{(-n_1\check{\tau}_1^2\check{\sigma}_2^2 - n_2\check{\sigma}_1^2\check{\tau}_2^2)^2}(-\check{\tau}_2^2\sqrt{n_1}Q_{1n_1}(\eta_0,0,0) + \frac{\sqrt{n_1}\check{\tau}_2\check{\tau}_1}{\sqrt{n_2}}\sqrt{n_2}Q_{2n_2}(\eta_0,0,0))^2 + O(n\varepsilon_n^4) \\
&\xrightarrow{\mathfrak{D}} \frac{1}{(p\tau_1^2\sigma_2^2 + \sigma_1^2\tau_2^2)^2}\tau_2^2(\tau_2^2\sigma_1^2 + p\tau_1^2\sigma_2^2)\chi_1^2 \\
&= \frac{1}{(p\tau_1^2\sigma_2^2 + \sigma_1^2\tau_2^2)}\tau_2^2\chi_1^2.
\end{aligned}
$$

From the equation (A.7), we obtain the equation as follows,

$$-n_1\check{\tau}_1(\eta_0)\beta_1 - n_2\check{\tau}_2(\eta_0)\beta_2 = O(\varepsilon_n^2),$$

and

$$\frac{\check{\tau}_1(\eta_0)}{\check{\tau}_2(\eta_0)} = -\frac{\lambda_2}{\lambda_1} + O(n^{-1}\varepsilon_n).$$

Finally, we have

$$\begin{aligned}
& -2\ln R(\eta_E) \\
&= \frac{\lambda_1^2}{n_1}\check{\sigma}_1^2(\eta_E) + \frac{\lambda_2^2}{n_2}\check{\sigma}_2^2(\eta_E) + O(n\varepsilon_n^3) \\
&= \frac{\lambda_1^2}{n_1}\check{\sigma}_1^2(\eta_E)(1 + \frac{\lambda_2^2 n_1\check{\sigma}_2^2(\eta_E)}{n_2\lambda_1^2\check{\sigma}_1^2(\eta_E)}) + O(n\varepsilon_n^3) \\
&= \frac{\lambda_1^2}{n_1}\check{\sigma}_1^2(\eta_E)(1 + \frac{\check{\tau}_1^2 n_1\check{\sigma}_2^2(\eta_E)}{n_2\check{\tau}_2^2\check{\sigma}_1^2(\eta_E)}) + o(1) \\
&\xrightarrow{\mathfrak{D}} \sigma_1^2\frac{1}{(p\tau_1^2\sigma_2^2 + \sigma_1^2\tau_2^2)}\tau_2^2\chi_1^2\frac{(\tau_2^2\sigma_1^2 + \tau_1^2 p\sigma_2^2)}{\tau_2^2\sigma_1^2} \quad a.s. \\
&= \chi_1^2 \quad a.s.
\end{aligned}$$

□

Appendix B

SIMULATION RESULTS

Table 1: 90% coverage probability for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$ with 10% censoring rate at point $p = 0.2$.

n_1	n_2	$chi-square$	$exponential$	$Weibull$
30	30	0.873 (4)	0.915 (4.5)	0.919(0.5)
50	50	0.915 (4)	0.916(4.5)	0.866(0.5)
100	100	0.907 (4)	0.895(4.5)	0905(0.5)
survival time		chi-square $1, 2$	exponential $1, 1.5$	Weibull $1, 1.5$
censoring time		exponential $0.1, 0.05$	exponential $0.11, 0.15$	exponential $0.1, 0.075$

Table 2: 95% coverage probability for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$ with 10% censoring rate at point $p = 0.2$.

n_1	n_2	$chi-square$	$exponential$	$Weibull$
30	30	0.965 (4)	0.958 (4.5)	0.924(0.5)
50	50	0.956 (4)	0.960(4.5)	0.956(0.5)
100	100	0.958 (4)	0.956(4.5)	0.943(0.5)
survival time		chi-square $1, 2$	exponential $1, 1.5$	Weibull $1, 1.5$
censoring time		exponential $0.1, 0.05$	exponential $0.11, 0.15$	exponential $0.1, 0.075$

