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Exact confidence interval estimation for the Youden index and its corresponding optimal cut-point

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Abstract

In diagnostic studies, the receiver operating characteristic (ROC) curve and the area under the ROC curve are important tools in assessing the utility of biomarkers in discriminating between non-diseased and diseased populations. For classifying a patient into the non-diseased or diseased group, an optimal cut-point of a continuous biomarker is desirable. Youden's index (J), defined as the maximum vertical distance between the ROC curve and the diagonal line, serves as another global measure of overall diagnostic accuracy and can be used in choosing an optimal cut-point. The proposed approach is to make use of a generalized approach to estimate the confidence intervals of the Youden index and its corresponding optimal cut-point. Simulation results are provided for comparing the coverage probabilities of the confidence intervals based on the proposed method with those based on the large sample method and the parametric bootstrap method. Finally, the proposed method is illustrated via an application to a data set from a study on Duchenne muscular dystrophy (DMD).

Keywords

Confidence interval; ROC curve; Sensitivity and specificity; Youden index; Optimal cut-point; Generalized pivotal quantity

1. Introduction

In diagnostic studies, the ROC curve, a plot of a test's sensitivity versus (1-specificity) for every possible cut-point or criterion value, and the area under the ROC curve (AUC) are important tools in assessing the diagnostic utility of biomarkers in discriminating between non-diseased and diseased populations (Goddard and Hinberg, 1990; Zweig and Campbell, 1993; Pepe, 2004). However, finding an optimal cut-point of a continuous biomarker for discriminating between non-diseased and diseased groups is also of paramount importance, and cannot be accomplished using the AUC. The Youden index (Youden, 1950), defined as

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$$J = \max_c \{\text{sensitivity}(c) + \text{specificity}(c) - 1\}, \quad (1)$$

serves as another global measure of overall diagnostic accuracy and can be used to find an optimal cut-point, where $-\infty < c < \infty$ and the value of J is between 0 and 1. When J equals 1, the distributions of the biomarker values for the diseased and the non-diseased populations are completely separated, and hence the diagnostic test is perfectly accurate. When J equals 0, the distributions of these two populations are completely overlapped, and hence the diagnostic test is completely ineffective. From the ROC curve plot, this index is the maximum vertical distance or difference between the ROC curve and the diagonal line and acts as a global measure of the optimum diagnostic utility (Schisterman and Perkins, 2007). An alternative method used to establish the "optimal" cut-point is that of finding the point on the ROC curve closest to (0, 1). Perkins and Schisterman (2006) obtained the inconsistency of optimal cut-points using the Youden index and the point closest to (0, 1) on the ROC curve.

There are several approaches for confidence interval or point estimation of the Youden index and its corresponding optimal cut-point. For instance, Schisterman et al. (2005) presented a method for estimating this index and the optimal cut-point, and extended its applications to pooled samples; Fluss et al. (2005) examined two parametric approaches (normal assumptions and transformations to normality) and two non-parametric approaches (the empirical method and the kernel method) for estimating J and the optimal cut-point; Schisterman and Perkins (2007) used the delta method to estimate the confidence intervals of the Youden index and its corresponding optimal cut-point under assumptions of normal and gamma distributions.

The purpose of this paper is to provide an alternative method for constructing the exact confidence intervals of the Youden index and its corresponding optimal cut-point under the assumption of normal distributions, especially for small to moderate sample sizes. Our approach is based on the concepts of the generalized confidence intervals introduced by Weerahandi (1993). The exact confidence intervals developed in this article are based on an exact probability statement rather than any approximation to the normal distribution. This idea of generalized inference has been widely applied to many different problems where a conventional exact confidence interval based on sufficient statistics does not exist; see Gamage et al. (2004), Lee and Lin (2004), Liu et al. (2006), Tian and Wilding (2008) and many others. In particular, the generalized inference is very efficient when the sample sizes are small; see Weerahandi (1995), Krishnamoorthy and Lu (2003), Tian and Cappelleri (2004), Lin et al. (2007), Li et al. (2008) and so on. Further details on generalized confidence intervals can be found in Weerahandi's books (1995, 2004).

This paper is organized as follows. In Section 2, the preliminary knowledge about the Youden index and its corresponding optimal cut-point is presented. In Section 3, the generalized inferences for the Youden index (J) and cut-point (c) are proposed. In Section 4, simulation results are presented for evaluating the coverage probabilities and the mean lengths of the confidence intervals based on the generalized pivotal quantity in comparison with those of the confidence intervals based on the large sample method of Schisterman and

Perkins (2007) and the parametric bootstrap method. In Section 5, the proposed approach is applied to a data set on Duchenne muscular dystrophy (DMD). A summary and discussion are presented in Section 6. The Appendix covers the basic concepts of generalized confidence intervals.

2. Preliminaries

In the following, we will briefly review the confidence interval estimation of J and c via the large sample method for which further details can be found in Schisterman and Perkins (2007).

Let Y_1 and Y_2 denote the diagnostic biomarker measurements for the diseased (case) and non-diseased (control) populations, respectively. Assume that $Y_1 \sim N(\mu_1, \sigma_1^2)$ and $Y_2 \sim N(\mu_2, \sigma_2^2)$ and that they are independent. Without loss of generality, assume that $\mu_1 > \mu_2$; otherwise take the negative of the biomarker values. Under the normality assumptions for these two populations, the value of c can be obtained from Eq. (1) such that J achieves the maximum. The optimal cut-point c and J as stated in Schisterman and Perkins (2007) are

$$c = \frac{\mu_2(b^2-1) - a + b\sqrt{a^2 + (b^2-1)\sigma_2^2 \ln(b^2)}}{b^2-1} \quad (2)$$

and

$$J = \Phi\left(\frac{\mu_1 - c}{\sigma_1}\right) + \Phi\left(\frac{c-\mu_2}{\sigma_2}\right) - 1, \quad (3)$$

where $a = \mu_1 - \mu_2$, $b = \frac{\sigma_1}{\sigma_2}$, and $\phi(\cdot)$ denotes the standard normal cumulative distribution function. When variances are equal, Eq. (2) is undefined and it can be replaced by

$$c = \frac{\mu_1 + \mu_2}{2}, \quad (4)$$

which is the limit of (2) as $b \to 1$.

