Tests for some statistical hypotheses for dependent competing risks

Isha Dewan
Indian Statistical Institute
New Delhi-110016
India
isha@isid.ac.in

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Abstract

Suppose an individual is exposed to two dependent competing risks. Here we review some tests based on time to failure and cause of failure for testing hypotheses for equality of sub-distribution (sub-survival) functions and cause specific hazard rates.

1 Introduction

The competing risks situation arises in life studies when a unit is subject to many, say k, modes of failure and the actual failure can be ascribed to a unique mode. Suppose that the continuous positive valued random variable T represents the lifetime of the unit and δ taking values $1, 2, \ldots, k$ represent the risk which caused the failure of the unit.

The joint probability distribution of (T, δ) is specified by the set of k sub-distribution functions $F(i,t) = P[T \leq t, \delta = i]$, or equivalently by the subsurvival functions $S(i,t) = P[T > t, \delta = i],\ i = 1, 2, \ldots, k$. Let $H(t)$ and $S(t)$ denote , respectively the distribution function and the survivor function of T. Let $f(i,t)$ denote the sub-density function corresponding to ith risk. Then the density function of T is $h(t) = \sum_{i=1}^{k} f(i,t)$ and $p_i = F(i, \infty)$ is the probability of failure due to the ith risk. Let cause specific hazard rate be given by $\lambda(i,t) = \frac{f(i,t)}{S(t)}$.

A commonly used description of the competing risks situation is the latent failure time model. Let $X_1, X_2, \ldots, X_k$ be the latent failure times of any unit exposed to k risks, where X_i represents the time to failure if cause i were the only cause of failure present in the situation. F_i denotes the marginal distribution of X_i. The observable random variables are still the time to failure T, and the cause of failure δ where $\delta = j$ if $X_j = \min(X_1, X_2, \ldots, X_k)$. If $X_1, X_2, \ldots, X_k$ are independent then the marginal and hence the joint distribution is identifiable from the probability distribution of the observable random variables (T, δ). However, in general when the risks are not independent, neither the joint distribution of $X's$ nor their marginals are identifiable from the probability distribution of (T, δ) (Crowder (2001)). The independence or otherwise of the latent lifetimes $(X_1, X_2, \ldots, X_k)$ cannot be statistically tested from any data collected on (T, δ). Also, the marginal distribution functions $F_i(x)$ may not represent the probability distribution of lifetimes in any practical situation. Elimination of jth risk may change the environment in such a way that $F_i(x)$ does not represent the lifetime of X_i in the changed scenario.

In view of the above considerations, unless one can assume independence, it is necessary to suggest appropriate models, develop methodology and carry out the data analysis in terms of the observable random variables (T, δ) alone. For recent work on these lines see Deshpande (1990), Aras and Deshpande (1992),Aly, Kochar and McKeague (1994), Sun and Tiwari (1995), Deshpande and Dewan (2000) , Crowder

(2001),Kalbfleisch and Prentice (2002), Dewan and Kulathinal (2003), and Dewan, Deshpande and Kulathinal (2004),

2 Locally Most Powerful Rank Tests

Suppose $k = 2$, that is , a unit is exposed to two risks of failure denoted by 1 and 0. When n units are put to trial , the data consists of $(T_i, {\delta^*}_i), i = 1, \ldots, n$ where $\delta^* = 2 - \delta$. Suppose we wish to test the hypothesis $H_0 : F(1,t) = F(2,t)$, for all t. Let $\underline{T} = (T_1, \ldots, T_n), \underline{\delta^*} = (\delta_1, \ldots, \delta_n)$. Let $f(1,t) = f(t,\theta), f(2,t) = h(t) - f(t,\theta)$ where $h(t)$ and $f(t,\theta)$ are known density functions and incidence density such that $f(t,\theta_0) = \frac{1}{2}h(t)$. Let $T_{(1)} \leq T_{(2)} \leq \ldots \leq T_{(n)}$ denote the ordered failure times. Let

$$W_i = \begin{cases} 1 & \text{if } T_{(i)} \text{ corresponds to first risk} \\ 0 & \text{otherwise.} \end{cases} \tag{1}$$

Let R_j be the rank of T_j among $T_1, \ldots, T_n$.

Theorem **2.1** *If $f'(t,\theta)$ is the derivative of $f(t,\theta)$ with respect to θ, then the locally most powerful rank test for $H_0 : \theta = \theta_0$ against $H_1 : \theta > \theta_0$ is given by: reject H_0 for large values of $L_c = \sum_{i=1}^n w_i a_i$, where*

$$a_i = \int \cdots \int_{0<t_1<\ldots<t_n<\infty} \frac{f'(t_i,\theta_0)}{f(t_i,\theta_0)} \prod_{i=1}^{n} [f(t_i,\theta_0) dt_i]. \tag{2}$$

Note that for Deshpande's (1990) model with $\theta_0 = 1/2$, then sign test U_1 is the LMPR test. When the underlying distribution is logistic , the LMPR test is based on the statistic $W^+ = \sum_{i=1}^n W_i R_i$, which is the analogue of the Wilcoxon signed rank statistic for competing risks data. For Lehmann type alternative LMPR test is based on scores $a_i = E(E_{(j)})$ where $E_{(j)}$ is the jth order statistic from a random sample of size n from standard exponential distribution.