Table 3: 90% coverage probability for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$ with 10% censoring rate at point $p = 0.7$.

n_1	n_2	$chi-square$	$exponential$	$Weibull$
30	30	0.931 (1.6)	0.925 (10)	0.912(5.5)
50	50	0.925 (1.6)	0.921(10)	0.893(5.5)
100	100	0.905 (1.6)	0.908(10)	0.906(5.5)
survival time		chi-square $1, 2$	exponential $1, 1.5$	Weibull $1, 1.5$
censoring time		exponential $0.1, 0.05$	exponential $0.11, 0.15$	exponential $0.1, 0.075$

Table 4: 95% coverage probability for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$ with 10% censoring rate at point $p = 0.7$.

n_1	n_2	$chi-square$	$exponential$	$Weibull$
30	30	0.965 (1.6)	0.965 (10)	0.966(5.5)
50	50	0.965 (1.6)	0.963(10)	0.954(5.5)
100	100	0.959 (1.6)	0.955(10)	0.952(5.5)
survival time		chi-square $1, 2$	exponential $1, 1.5$	Weibull $1, 1.5$
censoring time		exponential $0.1, 0.05$	exponential $0.11, 0.15$	exponential $0.1, 0.075$

Table 5: 90% coverage probability for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$ with 40% censoring rate at point $p = 0.2$.

n_1	n_2	$chi-square$	$exponential$	$Weibull$
30	30	0.921(10)	0.892 (0.5)	0.891(1.5)
50	50	0.903 (10)	0.914(0.5)	0.896(1.5)
100	100	0.892 (10)	0.910(0.5)	0.905(1.5)
survival time		chi-square $1, 2$	exponential $1, 1.5$	Weibull $1, 1.5$
censoring time		exponential $0.95, 0.35$	exponential $0.67, 1$	exponential $0.7, 0.45$

Table 6: 95% coverage probability for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$ with 40% censoring rate at point $p = 0.2$.

n_1	n_2	$chi-square$	$exponential$	$Weibull$
30	30	0.948 (10)	0.924 (0.5)	0.961(1.5)
50	50	0.937 (10)	0.943(0.5)	0.958(1.5)
100	100	0.938 (10)	0.944(0.5)	0.953(1.5)
survival time		chi-square $1, 2$	exponential $1, 1.5$	Weibull $1, 1.5$
censoring time		exponential $0.95, 0.35$	exponential $0.67, 1$	exponential $0.7, 0.45$

Table 7: 90% coverage probability for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$ with 40% censoring rate at point $p = 0.7$.

n_1	n_2	$chi-square$	$exponential$	$Weibull$
30	30	0.934 (7)	0.874 (0.08)	0.924(0.15)
50	50	0.921 (7)	0.886(0.08)	0.915(0.15)
100	100	0.896 (7)	0.893(0.08)	0.919(0.15)
survival time		chi-square $1, 2$	exponential $1, 1.5$	Weibull $1, 1.5$
censoring time		exponential $0.95, 0.35$	exponential $0.67, 1$	exponential $0.7, 0.45$

Table 8: 95% coverage probability for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$ with 40% censoring rate at point $p = 0.7$.

n_1	n_2	$chi-square$	$exponential$	$Weibull$
30	30	0.970 (7)	0.905 (0.08)	0.962(0.15)
50	50	0.963 (7)	0.923(0.08)	0.961(0.15)
100	100	0.949 (7)	0.919(0.08)	0.952(0.15)
survival time		chi-square $1, 2$	exponential $1, 1.5$	Weibull $1, 1.5$
censoring time		exponential $0.95, 0.35$	exponential $0.67, 1$	exponential $0.7, 0.45$

Table 9: Average length for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$, chi-square distribution with 10% censoring rate.