Suppose that $Y_{1k} \sim N(\mu_1, \sigma_1^2)$ for $k = 1, \dots, n_1$ and $Y_{2l} \sim N(\mu_2, \sigma_2^2)$ for $l = 1 \dots n_2$ are the diagnostic biomarker measures for the diseased and non-diseased subjects, respectively. Under the normality assumptions, when distributional parameters are unknown, estimators $\hat{J}$ and $\hat{c}$ can be found by substituting sample means, $\overline{Y}_1$ and $\overline{Y}_2$, and sample variances, S_1^2 and S_2^2, for μ_1, μ_2, σ_1^2 and σ_2^2, respectively, in Eqs. (2) and (3), or Eqs. (3) and (4) for the equal variance case. Consequently, on the basis of the delta method, the approximate variances of $\hat{J}$ and $\hat{c}$ as follows:

$$\mathrm{Var}(\hat{J}) \approx \left(\frac{\partial J}{\partial \mu_1}\right)^2 \mathrm{Var}(\hat{\mu}_1) + \left(\frac{\partial J}{\partial \sigma_1}\right)^2 \mathrm{Var}(\hat{\sigma}_1) + \left(\frac{\partial J}{\partial \mu_2}\right)^2 \mathrm{Var}(\hat{\mu}_2) + \left(\frac{\partial J}{\partial \sigma_2}\right)^2 \mathrm{Var}(\hat{\sigma}_2) \quad (5)$$

and

$$\mathrm{Var}(\hat{c}) \approx \left(\frac{\partial c}{\partial \mu_1}\right)^2 \mathrm{Var}(\hat{\mu}_1) + \left(\frac{\partial c}{\partial \sigma_1}\right)^2 \mathrm{Var}(\hat{\sigma}_1) + \left(\frac{\partial c}{\partial \mu_2}\right)^2 \mathrm{Var}(\hat{\mu}_2) + \left(\frac{\partial c}{\partial \sigma_2}\right)^2 \mathrm{Var}(\hat{\sigma}_2). \quad (6)$$

The $(1 - \alpha)$ 100% confidence intervals for J and c are respectively given by $\hat{J} \pm z_{(1-\alpha/2)} \sqrt{\mathrm{Var}(\hat{J})}$ and $\hat{c} \pm z_{(1-\alpha/2)} \sqrt{\mathrm{Var}(\hat{c})}$, where $z_{(1-\alpha/2)}$ is defined by $\phi(z_{(1-\alpha/2)}) = (1 - \alpha/2)$.

3. A generalized confidence interval

In this section, we will propose generalized confidence intervals of the Youden index and its corresponding optimal cut-point, and also the corresponding algorithm is given.

Let $\bar{y}_i$ and s_i^2 be respectively the observed values of $\overline{Y}_i$ and S_i^2, $i = 1, 2$. The generalized pivotal quantity for estimating μ_i can be expressed as

$$R_{\mu_i} = \overline{y}_i - \left(\frac{\overline{Y}_i - \mu_i}{\sigma_i / \sqrt{n_i}}\right) \frac{\sigma_i}{S_i} \frac{s_i}{\sqrt{n_i}} = \overline{y}_i - \frac{Z_i}{\sqrt{V_i/(n_i - 1)}} \frac{s_i}{\sqrt{n_i}} = \overline{y}_i - t_i \frac{s_i}{\sqrt{n_i}}, \quad (7)$$

where $Z_i = \frac{\sqrt{n_i}(\overline{Y}_i - \mu_i)}{\sigma_i} \sim N(0, 1)$, $V_i = \frac{(n_i - 1)S_i^2}{\sigma_i^2} \sim \chi^2_{n_i - 1}$, and $t_i = \frac{Z_i}{\sqrt{V_i/(n_i-1)}}$ follows a Student's t-distribution with degrees $_i$ of freedom $n_i - 1$, for $i = 1, 2$. The generalized pivotal quantity for estimating σ_i^2 can be expressed as

$$R_{\sigma_i^2} = \frac{\sigma_i^2}{(n_i - 1)S_i^2}(n_i - 1)s_i^2 = \frac{(n_i - 1)s_i^2}{V_i}, \quad \text{for } i = 1, 2. \quad (8)$$

Therefore, the generalized pivotal quantity for estimating σ_i is defined as $R_{\sigma_i} = \sqrt{R_{\sigma_i^2}}$.

The generalized pivotal quantities R_c and R_J for c and J can be obtained by substituting a and b in Eq. (2) with corresponding generalized pivotal quantities

$$R_a = R_{\mu_1} - R_{\mu_2} \quad \text{and} \quad R_b = R_{\sigma_1}/R_{\sigma_2}. \quad (9)$$

Consequently, the generalized pivotal quantity for the optimal cut-point, R_c, with unequal variances, is given by

$$R_c = \frac{R_{\mu_2}(R_b^2 - 1) - R_a + R_b \sqrt{R_a^2 + (R_b^2 - 1) R_{\sigma_2^2} \ln(R_b^2)}}{R_b^2 - 1}. \quad (10)$$

When the variances are equal, Eq. (10) is undefined and it can be replaced by

$$R_c = \frac{R_{\mu_1} + R_{\mu_2}}{2}, \quad (11)$$

which is the limit of (10) as $R_b \to 1$. After substituting μ_i, σ_i, and c with their generalized pivotal values R_{μ_i}, R_{σ_i} and R_c into J, the generalized pivotal quantity for the Youden index can be derived as

$$R_J = \Phi\left(\frac{R_{\mu_1} - R_c}{R_{\sigma_1}}\right) + \Phi\left(\frac{R_c - R_{\mu_2}}{R_{\sigma_2}}\right) - 1. \quad (12)$$

It is easy to check that R_J and R_c satisfy the two conditions necessary for them to be the generalized pivotal quantities described in Appendix. For given $\bar{y}_i$ and s_i, $i = 1, 2$: (1) the distributions of R_J and R_c are independent of any unknown parameters; and (2) the values of R_J and R_c are J and c, respectively, as $\bar{Y}_i = \bar{y}_i$ and $S_i = s_i$ for $i = 1, 2$.

Let $R_{J,\alpha}$ and $R_{c,\alpha}$ denote the αth quantiles of the distributions of R_J and R_c, respectively. Then the 100(1 − α)% confidence intervals of J and c based on R_J and R_c are ($R_{J,\alpha/2}$, $R_{J,\,1-\alpha/2}$) and ($R_{c,\alpha/2}$, $R_{c,\,1-\alpha/2}$), respectively. The distributions of R_J and R_c are estimated by simulation as described below.

Computing algorithm

For a given data set including $y_{11}, \ldots y_{1n_1}$, and $y_{21}, \ldots y_{2n_2}$, the generalized confidence intervals are computed on the basis of the following algorithm.

1. Compute the sample mean $\bar{y}_i$ and sample variance s_i^2, for $i = 1, 2$.
2. For k = 1, … K.
   - Generate t_{n_1-1} and t_{n_2-1}.
   - Generate V_i from $\chi^2_{n_i-1}$, $i = 1, 2$.
   - Compute R_{μ_i} and R_{σ_i}, $i = 1, 2$, following (7) and (8).
   - Compute $R_{c,k}$ and $R_{J,k}$ following (10)–(12).

   (end k loop)
3. Compute the 100(α/2)th percentile $R_{J,\alpha/2}$ and the 100(1 − α/2)th percentile $R_{J,\,1-\alpha/2}$ of $R_{J,1}, \ldots, R_{J,K}$. Then, ($R_{J,\alpha/2}$, $R_{J,\,1-\alpha/2}$) is a 100(1 − α)% confidence interval of J.
4. Compute the 100(α/2)th percentile $R_{c,\alpha/2}$ and the 100(1 − α/2)th percentile $R_{c,\,1-\alpha/2}$ of $R_{c,1}, \ldots, R_{c,K}$. Then, ($R_{c,\alpha/2}$, $R_{c,\,1-\alpha/2}$) is a 100(1 − α)% confidence interval of c.

