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# Empirical Likelihood Confidence Intervals for the Sensitivity of a Continuous-Scale Diagnostic Test

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# EMPIRICAL LIKELIHOOD CONFIDENCE INTERVALS FOR THE SENSITIVITY OF A CONTINUOUS-SCALE DIAGNOSTIC TEST

by

ANGELA E. DAVIS

Under the Direction of Gengsheng Qin

## ABSTRACT

Diagnostic testing is essential to distinguish non-diseased individuals from diseased individuals. More accurate tests lead to improved treatment and thus reduce medical mistakes. The sensitivity and specificity are two important measurements for the diagnostic accuracy of a diagnostic test. When the test results are continuous, it is of interest to construct a confidence interval for the sensitivity at a fixed level of specificity for the test. In this thesis, we propose three empirical likelihood intervals for the sensitivity. Simulation studies are conducted to compare the empirical likelihood based confidence intervals with the existing normal approximation based confidence interval. Our studies show that the new intervals had better coverage probability than the normal approximation based interval in most simulation settings.

INDEX WORDS: Empirical Likelihood, Confidence Intervals, Diagnostic Test, Sensitivity, Specificity

# EMPIRICAL LIKELIHOOD CONFIDENCE INTERVALS FOR THE SENSITIVITY OF A CONTINUOUS-SCALE DIAGNOSTIC TEST

by

ANGELA E. DAVIS

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by

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| | |
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Electronic Version Approved:

*"To whom much is given, much more is also required."*

To those who stood in the gap, this is dedicated to you.

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# Chapter I

# INTRODUCTION

Diagnostic testing, an integral facet of medical testing, aids in classifying the presence or absence of a disease or condition. There are two types of diagnostic tests: qualitative and quantitative. A qualitative test classifies patients as diseased or non-diseased based on clinical signs or symptoms. A quantitative test classifies patients according to $c$, a predetermined cutoff point. Disease or non-disease status is dependent upon whether or not the test result falls above or below the cutoff point. A more accurate diagnostic test leads to more effective treatment and thus reduces medical malpractice and mortality. The results of a diagnostic test help to answer two questions: If the test is positive, what is the probability that the person actually has the disease, and if the test is negative, what is the probability that the person actually doesn't have the disease? These questions can simply be answered in terms of the test's sensitivity and specificity respectively. A model test would have high sensitivity and high specificity.

The Receiver Operating Characteristic (ROC) curve, developed in World War II, was initially used in signal detection theory. It has since become widely used in diagnostic medicine as an efficient way to graphically display the tradeoff between sensitivity and specificity. When the specificity is high, the sensitivity is low and vice versa. More specifically, a ROC curve is a plot of 1 - specificity against sensitivity. In order to classify the results of a diagnostic test as positive or negative, a cutoff point $c$

must be defined when the response is continuous. When a level of specificity is chosen (commonly 80 %, 90% or 95%), it is of interest to construct confidence intervals for the sensitivity at the selected level of specificity.

Empirical likelihood (EL), introduced by Owen (1988, 1990), is a powerful non-parametric method. The EL method has many advantages over normal approximation based methods. For example, it has better small sample performance than approaches based on normal approximation; EL-based confidence regions are range preserving and transformation respecting; the regularity conditions for EL-based methods are weak and natural etc. The use of EL methods has becoming increasingly common in recent years and is attractive in many applied area (Wu and Rao, 2006). Claeskens et al. (2003), one of few studies on the EL method for ROC analysis, developed an empirical likelihood confidence interval for a ROC curve. Their EL confidence interval had better coverage probability than the normal approximation based interval. However, their method still needs kernel distribution estimation and the selection of smoothing parameters are problematic. It thus has not been well applied in practice.

In this thesis, we propose new empirical likelihood based confidence intervals and compare them with the existing normal approximation based interval. The thesis is organized in the following manner: Chapter I is an introduction, Chapter II lists concepts and terminology used throughout the thesis, existing confidence intervals for sensitivity at a fixed level of specificity for a continuous-scale test are presented in Chapter III, Chapter IV introduces three new empirical likelihood intervals for sensitivity at a fixed level of specificity, in Chapter V we conduct simulations studies to evaluate the

performance of new confidence intervals and in Chapter VI we apply the proposed methods to a real dataset. Lastly, there is a discussion of our findings in Chapter VII.

# Chapter II

# CONCEPTS AND TERMINOLOGY

## 2.1 Sensitivity and Specificity of a Binary Diagnostic Test

**Sensitivity** – probability that a diseased patient will have a positive test result.
P(positive test | patient has the disease)

**Specificity** – probability that a non-diseased patient will have a negative test result.
P(negative test | patient doesn't have the disease)

Classification of individuals according to diagnostic test results are shown in the following table:

| Test Result | Disease/Condition | |
|---|---|---|
| | **Present** | **Absent** |
| **Positive** | True Positive (TP) | False Positive (FP) |
| **Negative** | False Negative (FN) | True Negative (TN) |

Figure 1. 2x2 classification table of diagnostic test results

The following formulas are used to estimate the sensitivity and specificity:

$$Sensitivity = \frac{TP}{TP + FN}$$

$$Specificity = \frac{TN}{FP + TN}$$

## 2.2 Sensitivity and Specificity of a Continuous-Scale Diagnostic Test

For a continuous-scale diagnostic test, let $X$ be the test result from a non-diseased patient, and let $Y$ be the test result from a diseased patient. At a given cutoff point $c$, the sensitivity and specificity are defined as

$$S_e = P(Y \geq c), \quad S_p = P(X \leq c),$$

respectively. If $F$ is the distribution function of $X$ and $G$ is the distribution function of $Y$, the sensitivity and specificity can then be written as

$$S_e = 1-G(c), \quad S_p = F(c).$$

At a fixed level $p$ of specificity, the corresponding sensitivity of the test is

$$R(p) = 1 - G(F^{-1}(p)),$$

where $F^{-1}$ is the inverse function of $F$.

One problem that arises is how to construct a $(1-\alpha)100\%$ confidence interval for $R(p)$ based on, $X_1,...,X_m$, the results from the non-diseased group, and $Y_1,...,Y_{n,}$, the results from the diseased group.

# Chapter III

# EXISTING METHODS

## 3.1 Normal Approximation Based Confidence Interval

If $R(p) = P(Y \geq F^{-1}(p))$, then the estimator for $R(p)$ is the observed sensitivity at the $p$-th sample quantile from the test results of the non-diseased individuals. If we let $\hat{F}$ be the empirical distribution function based on $X_1, ..., X_m$, then the estimator for $R(p)$ becomes

$$\hat{R}(p) = \frac{\sum_{j=1}^{n} I(Y_j \geq \hat{F}^{-1}(p))}{n}. \qquad (1)$$

Linnet (1987) presented a formula for the variance of $\hat{R}(p)$ defined as

$$Var(\hat{R}(p)) = \frac{R(p)(1 - R(p))}{n} + \frac{p(1-p)}{m} \cdot \frac{g^2(F^{-1}(p))}{f^2(F^{-1}(p))}, \qquad (2)$$

where $f$ and $g$ are the probability density functions of $F$ and $G$ respectively. It has been shown that when both $m$ and $n$ are large, $\hat{R}(p)$ has an approximately normal distribution with mean $R(p)$ and variance $Var(\hat{R}(p))$, given by (2). By substituting unknown quantities in (2) by their corresponding sample estimates, we can obtain a $(1-\alpha)100\%$ normal approximation based confidence interval for $R(p)$. However, this interval may be greatly affected by poor empirical density and quantile estimation. Platt et al. (2000)

studied this issue and found via simulation study that the normal approximation based confidence interval could have poor coverage probability.