points	n_1	n_2	95%C.I.
	30	30	0.1422
	30	50	0.1428
	50	30	0.1165
	50	50	0.1175
	30	100	0.1438
0.2	100	30	0.0982
	50	100	0.1118
	100	50	0.0963
	100	100	0.0932
	30	30	0.1467
	30	50	0.1201
	50	30	0.1435
0.7	50	50	0.1161
	30	100	0.0900
	100	30	0.1345
	50	100	0.0807
	100	50	0.1003
	100	100	0.0687

Table 10: Average length for $ROC(p) = 1 - F_1(F_2^{-1}(1-p))$, chi-square distribution with 40% censoring rate.

points	n_1	n_2	95%C.I.
	30	30	0.2280
	30	50	0.2354
	50	30	0.1938
	50	50	0.1913
0.2	30	100	0.2552
	100	30	0.1868
	50	100	0.2046
	100	50	0.1849
	100	100	0.173
	30	30	0.4345
	30	50	0.3771
	50	30	0.4014
0.7	50	50	0.3383
	30	100	0.3298
	100	30	0.3952
	50	100	0.2944
	100	50	0.3071
	100	100	0.2489

Appendix C

R CODE OF COVERAGE PROBABILITY

```
 library(rootSolve)
library(survival)
#testchi<-function(t,cc,R,n1,n2,distribution)
testchi<-function(t,n1,n2,R,distribution,censor)
{
cc=1
k=0
pp=0
l=1
eta1=-0.5
eta2=0.5
####### no. of iterations #######
eta.string=rep(0,R)
rho1.string=rep(0,R)
rho2.string=rep(0,R)
chi.string=rep(0,R)
count=rep(0,length(cc))
```

```
count90=rep(0,length(cc))
while (k<R)    ######### repeat 1000 times ########## {
{
difference.estimate=0
difference.likelihood=0
### True Value ###
if (distribution==1)
theta<-1-pchisq(qchisq(1-t, 2),1 )
if (distribution==2)
theta<-1-pexp(qexp(1-t, 1.5),1 )
if (distribution==3)
theta<-1-pweibull(qweibull(1-t,1,1.5),1,1)
kernal1<-function(u)
{n1<-length(u)
 temp<-rep(0, n1)
  for (i in 1:n1)
 {
  if (abs(u)[i]<=abs(h1))
   temp[i]<-3/(4*h1)*(1-u[i]^2/h1^2)
 }
return(temp)
```

```
}
kernal2<-function(u)
{
n2<-length(u)
 temp<-rep(0, n2)
  for (i in 1:n2)
 {
  if (abs(u)[i]<=abs(h2))
   temp[i]<-3/(4*h2)*(1-u[i]^2/h2^2)
 }
return(temp)
}
G1<-function(u)
{
 n1<-length(u)
 temp<-rep(0, n1)
  for (i in 1:n1)
 {
  if (abs(u)[i]<=h1)
   temp[i]<-  3/4*(u[i]/h1-u[i]^3/(3*h1^3)+2/3)
  if (u[i]>h1)
```

```
   temp[i]<-1
  if (u[i]< (-h1))
   temp[i]<-0
 }
return(temp)
}
G2<-function(u)
{
 n2<-length(u)
 temp<-rep(0, n2)
  for (i in 1:n2)
 {
  if (abs(u)[i]<=h2)
   temp[i]<-3/4*(u[i]/h2-u[i]^3/(3*h2^3)+2/3)
  if (u[i]>h2)
   temp[i]<-1
  if (u[i]<(-h2))
   temp[i]<-0
 }
return(temp)
}
```

```
ln<- function(x)  ##### set new ln function to define -Inf*0
{
 temp<-rep(0,length(x))
  for (i in 1:length(x))
 {
  if (x[i]>0)
   temp[i]<-log(x[i])
 }
return(temp)
}
inverse <-function(x)  ##### to deal with the 1/0 issue
{
 temp<-rep(0,length(x))
  for (i in 1:length(x))
 {
  if (abs(x[i])>10e-6)
  temp[i]<-1/x[i]
 }
 return(temp)
}
########## Generate Data #########
```

```
m<-1
while (m>=1)