4. Simulation results

Simulation studies are performed to evaluate the coverage probabilities and the mean lengths of the confidence intervals based on the generalized pivotal quantity in comparison with those of the confidence intervals based on the large sample method by Schisterman and Perkins (2007) and the parametric bootstrap method.

In this simulation study, we are primarily interested in the small to moderate sample sizes. However, large sample sizes are also considered. Under the normality assumption, control groups were normally distributed with mean $\mu_2 = 0$ and variance $\sigma_2^2=1$, and case groups with mean $\mu 1$ and variances $\sigma_1^2=(0.5, 1, 3, 5)$. The specific values for $\mu 1$ were chosen to correspond to $J = 0.2, 0.4, 0.6, 0.8, 0.9$. Using the R statistical software package, 2000 samples of n_1 cases and n_2 controls for each parameter set were randomly generated. To estimate the confidence intervals by the proposed approach and the parametric bootstrap method, within each of the 2000 samples, 2500 sets of random numbers are generated in order toestimate the distributions of R_c and R_J. We generated samples of sizes (n_1, n_2) = (10, 10), (20, 20), (30, 30), (10, 30), (30, 20), (50, 20), (50, 50), (100, 100) with normal distributional assumptions.

For each of the 2000 samples, 95% confidence intervals and the mean lengths were constructed via the generalized pivotal quantity method, the large sample method and the parametric bootstrap method. When $|b - 1| < 0.01$ and $|R_b - 1| < 0.01$, they will be considered as $b \to 1$ and $R_b \to 1$, respectively. According to the large sample theory, an estimated probability will be between 0.9405 and 0.9596 at the 95% nominal confidence level.

Tables 1 and 2 present the simulation results of coverage probabilities of 95% confidence intervals and the mean lengths for J and c, respectively. The simulation results indicate that our proposed method appears satisfactory except that it tends to be slightly conservative for some scenarios, while the large sample method and the parametric bootstrap method appear liberal for many cases, especially when sample sizes are small or unequal.

To investigate the robustness of the proposed procedure under other types of distribution other than normal assumptions, simulation studies are conducted for the contaminated normal data and t distribution data. The results are displayed in Tables 3–6. For each parameter setting presented, the contaminated normal data are generated as a mixture of two normal distributions, that is, $Y_i \sim (1-B_i) N(\mu_i, \frac{1}{1.1}\sigma_i^2) + B_i N(\mu_i, \frac{2}{1.1}\sigma_i^2)$ where $B_i \sim$ Bernoulli(0.1) for $i = 1, 2$. From Tables 3 and 4, when sample sizes are increasing, the coverage probabilities of the generalized pivotal quantity method appear liberal for J and c, respectively. For t distribution data, Y_1 is generated from a non-central t distribution and Y_2 is generated from a central t distribution, that is, $Y_1 \sim t(\nu\ \delta)$ and $Y_2 \approx t(\nu, 0)$ where ν is the degree of freedom and δ is a non-centrality parameter. From Tables 5 and 6, when ν and the sample size are increasing, the coverage probability of the generalized pivotal quantity method is close to the 95% nominal confidence level for J and c, respectively.

5. Example

In this section, the proposed approach for confidence intervals of J and c will be applied to a data set on Duchenne muscular dystrophy (DMD) available from Carnegie Mellon University Statlib Datasets Archive at http://lib.stat.cmu.edu/ datasets/biomed.desc. The data set was discussed by Cox et al. (1982) and has been analyzed for ROC analysis. DMD is a typical X-linked disorder involving rapidly worsening muscle weakness. The disease is inherited from mothers to their children, primarily affecting boys. Females can be carriers of the disease but usually do not show symptoms. Currently, there is no known treatment for Duchenne muscular dystrophy. Therefore, the screening of females as potential DMD carriers is important.

The data set contains 38 carriers and 87 normals for which blood samples were obtained and four different variables were measured. For illustrative purposes, we consider the first biomarker in this data set and randomly select 24 carriers and 29 normals. Because the data set appears to be non-normal for both the carrier and normal groups, we take a logarithmic transformation for this data set to improve the normality. The sample means for carrier and normal groups are $\bar{y}_1$ = 4.7501 and $\bar{y}_2$ = 3.6382, respectively. The sample variances for carrier and normal groups are $s_1^2=0.6902$ and $s_2^2=0.1601$, respectively. The point estimates for J and c are 0.6654 and 4.1922, respectively. The 95% confidence intervals for J are (0.4951, 0.8104), (0.5014, 0.8242) and (0.5033, 0.8275) for the GPQ method, the large sample method and the parametric bootstrap method, respectively; the 95% confidence intervals for c are (4.0492, 4.3572), (4.0334, 4.3451) and (4.0422, 4.3422) for the GPQ method, the large sample method and the parametric bootstrap method, respectively. Therefore, when the sample sizes are moderate, the confidence intervals with the proposed approach are close to those for the large sample approach and the parametric bootstrap method.

6. Summary and discussion

In this article, we provide an alternative approach for estimating the confidence intervals of the Youden index and its corresponding optimal cut-point based on the concepts of generalized inference. From the simulation study, the generalized pivotal quantity method was found to be better, especially when sample sizes are small. And the simulation results from the generalized pivotal quantity method, the large sample method and the parametric bootstrapping method are very close when the sample sizes are large enough for each group.

The confidence intervals based on the concept of the generalized pivotal quantity were derived based on the assumption of normal distributions. The violation of normality assumption could result in potential bias in the estimation of confidence intervals. Before applying the generalized pivotal quantity method, the model assumption of original data should be checked and an appropriate transformation of the data carried out, if necessary.

The results of simulations show that the proposed method based on the generalized pivotal quantity is an efficient inferential procedure. Moreover, this method is based on a simple algorithm, so it is relatively easy to implement without calculating the complicated variance estimation as in the large sample approach. Thus, the generalized pivotal quantity method for estimating the confidence intervals of the Youden index and its corresponding optimal cut-point is applicable for practical use.

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Appendix

In the following, we will briefly review the basic concept of the generalized confidence interval proposed by Weerahandi (1993).

Suppose that Y is a random variable whose distribution depends on (θ, δ), where θ is a parameter of interest and δ is a nuisance parameter. Let y be the observed value of Y. A generalized pivotal quantity $R(Y; y, \theta\, \delta)$, a function of Y, y, θ, and δ, for interval estimation, defined in Weerahandi (1993), satisfies the following two conditions:

1. $R(Y; y, \theta\, \delta)$ has a distribution free of all unknown parameters.
2. The value of $(Y; y, \theta\, \delta)$ at $Y = y$ is θ, the parameter of interest.

Let R_α denote the αth quantile of the distribution of R. Then the 100(1 − α)% confidence interval of θ based on R is $(R_{\alpha/2}, R_{1-\alpha/2})$.

