The Korean Communications
in Statistics Vol. 11 No. 3, 2004
pp. 447-454

# Bootstrap Confidence Intervals for the Difference of Quantiles of Right Censored Data

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## Abstract

In this paper, we consider the bootstrap method to the interval estimation of the difference of quantiles of right censored data. We showed the validity of bootstrap method and compare with others with real data example. In simulation various resampling schemes for right censored data are also considered.

*Keywords* : Bootstrap interval estimation; Difference of quantiles; Right censored data

## 1. Introduction

Suppose that we have two independent non-negative valued random samples $X_{11}, \ldots, X_{1n_1}$ and $X_{21}, \ldots, X_{2n_2}$ with continuous distribution functions $F_1$ and $F_2$, respectively. Since the right censoring schemes are involved, we may only observe that for $i=1,2$ and $j=1, \ldots, n_i$

$$T_{ij} = \min(X_{ij}, C_{ij}), \quad \delta_{ij} = I(X_{ij} \le C_{ij}),$$

where $C_{11}, \ldots, C_{1n_1}$ and $C_{21}, \ldots, C_{2n_2}$ are two independent censoring random samples with arbitrary distribution functions. In order to avoid the identifiability problem, we assume the independence between $X_{ij}$ and $C_{ij}$ for each $i$ and $j$.

Based on these samples, Wang and Hettmansperger (1990), Kim (1993) and Su and Wei (1993) proposed the interval estimates of the difference between two medians. Wang and Hettmansperger proposed a procedure by obtaining two one-sample confidence intervals and then cooking up both intervals as one confidence interval for the difference of medians with a certain coefficient. Also they obtained asymptotic normality for appropriately defined confidence limits for each samples. Whereas Kim considered obtaining the interval estimation using the bootstrap method for right censored data. However he did not provide any asymptotic result. Su and Wei considered a procedure by defining an equation which contains the difference of medians as a parameter. The important feature of their approach does not require the

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estimates of densities. In this paper, also we consider the interval estimate of the difference between quantiles. For the motivation of this study, we investigate the relation of the control percentile test statistics (Gastwirth and Wang, 1988), and the estimates of differences of quantiles for right censored data. Then we may obtain the equivalence relation in the following manner.

Let $\widehat{F}_i$ be the Kaplan-Meier estimates for $F_i$ for each $i$. For any $p$, $0 < p < 1$, let

$$\theta_i(p) = F_i^{-1}(p) = \inf\{ t : F_i(t) \geq p\} \text{ and } \widehat{\theta}_i(p) = \widehat{F}_i^{-1}(p) = \inf\{ t : \widehat{F}_i(t) \geq p\}$$

be the $p$-th quantiles of $F_i$ and $\widehat{F}_i$, respectively for each $i = 1, 2$. Using these notations, Gastwirth and Wang (1988) proposed the contol percentile test statistics as follows:

$$W_{mn} = \widehat{F}_2(\widehat{F}_1^{-1}(p)) - p = \widehat{F}_2(\widehat{\theta}_1(p)) - p.$$

Since with probability one, $\widehat{F}_2^{-1}(\widehat{F}_2(t)) = t$, we see that by taking $\widehat{F}_2^{-1}$ on both terms of $W_{mn}$,

$$\begin{aligned} \widehat{F}_2^{-1}(\widehat{F}_2(\widehat{F}_1^{-1}(p))) - \widehat{F}_2^{-1}(p) &= \widehat{F}_2^{-1}(\widehat{F}_2(\widehat{\theta}_1(p))) - \widehat{F}_2^{-1}(p) \\ &= \widehat{\theta}_1(p) - \widehat{\theta}_2(p). \end{aligned}$$

Therefore the control percentile test statistics and the differences between two quantiles for any given $p$ are equivalent. This point urges us to consider the asymptotic properties for the point estimates $\widehat{\theta}_1(p) - \widehat{\theta}_2(p)$ for each given $p$. We note that $\widehat{\theta}_1(p) - \widehat{\theta}_2(p)$ is the form of the estimates of the differences of quantiles proposed by Kim (1993). In the next section, we consider the asymptotic normality for $\widehat{\theta}_1(p) - \widehat{\theta}_2(p)$.