 {
           ####### Sample Size #######
   #######  Quantile: Set t=0.2 & t=0.7  ######
 if (distribution==1&&censor==0.1)
 {
T1<-rchisq(n1,1)          #Simulation 1: Chi-square
 T2<-rchisq(n2,2)
theta1=0.1
theta2=0.05
 }
if (distribution==2&&censor==0.1)
  {
    T1<-rexp(n1,1)          #Simulation 2: Exponential
    T2<-rexp(n2,1.5)
theta1=0.11
theta2=0.15
  }
if (distribution==3&&censor==0.1)
 {
```

```
 T1<-rweibull(n1,1,1)       #Simulation 3: Weibull
 T2<-rweibull(n2,1,1.5)
 theta1=0.1
 theta2=0.075
 }
 if (distribution==1&&censor==0.4)
 {
T1<-rchisq(n1,1)          #Simulation 1: Chi-square
 T2<-rchisq(n2,2)
theta1=0.95
theta2=0.35
 }
if (distribution==2&&censor==0.4)
  {
    T1<-rexp(n1,1)          #Simulation 2: Exponential
    T2<-rexp(n2,1.5)
theta1=0.67
theta2=1.0
  }
if (distribution==3&&censor==0.4)
 {
```

```
 T1<-rweibull(n1,1,1)       #Simulation 3: Weibull
 T2<-rweibull(n2,1,1.5)
theta1=0.7
theta2=0.45
 }
 C1<-rexp(n1,theta1)
 C2<-rexp(n2,theta2)
 X1<-pmin(T1,C1)          ##generate the data
 X2<-pmin(T2,C2)
 delta1<-rep(1,n1)
 delta2<-rep(1,n2)
 count1<-0
 count2<-0
for (i in 1:n1)
      {
          if (T1[i]>C1[i])
            {
                delta1[i]<-0
             count1<-count1+1
            }
    }
```

```
 for (i in 1:n2)
    {
          if (T2[i]>C2[i])
                {
delta2[i]<-0
                count2<-count2+1
           }
     }
 count1/n1
 count2/n2
  if ( abs(count1/n1-censor)<=0.05
  &&abs(count2/n2-censor)<=0.05) #censoring rate=10%
  break
 else
  m<-m+1
 }
######### Using EL method #######
sort.delta1<-delta1[order(X1)]
sort.delta2<-delta2[order(X2)]
sort.X1<-sort(X1)
sort.X2<-sort(X2)
```

```
ii1<-1:n1

r1<-n1-ii1+1    ###### number of patients at risk before T_{ji}

ii2<-1:n2

r2<-n2-ii2+1

###   Eta Hat &  Theta Hat    ###

Fn1<-rep(1, n1)

M<-1

for (i in 1:n1)

 {

  M<- M*(1-sort.delta1[i]*inverse(r1[i]))

  Fn1[i]<-1-M

 }


Fn2<-rep(1, n2)

M<-1

for (i in 1:n2)

 {

   M<- M*(1-sort.delta2[i]*inverse(r2[i]))

   Fn2[i]<-1-M

 }

#### ETA.HAT ####
```

```
M<-1
eta.hat<-0
for (i in 1:(n2-1))
{
  if (Fn2[i]<1-t & Fn2[i+1]>1-t)
  eta.hat<-(sort.X2[i]+sort.X2[i+1])/2
}
#### THETA.HAT ####
M<-1
for (i in 1:(n1-1))
{
     M<- M*(1-sort.delta1[i]*inverse(r1[i]))
    if(sort.X1[i]>eta.hat)
    break
}
 theta.hat<-M
##############################NLM#########################################
equation<-function(x, y0)
{
F=numeric(3)
 F[1]<-ln(1-sort.delta1*inverse(r1+x[2]*G1(x[1]-sort.X1)))%*%G1(x[1]-sort.X1)
```

```
 F[2]<-ln(1-sort.delta2*inverse(r2+x[3]*G2(x[1]-sort.X2)))%*%G2(x[1]-sort.X2)