### 3.2 Empirical Likelihood Interval

Let $\theta = R(p) = 1 - G(F^{-1}(1-p))$ then there exists a quantity $\eta$ such that

$$F^{-1}(1-p) = G^{-1}(1-\theta) = \eta .$$

Using this relationship between sensitivity and specificity, Claeskens, Jing, Peng and Zhou (2003) proposed a smoothed empirical likelihood for $R(p)$ defined as follows:

$$L(\theta) = \sup_{p,q,\eta} \left( \prod_{i=1}^{n} p_i \right) \left( \prod_{j=1}^{m} q_j \right)$$

subject to the following constraints

$$\sum_{i=1}^{n} p_i G_1 \left( \frac{\eta - Y_i}{h_1} \right) = 1 - \theta, \quad \sum q_j G_2 \left( \frac{\eta - X_j}{h_2} \right) = 1 - p$$

where **p** and **q** are probability vectors, $G_1$ and $G_2$ are known functions and $h_j$'s are unknown smoothing parameters. Claeskens et al (2003), under certain conditions, illustrated that the empirical log-likelihood ratio is a chi-square distribution,

$$\ell(\theta) \rightarrow \chi_1^2 ,$$

and by inversing $\ell(\theta)$, they obtained an empirical likelihood confidence interval for $R(p)$ defined as

$$\{\theta : \ell(\theta) \leq \chi_1^2(1-\alpha)\}. \tag{3}$$

Their new confidence interval performed much better than the normal approximation based interval. However, the smoothed empirical likelihood method has two main drawbacks: (1) The method is computationally extensive, three nonlinear equations have to be solved to calculate the value of $\ell(\theta)$; (2) Two smoothing parameters $h_j's$ have to be selected, which is problematic in practice.

# Chapter IV

# NEW CONFIDENCE INTERVALS

Qin and Zhou (2006) successfully applied the empirical likelihood method to the inference for an area under the ROC curve. We will define the empirical likelihood method in this section for the sensitivity of a diagnostic test. Pepe (2003) defined a placement value for a given test value $Y$ from a diseased subject as

$$U = 1 - F(Y).$$

This value is the proportion of the non-diseased population with a test value greater than $Y$, essentially marking the placement of $Y$ within the non-diseased distribution. It is evident that

$$E(I(U \leq p)) = P(F(Y) \geq p) = P(Y \geq F^{-1}(p)) = R(p).$$

Based on the relationship between $R(p)$ and the placement value U, an empirical likelihood procedure is derived for the sensitivity of a diagnostic test. Let $\mathbf{p} = (p_1, p_2, ..., p_n)$ be a probability vector, i.e., $\sum_{j=1}^{n} p_j = 1$ and $p_j \geq 0$ for all $j$. The profile empirical likelihood for $R(p)$ can be defined as

$$\widetilde{L}(R(p)) = \sup\left\{ \prod_{j=1}^{n} p_j : \sum_{j=1}^{n} p_j = 1, \quad \sum_{j=1}^{n} p_j W_j(p) = 0 \right\},$$

where $W_j(p) = I(U_j \leq p) - R(p)$ with $U_j = 1 - F(Y_j)$, $j = 1, 2, ..., n$. Placement values, $U_j$'s, depend on the unknown distribution function $F$ of the non-diseased population.

Therefore, by replacing $F$ by its empirical distribution $\hat{F}$, we get an adjusted empirical likelihood for $R(p)$:

$$L(R(p)) = \sup\left\{\prod_{j=1}^{n} p_j : \sum_{j=1}^{n} p_j = 1, \quad \sum_{j=1}^{n} p_j \hat{W}_j(p) = 0 = 0\right\},$$

where $\hat{W}_j(p) = I(\hat{U}_j \le p) - R(p)$ with $\hat{U}_j = 1 - \hat{F}(Y_j)$ $j = 1,2,...,n.$ Then, by Lagrange multiplier, we get

$$p_j = \frac{1}{n}\left\{1 + \lambda \hat{W}_j(p))\right\}^{-1}, \quad j = 1,2,...n,$$

where $\lambda$ is the solution of

$$\frac{1}{n}\sum_{j=1}^{n} \frac{\hat{W}_j(p)}{1 + \lambda \hat{W}_j(p)} = 0. \tag{4}$$

Note that $\prod_{j=1}^{n} p_j$, subject to $\sum_{j=1}^{n} p_j = 1$, attains its maximum $n^{-n}$ at $p_j = n^{-1}$. So the empirical likelihood ratio for $R(p)$ is defined as

$$r(R(p)) = \prod_{j=1}^{n} (np_j) = \prod_{j=1}^{n}\left\{1 + \lambda \hat{W}_j(p)\right\}^{-1}.$$

The resulting log-pseudo-empirical likelihood ratio is

$$l(R(p)) = -2\log r(R(p)) = 2\sum_{j=1}^{n} \log\left\{1 + \lambda \hat{W}_j(p)\right\}, \tag{5}$$

where $\lambda$ is the solution of (4).

Qin (2006) established the following theorem for the asymptotic distribution for the log-pseudo-empirical likelihood ratio.

**Theorem 3.1.** *If $R_0(p)$ is the true value of sensitivity $R(p)$ at a fixed level $p$ of specificity, and $0 < R(p) < 1$ for $0 < p < 1$, then the limiting distribution of $l(R_0(p))$, defined by (5), is a scaled chi-square distribution with one degree of freedom. That is,*

$$c(p)l(R_0(p)) \longrightarrow \chi_1^2, \tag{6}$$

*where the scale constant $c(p)$ is*

$$c(p) = \frac{\sigma^2(p)}{\sigma_1^2(p)}$$

with

$$\sigma^2(p) = R(p)(1 - R(p)),$$

$$\sigma_1^2(p) = \sigma^2(p) + \frac{n}{m} \cdot p(1-p) \cdot \frac{g^2(F^{-1}(p))}{f^2(F^{-1}(p))}.$$

