# TESTING WHETHER ONE RISK PROGRESSES FASTER THAN THE OTHER IN A COMPETING RISKS PROBLEM 

Richard Dykstra, Subhash Kochar and Tim Robertson

Received :


#### Abstract

We consider the problem of testing the null hypothesis of proportionality of two cause specific hazard rates against the alternative that the ratio of the two hazard rates is monotone in the competing risks model. No assumption is made about the independence of the notional risks. The problem is seen to be equivalent to testing independence of $T$ and $C$ against positive likelihood ratio dependence, where $T$ denotes time to failure and $C$ indicates cause of failure. Thus $T$ is assumed to be a continuous random variable while $C$ is discrete. We consider conditional as well as unconditional tests. Whereas the conditional test is exactly distribution-free, the unconditional tests are asymptotically distribution-free.


## 1. Introduction

Competing risks survival analysis is a generalization of ordinary survival analysis in which each unit under study is exposed to a number of different risks but the actual failure results from just one of these risks.

AMS 1991 Subject Classification: Primary, 62G10; Secondary, 62E20.
Key words and phrases: Cause specific hazard rate, positive likelihood ratio dependence, peakedness of distributions, conditional tests, Brownian bridge.

Suppose that there are only two possible causes of failure labeled 1 and 2 and that the notional times to failure of a unit under these two risks are denoted by random variables $X$ and $Y$, respectively. We assume that the joint distribution of $X$ and $Y$ is absolutely continuous with respect to Lebesgue measure on $\mathcal{R}^{2}$ so that $P(X=Y)=0$. Thus, the cause of failure, $C$, is 1 if and only if $X<Y$. However, all that we can observe is $T=\min (X, Y)$, the time to failure, and the corresponding cause of failure, C. Data of this type can also arise in two-component series systems in reliability models.

Let the joint probability density of $X$ and $Y$ be denoted by $f(x, y)$ and the corresponding survival function by $\bar{F}(x, y)=P(X>x, Y>y)$. The survival function corresponding to $T$ is, of course, given by $\bar{H}(t)=\bar{F}(t, t)=P(T>t)$. (Ordinarily, being lifetimes, $X$ and $Y$ would be positive, but we need not make this assumption.)

It is common in the literature to assume that $X$ and $Y$ are independent. However, as noted by Gail [12], among others, this assumption is often unrealistic since the two risks act under the same environment. The problem is compounded by the fact that independence of $X$ and $Y$ cannot be tested on the basis of observed data of the form ( $T, C$ ) (cf. Cox [8] ).

To quantify the risks of failure from the various causes, the concept of cause specific hazard rate is often used. This is an extension of the ordinary definition of hazard rate to the competing risks situation. The cause specific hazard rate corresponding to the $i$ th cause is defined as

$$
g_{i}(t)=\lim _{\Delta t \rightarrow \infty} \frac{1}{\Delta t} P(t<T \leq t+\Delta t, C=i \mid T>t), i=1,2 .
$$

In terms of the joint density $f(x, y)$, we can write,

$$
\begin{aligned}
& g_{1}(t)=\int_{t}^{\infty} f(t, y) d y / \bar{H}(t), \quad \text { and } \\
& g_{2}(t)=\int_{t}^{\infty} f(y, t) d y / \bar{H}(t)
\end{aligned}
$$

In essence, $g_{i}(t)$ is the instantaneous rate of failure at time $t$ from the $i$ th cause given that the item has survived up to time $t$. Observe that the sum $g_{1}(t)+g_{2}(t)$, is equal to the hazard rate $r_{T}(t)$ of $T$. It is easy to see that if $X$ and $Y$ are independent, then $g_{1}$ and $g_{2}$ are simply the hazard rates corresponding to the marginal distributions of $X$ and $Y$, respectively.

It is important to compare the relative risks of failure due to the two causes at various times. Aly, Kochar and McKeague [1] and Dykstra, Kochar and Robertson [11], among others, have proposed distribution-free tests for testing the equality of cause specific
hazard rates against ordered alternatives. Sen [21] has also proposed nonparametric tests for testing the interchangeability of two risks under a competing risks model.