 F[3]<-x[2]*ln(1-sort.delta1*inverse(r1+x[2]*G1(x[1]-sort.X1)))

 %*%kernal1(x[1]-sort.X1)

 +x[3]*ln(1-sort.delta2*inverse(r2+x[3]*G2(x[1]-sort.X2)))

 %*%kernal2(x[1]-sort.X2)

 res<- sum((F-y0)^2)

return(res)

}

if(censor==0.1)

{

if(t==0.2&&distribution==1)

{

cc=4

eta1=2

eta2=-2

}

if(t==0.2&&distribution==2)

{

cc=4.5

eta1=0.5

eta2=-0.5
```

```
}
if(t==0.2&&distribution==3)
{
cc=0.5
eta1=0.25
eta2=-0.25
}
if(t==0.7&&distribution==1)
{
cc=1.7
eta1=2
eta2=-2
}
if(t==0.7&&distribution==2)
{
cc=10
eta1=0.5
eta2=-0.5
}
if(t==0.7&&distribution==3)
{
```

```
cc=5.5

eta1=0.25

eta2=-0.25

}

}

if(censor==0.4)

{

if(t==0.2&&distribution==1)

{

cc=10

eta1=0.75

eta2=-0.75

}

if(t==0.2&&distribution==2)

{

cc=0.48

eta1=-0.1

eta2=0.1

}

if(t==0.2&&distribution==3)

{
```

```
cc=1.5

eta1=0.25

eta2=-0.25

}

if(t==0.7&&distribution==1)

{

cc=7

eta1=0.2

eta2=-0.2

}

if(t==0.7&&distribution==2)

{

cc=0.085

eta1=-0.2

eta2=0.2

}

if(t==0.7&&distribution==3)

{

cc=0.14

eta1=0.25

eta2=-0.25
```

```
}

}

 h1<-cc[l]*n1^(-1/3)          ## bandwidth ##

  h2<-cc[l]*n2^(-1/3)      ## bandwidth ##

 theta.L<-nlm(equation,c(eta.hat,eta1,eta2),c(ln(theta),ln(t),0))

theta.L

error=theta.L$minimum

x=theta.L$estimate

F4=(r1-sort.delta1)%*%ln(1+x[2]*G1(x[1]-sort.X1)*inverse(r1-sort.delta1))

-r1%*%ln(1+x[2]*G1(x[1]-sort.X1)*inverse(r1))

+(r2-sort.delta2)%*%ln(1+x[3]*G2(x[1]

-sort.X2)*inverse(r2-sort.delta2))-r2%*%ln(1+x[3]

*G2(x[1]-sort.X2)*inverse(r2))

F4.L=-2*F4

pp=pp+1

if ( F4.L>0 && theta.L$estimate/eta.hat<2 && error<10^(-4))

{

k=k+1

eta.string[k]=theta.L$estimate[1]

rho1.string[k]=eta.hat

rho2.string[k]=abs(x[1])<3 && error<10^(-4)
```

```
chi.string[k]=F4.L


if(F4.L<1.96^2)

{count[l]=count[l]+1}

if(F4.L<1.64^2)

{count90[l]=count90[l]+1}

     #}

}

}

eta11=eta1

cc1=cc

h11=h1

#return(F4.L,eta.hat,x,eta11,cc1,abs(x[1])<3&&error<10^(-5))

countr11=count/R

countr21=count90/R

countr=matrix(0,length(cc),2)

countr[,1]=countr11

countr[,2]=countr21

return(countr,chi.string,eta.string,rho1.string,pp)

#return(count,pp,k,R,chi.string,eta.string,rho1.string,rho2.string)

}
```

```
testchi(0.2,100,100,1000,1,0.1)

testchi(0.7,100,100,1000,1,0.1)

testchi(0.2,100,100,1000,2,0.1)

testchi(0.7,100,100,1000,2,0.1)

testchi(0.2,100,100,1000,3,0.1)

testchi(0.7,100,100,1000,3,0.1)

testchi(0.2,100,100,1000,1,0.4)

testchi(0.7,100,100,1000,1,0.4)

testchi(0.2,100,100,1000,2,0.4)

testchi(0.7,100,100,1000,2,0.4)

testchi(0.2,100,100,1000,3,0.4)

testchi(0.7,100,100,1000,3,0.4)
```