*Here f and g are the density functions of F and G respectively.*

In order to construct confidence intervals for $R(p)$ based on Theorem 3.1, we need to estimate $\sigma^2(p)$ and $\sigma_1^2(p)$. Let

$$\hat{\sigma}^2(p) = \hat{R}(p)(1 - \hat{R}(p)),$$

$$\hat{\sigma}_1^2(p) = \hat{\sigma}^2(p) + \frac{n}{m} \cdot p(1-p) \cdot \frac{\hat{g}^2(\hat{F}^{-1}(p))}{\hat{f}^2(\hat{F}^{-1}(p))}.$$

where $\hat{F}^{-1}(p)$ is the *p-th* sample quantile of $X_i$'s, $\hat{f}$ and $\hat{g}$ are the estimates of density functions $f$ and $g$. Then, a $(1-\alpha)$-*th* empirical likelihood based confidence interval, called ELI interval, for $R(p)$, is defined by

$$CI_{2,\alpha}(R(p)) = \{R(p) : \hat{c}(p)\ell R(p)) \le \chi_1^2(1-\alpha)\}, \tag{7}$$

where $\hat{c}(p) = \dfrac{\hat{\sigma}^2(p)}{\hat{\sigma}_1^2(p)}$. By Theorem 3.1, $CI_{1,\alpha}(R(p))$ gives an approximate confidence interval for $R_0(p)$ with asymptotically correct coverage probability 1-α, i.e.,

$$P(R_0(p) \in CI_{2,\alpha}(R(p))) = 1 - \alpha + o(1).$$

The performance of the ELI interval depends on the density estimates $\hat{f}$ and $\hat{g}$, particularly when the sample sizes are small. We now propose a bootstrap method to estimate $\sigma_1^2(p)$. The bootstrap estimate is motivated by the fact that $\sigma_1^2(p)$ is the asymptotic variance of $n^{1/2}(\hat{R}(p) - R(p))$. The procedure for computing the bootstrap variance can be summarized in the following steps:

1. Draw a resample of size $n$, $Y_i^*$'s, with replacement from the diseased sample $Y_i$'s and a separate resample of size $m$, $X_i^*$'s, with replacement from the non-diseased sample $X_i$'s.

2. Calculate the bootstrap version of $\hat{R}(p)$,

$$\hat{R}^*(p) = \frac{\sum_{i=1}^n I\left[Y_i^* \ge \hat{F}^{-1*}(p)\right]}{n},$$

where $\hat{F}^{-1*}(p)$ is the $p$-th sample quantile based on the bootstrap resample $X_j^*$'s.

3. Repeat the first two steps B times to obtain the set of bootstrap replications $\{\hat{R}^{*b}(p) : b = 1, 2, ..., B\}$ Then, the bootstrap estimate $\sigma_1^{*2}(p)$ for $\sigma_1^2(p)$ is defined by

$$\sigma_1^{*2}(p) = \frac{n}{B-1} \sum_{b=1}^{B} (\hat{R}^{*b}(p) - \overline{R}^{*}(p))^2,$$

where $\overline{R}^{*}(p) = (1/B) \sum_{b=1}^{B} R^{*b}(p).$

Now we propose two new empirical likelihood based confidence intervals

for $R(p)$ by using the bootstrap variance $\sigma_1^{*2}(p)$.

The first one, called ELII interval, is defined by

$$\{R(p) : c_1^{*}(p)l(R(p)) \leq \chi_1^2(1-\alpha)\}, \tag{8}$$

where $c_1^{*}(p) = \dfrac{\hat{\sigma}^2(p)}{\hat{\sigma}_1^{*2}(p)}.$

The second one, called ELIII interval, is defined by

$$\{R(p) : c_2^{*}(p)l(R(p)) \leq \chi_1^2(1-\alpha)\}, \tag{9}$$

where $c_2^{*}(p) = \dfrac{\overline{R}^{*}(p)(1 - \overline{R}^{*}(p))}{\hat{\sigma}_1^{*2}(p)}.$

# Chapter V

# SIMULATION STUDIES FOR THE CONFIDENCE INTERVALS

We conducted three simulation studies to compare the coverage accuracy of the newly proposed intervals to that of the normal approximation based interval. In simulation studies, we generate 3,000 random samples of size $m$ from the distribution function $F$ for test responses of non-diseased patients and another independent random sample of size $n$ from the distribution function $G$ for test responses of diseased patients. In these studies, the sample sizes *(m,n)* were chosen to be (20,50), (50,20), (50,100), (100,50), (50,50) and (100,100), respectively.

In the first simulation study, the distribution function $F$ was chosen to be a standard normal distribution whereas the distribution function $G$ was a normal distribution with mean $\mu$ and variance 1. The specificity was fixed at 80% or 90% level for different values of $\mu$ (See Table I). The results of the simulation study at the nominal level of 95% are given in Tables IV-IX.

Table I. Parameter settings for the normal distribution at fixed levels of specificity.

| Run | $\mu$ | Specificity (p) | Sensitivity (R(p)) |
|-----|-------|------------|-------------|
| 1 | 2.9264 | 0.90 | 0.95 |
| 2 | 2.5631 | 0.90 | 0.90 |
| 3 | 2.1231 | 0.90 | 0.80 |
| 4 | 2.4865 | 0.80 | 0.95 |
| 5 | 1.6832 | 0.80 | 0.80 |

Our distributions, *F* and *G*, were beta distributions with parameters $(a_0,b_0)$ and $(a_1,b_1)$ respectively in the second simulation study. The specificity was also fixed at 80% or 90% for different values of $(a_0,b_0)$ and $(a_1,b_1)$ to get the corresponding sensitivities (See Table II). The coverage probabilities resulting from the simulation study at the nominal level of 95% are given in Tables X-XV.

Table II. Parameter setting for the Beta Distribution at fixed levels of specificity.

| Run | $(a_1,b_1)$ | $(a_0,b_0)$ | Specificity (*p*) | Sensitivity ($R(p)$) |
|-----|-------------|-------------|-------------------|----------------------|
| 1 | (4,1) | (1,3.5) | 0.90 | 0.95 |
| 2 | (3,1) | (1,3) | 0.80 | 0.93 |
| 3 | (3,1) | (1,3) | 0.90 | 0.85 |
| 4 | (4,2) | (2,4) | 0.80 | 0.82 |
| 5 | (3,2) | (2,3) | 0.80 | 0.55 |

In the third simulation study, we chose the distributions *F* and *G* to be the standard exponential distribution (with rate = 1) and an exponential distribution with rate = $1/\delta$ - 1, where $\delta$ represents the area under the receiver operating characteristic curve (AUC). Here, $\delta$ was taken to be 0.95. Specificity was set at 0.60, 0.70, 0.80, 0.90 and 0.95 along with the corresponding sensitivities (See Table III). The coverage probabilities resulting from the simulation study at the nominal level of 95% are given in Tables XVI-XXI.

Table III. Parameter settings for the exponential distribution

| Run | $\delta$ | Specificity (p) | Sensitivity (R(p)) |
|---|---|---|---|
| 1 | 0.95 | 0.60 | 0.95 |
| 2 | 0.95 | 0.70 | 0.94 |
| 3 | 0.95 | 0.80 | 0.92 |
| 4 | 0.95 | 0.90 | 0.89 |
| 5 | 0.95 | 0.95 | 0.85 |

The simulation studies illustrate that the newly proposed intervals generally performed better than the normal approximation based interval at the 95% nominal level in most settings.

# Chapter VI

# REAL APPLICATION

In this chapter, we apply the newly proposed intervals to a real life data example. The data is from 403 subjects out of a group of 1046 who were selected to gain more understanding regarding the prevalence of diabetes, obesity, etc. among African Americans in central Virginia. The risk factors that were chosen from the study were the waist and hip measurements, as they have been known to be a predictor of diabetes.