In this paper, we shall consider a somewhat different problem. Typically, $g_{1}(t)$ and $g_{2}(t)$ are changing with time. In many applications, particularly in the medical field, it is of interest to determine whether the two cause specific hazard rates are proportional to each other or whether one risk progresses faster than the other. That is, we wish to test whether the relative risk (or equivalently the cause specific hazard ratio) is constant, against the alternative that this ratio is monotone increasing (or decreasing). The proportional cause specific hazard model has been widely used in the literarture (cf. Chiang [5], [6], [7] Chapter II and Holt [15]). As Kalbfleisch and Prentice ([16], pp 170-171) observe, this proportionality assumption greatly simplifies the further analysis of competing risks data. On the other hand, there are many practical situations where one risk progresses faster than the other. For example, it is generally recognized that beyond the onset of menopause, the cause specific hazard rate for heart disease in women increases much faster than the cause specific hazard rates for many other risks. The recognition of this fact has led to significant changes in medical care for women. Thus, our goal is to provide a solution to the following problem:

On the basis of a random sample $\left(T_{1}, C_{1}\right), \ldots,\left(T_{n}, C_{n}\right)$ on $(T, C)$, we wish to test the null hypothesis,

$$
H_{0}: g_{2}(t)=c g_{1}(t), \quad t \geq 0
$$

for some unknown constant $c$, against the alternative,

$$
H_{A}: g_{2}(t) / g_{1}(t) \text { is nondecreasing in } t \text { (but not constant). }
$$

To further understand these hypotheses define the regression functions:

$$
\pi_{i}(t)=P(C=i \mid T=t), i=1,2
$$

It is easy to see that $\pi_{i}(t)=g_{i}(t) / r_{T}(t)$ and $\pi_{1}(t)+\pi_{2}(t)=1$. In terms of the $\pi_{i}$ 's, the above hypotheses are
$H_{0}: \pi_{2}(t)$ (and hence $\left.\pi_{1}(t)\right)$ is constant in $t$,
$H_{A}: \pi_{2}(t)$ is nondecreasing in $t$ (but not a constant).
Given that a failure has occurred at time $t$, the conditional probability that this failure is due to cause 2 , remains constant in $t$ under the null hypothesis, but under the alternative, $\pi_{2}(t)$ is increasing with time. The hypothesis $H_{A}$ says that as time passes, the probability that a failure is due to cause 2 , increases and the probability that it is due to cause 1 decreases. Another way of formulating the alternative $H_{A}$ is to note that it is equivalent
to $T$ and $C$ being positively likelihood ratio dependent (cf. Lehmann [18]). Observe that $T$ and $C$ are independent under $H_{0}$.

These hypotheses are of interest in parametric models as well. Gumbel's bivariate exponential distribution (Gumbel, 1960) has joint survival function

$$
\bar{F}(x, y)=\exp \left[-\left\{\lambda_{1} x+\lambda_{2} y+\lambda_{3} x y\right\}\right], \quad x, y \geq 0
$$

for $\lambda_{1}, \lambda_{2}, \lambda_{3} \geq 0$. Since the cause specific hazard rates are $g_{i}(t)=\lambda_{i}+\lambda_{3} t, i=1,2$, it easily follows that $g_{1}(t) / g_{2}(t)$ is nondecreasing in $t$ if and only if $\lambda_{1}<\lambda_{2}$ when $\lambda_{3}>0$ while $g_{1}(t) / g_{2}(t)$ is constant in $t$ if either $\lambda_{1}=\lambda_{2}$ or $\lambda_{3}=0$.

However, for the absolutely continuous bivariate exponential (ACBVE) distribution of Block and Basu [4] with joint survival function

$$
\begin{aligned}
\bar{F}(x, y) & =\frac{\lambda}{\lambda_{1}+\lambda_{2}} \exp \left[-\lambda_{1} x-\lambda_{2} y-\lambda_{3} \max (x, y)\right] \\
& -\frac{\lambda_{3}}{\lambda_{1}+\lambda_{2}} \exp [-\lambda \max (x, y)], \quad x, y \geq 0
\end{aligned}
$$

the cause specific hazard rates are given by $g_{j}(t)=\frac{\lambda \lambda_{j}}{\left(\lambda_{1}+\lambda_{2}\right)}, j=1,2$ where $\lambda_{1}, \lambda_{2}, \lambda_{3}$ are nonnegative parameters and $\lambda=\lambda_{1}+\lambda_{2}+\lambda_{3}$. For this model, the ratio of the cause specific hazard rates is always constant.