Appendix D

R CODE OF AVERAGE LENGTH

```
library(survival)

library(rootSolve)

testchi<-function(t,R,cc,n1,n2)

{

### True Value ###

theta<-1-pchisq(qchisq(1-t, 1),0.8 )

######### Initial Set-Up ##########

z<-0

l=0         ####### no. of iterations #######

k<-1

eta.string=rep(0,R)

rho1.string=rep(0,R)

rho2.string=rep(0,R)

chi.string=rep(0,R)

diff=rep(0,length(cc))

count=rep(0,length(cc))

count90=rep(0,length(cc))
```

```
for(l in 1:length(cc))

{

for(k in 1:R)    ######### repeat 1000 times ########## {

{

########## Generate Data #########

m<-1

while (m>=1)

{

                                                #####q<-n*(1-p) ####

 alpha<-0.1

 h1<-cc[l]*n1^(-1/3)          ## bandwidth ##

 h2<-cc[l]*n2^(-1/3)     ## bandwidth ##

 T1<-rchisq(n1,0.3)          #Simulation 1: Chi-square

T2<-rchisq(n2,1)

theta1<-2/3            #Distribution of Censoring time, Cj

theta2<-1/8

C1<-rexp(n1,theta1)

C2<-rexp(n2,theta2)

X1<-pmin(T1,C1)          ##generate the data

X2<-pmin(T2,C2)

delta1<-rep(1,n1)
```

```
delta2<-rep(1,n2)
for (i in 1:n1)
     {
         if (T1[i]>C1[i])
       delta1[i]<-0
   }
for (i in 1:n2)
   {
         if (T2[i]>C2[i])
               delta2[i]<-0
      }
count1<-0
count2<-0
 for (j in 1:n1)
      {
         if (delta1[j]==0)
               count1<-count1+1     # censoring side
       }
for (i in 1:n2)
   {
       if (delta2[i]==0)
```

```
              count2<-count2+1          # censoring side
   }
count1/n1
count2/n2
 if ( abs(count1/n1-0.1)<=0.05 & abs(count2/n2-0.1)<=0.05)
 break
else
 m<-m+1
}
######### Using EL method #######
sort.delta1<-delta1[order(X1)]
sort.delta2<-delta2[order(X2)]
sort.X1<-sort(X1)
sort.X2<-sort(X2)
ii1<-1:n1
r1<-n1-ii1+1    ###### number of patients at risk before T_{ji}
ii2<-1:n2
r2<-n2-ii2+1
###   Eta Hat &  Theta Hat    ###
Fn1<-rep(1, n1)
M<-1
```

```
for (i in 1:n1)
{
 M<- M*(1-sort.delta1[i]*inverse(r1[i]))
 Fn1[i]<-1-M
}
Fn2<-rep(1, n2)
M<-1
for (i in 1:n2)
{
  M<- M*(1-sort.delta2[i]*inverse(r2[i]))
  Fn2[i]<-1-M
}
#### ETA.HAT ####
M<-1
eta.hat<-0
for (i in 1:(n2-1))
{
 if (Fn2[i]<1-t & Fn2[i+1]>1-t)
 eta.hat<-(sort.X2[i]+sort.X2[i+1])/2
