

Journal of the Korean
Statistical Society
Vol. 23, No. 1, 1994

Nonparametric Test for Equality of Survival Distributions Using Probit Scale†

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ABSTRACT

To test the equality of survival distributions in the presence of arbitrary right censorship, the choice of weights which are functions of the number of individuals at risk at the time of each death is very important in increasing the power of the test. In this paper a weight by probit scale is derived and the efficiencies relative to the other weight's are also investigated.

KEYWORDS: Distribution-free test, Survival distribution, Failure or uncensored time, Censoring time, Probit scale, Relative efficiency.

1. INTRODUCTION

A distribution-free two-sample test is proposed, which is an extension of the Wilcoxon test, to samples with arbitrary censoring on the right. Suppose that the failure times or censoring times are observed for two different populations. For the first population, let the failure times, T_1, T_2, \dots, T_m be iid each with distribution function F_1 , and C_1, C_2, \dots, C_m be iid each with distribution

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† This research is supported by Korean Research Foundation, 1988.

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function G_1 where C_i is the censoring time associated with T_i . We can observe $(X_1, I_1), \dots, (X_m, I_m)$ where X_i is defined as the minimum of T_i and C_i , and I_i is a binary random variable equaling 1 if $T_i \leq C_i$ and 0 otherwise. For the second population, let, U_1, U_2, \dots, U_n be iid each with distribution function F_2 , and D_1, D_2, \dots, D_n be iid each with distribution function G_2 where D_j is the censoring time associated with U_j . We can observe $(Y_1, J_1), \dots, (Y_n, J_n)$ where Y_j is defined as the minimum of U_j and D_j , and J_j is a binary random variable equaling 1 if $U_j \leq D_j$ and 0 otherwise.

In this study we consider a generalized Wilcoxon procedure by Mantel and Haenszel(1959), and Gehan(1965) to test the equality of survival distributions of two populations. Taron and Ware(1977) demonstrate that the test statistics for these two methods differ only in the choice of weights which are functions of the number of individuals at risk at the time of each failure or censoring. Additionally they proposed a third statistic which is constructed with different weights. Based on the suggestions of Cochran(1954) regarding the combination of 2×2 contingency tables, a fourth statistic using probit scale is proposed which may be more satisfactory when the form of the alternatives is in question.

2. MODIFIED WILCOXON TEST STATISTICS

Let $Z_{(k)}, k = 1, 2, \dots, m + n$, be the combined ordered sample based on the two samples, and let $K_{(k)}$ be the indicator of uncensoredness associated with $Z_{(k)}$, i.e., $K_{(k)} = 1$ if $Z_{(k)}$ is uncensored and $K_{(k)} = 0$ otherwise. For each failure time point a 2×2 contingency table is constructed. For the i th failure time point (uncensored observation) the contingency table is as follows:

	# failure	# alive	
X(Population 1)	a_i		n_{i_1}
Y(Population 2)			
	m_{i_1}		n_i

where a_i is the number of uncensored observation in the first population at time t_i where t_i is the time of the i th uncensored observation, and m_{i_1} is the number of uncensored observation in the combined ordered sample at time t_i . If we

assume no ties, $m_{i1} = 1$ and $a_i = 0$ or 1 . n_{i1} is the number of X 's remaining at time t_i^- , and n_i is the number of Z 's remaining at time t_i^- . Given marginals fixed in the i th 2×2 table, the random variable A_i , which is the entry in the $(1, 1)$ cell of the i th contingency table, has a hypergeometric distribution with mean $(n_{i1} \cdot m_{i1})/n_i$ and variance $\{n_{i1} \cdot m_{i1} \cdot (n_i - n_{i1})(n_i - m_{i1})\}/\{n_i^2 \cdot (n_i - 1)\}$. After construction of a 2×2 table for each of the k uncensored observations, Tarone and Ware (1977) suggest weighting each table, forming

$$\sum_{i=1}^k W_i \{a_i - E_0(A_i)\} = \sum_{i=1}^k W_i \left\{a_i - \frac{m_{i1} n_{i1}}{n_i}\right\}, \quad (2.1)$$

where W_i is the weight given to each table and $E_0(A_i)$ is the expectation under the null hypothesis for random variable A_i , and a_i, m_{i1}, n_{i1} and n_i are taken from the 2×2 table. For the variance, use

$$\sum_{i=1}^k W_i^2 \text{Var}_0(A_i) = \sum_{i=1}^k W_i^2 \left\{ \frac{m_{i1}(n_i - m_{i1})}{n_i - 1} \right\} \left\{ \frac{n_{i1}}{n_i} \left(1 - \frac{n_{i1}}{n_i}\right) \right\}, \quad (2.2)$$

where $\text{Var}_0(A_i)$ is the variance of A_i calculated under the null hypothesis. And the test statistic

$$S^2 = \frac{\left[\sum_{i=1}^k W_i \{a_i - E_0(A_i)\} \right]^2}{\sum_{i=1}^k W_i^2 \text{Var}_0(A_i)} \quad (2.3)$$

is shown to be approximately distributed as χ^2 with 1 degree of freedom. This is an approximation to the exact conditional distribution under the null hypothesis.