## 2. Asymptotic Normality for $\widehat{\theta}_1(p) - \widehat{\theta}_2(p)$

In order to derive the asymptotic normality for $\widehat{\theta}_1(p) - \widehat{\theta}_2(p)$, we review some results for the Bahadur type representation theorem for quantiles, which was considered by Cheng (1984) and Lo and Singh (1985) with several assumptions for $F$. We will follow the idea of Lo and Singh in the following lemma. For this purpose, we introduce some notations. For each $i = 1, 2$,

$$1 - H_{F_i}(u) = P\{ T_{ij} > u\}, \quad F_i^1(u) = P\{ T_{ij} \leq u, \delta_{ij} = 1\},$$

$$\xi(T_{ij}, \delta_{ij}, t) = (1 - F_i(t)) \left\{ \frac{I(T_{ij} \leq t, \delta_{ij} = 1)}{1 - H_{F_i}(T_{ij})} - \int_0^t \frac{I(T_{ij} \geq u) dF_i^1(u)}{(1 - H_{F_i}(u))^2} \right\}$$

and finally $\theta_i$ is the upper limit of the support of $H_{F_i}$, in other words, $\theta_i = \inf\{ t : H_{F_i}(t) = 1\}$.

Now we state the assumptions which is needed in the following lemma:

Assumption 1. For each $p$ and for each $i = 1, 2$, $F_i$ is continuous and twice differentiable at $\theta_i(p) < \theta_i$.

Assumption 2. For each $p$ and for each $i = 1, 2$, $f_i(\theta_i(p)) > 0$ for $\theta_i(p) < \theta_i$, where $f_i$ is the densities for $F_i$.

**Lemma** 1. For any given $p$ and for each $i=1,2$, with the assumptions 1 and 2 for $F_i$, we have that with probability one, as $n_i\to\infty$,

$$\hat{\theta}_i(p) - \theta_i(p) = -\frac{1}{n_i}\sum_{j=1}^{n_i}\frac{\xi(T_{ij},\delta_{ij},\theta_i(p))}{f_i(\theta_i(p))} + O(n_i^{-3/4}(\log n_i)^{3/4}).$$

**Proof.** It follows from Theorem 2 in Lo and Singh (1985).

The mean and variance for $\xi(T_{ij},\delta_{ij},t)$ are as follows:

$$E[\xi(T_{ij},\delta_{ij},t)]=0$$

and

$$Var[\xi(T_{ij},\delta_{ij},t)]=(1-F_i(t))^2\int_0^t(1-H_{F_i}(u))^2dF_i^1(u).$$

Then the asymptotic normality for

$$\sqrt{n}\{(\hat{\theta}_1(p)-\hat{\theta}_2(p))-(\theta_1(p)-\theta_2(p))\}$$

with $n=n_1+n_2$ follows in the following theorem.

**Theorem** 1. With the assumptions 1 and 2 for $F_i$ and $n_1/n\to\lambda$,

$$\sqrt{n}\{(\hat{\theta}_1(p)-\hat{\theta}_2(p))-(\theta_1(p)-\theta_2(p))\}$$

converges weakly to a normal random variable with 0 mean and variance $\sigma^2(p)$, where

$$\begin{aligned}\sigma^2(p) &= \frac{1}{\lambda}\frac{(1-F_1(\theta_1(p))^2}{f_1^2(\theta_1(p))}\int_0^{\theta_1(p)}\frac{dF_1^1(u)}{(1-H_{F_1}(u))^2} \\ &\quad+\frac{1}{1-\lambda}\frac{(1-F_2(\theta_2(p))^2}{f_2^2(\theta_2(p))}\int_0^{\theta_2(p)}\frac{dF_2^1(u)}{(1-H_{F_2}(u))^2} \\ &=\frac{1}{\lambda}\frac{(1-p)^2}{f_1^2(\theta_1(p))}\int_0^{\theta_1(p)}\frac{dF_1^1(u)}{(1-H_{F_1}(u))^2}+\frac{1}{1-\lambda}\frac{(1-p)^2}{f_2^2(\theta_2(p))}\int_0^{\theta_2(p)}\frac{dF_2^1(u)}{(1-H_{F_2}(u))^2}.\end{aligned}$$