3 Tests for bivariate symmetry

Assume that the latent failure times X and Y are dependent. Suppose their joint distribution is given by $F(x,y)$. On the basis of independent pairs $(T_i, {\delta^*}_i)$ we want to test whether the forces of two risks are equivalent against the alternative that the force of one risk is greater than that of the other. That is we test the null hypothesis of bivariate symmetry

$$H_0 : F(x,y) = F(y,x) \text{ for every } (x,y) \tag{3}$$

Theorem **3.1** *Under the null hypothesis of bivariate symmetry we have*
(i)$F(1,t) = F(2,t)$ $S(1,t) = S(2,t)$ $\lambda(1,t) = \lambda(2,t)$ for all t,
(ii) $P[\delta^* = 1] = P[\delta^* = 0]$ and T and δ^* are independent.

The following alternatives to the null hypothesis are worth considering.

$$H_1 : \lambda(1,t) < \lambda(2,t); \quad H_2 : F(1,t) < F(2,t); \quad H_3 : S(1,t) > S(2,t). \tag{4}$$

For testing H_0 against H_1 recently Kochar and Dewan have suggested considering the following measure of deviation between H_0 and H_1, $\Delta = \int_{0<x<y<\infty} [\psi(x) - \psi(y)]\, dF(x)\, dF(y)$. Its empirical estimator leads to the statistic

$$U_2 = \sum_{i=1}^{n-1} i(n-i) W_{i+1}. \tag{5}$$

Rejecting H_0 for small values of U_2. Under H_0, $n^{\frac{1}{2}}\{\frac{U_2}{n^3} - \frac{1}{12}\} \xrightarrow{\mathcal{L}} N(0, \frac{1}{120})$.

Deshpande (1990) proposed two tests for testing H_0 versus H_2 on heuristic grounds. The first test is the Wilcoxon signed rank type statistic $W^+ = \sum_{i=1}^{n}(1-\delta^*{}_i)R_i$. Another test is based on the U-statistic U_3 where

$$\binom{n}{2}U_3 = \sum_{i=1}^{n}(n - R_i + 1)\delta^*{}_i. \tag{6}$$

For testing H_0 against H_2, one can consider the measure of deviation $F(2,t) - F(1,t)$, which is non-negative under H_2. Then $\int_0^\infty [F(2,t) - F(1,t)]dH(t) = P[\delta^*{}_1 = 0, T_1 \leq T_2] - \frac{1}{2}$. A U-statistic estimator of this parameter is the statistic U_3 discussed above. Similarly for testing H_0 against H_3 consider the measure of deviation $S(1,t) - S(2,t)$, which is non-negative under H_3. Then $\int_0^\infty [S(1,t) - S(2,t)]dH(t) = P[\delta^*{}_1 = 1, T_1 > T_2] - \frac{1}{2}$. A U-statistic estimator is given by

$$\binom{n}{2}U_4 = \sum_{i=1}^{n}(R_i - 1)\delta^*{}_i. \tag{7}$$

This statistic was earlier proposed by Bagai, Deshpande and Kochar (1989) to test for equality of failure rates of independent latent competing risks. Aly , Kochar and Mckeague (1994) proposed Kolmogrov-Smirnov type tests for testing the equality of two competing risks against the alternatives H_1 and H_2. Most of the above tests can be generalized to the case when the data is right censored (Aly et al (1994), Sun and Tiwari (1995).

Remarks

(i) The various tests are distribution-free under H_0 and consistent against their intended alternatives.

(ii) We can also use these tests for the hypothesis $\lambda_1(t) = \lambda_2(t)$ against the alternative that cause-specific hazards are ordered.

(iii) The statistic U_2 puts more weight on the middle observations and is less sensitive to the observations in the beginning and the end of the experiment. On the other hand, U_3 puts more weight to later observations and U_4 puts higher weight to observations in the beginning.

(iv) Deshpande and Dewan (2000) proposed tests for testing bivariate symmetry aginst dispersive asymmetry. Here the alternatives can be expressed in terms of ordering of sub-survival functions and ordering of sub-distributions of the maximum of observations and δ . The statistic is a linear combination of two statistics, the first one is a U-statistic based on minimum and δ and the other one is a U-statistic based on maximum and δ. The one based on minimum and δ is the statistic U_4

(v) The statistics U_2, U_3, U_4 are all linear combinations of the sign statistic and the Wilcoxon-signed rank type statistic.

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