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Weighted Quantile Test for Comparing Several Treatments with a Control Under Right Censorship

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ABSTRACT

A test based on quantiles is proposed for homogeneity of several treatments against the simple tree alternatives when the samples are subject to the right censorship. The proposed test is a generalization of Park and Kim(1989)'s one. The size and the power of the test is examined in a simulation study.

I. Introduction

In certain life-testing experiments and clinical trials for survival analysis, where cost of experimentation is high, it is desirable to terminate the experimentation or the study as soon

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as enough data become available to reach a decision. When we compare several treatments with a control, an easy way to compare them is to compare specified quantiles among groups. The most desirable aspect of this statistical method is for the experimenter to terminate the experiment when we collect the data until specified quantile points.

The quantile test was introduced by Mathisen(1943) and used in survival analysis in situations where the cost of continuing an experiment is high. Further developments of the procedure are due to Gart(1963), Gastwirth(1968). Recently Chakraborti and Desu(1988) discussed the quantile test procedures extensively and Park and Kim(1989) obtained weighted quantile test for the simple tree alternatives. These researches assume no censoring data.

For the case of censored data, Brookmeyer and Crowley(1982) extended the median test procedure to the case of censored data consisting two or more samples. Recently Gastwirth and Wang(1988) and Chakraborti(1988, 1990a 1990b), Chakraborti and Desu(1990), Park(1990) discussed about quantile test procedures with right random censored data.

This research was motivated by combining Park and Kim(1989) with Chakraborti and Desu(1990). It aims for developing the weighted quantile test for the simple tree with right random censored data and showing how much the proposed test is more powerful than the Chakraborti and Desu one. We present the limiting distribution of quantile test statistic in section 2. In section3, we propose weighted quantile test by combining several quantile statistics with reasonable weights. Finally, we examing the approximate powers of weighted quantile test in various sample size configurations and compare it with Chakraborti and Desu one through simulations.

Ⅱ. Quantile Test

Here we have $(k+1)$ independent random samples of sizes $n_0, n_1, \cdots, n_k$, from $(k+1)$ populations with continuous distribution functions $F_0, F_1, \cdots, F_k$, respectively. For the j-th unit in the i-th sample we observe the pair (X_{ij}, δ_{ij}), where X_{ij} denotes either the lifetime (T_{ij}) or the observation time corresponding to the unit and δ_{ij} denotes whether the lifetime was censored or not, $i=0, 1, 2, \cdots, k$ and $j=1, 2, \cdots, n_i$.

Suppose that we have the random censoring model and that the censoring variables C_{ij}'s are $i.i.d.$ random variables with a continuous cumulative distribution function G_i, $i=0, 1, \cdots, k$, $j=1, 2, \cdots, n_i$. In the random censoring model, the C_{ij}'s and the T_{ij}'s are independent. Hence, X_{ij} are also $i.i.d.$ with continuous distribution function H_i, given by

$$(2.1) \qquad H_i(X) = 1-(1-F_i(X))(1-G_i(X)).$$

The null hypothesis of interest is that the effect of each of the k treatments is the same as the control,

$$(2.2) \qquad H_0 : F_0 = F_i, i=1, 2, \cdots, k,$$

We consider the one-sided alternatives that at least one of the treatments is better than the control which is formulated as

$$(2.3) \qquad H_1 : F_0 \geq F_i, i=1, 2, \cdots, k,$$

with strict inequality for at least one i. This alternatives are also referred as "simple tree alternatives".

Remark 1. The alternatives (2.3) can be changed in some situations like

$$H_2 : F_0 \leq F_i, i=1, 2, \cdots, k,$$

or

$$H_3 : F_0 \neq F_i, i=1, 2, \cdots, k.$$

One obvious way to test the alternatives (2.3) is to compare the prechosen p-quantile β of the control sample with the relative quantile of β of the treatment samples. Let $\hat{F}_i$ be the Kaplan-Meier estimator of F_i and
let $\hat{F}_0^{-1}(p)$ be defined as

$$\hat{F}_0^{-1}(p) = \inf\{t : \hat{F}_0(t) \geq p\},$$

an estimator of β. Further let the random vector U

$$\mathrm{U} = (U_1 - n_1 F_1(\beta), U_2 - n_2 F_2(\beta), \cdots, U_k - n_k F_k(\beta))'$$

where $U_i = n_i \hat{F}_i(\hat{F}_0^{-1}(p))$, and let

$$(2.4) \qquad \sigma_{ii} = [1 - F_i(\beta)]^2 \int_0^\beta (1-F_i)^{-2}(1-G)^{-1} dF_i,$$

$$i=1, 2, \cdots, k.$$

If there are no censored observations and $k=1$, $p=1/2$, U_1 reduces to counting the number of treatment observations that precede the pre-assigned quantile of the control sample, the statistic proposed by Mathisen(1943).