**Proof.** From Lemma 1, we note that with probability one,

$$\begin{aligned}&\sqrt{n}\{(\hat{\theta}_1(p)-\hat{\theta}_2(p))-(\theta_1(p)-\theta_2(p))\} \\ &=\sqrt{n/n_1}\sqrt{n_1}(\hat{\theta}_1(p)-\theta_1(p))-\sqrt{n/n_2}\sqrt{n_2}(\hat{\theta}_2(p)-\theta_2(p)) \\ &=\sqrt{\frac{n}{n_1}}\sqrt{\frac{1}{n_1}}\sum_{j=1}^{n_1}\frac{\xi(T_{1j},\delta_{1j},\theta_1(p))}{f_1(\theta_1(p))}-\sqrt{\frac{n}{n_2}}\sqrt{\frac{1}{n_2}}\sum_{j=1}^{n_2}\frac{\xi(T_{2j},\delta_{2j},\theta_2(p))}{f_2(\theta_2(p))} \\ &\qquad+O(n^{-3/4}(\log n)^{3/4}).\end{aligned}$$

Thus the result follows from the central limit theorem with Slutsky's theorem.

From the Theorem, we have that

$$\sqrt{n}\{(\hat{\theta}_1(p)-\hat{\theta}_2(p))-(\theta_1(p)-\theta_2(p))\}/\sigma(p)$$

is asymptotically normally distributed with 0 mean and unit variance. Thus

$$(\hat{\theta}_1(p)-\hat{\theta}_2(p))\pm z_{\alpha/2}\sigma(p)/\sqrt{n}$$

is an asymptotic $(1-\alpha)\times 100\%$ confidence interval for $\theta_1(p)-\theta_2(p)$, where $z_{\alpha/2}$ is a percentile point such that $\Phi(z_{\alpha/2})=1-\alpha/2$ for the standard normal cumulative distribution $\Phi$ Then we need the consistent estimate of $\sigma^2(p)$ for calculating the end points. However, the result may be unstable since we have to consider estimating the densities. In order to detour this difficulty, we consider applying the bootstrap method to obtain the confidence interval of $\theta_1(p)-\theta_2(p)$ in the next section.

## 3. Bootstrap Interval Estimations for the Difference of Quantiles

In this section we will show the validity of bootstrap method and also introduce various resampling schemes which are useful for censored surviving data. Let $\hat{\theta}_i(p)$, $i=1,2$ be the estimators defined in the previous section and let $\hat{\theta}_i^*(p)$, $i=1,2$ be the corresponding estimators based on bootstrap samples.

**Theorem 2.** Under the assumptions for $F_1$ and $F_2$ in Lemma 1 and $n_1/n\to\lambda$,

$$\sqrt{N}[\hat{\theta}_1^*(p)-\hat{\theta}_2^*(p)-(\hat{\theta}_1(p)-\hat{\theta}_2(p))]$$

converges in distribution to a normal random variable with mean 0 and variance $\sigma^2(p)$, where

$$\sigma^2(p)=\frac{1}{\lambda}\frac{(1-p)^2}{f_1^2(\theta_1(p))}\int_0^{\theta_1(p)}\frac{dF_1^1(u)}{(1-H_{F_1}(u))^2}+\frac{1}{1-\lambda}\frac{(1-p)^2}{f_2^2(\theta_2(p))}\int_0^{\theta_2(p)}\frac{dF_2^1(u)}{(1-H_{F_2}(u))^2}.$$

**Proof**. For detailed derivations, see Appendix in Park and Na (2000).

This means that for the approximate distribution for $\hat{\theta}_1(p)-\hat{\theta}_2(p)$, we may use the approximate bootstrap distribution based on $\hat{\theta}_{1^*}(p)-\hat{\theta}_{2^*}(p)$.