Radhakrishna(1965) investigated the choice of efficient weights in the combination of 2×2 tables for various alternatives of the form $f(p_{1i}) - f(p_{2i}) = c$, where p_{1i} and p_{2i} are the response probabilities in the i th table; $f(p)$ is a known monotonic function for $0 < p < 1$, and c is a constant. There are three special cases:

- (i) Mantel and Haenszel(MH:1959) consider a logit scale which results in $W_i = 1$,
- (ii) Gehan(1965) considers a constant scale which results in $W_i = n_i$, and
- (iii) Tarone and Ware(TW:1977) suggest an arcsin scale which results in $W_i = \sqrt{n_i}$.

In this paper a probit scale is studied which can be considered a fourth weight.

3. WEIGHT BY PROBIT SCALE

The weight which is optimal for constant differences on the probit scale, $\Phi^{-1}(p)$, is estimated from continuous life time data, where

$$\Phi(p) = \int_{-\infty}^p \frac{1}{\sqrt{2\pi}} e^{-\frac{x^2}{2}} dx.$$

Radhakrishna(1965) showed that the weight by probit scale is

$$W_i = \frac{\exp[-\{\Phi(\Pi_i)\}^2/2]}{\sqrt{2\pi}\Pi_i(1 - \Pi_i)} \quad (3.1)$$

where Π_i denotes the expected response of marginals for the i th table. Since the estimate of Π_i is $1/n_i$, the weight W_i is estimated as

$$\widehat{W}_i = \frac{\exp[-\{\Phi(1/n_i)\}^{-2}/2]}{\sqrt{2\pi}} \cdot \frac{n_i^2}{n_i - 1}. \quad (3.2)$$

But using the Mclaurin series and after some manipulation, it can be shown that

$$\exp[-\{\Phi(1/n_i)\}^{-2}/2] = e^{-2}\left(1 + \frac{8}{\sqrt{2\pi}n_i}\right) + O\left(\frac{1}{n_i^2}\right)$$

where $-0.1865 < O\left(\frac{1}{n_i^2}\right) < 0.1723$.

Constant multiplications to weight, W_i , do not change the test statistics of equation. Hence the estimate of weight becomes from (3.2)

$$\widehat{W}_i = n_i + \frac{8}{\sqrt{2\pi}}$$

by letting $\frac{n_i}{n_i-1} \cong 1$. Thus the weight by probit scale is shown to be a combination of the weights by logit and constant scale of section 2-(i) and (ii).

4. ASYMPTOTIC RELATIVE EFFICIENCY

Asymptotic relative efficiencies for test statistics by logit, arcsin and constant scales which result in MH, TW, and Gehan statistics, are compared by Tarone and Ware(1977) using Pitman efficiencies at several alternatives under the assumption of no censorship and equal sample sizes. The alternatives considered are

- (i) Lehmann alternative; $F_2(x) = F_1^\theta(x)$
- (ii) Logistic alternative; $F_2(x) = [1 + e^\theta \{1 - F_1(x)\} / F_1(x)]^{-1}$
- (iii) Scale alternative; $F_2(x) = F_1(\theta x)$
- (iv) Translation alternative; $F_2(x) = F_1(x + \theta)$.

In addition, we can introduce a probit scale for comparison. In order to obtain the Pitman efficiencies we adapt the Crowley's representation(see [2]), which is used to provide a proof of the asymptotic normality of a nonparametric two-sample test statistic, under the above assumptions. After some manipulation we can obtain the Pitman efficacy for each statistic, then we know that the efficiencies depend upon the censoring distributions in a complicated manner and the total sample sizes of the combined sample. The null density function, $f(t)$, is specified in the table 1, and the total sample sizes given to the left entry in the table represent the examples of a small sample size and an asymptotic case. For each alternative, Table 1 lists the Pitman efficiencies relative to the statistic which, of the four statistics considered, has the highest efficacy at the specified alternative.

5. DISCUSSION

One can observe from Table 1 that the test statistic by probit scale(S_P) tends to be the same with the test statistic by logit scale(S_G) as $n \rightarrow \infty$.

Table 1. Relative efficiencies of the two sample rank tests when there is no censorship.

n	S_{MH}	S_G	S_{TW}	S_P
Lehman alternative; $f(t) = \exp(-t), t > 0$				
20	100	75	89	78
50	100	75	89	76
∞	100	75	89	75
Logistic alternative; $f(t) = \exp(-t), t > 0$				
20	68	90	87	100
50	72	95	92	100
∞	75	100	96	100
Scale alternative; $f(t) = 2t \exp(-t^2), t > 0$				
20	100	75	89	78
50	100	75	89	78
∞	100	75	89	75
Translation alternative; $f(t) = 2t \exp(-t^2), t > 0$				
20	67	100	89	78
50	67	100	89	75
∞	67	100	89	75

In equation (3.2), it is obvious that the weight by probit scale shows that the term with n_i will dominate as $n_i \rightarrow \infty$. But when n_i is small it seems that S_P neutralizes S_G . The exact calculation of test statistics and application to different types of censoring distributions may enlighten the usage of probit scale.

We know that the results in Table 1 are obtained from assuming no censorship, and it may be more practical to calculate the test power using the various simulation methodologies such as Monte-Carlo simulation methodology when there exists censorship. To get the results of applying the simulation methodologies, further study is needed later.

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