Table 1

The coverage probabilities and mean lengths of the 95% confidence interval for the Youden index *J*.

σ_1^2	n_1	n_2	*J*	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
0.5	10	10	0.2	0.9560	0.5165	0.8755	0.5626	0.9340	0.5198
			0.4	0.9570	0.5835	0.9250	0.6025	0.9250	0.5760
			0.6	0.9640	0.5460	0.9150	0.5397	0.9245	0.5146
			0.8	0.9690	0.4189	0.8895	0.3938	0.9175	0.3605
			0.9	0.9710	0.3105	0.8575	0.2668	0.9160	0.2412
	20	20	0.2	0.9510	0.3920	0.9275	0.4213	0.9445	0.3935
			0.4	0.9505	0.4335	0.9365	0.4360	0.9365	0.4307
			0.6	0.9485	0.3916	0.9325	0.3893	0.9275	0.3830
			0.8	0.9535	0.2931	0.9145	0.2848	0.9305	0.2742
			0.9	0.9520	0.2077	0.8970	0.1921	0.9280	0.1837
	30	30	0.2	0.9600	0.3351	0.9420	0.3519	0.9355	0.3357
			0.4	0.9610	0.3578	0.9515	0.3591	0.9360	0.3569
			0.6	0.9575	0.3206	0.9475	0.3206	0.9320	0.3164
			0.8	0.9610	0.2381	0.9355	0.2349	0.9265	0.2274
			0.9	0.9560	0.1655	0.9190	0.1581	0.9250	0.1517
	10	30	0.2	0.9550	0.4247	0.9075	0.4546	0.9140	0.4176
			0.4	0.9540	0.4731	0.9290	0.4734	0.9195	0.4596
			0.6	0.9580	0.4325	0.9190	0.4220	0.9155	0.4105
			0.8	0.9645	0.3284	0.9040	0.3072	0.9210	0.2928
			0.9	0.9635	0.2373	0.8845	0.2067	0.9210	0.1957
	30	20	0.2	0.9535	0.3720	0.9205	0.3959	0.9335	0.3733
			0.4	0.9555	0.4070	0.9320	0.4071	0.9355	0.4038
			0.6	0.9540	0.3670	0.9320	0.3643	0.9285	0.3583
			0.8	0.9595	0.2746	0.9195	0.2677	0.9235	0.2570
			0.9	0.9605	0.1940	0.9050	0.1810	0.9245	0.1721
	50	20	0.2	0.9510	0.3569	0.9250	0.3724	0.9385	0.3548
			0.4	0.9535	0.3834	0.9375	0.3814	0.9345	0.3813

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
			0.6	0.9575	0.3426	0.9315	0.3415	0.9310	0.3381
			0.8	0.9545	0.2546	0.9205	0.2515	0.9315	0.2434
			0.9	0.9495	0.1785	0.9005	0.1703	0.9295	0.1631
	50	50	0.2	0.9485	0.2691	0.9425	0.2761	0.9470	0.2696
			0.4	0.9480	0.2792	0.9465	0.2797	0.9485	0.2785
			0.6	0.9510	0.2499	0.9465	0.2502	0.9440	0.2476
			0.8	0.9515	0.1850	0.9450	0.1838	0.9420	0.1795
			0.9	0.9485	0.1271	0.9360	0.1238	0.9415	0.1200
	100	100	0.2	0.9485	0.1950	0.9510	0.1969	0.9465	0.1955
			0.4	0.9455	0.1981	0.9530	0.1986	0.9460	0.1981
			0.6	0.9480	0.1772	0.9510	0.1776	0.9450	0.1765
			0.8	0.9510	0.1307	0.9450	0.1304	0.9480	0.1287
			0.9	0.9500	0.0888	0.9410	0.0877	0.9500	0.0862
1	10	10	0.2	0.9530	0.5319	0.8895	0.5910	0.9250	0.5380
			0.4	0.9605	0.5891	0.9295	0.6136	0.9225	0.5807
			0.6	0.9655	0.5488	0.9130	0.5446	0.9205	0.5163
			0.8	0.9695	0.4205	0.8905	0.3952	0.9200	0.3610
			0.9	0.9715	0.3117	0.8575	0.2669	0.9145	0.2412
	20	20	0.2	0.9440	0.4089	0.9285	0.4486	0.9340	0.4107
			0.4	0.9475	0.4398	0.9405	0.4468	0.9280	0.4377
			0.6	0.9520	0.3947	0.9285	0.3940	0.9310	0.3860
			0.8	0.9545	0.2945	0.9125	0.2860	0.9315	0.2752
			0.9	0.9540	0.2084	0.8940	0.1921	0.9290	0.1841
	30	30	0.2	0.9590	0.3517	0.9405	0.7781	0.9350	0.3530
			0.4	0.9595	0.3649	0.9490	0.3686	0.9350	0.3641
			0.6	0.9580	0.3238	0.9440	0.3247	0.9315	0.3195
			0.8	0.9580	0.2391	0.9310	0.2359	0.9300	0.2284
			0.9	0.9570	0.1657	0.9145	0.1582	0.9275	0.1519
	10	30	0.2	0.9455	0.4636	0.9105	0.5036	0.9125	0.4544
			0.4	0.9475	0.5052	0.9225	0.5077	0.9145	0.4925

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
			0.6	0.9580	0.4586	0.9110	0.4490	0.9125	0.4377
			0.8	0.9620	0.3466	0.8980	0.3266	0.9140	0.3104
			0.9	0.9670	0.2523	0.8760	0.2205	0.9095	0.2078
1	30	20	0.2	0.9530	0.3820	0.9270	0.4152	0.9300	0.3839
			0.4	0.9555	0.4059	0.9350	0.4101	0.9315	0.4027
			0.6	0.9555	0.3628	0.9320	0.3616	0.9275	0.3540
			0.8	0.9625	0.2703	0.9230	0.2628	0.9230	0.2524
			0.9	0.9630	0.1899	0.9065	0.1766	0.9250	0.1682
	50	20	0.2	0.9490	0.3602	0.9300	0.3843	0.9355	0.3594
			0.4	0.9550	0.3740	0.9340	0.3764	0.9330	0.3722
			0.6	0.9530	0.3315	0.9330	0.3315	0.9360	0.3265
			0.8	0.9510	0.2450	0.9195	0.2410	0.9360	0.2333
			0.9	0.9525	0.1703	0.9065	0.1618	0.9325	0.1555
	50	50	0.2	0.9460	0.2855	0.9475	0.2993	0.9435	0.2872
			0.4	0.9475	0.2859	0.9505	0.2878	0.9465	0.2856
			0.6	0.9465	0.2528	0.9480	0.2535	0.9420	0.2505
			0.8	0.9485	0.1859	0.9440	0.1845	0.9415	0.1802
			0.9	0.9510	0.1272	0.9325	0.1237	0.9410	0.1199
	100	100	0.2	0.9455	0.2107	0.9560	0.2148	0.9475	0.2111
			0.4	0.9435	0.2036	0.9580	0.2046	0.9435	0.2035
			0.6	0.9465	0.1794	0.9565	0.1800	0.9445	0.1786
			0.8	0.9490	0.1312	0.9465	0.1310	0.9470	0.1292
			0.9	0.9500	0.0887	0.9425	0.0877	0.9505	0.0862
3	10	10	0.2	0.9660	0.4965	0.8845	0.5310	0.9430	0.4973
			0.4	0.9630	0.5774	0.9315	0.5868	0.9315	0.5686
			0.6	0.9655	0.5440	0.9195	0.5317	0.9210	0.5122
			0.8	0.9715	0.4175	0.8920	0.3915	0.9185	0.3597
			0.9	0.9745	0.3091	0.8600	0.2664	0.9145	0.2408
	20	20	0.2	0.9595	0.3738	0.9265	0.3930	0.9410	0.3736
			0.4	0.9540	0.4234	0.9440	0.4229	0.9305	0.4198