Now we briefly state three types of resampling plans (Resampling I ~ III below) for censored data which are used in Section 4. Suppose that $F$ and $G$ are the distribution functions of $X$ and C, respectively. Let $1-\hat{F}(x)$ be the product-limit (or Kaplan-Meier) estimate of the failure time survivor function and $1-\hat{G}(x)$ be the product limit estimate of the censoring survivor function.

Resampling I : Ordinary (or Case) Bootstrap

When the data are homogeneous sample subject to random censorship, the most direct way to bootstrap is to set $T^*=\min(X^*,C^*)$, where $X^*$ and $C^*$ are independently generated from $\hat{F}$ and $\hat{G}$ respectively. This implies that

$$P\{T^*>x\}=\{1-\hat{G}(x)\}\{1-\hat{F}(x)\}=\prod_{j:x_j\le x}\left(\frac{n-j}{n+1-j}\right),$$

which corresponds to the empirical distribution function (EDF) that places mass $n^{-1}$ on each of the n cases $(t_j,\delta_j)$.

Resampling II : Conditional Bootstrap

For $r=1,\dots,R$,

1. Generate $X_1^*,\dots,X_n^*$ independently from $\hat{F}$
2. For $j=1,\dots,n$, make simulated censoring variables by setting $C_j^*=x_j$ if $\delta_j=0$, and if $\delta_j=1$, generating $C_j^*$ from $\{\hat{G}(x)-\hat{G}(x_j)\}/\{1-\hat{G}(x_j)\}$, which is the estimated distribution of $C_j$ conditional on $C_j > x_j$ ; then
3. Set $T_j^*=\min(X_j^*, C_j^*)$, for $j=1,\dots,n$.

Resampling Ⅲ: Wierd Bootstrap

When interest is focused on the survival or hazard functions, a third and quite different approach uses direct simulation from the Nelson-Aalen estimate $\hat{A}(x) = \sum_{j:x_j\le x}\left\{\delta_j / \sum_{k=1}^{n} H(x_j-x_k)\right\}$ of the cumulative hazard, where $H(u)$ is the Heaviside function, which equals zero if $u<0$ and equals one otherwise. The idea is to treat the numbers of failures at each observed failure time as independent binomial variables with denominators equal to the numbers of individuals at risk, and means equal to the numbers that actually failed. Thus when $x_1<\cdots<x_n$, we take the simulated number to fail at time $x_j$, $N_j^*$, to be binomial with denominator $n-j+1$ and probability of failure $d_j/(n-j+1)$. A simulated Nelson-Aalen estimate is then

$$\hat{A}(x) = \sum_{j=1}^{n}\frac{N_j^*}{\sum_{k=1}^{n} H(x_j-x_k)},$$

which can be used to estimate the uncertainty of the original estimate $\hat{A}(x)$

## 4. Comparison with Others

### 4.1 Other Procedures

For comparison with other procedures, we briefly describe the following two methods among others.

(A) Wang and Hettmansperger's (WH) method

Frist of all, we obtain two univariate confidence intervals $(L_1, U_1)$ and $(L_2, U_2)$ for two medians, $\theta_1$ and $\theta_2$ with some confidence coefficients, $\gamma_1$ and $\gamma_2$, respectively. Then for the confidence interval $\theta_1-\theta_2$, Wang and Hettmansperger (1990) proposed

$$(L_1-U_2, U_1-L_2)$$

with some confidence coefficient $\gamma$.