Recently, Ryu [22] has extended the bivariate exponential model of Marshall and Olkin in such a way that it is absolutely continuous (although it need not be memoryless). His model allows both $H_{0}$ and $H_{A}$ to be true for appropriate choices of the parameters.

As another example, consider the contaminated model,

$$
f(x, y)=(1-\epsilon) f_{1}(x) f_{2}(y)+\epsilon f_{3}(x) f_{4}(y), \quad 0<\epsilon<1
$$

where the hazard rates for the $f_{i}$ 's are proportional. That is, the hazard rates satisfy $r_{i}(t)=\lambda_{i} r(t)$ and as a consequence, their survival functions satisfy $\bar{F}_{i}(t)=[\bar{F}(t)]^{\lambda_{i}}$, $i=1,2,3,4$. Observe that $X$ and $Y$ will not be independent. It can be seen after some simplifications that $g_{1}(t)$ is proportional to $g_{2}(t)$ if either $\lambda_{1} / \lambda_{2}=\lambda_{3} / \lambda_{4}$ or $\lambda_{3}+\lambda_{4}=$ $\lambda_{1}+\lambda_{2}$; and $g_{1}(t) / g_{2}(t)$ is nondecreasing if and only if $\left(\lambda_{2} \lambda_{3}-\lambda_{1} \lambda_{4}\right)\left[\lambda_{3}+\lambda_{4}-\lambda_{1}-\lambda_{2}\right]>0$.

The assumption of absolute continuity of the joint distribution of $(X, Y)$ is crucial in our development. This assumption ensures that $P(X=Y)=0$. However, there are many bivariate models of practical interest that are not absolutely continuous. An important example is the Marshall-Olkin bivariate exponential distribution. When the event $\{X=Y\}$ occurs the cause of failure cannot be uniquely assigned to the different
risks and this leads to identifiability problems. The occurrence of the event $\{X=Y\}$ does not provide any information to compare the relative risks.

Prentice et al. [19] emphasize that only quantities that are expressible in terms of cause specific hazard rates are identifiable and thus can be estimated from competing risks data. In this paper, our hypotheses are phrased in terms of the cause specific hazard rates and hence identifiability is not a problem.

In Section 2, we propose two asymptotically distribution-free tests for the above testing problem. The first test is based on an estimate of the average deviation between $H_{0}$ and $H_{A}$. The test statistic can be expressed as a linear rank statistic. The second test we propose is of the Kolmogorov type and its asymptotic null distribution is the same as that of the one-sample, one-sided Kolmogorov test for goodness-of-fit. Our tests are less subjective than the graphical procedures based on inspection of the empirical cause specific hazard rates suggested by Kalbfleisch and Prentice [16]. In Section 3, the powers of the tests proposed in this paper have been compared with the help of a simulation study. In the fourth section, the procedures developed in this paper are illustrated with a numerical example on survival data. Finally, in the last section, it is briefly noted that by conditioning on the observed number of failures from the first cause, completely distribution-free versions of the above tests can be obtained.

## 2. The Proposed Tests

We propose two asymptotically distribution-free tests for our testing problem. The first test is based on an estimator of the average measure of deviation between $H_{0}$ and $H_{A}$ and the second test considers the supremum of a measure of deviation between $H_{0}$ and $H_{A}$.

For $x \geq y$, let $\delta(x, y)=\pi_{2}(x)-\pi_{2}(y)=\pi_{1}(y)-\pi_{1}(x)$. Under $H_{0}, \delta(x, y)=0$, but under $H_{A}$, it is nonnegative for all $x \geq y$ and $\delta(x, y)>0$ for some $x>y$. Consider the following measure of average deviation between $H_{0}$ and $H_{A}$,

$$
\begin{aligned}
\Delta & =\iint_{x \geq y} \delta(x, y) d H(x) d H(y) \\
& =\int_{-\infty}^{\infty}\left[S_{1}(y)-\tilde{S}_{1}(y)\right] d H(y)
\end{aligned}
$$

where,

$$
\begin{aligned}
S_{1}(y) & =\int_{-\infty}^{y} \pi_{1}(t) d H(t) \\
& =P[C=1, T<y], \\
\tilde{S}_{1}(y) & =\int_{y}^{\infty} \pi_{1}(t) d H(t) \\
& =P[C=1, T>y]
\end{aligned}
$$