## 6.1 Detection of Diabetes

Diabetes is a disease resulting from the way our bodies use blood glucose. The glucose (sugar) is your body's energy source. Insulin, produced by the pancreas, helps the body produce sugar, which is used for energy. Too little insulin or the body using it improperly causes diabetes. It is the 5th leading cause of death in America and more prevalent among African Americans. Left untreated, diabetes leads to amputations, organ failure and even death in some cases.

Our study used the waist and hip measurements (in inches) of 388 female and male subjects to determine the waist/hip ratio (WHR). The waist/hip ratio is just one way of detecting diabetes in patients. Excess abdominal fat has been associated with higher levels of insulin, which can raise blood sugar and pressure among other things. A WHR greater than 0.8 in women and 0.9 in men is said to increase the risk of diabetes in

patients. Snijder et al. (2004) found that waist and hip measurements are important factors in predicting diabetes and other diseases.

The new empirical likelihood confidence intervals were applied to the data to determine the accuracy of the WHR in predicting diabetes. There were 305 non-diseased patients and 83 diseased patients. The results of the computation are found in Table XXII. The interval lengths were shorter when specificity was fixed at 90% and 95%.

# Chapter VII

# DISCUSSION

Diagnostic testing is essential in distinguishing diseased patients from non-diseased patients. When the result of a test is more accurate, there is less misconduct and better treatment options can be implemented. The ROC curve provides a summary of the performance of a diagnostic test (Claeskens et. al, 2003). For a quantitative test, the cutoff point $c$ is imperative because it determines which patients will be classified as diseased and non-diseased. When the response of a test is continuous, it is of interest to construct confidence intervals for the sensitivity of the test at this point. Calculating the sensitivity and specificity of a test at various cutoff points is effective in determining the best point at which to classify the test. The normal approximation confidence intervals are inadequate when the distribution is skewed or the parameter range is restricted (Wu and Rao, 2006). We proposed three new empirical likelihood confidence intervals for the sensitivity of a continuous scale diagnostic test at a fixed level of specificity. The newly proposed intervals were shown to generally perform better than the normal approximation based interval at the 95% nominal level in most simulation settings.

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# APPENDIX I: SIMULATION TABLES

## A. Normal Distribution Tables

Table IV. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the normal distribution with m=20 and n=50.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9957 |
|   | ELI | 0.9810 |
|   | ELII | 0.9793 |
|   | ELIII | 0.9836 |
| 2 | Normal | 0.9280 |
|   | ELI | 0.9746 |
|   | ELII | 0.9628 |
|   | ELIII | 0.9678 |
| 3 | Normal | 0.8500 |
|   | ELI | 0.9557 |
|   | ELII | 0.9412 |
|   | ELIII | 0.9335 |
| 4 | Normal | 0.9987 |
|   | ELI | 0.9895 |
|   | ELII | 0.9717 |
|   | ELIII | 0.9745 |
| 5 | Normal | 0.9277 |
|   | ELI | 0.9790 |
|   | ELII | 0.9619 |
|   | ELIII | 0.9519 |

Table V. Coverage probabilities of intervals at the
nominal level of 95 percent when the data are generated
from the normal distribution with m=50 and n=20.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9983 |
|   | ELI | 0.9576 |
|   | ELII | 0.9731 |
|   | ELIII | 0.9759 |
|   |  |  |
| 2 | Normal | 0.9910 |
|   | ELI | 0.9736 |
|   | ELII | 0.9821 |
|   | ELIII | 0.9842 |
|   |  |  |
| 3 | Normal | 0.8510 |
|   | ELI | 0.9708 |
|   | ELII | 0.9785 |
|   | ELIII | 0.9795 |
|   |  |  |
| 4 | Normal | 0.9983 |
|   | ELI | 0.9668 |
|   | ELII | 0.9706 |
|   | ELIII | 0.9745 |
|   |  |  |
| 5 | Normal | 0.8953 |
|   | ELI | 0.9780 |
|   | ELII | 0.9791 |
|   | ELIII | 0.9832 |

Table VI. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the normal distribution with m=50 and n=100.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9793 |
|   | ELI    | 0.9820 |
|   | ELII   | 0.9716 |
|   | ELIII  | 0.9737 |
|   |        |        |
| 2 | Normal | 0.9220 |
|   | ELI    | 0.9670 |
|   | ELII   | 0.9616 |
|   | ELIII  | 0.9543 |
|   |        |        |
| 3 | Normal | 0.8873 |
|   | ELI    | 0.9267 |
|   | ELII   | 0.9583 |
|   | ELIII  | 0.9543 |
|   |        |        |
| 4 | Normal | 0.9940 |
|   | ELI    | 0.9884 |
|   | ELII   | 0.9700 |
|   | ELIII  | 0.9714 |
|   |        |        |
| 5 | Normal | 0.9367 |
|   | ELI    | 0.9730 |
|   | ELII   | 0.9600 |
|   | ELIII  | 0.9533 |

Table VII. Coverage probabilities of intervals at the
nominal level of 95 percent when the data are generated
from the normal distribution with m=100 and n=50.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9907 |
|   | ELI | 0.9802 |
|   | ELII | 0.9833 |
|   | ELIII | 0.9832 |
|   |    |    |
| 2 | Normal | 0.9333 |
|   | ELI | 0.9729 |
|   | ELII | 0.9736 |
|   | ELIII | 0.9730 |
|   |    |    |
| 3 | Normal | 0.9067 |
|   | ELI | 0.9433 |
|   | ELII | 0.9703 |
|   | ELIII | 0.9673 |
|   |    |    |
| 4 | Normal | 0.9977 |
|   | ELI | 0.9835 |
|   | ELII | 0.9816 |
|   | ELIII | 0.9835 |
|   |    |    |
| 5 | Normal | 0.9383 |
|   | ELI | 0.9620 |
|   | ELII | 0.9690 |
|   | ELIII | 0.9627 |

Table VIII. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the normal distribution with m=n=50.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9947 |
|   | ELI | 0.9782 |
|   | ELII | 0.9798 |
|   | ELIII | 0.9844 |
| 2 | Normal | 0.9133 |
|   | ELI | 0.9771 |
|   | ELII | 0.9750 |
|   | ELIII | 0.9757 |
| 3 | Normal | 0.8853 |
|   | ELI | 0.9343 |
|   | ELII | 0.9637 |
|   | ELIII | 0.9567 |
| 4 | Normal | 0.9983 |
|   | ELI | 0.9859 |
|   | ELII | 0.9821 |
|   | ELIII | 0.9840 |
| 5 | Normal | 0.9313 |
|   | ELI | 0.9663 |
|   | ELII | 0.9646 |
|   | ELIII | 0.9600 |