Even though the confidence interval does not contain the unknown densities, the confidence coefficient requires some complicated calculations and is obtainable some special cases with relatively easy manners. For more detailed contents, see Wang and Hettmansperger (1990).

(B) Su and Wei's (SW) method

For each $i=1,2$ let $S_i(\cdot)$ be the survival function for group $i$ and let $\hat{S}_i(\cdot)$ be the corresponding Kaplan-Meier estimate. For $i=1,2$, let $\theta_i=\theta_i(p)$ be the $p$-th quantile of the distribution $F_i$ and let $\hat{\theta}_i$ be a consistent estimate of $\theta_i$ which can be easily obtained by solving the equation $\hat{S}_i(\theta_i)=p$. Suppose that we are interested in making inferences about $\Delta=\theta_1-\theta_2$ and suppose that $\theta_2$ can be expressed as $h(\Delta,\theta_1)$.

Su and Wei (1993) used a functional equation such as

$$W(\Delta,\theta_1)=\frac{(\hat{S}_1(\theta_1)-1/2)^2}{\hat{\sigma}_1^2(\hat{\theta}_1)}+\frac{\hat{S}_2(h(\Delta,\theta_1))-1/2)^2}{\hat{\sigma}_2^2(\hat{\theta}_2)},$$

where $\hat{\sigma}_i^2(t)$ is the usual Greenwood's formula for the variance of $\hat{S}_i(t)$ and $\theta_1$ is a nuisance parameter. To eliminate $\theta_1$, we have to minimize $W(\Delta,\theta_1)$ with respect to $\theta_1$. Let $G(\Delta)$ be the resulting statistic. Then $G(\Delta)$ is asymptotically chi-square distributed with 1 degree of freedom. A confidence interval for $\Delta$ with confidence coefficient $1-\alpha$ can be constructed by inverting $G(\cdot)$, where $\{\Delta: G(\Delta)<\chi_1^2(\alpha)\}$ and $\chi_1^2(\alpha)$ is the $100\times\alpha$ upper percentage point of $\chi_1^2$.

### 4.2 A Practical Example

In this section we show an example for illustration of our bootstrap interval estimation procedures. We consider the data in Table 1 cited from Efron (1988). These data arose in a clinical trial of cancer of the head and neck, comparing radiation only with radiation plus chemotherapy. Subjects were randomly allocated to the two treatment groups. $x$ is observed numbered number of days following treatment before relapse. $\delta=1$ if the relapse was observed and $\delta=0$ if the experiment was terminated before the relapse was observed.

<Table 1> Head and Neck Cancer Data, Efron(1988)

| Radiation Alone | | | | | | Radiation plus Chemotherapy | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| x | $\delta$ | x | $\delta$ | x | $\delta$ | x | $\delta$ | x | $\delta$ | x | $\delta$ |
| 7 | 1 | 146 | 1 | 297 | 1 | 37 | 1 | 194 | 1 | 1092 | 0 |
| 34 | 1 | 149 | 1 | 319 | 0 | 84 | 1 | 195 | 1 | 1245 | 0 |
| 42 | 1 | 154 | 1 | 405 | 1 | 92 | 1 | 209 | 1 | 1331 | 0 |
| 63 | 1 | 157 | 1 | 417 | 1 | 94 | 1 | 249 | 1 | 1557 | 1 |
| 64 | 1 | 160 | 1 | 420 | 1 | 110 | 1 | 281 | 1 | 1642 | 0 |
| 74 | 0 | 160 | 1 | 440 | 1 | 112 | 1 | 319 | 1 | 1771 | 0 |
| 83 | 1 | 165 | 1 | 523 | 0 | 119 | 1 | 339 | 1 | 1776 | 1 |
| 84 | 1 | 173 | 1 | 523 | 1 | 127 | 1 | 432 | 1 | 1897 | 0 |
| 91 | 1 | 176 | 1 | 583 | 1 | 130 | 1 | 469 | 1 | 2023 | 0 |
| 108 | 1 | 185 | 0 | 594 | 1 | 133 | 1 | 519 | 1 | 2146 | 0 |
| 112 | 1 | 218 | 1 | 1101 | 1 | 140 | 1 | 528 | 0 | 2297 | 0 |
| 129 | 1 | 225 | 1 | 1116 | 0 | 146 | 1 | 547 | 0 | | |
| 133 | 1 | 241 | 1 | 1146 | 1 | 155 | 1 | 613 | 0 | | |
| 133 | 1 | 248 | 1 | 1226 | 0 | 159 | 1 | 633 | 1 | | |
| 139 | 1 | 273 | 1 | 1349 | 0 | 169 | 0 | 725 | 1 | | |
| 140 | 1 | 277 | 1 | 1412 | 0 | 173 | 1 | 759 | 0 | | |
| 140 | 1 | 279 | 0 | 1417 | 1 | 179 | 1 | 817 | 1 | | |