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
			0.6	0.9515	0.3872	0.9260	0.3835	0.9325	0.3785
			0.8	0.9535	0.2915	0.9135	0.2834	0.9265	0.2736
			0.9	0.9570	0.2073	0.8950	0.1921	0.9275	0.1843
	30	30	0.2	0.9545	0.3158	0.9390	0.3252	0.9485	0.3156
			0.4	0.9625	0.3487	0.9470	0.3469	0.9400	0.3466
			0.6	0.9590	0.3167	0.9420	0.3154	0.9385	0.3122
			0.8	0.9570	0.2367	0.9300	0.2339	0.9320	0.2270
			0.9	0.9595	0.1650	0.9175	0.1585	0.9305	0.1524
	10	30	0.2	0.9555	0.4594	0.9025	0.4730	0.9280	0.4403
			0.4	0.9490	0.5250	0.9275	0.5166	0.9195	0.5143
			0.6	0.9540	0.4844	0.9085	0.4699	0.9135	0.4663
			0.8	0.9595	0.3674	0.8920	0.3493	0.9080	0.3324
			0.9	0.9640	0.2702	0.8660	0.2395	0.9035	0.2244
	30	20	0.2	0.9620	0.3355	0.9405	0.3502	0.9425	0.3368
			0.4	0.9565	0.3762	0.9460	0.3751	0.9310	0.3727
			0.6	0.9610	0.3436	0.9370	0.3401	0.9290	0.3350
			0.8	0.9660	0.2584	0.9235	0.2510	0.9285	0.2420
			0.9	0.9660	0.1817	0.9090	0.1697	0.9260	0.1620
	50	20	0.2	0.9565	0.3031	0.9430	0.3105	0.9405	0.3011
			0.4	0.9570	0.3320	0.9415	0.3305	0.9365	0.3284
			0.6	0.9515	0.3014	0.9355	0.2989	0.9370	0.2952
			0.8	0.9485	0.2244	0.9255	0.2196	0.9375	0.2137
			0.9	0.9500	0.1553	0.9165	0.1478	0.9375	0.1427
	50	50	0.2	0.9475	0.2503	0.9515	0.2542	0.9530	0.2514
			0.4	0.9435	0.2707	0.9570	0.2700	0.9500	0.2701
			0.6	0.9455	0.2462	0.9520	0.2459	0.9460	0.2440
			0.8	0.9530	0.1840	0.9445	0.1829	0.9400	0.1787
			0.9	0.9555	0.1271	0.9350	0.1239	0.9400	0.1200
	100	100	0.2	0.9450	0.1801	0.9530	0.1807	0.9480	0.1801
			0.4	0.9480	0.1917	0.9565	0.1913	0.9465	0.1912

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	**Mean length**	**Coverage probability**	**Mean length**	**Coverage probability**	**Mean length**
			0.6	0.9485	0.1743	0.9560	0.1744	0.9460	0.1734
			0.8	0.9520	0.1299	0.9505	0.1298	0.9450	0.1281
			0.9	0.9520	0.0887	0.9470	0.0879	0.9445	0.0864
5	10	10	0.2	0.9655	0.4707	0.8900	0.4897	0.9360	0.4666
			0.4	0.9650	0.5651	0.9280	0.5624	0.9365	0.5558
			0.6	0.9655	0.5381	0.9190	0.5205	0.9250	0.5076
			0.8	0.9710	0.4141	0.8905	0.3883	0.9155	0.3584
			0.9	0.9730	0.3066	0.8580	0.2663	0.9150	0.2407
	20	20	0.2	0.9585	0.3493	0.9240	0.3596	0.9410	0.3476
			0.4	0.9550	0.4086	0.9425	0.4038	0.9350	0.4044
			0.6	0.9545	0.3802	0.9310	0.3744	0.9330	0.3720
			0.8	0.9515	0.2888	0.9165	0.2812	0.9275	0.2721
			0.9	0.9550	0.2062	0.8950	0.1923	0.9265	0.1844
	30	30	0.2	0.9585	0.2917	0.9400	0.2964	0.9480	0.2910
			0.4	0.9615	0.3346	0.9495	0.3308	0.9430	0.3324
			0.6	0.9585	0.3101	0.9440	0.3076	0.9435	0.3060
			0.8	0.9560	0.2345	0.9325	0.2322	0.9340	0.2257
			0.9	0.9615	0.1646	0.9170	0.1588	0.9285	0.1527
	10	30	0.2	0.9575	0.4445	0.8925	0.4452	0.9220	0.4208
			0.4	0.9490	0.5227	0.9295	0.5087	0.9165	0.5132
			0.6	0.9505	0.4898	0.9080	0.4725	0.9120	0.4733
			0.8	0.9555	0.3738	0.8870	0.3563	0.9035	0.3397
			0.9	0.9630	0.2760	0.8670	0.2464	0.9015	0.2305
	30	20	0.2	0.9605	0.3072	0.9430	0.3148	0.9370	0.3070
			0.4	0.9580	0.3563	0.9510	0.3523	0.9300	0.3527
			0.6	0.9595	0.3318	0.9380	0.3268	0.9355	0.3236
			0.8	0.9655	0.2521	0.9250	0.2452	0.9300	0.2370
			0.9	0.9660	0.1779	0.9130	0.1672	0.9245	0.1596
	50	20	0.2	0.9535	0.2704	0.9455	0.2722	0.9440	0.2674
			0.4	0.9605	0.3077	0.9500	0.3037	0.9440	0.3034

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	**Mean length**	**Coverage probability**	**Mean length**	**Coverage probability**	**Mean length**
			0.6	0.9545	0.2848	0.9380	0.2811	0.9410	0.2787
			0.8	0.9515	0.2142	0.9285	0.2098	0.9405	0.2047
			0.9	0.9525	0.1487	0.9185	0.1421	0.9365	0.1375
	50	50	0.2	0.9435	0.2290	0.9515	0.2313	0.9540	0.2296
			0.4	0.9465	0.2587	0.9545	0.2571	0.9520	0.2581
			0.6	0.9465	0.2406	0.9500	0.2396	0.9445	0.2385
			0.8	0.9525	0.1824	0.9425	0.1815	0.9415	0.1775
			0.9	0.9520	0.1270	0.9330	0.1242	0.9405	0.1202
	100	100	0.2	0.9465	0.1639	0.9510	0.1644	0.9485	0.1639
			0.4	0.9445	0.1827	0.9550	0.1820	0.9460	0.1823
			0.6	0.9495	0.1700	0.9535	0.1698	0.9475	0.1692
			0.8	0.9510	0.1288	0.9510	0.1288	0.9445	0.1272
			0.9	0.9505	0.0887	0.9465	0.0881	0.9460	0.0866

GPQ means the generalized pivotal quantity method. *Delta* means the large sample approach based on the delta method. *PB means the parametric bootstrap method.*.