Thus $\Delta$ becomes

$$
\begin{equation*}
\Delta=P\left[C_{1}=1, T_{1}<T_{2}\right]-P\left[C_{1}=1, T_{1}>T_{2}\right] \tag{2.1}
\end{equation*}
$$

where $\left(T_{1}, C_{1}\right)$ and $\left(T_{2}, C_{2}\right)$ are two independent copies of $(T, C)$.
Given a random sample $\left\{T_{i}, C_{i}\right\}, i=1, \cdots, n$ on $\{T, C\}$ we can estimate $\Delta$ by using a $U$-statistic with kernel

$$
\varphi\left(T_{1}, C_{1} ; T_{2}, C_{2}\right)=\left\{\begin{array}{lll}
1 & \text { if } & T_{2}>T_{1}, C_{1}=1, C_{2}=0 \quad \text { or }  \tag{2.2}\\
& & T_{1}>T_{2}, C_{1}=0, C_{2}=1 \\
-1 & \text { if } & T_{1}>T_{2}, C_{1}=1, C_{2}=0 \quad \text { or } \\
& & T_{2}>T_{1}, C_{1}=0, C_{2}=1 \\
0, & \text { otherwise. }
\end{array}\right.
$$

Our $U$-statistic estimator of $\Delta$ is

$$
\begin{equation*}
\left.U_{n}=\left[\binom{n}{2}\right]^{-1} \sum_{1 \leq k<l \leq n} \sum_{1} \varphi T_{k}, C_{k} ; T_{l}, C_{l}\right\} \tag{2.3}
\end{equation*}
$$

and large values of $U_{n}$ are significant for testing $H_{0}$ against $H_{A}$.
It is easy to compute the test statistic $U_{n}$ using the ranks of the observed times to failure. Let $T_{(1)}<T_{(2)}<\cdots<T_{(n)}$ be the ordered $T_{i}$ 's and let

$$
W_{j}= \begin{cases}1 & \text { if } T_{(j)} \text { corresponds to cause } 1 \\ 0, & \text { otherwise }\end{cases}
$$

Then $V_{n}=\binom{n}{2} U_{n}$ can be expressed as

$$
\begin{align*}
V_{n} & =\sum_{j=1}^{n}(n-2 j+1) W_{j} \\
& =\sum_{j=1}^{n} a_{j} W_{j}  \tag{2.4}\\
& =\sum_{j=1}^{n}\left(n-2 R_{j}+1\right) \delta_{j}
\end{align*}
$$

where $a_{j}=n-2 j+1, R_{j}$ is the rank of $T_{j}$, and $\delta_{j}=1$ if $C_{j}=1$ and 0 otherwise.

## The null distribution of $U_{n}$

We use the method of moment generating function to find the null distribution of $V_{n}$ (or $U_{n}$ ). As seen earlier, under $H_{0}, T_{1}, \ldots, T_{n}$ and $C_{1}, \ldots, C_{n}$ are mutually independent. As a result, $W_{1}, \ldots, W_{n}$ are independent and identically distributed Bernoulli random variables with $P\left(W_{i}=1\right)=P(C=1)=\theta$. Using this, we obtain the moment generating function of $V_{n}$ under $H_{0}$ as

$$
\begin{equation*}
M_{\theta}(t)=\prod_{j=1}^{n}\left[(1-\theta)+\theta e^{a_{j} t}\right] \tag{2.5}
\end{equation*}
$$

where $a_{j}=(n-2 j+1)$. This gives, under $H_{0}, E\left(V_{n}\right)=0$, and var $\left(V_{n}\right)=(4 / 3) n\left(n^{2}-\right.$ 1) $\theta(1-\theta)$. As shown in the Appendix, the null distribution of $V_{n}$ is symmetric about 0 and it depends only on the unknown parameter $\theta$. If $\theta$ is known, the exact distribution of $V_{n}$ can be obtained as in Bagai, Deshpandé and Kochar [2]. However, in general, $\theta$ is not known. The next theorem gives the least favorable distribution of $V_{n}$ under $H_{0}$.