Table IX. Coverage probabilities of intervals at the
nominal level of 95 percent when the data are generated
from the normal distribution with m=n=100.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9610 |
|   | ELI | 0.9837 |
|   | ELII | 0.9745 |
|   | ELIII | 0.9748 |
|   |   |   |
| 2 | Normal | 0.9253 |
|   | ELI | 0.9730 |
|   | ELII | 0.9673 |
|   | ELIII | 0.9620 |
|   |   |   |
| 3 | Normal | 0.9017 |
|   | ELI | 0.9320 |
|   | ELII | 0.9537 |
|   | ELIII | 0.9527 |
|   |   |   |
| 4 | Normal | 0.9787 |
|   | ELI | 0.9854 |
|   | ELII | 0.9661 |
|   | ELIII | 0.9678 |
|   |   |   |
| 5 | Normal | 0.9353 |
|   | ELI | 0.9563 |
|   | ELII | 0.9540 |
|   | ELIII | 0.9533 |

## B.  Beta Distribution Tables

Table X. Coverage probabilities of intervals at the
nominal level of 95 percent when the data are generated
from the beta distribution with m=20 and n=50.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9883 |
|   | ELI | 0.9757 |
|   | ELII | 0.9753 |
|   | ELIII | 0.9817 |
| 2 | Normal | 0.9900 |
|   | ELI | 0.9848 |
|   | ELII | 0.9770 |
|   | ELIII | 0.9803 |
| 3 | Normal | 0.8497 |
|   | ELI | 0.9645 |
|   | ELII | 0.9522 |
|   | ELIII | 0.9436 |
| 4 | Normal | 0.9297 |
|   | ELI | 0.9802 |
|   | ELII | 0.9758 |
|   | ELIII | 0.9670 |
| 5 | Normal | 0.8853 |
|   | ELI | 0.9283 |
|   | ELII | 0.9413 |
|   | ELIII | 0.9330 |

Table XI. Coverage probabilities of intervals at the
nominal level of 95 percent when the data are generated
from the beta distribution with m=50 and n=20.

| Run | Method | Coverage Probability |
|-----|--------|:---:|
|     |        | 95% |
| 1   | Normal | 0.9957 |
|     | ELI    | 0.9567 |
|     | ELII   | 0.9671 |
|     | ELIII  | 0.9726 |
|     |        |        |
| 2   | Normal | 0.9953 |
|     | ELI    | 0.9702 |
|     | ELII   | 0.9757 |
|     | ELIII  | 0.9785 |
|     |        |        |
| 3   | Normal | 0.9457 |
|     | ELI    | 0.9726 |
|     | ELII   | 0.9823 |
|     | ELIII  | 0.9827 |
|     |        |        |
| 4   | Normal | 0.9240 |
|     | ELI    | 0.9724 |
|     | ELII   | 0.9794 |
|     | ELIII  | 0.9801 |
|     |        |        |
| 5   | Normal | 0.9023 |
|     | ELI    | 0.9330 |
|     | ELII   | 0.9603 |
|     | ELIII  | 0.9483 |

Table XII. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the beta distribution with m=50 and n=100.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9490 |
|   | ELI | 0.9760 |
|   | ELII | 0.9739 |
|   | ELIII | 0.9732 |
| 2 | Normal | 0.9697 |
|   | ELI | 0.9876 |
|   | ELII | 0.9705 |
|   | ELIII | 0.9685 |
| 3 | Normal | 0.8830 |
|   | ELI | 0.9363 |
|   | ELII | 0.9517 |
|   | ELIII | 0.9477 |
| 4 | Normal | 0.9380 |
|   | ELI | 0.9703 |
|   | ELII | 0.9527 |
|   | ELIII | 0.9470 |
| 5 | Normal | 0.9090 |
|   | ELI | 0.9220 |
|   | ELII | 0.9503 |
|   | ELIII | 0.9473 |

Table XIII. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the beta distribution with m=100 and n=50.

| Run | Method | Coverage Probability |
| --- | --- | --- |
| | | 95% |
| 1 | Normal | 0.9877 |
| | ELI | 0.9752 |
| | ELII | 0.9770 |
| | ELIII | 0.9804 |
| 2 | Normal | 0.9657 |
| | ELI | 0.9792 |
| | ELII | 0.9751 |
| | ELIII | 0.9764 |
| 3 | Normal | 0.8960 |
| | ELI | 0.9503 |
| | ELII | 0.9646 |
| | ELIII | 0.9586 |
| 4 | Normal | 0.9360 |
| | ELI | 0.9687 |
| | ELII | 0.9650 |
| | ELIII | 0.9573 |
| 5 | Normal | 0.9230 |
| | ELI | 0.9330 |
| | ELII | 0.9560 |
| | ELIII | 0.9533 |

Table XIV. Coverage probabilities of intervals at the
nominal level of 95 percent when the data are generated
from the beta distribution with m=n=50.

| Run | Method | Coverage Probability |
|-----|--------|----------------------|
|     |        | 95% |
| 1 | Normal | 0.9817 |
|   | ELI | 0.9702 |
|   | ELII | 0.9744 |
|   | ELIII | 0.9767 |
| 2 | Normal | 0.9800 |
|   | ELI | 0.9841 |
|   | ELII | 0.9789 |
|   | ELIII | 0.9813 |
| 3 | Normal | 0.8847 |
|   | ELI | 0.9558 |
|   | ELII | 0.9648 |
|   | ELIII | 0.9615 |
| 4 | Normal | 0.9260 |
|   | ELI | 0.9696 |
|   | ELII | 0.9616 |
|   | ELIII | 0.9566 |
| 5 | Normal | 0.9070 |
|   | ELI | 0.9290 |
|   | ELII | 0.9547 |
|   | ELIII | 0.9503 |

Table XV. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the beta distribution with m=n=100.

| Run | Method | Coverage Probability |
|-----|--------|:--------------------:|
|     |        | 95% |
| 1 | Normal | 0.9370 |
|   | ELI    | 0.9762 |
|   | ELII   | 0.9708 |
|   | ELIII  | 0.9684 |
|   |        |        |
| 2 | Normal | 0.9573 |
|   | ELI    | 0.9853 |
|   | ELII   | 0.9675 |
|   | ELIII  | 0.9651 |
|   |        |        |
| 3 | Normal | 0.8960 |
|   | ELI    | 0.9370 |
|   | ELII   | 0.9587 |
|   | ELIII  | 0.9530 |
|   |        |        |
| 4 | Normal | 0.9520 |
|   | ELI    | 0.9667 |
|   | ELII   | 0.9623 |
|   | ELIII  | 0.9590 |
|   |        |        |
| 5 | Normal | 0.9227 |
|   | ELI    | 0.9320 |
|   | ELII   | 0.9507 |
|   | ELIII  | 0.9483 |

## C. Exponential Distribution Tables

Table XVI. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the exponential distribution with m=20 and n=50.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9993 |
|   | ELI | 0.9837 |
|   | ELII | 0.9783 |
|   | ELIII | 0.9791 |
| 2 | Normal | 0.9940 |
|   | ELI | 0.9875 |
|   | ELII | 0.9811 |
|   | ELIII | 0.9840 |
| 3 | Normal | 0.9423 |
|   | ELI | 0.9860 |
|   | ELII | 0.9818 |
|   | ELIII | 0.9846 |
| 4 | Normal | 0.8893 |
|   | ELI | 0.9815 |
|   | ELII | 0.9737 |
|   | ELIII | 0.9690 |
| 5 | Normal | 0.8357 |
|   | ELI | 0.9369 |
|   | ELII | 0.9452 |
|   | ELIII | 0.9459 |