}
#### THETA.HAT ####
```

```
M<-1
for (i in 1:(n1-1))
{
     M<- M*(1-sort.delta1[i]*inverse(r1[i]))
    if(sort.X1[i]>eta.hat)
    break
}
 theta.hat<-M
 h1<-max(sort.X1)*n1^(-1/3)          ## bandwidth ##
 h2<-max(sort.X2)*n2^(-1/3)     ## bandwidth ##
############################NLM#########################################
equation<-function(x, y0)
{
F=numeric(3)
F[1]<-ln(1-sort.delta1*inverse(r1+x[2]*G1(x[1]-sort.X1)))%*%G1(x[1]-sort.X1)
F[2]<-ln(1-sort.delta2*inverse(r2+x[3]*G2(x[1]-sort.X2)))%*%G2(x[1]-sort.X2)
F[3]<-x[2]*ln(1-sort.delta1*inverse(r1+x[2]*G1(x[1]-sort.X1)))
%*%kernal1(x[1]-sort.X1)+x[3]*ln(1-sort.delta2*
inverse(r2+x[3]*G2(x[1]-sort.X2)))%*%kernal2(x[1]-sort.X2)
res<- sum((F-y0)^2)
return(res)
```

```
}
lnR<- function(theta0)
{
theta.L<-nlm(equation,c(eta.hat,0.21,-0.21),c(ln(theta0),ln(t),0))
x=theta.L$estimate
error=theta.L$minimum
F4=(r1-sort.delta1)%*%ln(1+x[2]*G1(x[1]-sort.X1)
*inverse(r1-sort.delta1))-r1%*%ln(1+x[2]*G1(x[1]-sort.X1)
*inverse(r1))+(r2-sort.delta2)%*%ln(1+x[3]*G2(x[1]-sort.X2)
*inverse(r2-sort.delta2))-r2%*%ln(1+x[3]*G2(x[1]-sort.X2)*inverse(r2))
a=c(2,1)
a[1]=-2*F4-1.96^2
a[2]=error
return(a)
}
upperbound<-function(t)
  {
    if (t>0.5)
    {lap=0.02}
     if (t<0.5)
    {lap=0.03}
```

```
     distance=0
    upper=t
value=c(-1,0)
    while(value[1]<0 & value[2]<10^(-5) & t+distance<1 & t+distance>0)
       {
        distance=distance+lap
        upper=t+distance
value=lnR(t-distance)
       }
    return(upper)
  }
lowerbound<-function(t)
  {
     if (t<0.5)
    lap=0.02
     if (t>0.5)
    lap=0.03
     distance=0
    lower=t
value=c(-1,0)
     while(value[1]<0 & value[2]<10^(-5)& t-distance<1 & t-distance>0.000001)
```

```
       {
        distance=distance+lap
         lower=t-distance
value=lnR(t-distance)
       }
    return(lower)
    }
diff[l]=diff[l]+upperbound(theta.hat)-lowerbound(theta.hat)
}
}
averagelength=diff/R
countr11=count/R
countr21=count90/R
countr=matrix(0,length(cc),3)
countr[,1]=cc
countr[,2]=countr11
countr[,3]=countr21
return(averagelength)
}
t<-0.2
R<-1000
```

```
cc=c(1)

testchi(t,R,cc,30,30)

testchi(t,R,cc,50,50)

testchi(t,R,cc,100,100)
```