Theorem 2.1. The least favorable distribution of $V_{n}$ under $H_{0}$ occurs at $\theta=1 / 2$ in the sense that $P_{\theta}\left(V_{n} \geq v\right) \leq P_{1 / 2}\left(V_{n} \geq v\right)$ for any $v>0$.

The proof of this theorem is given in the Appendix.
To give an idea of the difference between the actual value of $P_{\theta}\left(V_{n} \geq v\right)$ and the least favorable probability $P_{\frac{1}{2}}\left[V_{n} \geq v\right]$, we find that for $n=8, P_{\frac{1}{2}}\left(V_{n} \geq 11\right)=0.04687$ and $P_{\frac{1}{4}}\left(V_{n} \geq 11\right)=0.02856$ while for $n=10, P_{1 / 2}\left(V_{n} \geq 15\right)=0.05273$ and $P_{1 / 4}\left(V_{n} \geq\right.$ $15)=0.03294$. Asymptotically, these probabilities are 0.05 and 0.03 for $\theta=1 / 2$ and $1 / 4$, respectively.

If $n$ is large, $\theta$ can be estimated consistently by the corresponding sample proportion $\hat{\theta}_{n}=\frac{1}{n} \sum_{i=1}^{n} I_{\left\{C_{i}=1\right\}}$. Since $U_{n}$ is a $U$-statistic, it follows that an asymptotically distribution-free test for testing $H_{0}$ against $H_{A}$ at level $\alpha$ has rejection region

$$
\begin{equation*}
V_{n}^{*}=\left[3 /\left\{4\left(n^{2}-1\right) \hat{\theta}_{n}\left(1-\hat{\theta}_{n}\right)\right\}\right]^{1 / 2} \geq z_{\alpha} \tag{2.6}
\end{equation*}
$$

where $z_{\alpha}$ is the $(1-\alpha)$ th quantile of the standard normal distribution.

## A Kolmogorov type test

Let

$$
\begin{aligned}
\psi(t) & =S_{1}(t)-\theta H(t) \\
& =P[T \leq t, C=1]-P[C=1] P[T \leq t]
\end{aligned}
$$

Under $H_{0}, \psi(t) \equiv 0$, but under the alternative $H_{A}, \psi(t) \geq 0$, as positive likelihood ratio dependence implies positive quadrant dependence (cf. Lehmann [18]).

Let

$$
\begin{aligned}
S_{1 n}(t) & =\frac{1}{n} \sum_{i=1}^{n} I_{\left\{C_{i}=1, T \leq t\right\}} \\
H_{n}(t) & =\frac{1}{n} \sum_{i=1}^{n} I_{\left\{T_{i} \leq t\right\}}, \quad \text { and } \\
h_{n}(t) & =\left[\frac{n}{\hat{\theta}_{n}\left(1-\hat{\theta}_{n}\right)}\right]^{1 / 2}\left[S_{1 n}(t)-\hat{\theta}_{n} H_{n}(t)\right]
\end{aligned}
$$

Then our suggested test statistic is

$$
\begin{align*}
\sqrt{n} D_{n}^{+} & =\sup _{-\infty<t<\infty} h_{n}(t) \\
& =\left[\frac{1}{n \hat{\theta}_{n}\left(1-\hat{\theta}_{n}\right)}\right]^{1 / 2} \max _{1 \leq i \leq n}\left[N_{i n}-i \hat{\theta}_{n}\right] \tag{2.7}
\end{align*}
$$

where

$$
N_{i, n}=\#\left\{1 \leq k \leq i, W_{k}=1\right\} .
$$

Large values of $D_{n}^{+}$are significant for testing $H_{0}$ against $H_{1}$. To study the asymptotic null distribution of $\sqrt{n} D_{n}^{+}$, we use the following empirical convergence result due to Csörgo [9].