Table XVII. Coverage probabilities of intervals at the
nominal level of 95 percent when the data are generated
from the exponential distribution with m=50 and n=20.

| Run | Method | Coverage Probability 95% |
|---|---|---|
| 1 | Normal | 0.9983 |
|   | ELI | 0.9771 |
|   | ELII | 0.9766 |
|   | ELIII | 0.9776 |
|   |   |   |
| 2 | Normal | 0.9977 |
|   | ELI | 0.9493 |
|   | ELII | 0.9620 |
|   | ELIII | 0.9638 |
|   |   |   |
| 3 | Normal | 0.9950 |
|   | ELI | 0.9723 |
|   | ELII | 0.9733 |
|   | ELIII | 0.9729 |
|   |   |   |
| 4 | Normal | 0.9677 |
|   | ELI | 0.9770 |
|   | ELII | 0.9788 |
|   | ELIII | 0.9800 |
|   |   |   |
| 5 | Normal | 0.9733 |
|   | ELI | 0.9694 |
|   | ELII | 0.9729 |
|   | ELIII | 0.9765 |

Table XVIII. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the exponential distribution with m=50 and n=100.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9616 |
|   | ELI | 0.9899 |
|   | ELII | 0.9689 |
|   | ELIII | 0.9448 |
|   |   |   |
| 2 | Normal | 0.9520 |
|   | ELI | 0.9873 |
|   | ELII | 0.9669 |
|   | ELIII | 0.9599 |
|   |   |   |
| 3 | Normal | 0.9467 |
|   | ELI | 0.9850 |
|   | ELII | 0.9643 |
|   | ELIII | 0.9567 |
|   |   |   |
| 4 | Normal | 0.9363 |
|   | ELI | 0.9653 |
|   | ELII | 0.9647 |
|   | ELIII | 0.9597 |
|   |   |   |
| 5 | Normal | 0.9130 |
|   | ELI | 0.9337 |
|   | ELII | 0.9457 |
|   | ELIII | 0.9477 |

Table XIX. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the exponential distribution with m=100 and n=50.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9773 |
|   | ELI | 0.9709 |
|   | ELII | 0.9764 |
|   | ELIII | 0.9768 |
|   |  |  |
| 2 | Normal | 0.9806 |
|   | ELI | 0.9867 |
|   | ELII | 0.9765 |
|   | ELIII | 0.9779 |
|   |  |  |
| 3 | Normal | 0.9063 |
|   | ELI | 0.9763 |
|   | ELII | 0.9736 |
|   | ELIII | 0.9763 |
|   |  |  |
| 4 | Normal | 0.9087 |
|   | ELI | 0.9625 |
|   | ELII | 0.9678 |
|   | ELIII | 0.9655 |
|   |  |  |
| 5 | Normal | 0.9127 |
|   | ELI | 0.9489 |
|   | ELII | 0.9619 |
|   | ELIII | 0.9606 |

Table XX. Coverage probabilities of intervals at the
nominal level of 95 percent when the data are generated
from the exponential distribution with m=n=50.

| Run | Method | Coverage Probability |
|-----|--------|:---:|
|     |        | 95% |
| 1   | Normal | 0.9907 |
|     | ELI    | 0.9870 |
|     | ELII   | 0.9759 |
|     | ELIII  | 0.9773 |
|     |        |        |
| 2   | Normal | 0.9850 |
|     | ELI    | 0.9838 |
|     | ELII   | 0.9764 |
|     | ELIII  | 0.9792 |
|     |        |        |
| 3   | Normal | 0.9147 |
|     | ELI    | 0.9793 |
|     | ELII   | 0.9793 |
|     | ELIII  | 0.9806 |
|     |        |        |
| 4   | Normal | 0.9097 |
|     | ELI    | 0.9695 |
|     | ELII   | 0.9709 |
|     | ELIII  | 0.9702 |
|     |        |        |
| 5   | Normal | 0.9020 |
|     | ELI    | 0.9375 |
|     | ELII   | 0.9469 |
|     | ELIII  | 0.9496 |

Table XXI. Coverage probabilities of intervals at the nominal level of 95 percent when the data are generated from the exponential distribution with m=n=100.

| Run | Method | Coverage Probability 95% |
|-----|--------|--------------------------|
| 1 | Normal | 0.9397 |
|   | ELI | 0.9807 |
|   | ELII | 0.9582 |
|   | ELIII | 0.9548 |
| 2 | Normal | 0.9323 |
|   | ELI | 0.9799 |
|   | ELII | 0.9655 |
|   | ELIII | 0.9592 |
| 3 | Normal | 0.9523 |
|   | ELI | 0.9687 |
|   | ELII | 0.9563 |
|   | ELIII | 0.9543 |
| 4 | Normal | 0.9207 |
|   | ELI | 0.9550 |
|   | ELII | 0.9577 |
|   | ELIII | 0.9540 |
| 5 | Normal | 0.9247 |
|   | ELI | 0.9463 |
|   | ELII | 0.9580 |
|   | ELIII | 0.9580 |

# APPENDIX II: REAL APPLICATION TABLE

Table XXII. Confidence Intervals for R(p) for the real data application at the 95% nominal level.

| Specificity (p) | Method | Sensitivity R(p) | Confidence Intervals | Length |
|---|---|---|---|---|
| 0.95 | ELI | 0.1446 | (0.0714, 0.2473) | .1759 |
| | ELII | 0.1446 | (0.0591, 0.2741) | .2150 |
| | ELIII | 0.1446 | (0.0590, 0.2742) | .2152 |
| 0.90 | ELI | 0.2410 | (0.1457, 0.3576) | .2119 |
| | ELII | 0.2410 | (0.1521, 0.3480) | .1959 |
| | ELIII | 0.2410 | (0.1505, 0.3503) | .1998 |
| 0.85 | ELI | 0.3133 | (0.2055, 0.4366) | .2311 |
| | ELII | 0.3133 | (0.1989, 0.4454) | .2465 |
| | ELIII | 0.3133 | (0.1983, 0.4462) | .2479 |
| 0.80 | ELI | 0.4096 | (0.2920, 0.5347) | .2427 |
| | ELII | 0.4096 | (0.2864, 0.5410) | .2546 |
| | ELIII | 0.4096 | (0.2857, 0.5419) | .2562 |
| 0.70 | ELI | 0.5181 | (0.3941, 0.6406) | .2465 |
| | ELII | 0.5181 | (0.4094, 0.6256) | .2162 |
| | ELIII | 0.5181 | (0.4094, 0.5419) | .1325 |