Under the alternative H_1 at least one of the elements of U is expected to be small. Thus, a test of H_0 against H_1 can be obtained

$$\text{reject } H_0 \text{ in favor of } H_1 \text{ if } W = \sum_{i=1}^{k} \{U_i - n_i F_i(\beta)\} < C.$$

The remaining problem to implement the test is to either find C so that the size of the test is equal to a pre-assigned quantity, or to find the p-value of the test. For these purposes the distribution of W is required. Assuming random censorship, the following result was proved by Chakraborti(1988) under certain regularity conditions. Recently Gastwirth and Wang (1988) proved a similar result.

Theorem 1. $N^{-1/2}$ U converges weakly to a k dimensional normal distribution with mean vector 0 and dispersion matrix $\Gamma = ((\partial_{ij}))$, where

$$\partial_{ij} = \sigma_{00}\varphi_i\varphi_j\lambda_i\lambda_j\lambda_0^{-1} + \delta_{ij}\sigma_{ii}\lambda_i,$$

$N = \sum_{i=0}^{k} n_i$, $\lambda_i = \lim_{N\to\infty} \dfrac{n_i}{N}$ $(0<\lambda_i<1)$, $\varphi_i = \dfrac{F_i'(\beta)}{F_0'(\beta)}$, and δ_{ij} equals 1 if $i=j$, 0 otherwise.

Since $F_i(\beta) = p$ for all i under H_0, from theorem 1 it follows that $N^{-1/2} W$ converges weakly to the normal distribution with mean 0 and the variance

$$\sigma_W^2 = \{(1-\lambda_0)^2/\lambda_0\}\sigma_{00} + \sum_{i=1}^{k} \lambda_i\sigma_{ii}.$$

The quantity σ_W^2 can be consistently estimated by estimating σ_{ii} with the Greenwood estimate $\lambda = \dfrac{n_i}{\mathrm{N}}$ and

$$(2.5) \qquad \hat{\sigma}_{ii} = \{1-\hat{F}_0(\hat{\beta}_0)\}^2 \sum_{j=1} n_i d_{ij} \{R_{ij}(R_{ij}-d_{ij})\}^{-1},$$

where d_{ij} is the number of deaths at X_{ij}, R_{ij} is the number of 'risk' at X_{ij} and the sum is over all distinct X_{ij} such that $X_{ij} \leq \hat{\beta}$.

If $\hat{\sigma}_W^2$ is such an estimate of σ_W^2 it follows that the null distribution of $W^* = N^{-1/2} W/\hat{\sigma}_W$ can be approximated by the standard normal distribution from Theorem 1 and Slutsky's theorem. Hence an approximately size α version of the proposed test is

$$(2.6) \qquad \text{reject } H_0 \text{ in favor of } H_1 \text{ if } W^* < Z(\alpha)$$

Where $Z(\alpha)$ is the lower α -quantile of a standard normal distribution.

Remark 2. One might propose the following test, when the alternative hypothesis is H_2

reject H_0 in favor of H_2 if $W^* > Z(1-\alpha)$,

and when the alternative hypothesis H_3

reject H_0 in favor of H_3 if $W^{*2} > \chi^2(1;1-\alpha)$,

where $\chi^2(1;1-\alpha)$, is the $(1-\alpha)$th quantile of the chi-square distribution with 1 degree of freedom.

Remark 3. Chakraborti(1990a, b) proposed two tests for H_0 against H_1 by considering minimum of U_i and Behrens-Fisher type problem.

Ⅲ. Weighted Quantile Test

Park and Kim(1989) discussed weighted version of W^* assuming no censored data. They pointed out that we should use their test when we are interested in comparing several treatments with a control and especially, the sizes of samples are different. It has not been known that this result can be extended to the case of censored data. This research suggest that we would better use Park and Kim's weights to the censored data cases. The following result is from theroem 1 and Park and Kim(1989).