Theorem 2.2. If $H_{0}$ holds, then on an appropriate probability space, there exists a sequence of Brownian bridges $B_{n}(u), 0 \leq u \leq 1$, such that as $n \rightarrow \infty$,

$$
\sup _{\infty<t<\infty}\left|h_{n}(t)-B_{n}(H(t))\right| \longrightarrow 0 \quad \text { almost surely. }
$$

Using this result, it follows that under $H_{0}$,

$$
\sqrt{n} D_{n}^{+} \xrightarrow{\text { dist }} \sup _{0 \leq u \leq 1} B(u) \quad \text { as } \quad n \rightarrow \infty
$$

and it is well known that

$$
\begin{equation*}
P\left[\sup _{0 \leq u \leq 1} B(u)>t\right]=e^{-2 t^{2}}, t>0 \tag{2.8}
\end{equation*}
$$

(see, Shorack and Wellner [22]).
Thus the asymptotic null distribution of $\sqrt{n} D_{n}^{+}$is the same as that of the one-sided Kolmogorov-Smirnov test for goodness-of-fit

It is to be noted that our $V_{n}$ statistic is asymptotically equivalent to the statistic $\int_{-\infty}^{\infty} h_{n}(t) d H_{n}(t)$ which converges in distribution to a normal random variable $\int_{0}^{1} B(u) d u$, as has been established earlier.

## 3. A Monte Carlo Power Comparison

To compare the powers of our large sample tests, a simulation study was performed by generating 5000 random samples of different sizes from the distribution of $(X, Y)$, where $X$ and $Y$ are independent random variables having Weibull distributions with shape parameters 1 and $\lambda$, respectively. For $\left.\lambda>1, g_{2}(t) / g_{1}(t)\right)=\lambda t^{\lambda-1}$ is nondecreasing in t . The case $\lambda=1$ corresponds to $H_{0}$.

Table 3.1

Estimated powers of the $V_{n}$ and the $D_{n}^{+}$tests at $5 \%$ level

| n | $\lambda=1.25$ | $\lambda=1.25$ | $\lambda=2$ | $\lambda=2$ |
| ---: | :--- | :--- | :--- | :--- |
|  | $V_{n}$ | $D_{n}^{+}$ | $V_{n}$ | $D_{n}^{+}$ |
| 25 | .1518 | .1230 | .6065 | .5018 |
| 50 | .2370 | .2070 | .8701 | .8080 |
| 100 | .3815 | .3288 | .9888 | .9721 |

The $5 \%$ critical points of $V_{n}^{*}$ and $\sqrt{n} D_{n}^{+}$were estimated from the simulated data by taking $\lambda=1$. These values for $V_{n}^{*}$ and $\sqrt{n} D_{n}^{+}$are $1.74,1.69$ and 1.65 (1.14, 1.15 and 1.18) for $\mathrm{n}=25,50$ and 100 , respectively. From the asymptotic distributions of $V_{n}^{*}$ and $\sqrt{n} D_{n}^{+}$, the upper $5 \%$ critical values are 1.645 and 1.2238 , respectively. Thus we see that for $n=100$, the asymptotic approximation to the null distribution of $V_{n}^{*}$ is quite good, but that of $\sqrt{n} D_{n}^{+}$is somewhat conservative.

In the power comparison, we used the simulated critical points for $\lambda=1.25$ and $\lambda=2$. These estimated powers are reported in Table 3.1. It is seen from this table that for the above mentioned alternatives, the $V_{n}$ test performs better than the $D_{n}^{+}$test.

## 4. An Example

We consider some mortality data provided by Dr. H.E. Walburg, Jr. of the Oak Ridge National Laboratory (see Hoel [14]). The data was obtained from a laboratory experiment on RFM strain of male mice which had received a radiation dose of $300 r$ at an age of 5-6 weeks and were kept in a conventional environment. We consider only two major risks of death - the first risk is cancer and the second risk is the accumulation of all other risks into a single group. Table 4.1 gives autopsy data for 99 such mice.

## Table 4.1

Ages at death in days for 99 RFM conventional male mice which received a radiation dose of $300 r$ at the age 5-6 weeks due to cancer and due to all other causes

Other causes

| 40 | 42 | 51 | 62 | 163 | 179 | 206 | 222 | 228 | 249 |
| ---: | ---: | ---: | ---: | ---: | :--- | :--- | :--- | :--- | :--- |
| 252 | 282 | 324 | 333 | 341 | 366 | 385 | 407 | 420 | 431 |
| 441 | 461 | 462 | 482 | 517 | 517 | 524 | 564 | 567 | 586 |
| 619 | 620 | 621 | 622 | 647 | 651 | 686 | 761 | 763 |  |