# APPENDIX III: S-PLUS CODE FOR SIMULATION

```
# Computing the pseudo empirical likelihood ratio confidence intervals for ROC
   curve
#
# December 3, 2005
#
#############################################################################

   m<-20
   n<-50

   #sp<-0.7  # 0.90, 0.80, 0.70
   iter<-3000
   levelc1<-0.90
   levelc2<-0.95


############################################################################
#normal distribution.

   #muy<-1   # the mean of diseased population
   #sens<-1-pnorm(qnorm(sp),muy,1)

   #sp = 0.9; muy = 2.9264
   #sp = 0.9; muy = 2.5631
   #sp = 0.9; muy = 2.1231
   #sp = 0.8; muy = 2.4865
   #sp = 0.8; muy = 1.6832
   #sens<-1-pnorm(qnorm(sp),muy,1)
############################################################################
#Exponential distribution.

   #sp<- 0.95        #  specificity = 0.6, 0.7, 0.8, 0.9, 0.95
   #delta<- 0.95     #  AUC = 0.95
   #sens<- 1-pexp(qexp(sp), rate= (1/delta -1))
############################################################################

############################################################################
#Beta(a,b) distribution.

#Table 2:

#Run 1: specificity=1-tt=0.9, sensitivity=0.95
#sp<-0.9; a0<-1; b0<-3.5; a1<-4; b1<-1;# sensitivity=0.946002
    # Delete the "#" before "tt"  when you run "Run 1" for Beta(a,b)
   distribution.

#Run 2: specificity=1-tt=0.8, sensitivity=0.93
#sp<-0.8; a0<-1; b0<-3; a1<-3; b1<-1; # sensitivity=0.9284251
    # Delete the "#" before "tt"  when you run "Run 2" for Beta(a,b)
   distribution.

#Run 3: specificity=1-tt=0.9, sensitivity=0.85
```

```
#sp<-0.9; a0<-1; b0<-3; a1<-3; b1<-1; # sensitivity=0.8461462
    # Delete the "#" before "tt"  when you run "Run 3" for Beta(a,b)
   distribution.

#Run 4: specificity=1-tt=0.8, sensitivity=0.82
#sp<-0.8; a0<-2; b0<-4; a1<-4; b1<-2; # sensitivity=0.8245191
    # Delete the "#" before "tt"  when you run "Run 4" for Beta(a,b)
   distribution.

#Run 5: specificity=1-tt=0.8, sensitivity=0.55
#sp<-0.8; a0<-2; b0<-3; a1<-3; b1<-2; # sensitivity=0.5548815
    # Delete the "#" before "tt"  when you run "Run 5" for Beta(a,b)
   distribution.

#sens<- 1-pbeta(qbeta(sp,a0,b0),a1,b1)  #sensitivity
     # Delete the "#" before "Rtt"  when you run the S code for Beta(a,b)
   distribution.

##########################################################################


   p<-1-sp

   coverage1<-0
   coverage2<-0

   coverageb11<-0        # First bootstrap
   coverageb12<-0

   coverageb21<-0        # Second bootstrap
   coverageb22<-0

   coveraget1<-0
   coveraget2<-0

   CILT1<-c(rep(0,iter))
   CILT2<-c(rep(0,iter))


# Loop

Rp<-0

for ( i in c(1:iter))
{
   #normal distribution:
   #x<-rnorm(m,0,1)            # obs from non-diseased population
   #y<-rnorm(n,muy,1)          # obs from diseased population

   #Exponential distribution: rexp(n, rate=1, scale)
   #x<-rexp(m, rate= 1)              # obs from non-diseased population
   #y<-rexp(n, rate= (1/delta -1))   # obs from diseased population

   #Beta(a,b) distribution:
   #x<-rbeta(m,a0,b0) #nondesease:
                       # Delete the "#" before "x"  when you run the S code for
                          Beta(a,b) distribution.
   #y<-rbeta(n,a1,b1) #desease
```

```
                    # Delete the "#" before "y"  when you run the S code for
                      Beta(a,b) distribution.


u<-rep(100,n)              # hat U =1- hat F
for (j in 1:n)
{
    u[j]<-1-mean((x<=y[j]))
}

indU<-(u <= p)*1          # indicator function of U: I(U_j <=p)

Rp[i]<-mean(indU)

#   compute the scale constant c(p).
    if ((Rp[i]!=1) & (Rp[i]!=0))
        {
            sigma<-Rp[i]*(1-Rp[i])
                # estimate for sigma^2

            hg<-bandwidth.sj(y, nb=1000, method="dpi")
                # Uses the method of Sheather & Jones (1991)
                # to select the bandwidth of a Gaussian kernel density
                  estimator for g
            hf<-bandwidth.sj(x, nb=1000, method="dpi")
                # Uses the method of Sheather & Jones (1991)
                # to select the bandwidth of a Gaussian kernel density
                  estimator for f

            quantileF<-quantile(x,1-p)
            densityg<-density(y,n=1,window="g",width=hg, from=quantileF)$y
                #density(.): density estimate at (1-p)-th quantile of F.
            densityf<-density(x,n=1,window="g",width=hf, from=quantileF)$y
                #density(.): density estimate at tt-th quantile of F.
            hatsigma1<-sigma + n*p*(1-p)*densityg/(m*densityf)
                # estimate for sigma_1^2
            #sigma1<-sigma + n*p*(1-p)*dnorm(qnorm(1-p), muy,
                     1)/(m*dnorm(qnorm(1-p),0,1))
                # True value of sigma_1^2

            #bootstrap estimates for R(p). Bootstap variance estimate of R(p)
            test<-sensb(y,x,1-p,300,0)
            Rpboot<-mean(test)
            Rpvar<-var(test)

            cp<-sigma/hatsigma1
            cpstar1<- sigma/(n*Rpvar)
            cpstar2<- Rpboot*(1-Rpboot)/(n*Rpvar)


            #   cat("the scale constant cp=",cp, "\n")
            wjhat<-indU-sens

            funclambda<-function(lam)mean(wjhat/(1+lam*wjhat))
            lambda<-solveNonlinear(funclambda, c(0), c(0.01))$x
            #lambda<-sum(wjhat)/sum(wjhat^2)

            lroc<-2*sum( log(abs(1+lambda*wjhat)) )
```

```
              coverage1[i]<-(cp*lroc <= qchisq(levelc1,1))*1
              coverage2[i]<-(cp*lroc <= qchisq(levelc2,1))*1

              coverageb11[i]<-(cpstar1*lroc <= qchisq(levelc1,1))*1    # First
    bootstrap
              coverageb12[i]<-(cpstar1*lroc <= qchisq(levelc2,1))*1

              coverageb21[i]<-(cpstar2*lroc <= qchisq(levelc1,1))*1    # second
    bootstrap
              coverageb22[i]<-(cpstar2*lroc <= qchisq(levelc2,1))*1

          }else{
              coverage1[i]<-NA; coverage2[i]<-NA
              coverageb11[i]<-NA; coverageb12[i]<-NA
              coverageb21[i]<-NA; coverageb22[i]<-NA
              }


    #   compute the normal approximation based interval.

       hwidth1<-qnorm(1-(1-levelc1)/2)*(hatsigma1/n)^(1/2)
       tlow1<-Rp[i]-hwidth1          # lower limit of the CI
       tup1<- Rp[i]+hwidth1          # upper limit of the CI
       if ((tlow1 <= sens) & (tup1 >= sens))coveraget1<-coveraget1+1
       CILT1[i]<-2*hwidth1           # The length of CI

       hwidth2<-qnorm(1-(1-levelc2)/2)*(hatsigma1/n)^(1/2)
       tlow2<-Rp[i]-hwidth2          # lower limit of the CI
       tup2<- Rp[i]+hwidth2          # upper limit of the CI
       if ((tlow2 <= sens) & (tup2 >= sens))coveraget2<-coveraget2+1
       CILT2[i]<-2*hwidth2           # The length of CI

}

sink("pseudoelroc1bootres")

#Normal distribution: # Delete the "#"'s before "cat" when you run the S code
   for normal distribution.
#cat("Normal distribution: m=", m, "n=", n, "specificity=", sp, "sensitivity=",
   sens, "mu=", muy, "iter=", iter, "\n")

#Exponential distribution: # Delete the "#"'s before "cat" when you run the S
   code for Exponential distribution.
#cat("Exponential dist: m=", m, "n=", n, "sp=", sp, "sens=", sens, "AUC=",
   delta, "iter=", iter, "\n")

# Beta distribution: # Delete the "#"'s before "cat"  when you run the S code
   for Beta distribution.
#cat("Beta distribution:  m=", m, "n=", n, "iter=", iter, "\n")
#cat("specifity=",sp, "sens=", sens, "a0=",a0,"a1=",a1,"b0=",b0,"b1=",b1, "\n")


cat("CI for sensitivity at level=", levelc1, "\n")
cat("Coverage of the ELRCI :", mean(sort(coverage1)), "\n")
cat("First bootstrap method. Coverage of the ELRCI :", mean(sort(coverageb11)),
   "\n")
```

```
cat("second bootstrap method. Coverage of the ELRCI :",
    mean(sort(coverageb21)), "\n")
cat("Coverage of the Normal CI :", coveraget1/iter, "\n")
#cat("Average length of ELRCI:  ", mean(CIL), " STD=", (var(CIL))^(1/2), "\n")
cat("Average length of Normal CI:  ", mean(CILT1),  "  STD=",
    (var(CILT1))^(1/2), "\n")
#cat("Midpoint:", mean(Mid),  "  STD=", (var(Mid))^(1/2), "\n")
cat("-----------------------------------------------------------------","\n")

cat("CI for sensitivity at level=", levelc2, "\n")

cat("Coverage of the ELRCI :", mean(sort(coverage2)), "\n")
cat("First bootstrap method. Coverage of the ELRCI :", mean(sort(coverageb12)),
    "\n")
cat("second bootstrap method. Coverage of the ELRCI :",
    mean(sort(coverageb22)), "\n")
cat("Coverage of the Normal CI :", coveraget2/iter, "\n")
#cat("Average length of ELRCI:  ", mean(CIL), " STD=", (var(CIL))^(1/2), "\n")
cat("Average length of Normal CI:  ", mean(CILT2),  "  STD=",
    (var(CILT2))^(1/2), "\n")
#cat("Midpoint:", mean(Mid),  "  STD=", (var(Mid))^(1/2), "\n")
cat("Mean estimate for sensitivity:", mean(Rp),  "  STD=", (var(Rp))^(1/2),
    "\n")
cat("=================================================================","\n")
sink()
```