<Table 2> and <Table 3> summarize the $100(1-\alpha)\%$ bootstrap confidence intervals of the difference of quantiles. For $\alpha$=0.05, 0.1, we consider the quantiles for $p=0.5$ and 0.8. All the types of resampling schemes explained in above section are considered and all the results concerning bootstrap confidence intervals are based on 1000 replications. The confidence intervals from both standard and percentile bootstrap methods are given. Confidence interval based on standard bootstrap method is obtained by using the asymptotic normality of bootstrap estimator which is derived in Section 2, whereas the percentile method uses the percentiles of bootstrap estimates from resampled data. For detailed explanation of the bootstrap methods refered in this paper, see Efron and Tibshirani (1993). The results from standard bootstrap method are quite different from others since this method does not sufficiently reflect the asymmetricity of the quantile estimators. But the results from percentile bootstrap method are very similar to WH and SW's. The suggested bootstrap methods are very simple and easy to use and also does not involve any complicated calculation. All the simulations are carried out from Splus software.

<Table 2> Bootstrap Confidence Intervals for the Difference of Quantiles( $\alpha$ = 0.95)

| C.I. | Method | $p$=0.8 | $p$=0.5 |
|---|---|---|---|
| Standard Bootstrap | Ordinary | (-52, 50) | (-504, 262) |
| | Conditional | (-49, 47) | (-558, 316) |
| | Weird | (-50, 48) | (-395, 153) |
| Percentile Bootstrap | Ordinary | (-66, 29) | (-565, 64) |
| | Conditional | (-66, 24) | (-641, 79) |
| | Weird | (-69, 21) | (-473, 53) |
| SW | | (-81, 36) | (-643, 78) |
| WH | Equal coefficient | (-75, 28) | (-565, 68) |
| | Equal length | (-75, 21) | (-473, 68) |
| | Equal depth | (-50, 30) | (-283, 121) |

(SW: Su & Wei (1993), WH: Wang & Hettmansperger (1990))

<Table 3> Bootstrap Confidence Intervals for the Difference of Quantiles( $\alpha$ = 0.90)

| C.I. | Method | $p$=0.8 | $p$=0.5 |
|---|---|---|---|
| Standard Bootstrap | Ordinary | (-44, 42) | (-442, 200) |
| | Conditional | (-41, 39) | (-488, 246) |
| | Weird | (-42, 40) | (-351, 109) |
| Percentile Bootstrap | Ordinary | (-57, 23) | (-479, 39) |
| | Conditional | (-56, 21) | (-507, 45) |
| | Weird | (-62, 19) | (-415, 30) |
| SW | | (-70, 21) | (-559, 46) |
| WH | Equal coefficient | (-64, 20) | (-473, 64) |
| | Equal length | (-64, 21) | (-473, 64) |
| | Equal depth | (-50, 27) | (-185, 101) |

(SW: Su & Wei (1993), WH: Wang & Hettmansperger (1990))

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[ Received April 2004 , Accepted August 2004 ]