Theorem 2. Assuming no censored data, the relative maximin test statistic based on the quantile statistics is

$$V = \sum_{i=1}^{k} \{a_i U_i - a_i n_i F_i(\beta)\},$$

where $a_i = \sqrt{\dfrac{N-n_i}{n_i}}$. Under the regularity conditions, the statistic $V^* = N^{-1/2} V/\hat{\sigma}_V$ is approximately normally distributed with mean 0 and variance 1, where

$$(2.7) \qquad \hat{\sigma}_V^2 = \lambda_0^{-1}\hat{\sigma}_{00}\left(\sum_{i=1}^{k} a_i \lambda_i\right)^2 + \sum_{i=1}^{k} a_i^2 \lambda_i \hat{\sigma}_{ii}.$$

Hence, we propose an approximate α-level test based on V^*;

$$(2.8) \qquad \text{reject } H_0 \text{ in favor of } H_1 \text{ if } V^* < Z(\alpha)$$

Remark 4. See Park(1990) for the detailed asymptotic distribution of V^*.

One might conjecture V is not a relative maximin test statistic under the censored data. Since censoring mechanism is so complex, it might spoils the true differences among experimental differences. It is true! However, the censoring rate is not high and sample sizes are different, then we expect test based on V^* works better than Chakraborti and Desu unweighted quantile test. Besides if censoring distributions are same and proportional to lifetime distributions, then V^* is still the relative maximin test statistic. We will examine the powers of the proposed test and unweighted quantile test in next sections.

Ⅳ. Simulation Results and Conclusion

Some simulation study was conducted to examine the behavior of the proposed test in terms of the size and the power. The simulation consisted of the following steps.

(1) Two sets of random numbers from two probability distributions (one is the population distribution, the other is censoring distribution) were generated. In each simulation the generation was repeated 1000 times.

(2) In each repeat (run) we computed the test statistics and checked if H_0 was rejected or not. The proportion of times (out of 1000) the procedure rejected H_0 was recorded.

1. Population Distributions − Translation Exponential Distribution
   Censoring Distributions − Translation Exponential Distribution
   Censoring rate : 10%

〈Table 4.1 : k=2, n_0=50, n_1=30, n_2=40〉

Population Distr. Exponential			Unweighted test	weighted test
θ_0	θ_1	θ_2		
0.0	0.0	0.0	0.053	0.055
0.0	0.1	0.1	0.173	0.175
0.0	0.1	0.2	0.259	0.253
0.0	0.2	0.2	0.358	0.360
0.0	0.3	0.1	0.336	0.352
0.0	0.3	0.5	0.810	0.801
0.0	0.4	0.3	0.690	0.693
0.0	0.5	0.5	0.890	0.892

2. Population Distributions – Translation Exponential distribution
Censoring Distributions – Uniform distribution
Censoring rate : 10%

〈 Table 4.2 : k=2, n_0=50, n_1=40, n_2=50 〉

Population Distr. Exponential θ_0	θ_1	θ_2	Unweighted test	weighted test
0.0	0.0	0.0	0.053	0.058
0.0	0.1	0.2	0.172	0.155
0.0	0.0	0.4	0.451	0.409
0.0	0.2	0.2	0.353	0.355
0.0	0.4	0.2	0.576	0.591
0.0	0.6	0.4	0.887	0.892
0.0	0.6	0.6	0.965	0.966
0.0	0.8	0.0	0.879	0.909

〈 Table 4.3 : k=2, n_0=50, n_1=60, n_2=50 〉

Population Distr. Exponential θ_0	θ_1	θ_2	Unweighted test	weighted test
0.0	0.0	0.0	0.044	0.045
0.0	0.0	0.2	0.169	0.180
0.0	0.2	0.0	0.177	0.166
0.0	0.2	0.2	0.372	0.369
0.0	0.2	0.4	0.635	0.650
0.0	0.2	0.6	0.807	0.827
0.0	0.4	0.6	0.915	0.917
0.0	0.8	0.2	0.972	0.963

〈 Table 4.4 : k=2, n_0=50, n_1=60, n_2=70 〉

Population Distr. Exponential θ_0	θ_1	θ_2	Unweighted test	weighted test
0.0	0.0	0.0	0.043	0.044
0.0	0.0	0.2	0.202	0.188
0.0	0.2	0.0	0.165	0.180
0.0	0.2	0.2	0.401	0.406
0.0	0.4	0.2	0.617	0.633
0.0	0.2	0.4	0.665	0.649
0.0	0.4	0.4	0.809	0.809
0.0	0.6	0.4	0.927	0.933

We simulated various population and censoring models to compare two tests and found some interesting features ;

(i) both tests are comparable,

(ii) when certain treatment group has smaller sample size and bigger parameter value than the other treatment one, weighted quantile test is more powerful.

From the simulation studies weighted quantile test is not uniformly more powerful than unweighted quantile test, but weighted one is recommended in general.

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