# APPENDIX IV: S-PLUS CODE FOR REAL APPLICATION

```
# Computing the pseudo empirical likelihood ratio confidence intervals for ROC
    curve
#
# Jan. 3, 2006

    #Diabetes example
    xx<-NON[,1]             # obs from non-diseased population
    yy<-DIS[,1]              # obs from diseased population

    x<-sort(xx)
    y<-sort(yy)

    m<-length(x)
    n<-length(y)

    levelc<-0.95

    crit<-qchisq(levelc,1)

    sp<- 0.95          # specificity
    p<-1-sp          # p<-1-sp   # False Positive Rate

    ELlow<-0         # EL interval
    ELup<-0

    BELlow1<-0          # First bootstrap EL-based CI
    BELup1<-0

    BELlow2<-0          # Second bootstrap EL-based CI
    BELup2<-0

    u<-rep(100,n)             # hat U =1- hat F
    for (j in 1:n)
    {
       u[j]<-1-mean((x<=y[j]))
    }

    hg<-bandwidth.sj(y, nb=1000, method="dpi")
       # Uses the method of Sheather & Jones (1991)
       # to select the bandwidth of a Gaussian kernel density estimator for g
    hf<-bandwidth.sj(x, nb=1000, method="dpi")
       # Uses the method of Sheather & Jones (1991)
       # to select the bandwidth of a Gaussian kernel density estimator for f

    indU<-(u <= p)*1          # indicator function of U: I(U_j <=p)

    Rp<-mean(indU)            # estimate for R(p). Sensitivity

#   compute the scale constant c(p).

    sigma<-Rp*(1-Rp)         # estimate for sigma^2

    quantileF<-quantile(x,1-p)
```

```
    densityg<-density(y,n=1,window="g",width=hg, from=quantileF)$y
        #density(.): density estimate at (1-p)-th quantile of F.
    densityf<-density(x,n=1,window="g",width=hf, from=quantileF)$y
        #density(.): density estimate at tt-th quantile of F.
    hatsigma1<-sigma + n*p*(1-p)*densityg^2/(m*densityf^2)
        # estimate for sigma_1^2

#bootstrap estimates for R(p). Bootstap variance estimate of R(p)

    test<-sensb(y,x,1-p,1000,0)
    Rpboot<-mean(test)
    Rpvar<-var(test)

    cp<-sigma/hatsigma1
    cpstar1<- sigma/(n*Rpvar)
    cpstar2<- Rpboot*(1-Rpboot)/(n*Rpvar)

    #   cat("the scale constant cp=",cp, "\n")

        critcp_crit/cp               # EL interval

        critcps1_crit/cpstar1        # First bootstrap EL-based CI

        critcps2_crit/cpstar2        # second bootstrap EL-based CI


    # EL confidence intervals

        y<-elciroc(n,indU,critcp)        # calling "elciroc" to compute the EL
    interval.
        ELlow<-y[4]                  # lower limit of the EL CI
        ELup<-y[5]                   # upper limit of the EL CI


    # first bootstrap EL based CI:

        y<-elciroc(n,indU,critcps1)  # calling "elciroc" to compute the EL
    interval.
        BELlow1<-y[4]                # lower limit of the bootstrap EL CI
        BELup1<- y[5]                # upper limit of the bootstrap EL CI


    # Second bootstrap EL based CI:

        y<-elciroc(n,indU,critcps2)  # calling "elciroc" to compute the EL
    interval.
        BELlow2<-y[4]                # lower limit of the bootstrap EL CI
        BELup2<- y[5]                # upper limit of the bootstrap EL CI


sink("realexampleres")

cat("CI for sens at level=", levelc, "m=", m, "n=", n, "\n")
cat("specificity =", sp, "\n")
cat("R(p)=", Rp, "\n")

cat("lower limit of the EL CI :", ELlow, "\n")
```

```
cat("upper limit of the EL CI :", ELup, "\n")

cat("lower limit of the First bootstrap EL CI :", BELlow1, "\n")
cat("upper limit of the First bootstrap EL CI :", BELup1, "\n")

cat("lower limit of the second bootstrap EL CI :", BELlow2, "\n")
cat("upper limit of the second bootstrap EL CI :", BELup2, "\n")

cat("-------------------------------------------------------------","\n")

sink()
```