Appendix E

R CODE OF REAL APPLICATION

```
############ Real Application ##################

library(survival)

library(rootSolve)

###### Import Data #########

treatment<-read.table("C:\\Documents and Settings\\Hanfang Yang\\Desktop\\tr[1].txt")

placebo<-read.table("C:\\Documents and Settings\\Hanfang Yang\\Desktop\\pl[1].txt")

########## Initial Set-up #########

n1<-nrow(treatment)

n2<-nrow(placebo)

X1<-treatment[,1]

X2<-placebo[,1]

delta1<-1-treatment[,2]

delta2<-1-placebo[,2]

 count1=sum(delta1)

 count2=sum(delta2)

sort.delta1<-delta1[order(X1)]

sort.delta2<-delta2[order(X2)]
```

```
sort.X1<-sort(X1)

sort.X2<-sort(X2)

i<-1:n1

j<-1:n2

r1<-n1-i+1    ###### number of patients at risk before T_{ji}

r2<-n2-j+1

###   Eta Hat &  Theta Hat    ###

Fn1<-rep(1, n1)

M<-1

for (i in 1:n1)

{

 M<- M*(1-sort.delta1[i]*inverse(r1[i]))

 Fn1[i]<-1-M

}

Fn2<-rep(1, n2)

M<-1

for (i in 1:n2)

{

  M<- M*(1-sort.delta2[i]*inverse(r2[i]))

  Fn2[i]<-1-M

}
```

```
alpha<-0.05          #nominal level:1-alpha, set alpha=0.1 & alpha=0.05

                ##### Equal 0.5886076

    #### Equal 0.6103896

#### sorts of Function ####

lnR<- function(theta0,t,eta)

{

theta.L<-nlm(equation,c(eta,0.21,-0.21),c(ln(theta0),ln(t),0))

x=theta.L$estimate

error=theta.L$minimum

F4=(r1-sort.delta1)%*%ln(1+x[2]*G1(x[1]-sort.X1)*

inverse(r1-sort.delta1))-r1%*%ln(1+x[2]*G1(x[1]-sort.X1)

*inverse(r1))+(r2-sort.delta2)%*%ln(1+x[3]*G2(x[1]-sort.X2)

*inverse(r2-sort.delta2))-r2%*%ln(1+x[3]*G2(x[1]-sort.X2)*inverse(r2))

a=c(2,1)

a[1]=-2*F4-1.96^2

a[2]=error

return(a)

}

bisection<- function(point1,t,eta)

{ point=point1

left=0
```

```
if(lnR((left+point)/2,t,eta )>0)
   left=(left+point)/2
else point=(left+point)/2
point
right=1
point=point1
if(lnR((right+point)/2,t,eta )>0)
   right=(right+point)/2
else point=(right+point)/2
}
upperbound<-function(theta0,t,eta)
  { lap=0.005
    if (theta0>0.5)
    {lap=0.005}
     if (theta0<0.5)
    {lap=0.005}
     distance=0
    upper=theta0
value=c(-1,0)
    while(value[1]<0 & value[2]<10^(-5) & theta0+distance<1 & theta0+distance>0)
       {
```

```
        distance=distance+lap
        upper=theta0+distance
value=lnR(theta0-distance,t,eta)
       }
    return(upper)
  }
lowerbound<-function(theta0,t,eta)
  {  lap=0.005
     if (theta0<0.5)
    lap=0.005
     if (theta0>0.5)
    lap=0.005
     distance=0
    lower=theta0
value=c(-1,0)
     while(value[1]<0 & value[2]<10^(-5)& theta0-distance<1 & theta0-distance>0.00000
       {
        distance=distance+lap
         lower=theta0-distance
value=lnR(theta0-distance,t,eta)
```

```
       }
    return(lower)
    }

band<-function(t)
{
#### ETA.HAT ####
M<-1
eta.hat<-0
for (i in 1:(n2-1))
{
 if (Fn2[i]<1-t & Fn2[i+1]>1-t)
 eta.hat<-(sort.X2[i]+sort.X2[i+1])/2
}
#### THETA.HAT ####
M<-1
for (i in 1:(n1-1))
{
     M<- M*(1-sort.delta1[i]*inverse(r1[i]))
    if(sort.X1[i]>eta.hat)
    break
```

```
}
 theta.hat<-M
 h1<-2*n1^(-1/3)          ## bandwidth ##
 h2<-2*n2^(-1/3)     ## bandwidth ##
low=lowerbound(theta.hat,t,eta.hat)
upper=upperbound(theta.hat,t,eta.hat)
return(low,upper,eta.hat,theta.hat)
}
nnn=50
lowa=rep(0,nnn)
uppera=rep(0,nnn)
eta.hata=rep(0,nnn)
theta.hata=rep(0,nnn)

for (i in 1:nnn)
{
b=band(i/nnn*0.7+0.15)
lowa[i]=b$low
uppera[i]=b$upper
eta.hata[i]=b$eta.hat
theta.hata[i]=b$theta.hat
```

```
}

lowa

uppera

eta.hata

theta.hata

index=(1:nnn)/nnn*0.7+0.15

plot(index,lowa , type='l',col='green',xlab='1-specificity',ylab='sensitivity')

lines(index,uppera , type='l', col='green')

lines(index,theta.hata , type='l', col='black')

lines(index,index , type='l', col='blue')

legend(0.5, 0.38, legend = c("EL confidence bands", "45 degree diagonal", "Empirical

of the ROC curve"),lty = c(1),col = c(3,4, 1))
```