Table 2

The coverage probabilities and mean lengths of the 95% confidence interval for the optimal cut-point *c*.

σ_1^2	n_1	n_2	*J*	GPQ		Delta		PB	
				Coverage probability	**Mean length**	**Coverage probability**	**Mean length**	**Coverage probability**	**Mean length**
0.5	10	10	0.2	0.9685	4.7857	0.8905	6.1321	0.9385	4.0438
			0.4	0.9765	1.7723	0.9170	1.4860	0.9410	1.3870
			0.6	0.9695	1.0252	0.9300	0.7806	0.9380	0.8444
			0.8	0.9635	0.9058	0.9315	0.7868	0.9420	0.8427
			0.9	0.9530	0.9854	0.9275	0.9080	0.9445	0.9731
	20	20	0.2	0.9625	2.6189	0.9255	2.3240	0.9345	2.4927
			0.4	0.9605	0.8803	0.9370	0.7091	0.9330	0.7992
			0.6	0.9625	0.6109	0.9495	0.5436	0.9450	0.5642
			0.8	0.9585	0.5870	0.9400	0.5542	0.9490	0.5734
			0.9	0.9510	0.6616	0.9370	0.6409	0.9490	0.6628
	30	30	0.2	0.9625	1.6255	0.9400	1.2775	0.9440	1.5963
			0.4	0.9570	0.6403	0.9375	0.5698	0.9510	0.5968
			0.6	0.9560	0.4731	0.9515	0.4413	0.9465	0.4488
			0.8	0.9545	0.4671	0.9540	0.4516	0.9505	0.4607
			0.9	0.9475	0.5327	0.9435	0.5232	0.9440	0.5341
	10	30	0.2	0.9535	3.3922	0.9125	3.1559	0.9315	2.8695
			0.4	0.9550	1.2371	0.9230	0.8668	0.9330	1.0029
			0.6	0.9510	0.8104	0.9385	0.6696	0.9255	0.7042
			0.8	0.9500	0.7447	0.9295	0.6790	0.9225	0.7087
			0.9	0.9510	0.8202	0.9185	0.7753	0.9255	0.8051
	30	20	0.2	0.9620	2.2636	0.9360	1.9614	0.9510	2.1656
			0.4	0.9670	0.7602	0.9400	0.6283	0.9415	0.6927
			0.6	0.9610	0.5318	0.9490	0.4815	0.9415	0.4955
			0.8	0.9540	0.5167	0.9435	0.4918	0.9480	0.5081
			0.9	0.9535	0.5878	0.9320	0.5732	0.9475	0.5923
	50	20	0.2	0.9530	1.7720	0.9380	1.5530	0.9495	1.8061
			0.4	0.9480	0.6239	0.9410	0.5580	0.9550	0.5951

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
			0.6	0.9575	0.4586	0.9545	0.4252	0.9480	0.4360
			0.8	0.9520	0.4550	0.9500	0.4360	0.9495	0.4512
			0.9	0.9495	0.5242	0.9400	0.5130	0.9445	0.5309
	50	50	0.2	0.9500	0.9689	0.9550	0.7293	0.9515	0.9258
			0.4	0.9505	0.4666	0.9515	0.4385	0.9535	0.4440
			0.6	0.9525	0.3556	0.9580	0.3408	0.9540	0.3430
			0.8	0.9430	0.3562	0.9485	0.3487	0.9475	0.3530
			0.9	0.9480	0.4090	0.9420	0.4042	0.9430	0.4096
	100	100	0.2	0.9465	0.5261	0.9540	0.4869	0.9560	0.5253
			0.4	0.9570	0.3151	0.9485	0.3073	0.9515	0.3086
			0.6	0.9610	0.2445	0.9565	0.2400	0.9560	0.2405
			0.8	0.9480	0.2485	0.9545	0.2465	0.9550	0.2477
			0.9	0.9540	0.2870	0.9525	0.2861	0.9520	0.2876
1	10	10	0.2	0.9635	5.6782	0.8920	7.5766	0.9540	4.7775
			0.4	0.9755	2.2191	0.9210	1.3418	0.9475	1.7399
			0.6	0.9695	1.2628	0.9360	0.9383	0.9470	1.0291
			0.8	0.9620	1.0906	0.9270	0.9404	0.9400	1.0127
			0.9	0.9525	1.1810	0.9265	1.0875	0.9440	1.1695
	20	20	0.2	0.9600	3.4227	0.9040	3.0046	0.9490	3.1900
			0.4	0.9620	1.1437	0.9410	0.8862	0.9470	1.0117
			0.6	0.9660	0.7473	0.9510	0.6531	0.9460	0.6819
			0.8	0.9590	0.7030	0.9405	0.6619	0.9485	0.6868
			0.9	0.9485	0.7925	0.9345	0.7667	0.9455	0.7958
	30	30	0.2	0.9520	2.3636	0.9090	2.0642	0.9490	2.1727
			0.4	0.9595	0.8329	0.9400	0.7149	0.9535	0.7530
			0.6	0.9580	0.5755	0.9560	0.5290	0.9505	0.5405
			0.8	0.9560	0.5593	0.9530	0.5384	0.9470	0.5513
			0.9	0.9495	0.6393	0.9475	0.6239	0.9430	0.6412
	10	30	0.2	0.9520	4.1587	0.8915	5.5225	0.9545	4.0171
			0.4	0.9610	1.4703	0.9295	1.0396	0.9560	1.3009

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
			0.6	0.9590	0.9274	0.9475	0.7603	0.9355	0.8158
			0.8	0.9500	0.8483	0.9360	0.7659	0.9255	0.8151
			0.9	0.9500	0.9400	0.9240	0.8869	0.9265	0.9405
1	30	20	0.2	0.9510	2.9970	0.9090	2.4037	0.9410	2.7261
			0.4	0.9590	1.0050	0.9440	0.8076	0.9385	0.8811
			0.6	0.9565	0.6665	0.9510	0.5944	0.9430	0.6138
			0.8	0.9515	0.6339	0.9420	0.6029	0.9475	0.6233
			0.9	0.9535	0.7190	0.9340	0.6985	0.9445	0.7238
	50	20	0.2	0.9495	2.4171	0.9095	1.8781	0.9500	2.2967
			0.4	0.9535	0.8551	0.9445	0.7366	0.9465	0.7809
			0.6	0.9565	0.5935	0.9570	0.5437	0.9405	0.5586
			0.8	0.9500	0.5756	0.9490	0.5533	0.9440	0.5701
			0.9	0.9510	0.6571	0.9435	0.6420	0.9405	0.6621
	50	50	0.2	0.9475	1.5422	0.9165	1.0941	0.9495	1.4219
			0.4	0.9525	0.6061	0.9460	0.5476	0.9525	0.5653
			0.6	0.9500	0.4300	0.9620	0.4075	0.9530	0.4122
			0.8	0.9435	0.4259	0.9535	0.4154	0.9475	0.4225
			0.9	0.9485	0.4909	0.9435	0.4804	0.9445	0.4926
	100	100	0.2	0.9540	0.8860	0.9215	0.7484	0.9510	0.8295
			0.4	0.9555	0.4071	0.9460	0.3827	0.9485	0.3920
			0.6	0.9585	0.2943	0.9610	0.2866	0.9515	0.2882
			0.8	0.9470	0.2972	0.9585	0.2933	0.9545	0.2963
			0.9	0.9500	0.3449	0.9515	0.3388	0.9515	0.3457
3	10	10	0.2	0.9580	7.1981	0.9125	9.2707	0.9330	6.4606
			0.4	0.9615	2.5786	0.9165	1.5471	0.9315	2.1057
			0.6	0.9650	1.5396	0.9225	1.1911	0.9400	1.2902
			0.8	0.9590	1.3965	0.9305	1.2199	0.9385	1.3014
			0.9	0.9550	1.5275	0.9225	1.4054	0.9445	1.5028
	20	20	0.2	0.9520	3.2063	0.9400	3.5914	0.9450	3.0694
			0.4	0.9565	1.2413	0.9320	1.0350	0.9445	1.1500

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
			0.6	0.9575	0.9228	0.9380	0.8370	0.9390	0.8610
			0.8	0.9555	0.9071	0.9380	0.8602	0.9380	0.8846
			0.9	0.9560	1.0216	0.9325	0.9911	0.9430	1.0189
	30	30	0.2	0.9580	1.8981	0.9580	1.3017	0.9390	1.7417
			0.4	0.9585	0.9077	0.9495	0.8300	0.9310	0.8526
			0.6	0.9625	0.7211	0.9505	0.6807	0.9365	0.6871
			0.8	0.9570	0.7235	0.9505	0.6999	0.9450	0.7106
			0.9	0.9510	0.8227	0.9470	0.8063	0.9425	0.8199
	10	30	0.2	0.9590	4.6561	0.9390	7.2746	0.9470	5.6016
			0.4	0.9535	1.5270	0.9435	1.2229	0.9510	1.5352
			0.6	0.9615	1.0106	0.9430	0.8709	0.9500	0.9405
			0.8	0.9490	0.9929	0.9430	0.8984	0.9325	0.9723
			0.9	0.9520	1.1232	0.9315	1.0612	0.9305	1.1501
	30	20	0.2	0.9565	2.6175	0.9360	1.5814	0.9375	2.3694
			0.4	0.9515	1.1143	0.9380	0.9670	0.9275	1.0144
			0.6	0.9535	0.8599	0.9435	0.7940	0.9300	0.8076
			0.8	0.9515	0.8491	0.9385	0.8146	0.9375	0.8312
			0.9	0.9535	0.9545	0.9340	0.9308	0.9445	0.9502
	50	20	0.2	0.9510	2.0620	0.9350	1.3690	0.9345	1.8219
			0.4	0.9455	1.0164	0.9405	0.9121	0.9295	0.9400
			0.6	0.9465	0.8045	0.9430	0.7594	0.9350	0.7691
			0.8	0.9490	0.8019	0.9460	0.7787	0.9385	0.7894
			0.9	0.9535	0.9007	0.9405	0.8823	0.9395	0.8932
	50	50	0.2	0.9470	1.0883	0.9550	0.9206	0.9485	1.0500
			0.4	0.9500	0.6673	0.9515	0.6384	0.9445	0.6437
			0.6	0.9425	0.5446	0.9540	0.5261	0.9505	0.5280
			0.8	0.9440	0.5519	0.9525	0.5410	0.9490	0.5466
			0.9	0.9465	0.6306	0.9460	0.6233	0.9450	0.6310
	100	100	0.2	0.9475	0.6560	0.9555	0.6239	0.9455	0.6433
			0.4	0.9465	0.4566	0.9585	0.4480	0.9410	0.4480

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
			0.6	0.9490	0.3770	0.9570	0.3713	0.9480	0.3713
			0.8	0.9475	0.3856	0.9560	0.3822	0.9530	0.3838
			0.9	0.9480	0.4427	0.9510	0.4403	0.9545	0.4427
5	10	10	0.2	0.9640	6.7568	0.9250	5.8390	0.9355	6.1820
			0.4	0.9630	2.5408	0.9240	1.6069	0.9270	2.1225
			0.6	0.9625	1.6357	0.9265	1.3112	0.9335	1.3965
			0.8	0.9565	1.5449	0.9255	1.3587	0.9400	1.4379
			0.9	0.9545	1.7021	0.9225	1.5568	0.9435	1.6600
	20	20	0.2	0.9500	2.3486	0.9385	1.5640	0.9435	2.2524
			0.4	0.9525	1.2136	0.9360	1.0692	0.9365	1.1444
			0.6	0.9600	0.9984	0.9345	0.9236	0.9380	0.9413
			0.8	0.9540	1.0088	0.9360	0.9574	0.9435	0.9797
			0.9	0.9555	1.1332	0.9345	1.0944	0.9440	1.1227
	30	30	0.2	0.9575	1.4234	0.9535	1.1638	0.9380	1.3524
			0.4	0.9525	0.9188	0.9480	0.8645	0.9310	0.8758
			0.6	0.9585	0.7878	0.9480	0.7527	0.9310	0.7554
			0.8	0.9575	0.8053	0.9470	0.7789	0.9395	0.7881
			0.9	0.9555	0.9107	0.9465	0.8892	0.9430	0.9025
	10	30	0.2	0.9660	3.6319	0.9550	3.1423	0.9570	4.8076
			0.4	0.9540	1.4101	0.9535	1.1167	0.9515	1.4494
			0.6	0.9550	1.0337	0.9450	0.9148	0.9525	0.9755
			0.8	0.9510	1.0558	0.9425	0.9613	0.9420	1.0407
			0.9	0.9500	1.2040	0.9390	1.1402	0.9350	1.2428
	30	20	0.2	0.9565	1.9309	0.9360	1.3873	0.9340	1.7870
			0.4	0.9530	1.1267	0.9370	1.0191	0.9265	1.0501
			0.6	0.9510	0.9480	0.9430	0.8893	0.9315	0.8987
			0.8	0.9560	0.9572	0.9385	0.9182	0.9405	0.9324
			0.9	0.9530	1.0707	0.9360	1.0382	0.9415	1.0568
	50	20	0.2	0.9505	1.6405	0.9375	1.3024	0.9320	1.4483
			0.4	0.9405	1.0537	0.9400	0.9798	0.9295	0.9949

σ_1^2	n_1	n_2	J	GPQ		Delta		PB	
				Coverage probability	Mean length	Coverage probability	Mean length	Coverage probability	Mean length
			0.6	0.9465	0.9021	0.9435	0.8624	0.9330	0.8679
			0.8	0.9475	0.9160	0.9445	0.8885	0.9360	0.8956
			0.9	0.9530	1.0208	0.9405	0.9946	0.9365	1.0027
	50	50	0.2	0.9490	0.9454	0.9535	0.8704	0.9455	0.9187
			0.4	0.9470	0.6875	0.9470	0.6666	0.9400	0.6693
			0.6	0.9425	0.5987	0.9505	0.5827	0.9485	0.5831
			0.8	0.9425	0.6145	0.9505	0.6022	0.9470	0.6074
			0.9	0.9445	0.6965	0.9460	0.6870	0.9450	0.6950
	100	100	0.2	0.9460	0.6218	0.9550	0.6018	0.9540	0.6111
			0.4	0.9480	0.4756	0.9560	0.4691	0.9430	0.4686
			0.6	0.9460	0.4167	0.9550	0.4117	0.9485	0.4111
			0.8	0.9455	0.4293	0.9570	0.4253	0.9515	0.4267
			0.9	0.9505	0.4882	0.9540	0.4849	0.9560	0.4874

GPQ means the generalized pivotal quantity method. *Delta* means the large sample approach based on the delta method. *PB* means the parametric bootstrap method.

Table 3

Coverage probabilities of the 95% confidence interval for the Youden index J under the mixture model.

n_1	n_2	J	σ_1^2			
			0.5	**1**	**3**	**5**
10	10	0.2	0.9665	0.9640	0.9640	0.9640
		0.4	0.9660	0.9615	0.9620	0.9615
		0.6	0.9605	0.9600	0.9560	0.9535
		0.8	0.9530	0.9550	0.9580	0.9540
		0.9	0.9475	0.9505	0.9520	0.9470
20	20	0.2	0.9500	0.9430	0.9480	0.9435
		0.4	0.9430	0.9420	0.9455	0.9470
		0.6	0.9350	0.9330	0.9365	0.9380
		0.8	0.9240	0.9240	0.9330	0.9320
		0.9	0.9170	0.9180	0.9265	0.9235
10	30	0.2	0.9510	0.9455	0.9525	0.9535
		0.4	0.9500	0.9500	0.9520	0.9485
		0.6	0.9475	0.9415	0.9430	0.9455
		0.8	0.9425	0.9440	0.9440	0.9420
		0.9	0.9385	0.9420	0.9410	0.9435
50	50	0.2	0.9525	0.9520	0.9370	0.9310
		0.4	0.9485	0.9510	0.9375	0.9380
		0.6	0.9420	0.9395	0.9390	0.9385
		0.8	0.9155	0.9165	0.9170	0.9200
		0.9	0.9000	0.8995	0.9035	0.9095
100	100	0.2	0.9410	0.9480	0.9350	0.9300
		0.4	0.9370	0.9420	0.9390	0.9385
		0.6	0.9165	0.9190	0.9255	0.9285
		0.8	0.8905	0.8910	0.8940	0.8975
		0.9	0.8765	0.8740	0.8805	0.8830

The mixture model is defined as $Y_i \sim (1-B_i)N(\mu_i, \frac{1}{1.1}\sigma_i^2)+B_iN(\mu_i, \frac{2}{1.1}\sigma_i^2)$ where $B_i \sim$ Bernoulli(0.1) for i = 1, 2.

Table 4

Coverage probabilities of the 95% confidence interval for the optimal cut-point c under the mixture model.

n_1	n_2	J	σ_1^2			
			0.5	**1**	**3**	**5**
10	10	0.2	0.9510	0.9355	0.9640	0.9695
		0.4	0.9535	0.9540	0.9590	0.9575
		0.6	0.9670	0.9655	0.9510	0.9515
		0.8	0.9580	0.9615	0.9585	0.9565
		0.9	0.9415	0.9470	0.9450	0.9465
20	20	0.2	0.9420	0.9125	0.9410	0.9455
		0.4	0.9455	0.9340	0.9355	0.9315
		0.6	0.9535	0.9550	0.9415	0.9335
		0.8	0.9530	0.9535	0.9470	0.9405
		0.9	0.9345	0.9330	0.9320	0.9290
10	30	0.2	0.9410	0.9200	0.9435	0.9500
		0.4	0.9455	0.9400	0.9295	0.9335
		0.6	0.9570	0.9575	0.9485	0.9415
		0.8	0.9475	0.9495	0.9430	0.9415
		0.9	0.9420	0.9385	0.9350	0.9290
50	50	0.2	0.9255	0.8870	0.9465	0.9460
		0.4	0.9170	0.9135	0.9365	0.9350
		0.6	0.9395	0.9515	0.9505	0.9350
		0.8	0.9445	0.9455	0.9415	0.9360
		0.9	0.9260	0.9280	0.9265	0.9245
100	100	0.2	0.9150	0.8855	0.9250	0.9250
		0.4	0.9150	0.9120	0.9145	0.9185
		0.6	0.9400	0.9440	0.9385	0.9250
		0.8	0.9335	0.9425	0.9330	0.9275
		0.9	0.9270	0.9345	0.9275	0.9220

The mixture model is defined as $Y_i \sim (1-B_i)N(\mu_i, \frac{1}{1.1}\sigma_i^2) + B_i N(\mu_i, \frac{2}{1.1}\sigma_i^2)$ where $B_i \sim$ Bernoulli(0.1) for $i = 1, 2$.

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Table 5

Coverage probabilities of the 95% confidence interval for the Youden index J under the t distribution.

n_1	n_2	$\nu = 5$ J = 0.7329	$\nu = 8$ J = 0.7898	$\nu = 10$ J = 0.8068
10	10	0.9660	0.9725	0.9635
20	20	0.9485	0.9615	0.9665
10	30	0.9675	0.9725	0.9720
50	50	0.9315	0.9490	0.9640
100	100	0.9005	0.9455	0.9510

The t-distribution is defined as $Y_1 \sim t(\nu, \delta)$ and $Y_2 \sim t(\nu, 0)$ where ν is the degree of freedom and δ is a non-centrality parameter.

Table 6

Coverage probabilities of the 95% confidence interval for the optimal cut-point c under the t distribution.

n_1	n_2	$\nu = 5$	$\nu = 8$	$\nu = 10$
		J = 0.7329	J = 0.7898	J = 0.8068
10	10	0.9485	0.9605	0.9710
20	20	0.9420	0.9585	0.9635
10	30	0.9520	0.9605	0.9665
50	50	0.9290	0.9630	0.9620
100	100	0.9155	0.9505	0.9555

The t-distribution is defined as $Y_1 \sim t(\nu, \delta)$ and $Y_2 \sim t(\nu, 0)$ where ν is the degree of freedom and δ is a non-centrality parameter.