Cancer

| 159 | 189 | 191 | 198 | 200 | 207 | 220 | 235 | 245 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| 250 | 256 | 261 | 265 | 266 | 280 | 317 | 318 | 343 |
| 356 | 383 | 399 | 403 | 414 | 428 | 432 | 495 | 525 |
| 536 | 549 | 552 | 554 | 557 | 558 | 571 | 586 | 594 |
| 596 | 605 | 612 | 621 | 628 | 631 | 636 | 643 | 647 |
| 648 | 649 | 661 | 663 | 666 | 671 | 695 | 697 | 700 |
| 705 | 712 | 713 | 738 | 748 | 753 |  |  |  |

Let $g_{2}(t)$ and $g_{1}(t)$ denote the cause specific hazard rates of death due to cancer and all other causes combined, respectively. On the basis of the above data we wish to test $H_{0}$ against $H_{A}$. We rank these 99 observations from 1 to 99 . Ties are broken by randomization. The observed value of the standardized statistic $V_{n}^{*}$ given by (2.6) is 1.87 with the corresponding $p$-value as 0.0307 . The observed value of $\sqrt{n} D_{n}^{+}$is 1.259 and using (2.8) we find the $p$-value as 0.042 . Thus, there is sufficient evidence to reject $H_{0}$ at the $5 \%$ level of significance.

## 5. Conditional Tests

Let $N_{1}=\sum_{i=1}^{n} W_{i}$, the number of failures from cause 1. Then the conditional distribution of $\left(W_{1}, \ldots, W_{n}\right)$ given $N_{1}=n_{1}$ is independent of $\theta$ if $H_{0}$ is true and is given by

$$
P\left\{W_{1}=w_{1}, \ldots, W_{n}=w_{n} \mid \sum_{i=1}^{n} W_{i}=n_{1}\right\}= \begin{cases}\frac{1}{\binom{n}{n_{1}}}, & \text { if } \sum_{i=1}^{n} w_{i}=n_{1} \\ 0, & \text { otherwise }\end{cases}
$$

Since the statistics $V_{n}$ and $D_{n}^{+}$are based on $W_{i}$ 's, their conditional distributions given $N_{1}$ are independent of the parameter $\theta$ under the null hypothesis and the resulting conditional tests are exactly distribution-free. We feel that the statistic $N_{1}$ is ancillary for this problem although we have not obtained a rigorous proof for this. However, in case $T$ is decrete, Bhapkar [3] has shown that the statistic $N_{1}$ is strongly ancillary. It will be interesting to compare the performance of the conditional tests with the unconditional ones but we shall not pursue this matter here.

## Appendix

We need the following notion of peakedness of probability distributions.

Definition. A random variable $X_{1}$ with c.d.f. $F_{1}$ is said to be less peaked than $X_{2}$ with c.d.f. $F_{2}$ (written as $X_{1} \stackrel{p}{\leq} X_{2}$ or $F_{1} \stackrel{p}{\leq} F_{2}$ ) if $\left|X_{1}\right|$ is stochastically greater than $\left|X_{2}\right|$.

If $X_{1}$ and $X_{2}$ are symmetric about the origin, then $X_{1} \stackrel{p}{\leq} X_{2}$ if and only if

$$
P\left(X_{1}>x\right) \geq P\left(X_{2}>x\right)
$$

for all $x>0$.
It is easy to see that under $H_{0}$, when $W_{1}, \ldots, W_{n}$ are independent and identically distributed Bernoulli random variables with probability of success $\theta$, the distribution of $V$ is symmetric about the origin. This follows since the coefficients $a_{i}=(n-2 i+1)$ of $W_{i}$ in

$$
V=\sum a_{i} W_{i}
$$

satisfy $a_{i}=-a_{n-i+1}, i=1,2, \ldots, n$ with $\sum_{i=1}^{n} a_{i}=0$. Hence to prove Theorem 2.1, it is equivalent to prove the following:

Theorem 2.1. Let $W_{1}, \ldots, W_{n}$ be independent Bernoulli random variables each with parameter $\theta, 0<\theta<1$. Then the distribution of $V=\sum_{i=1}^{n} a_{i} W_{i}$ is least peaked when $\theta=\frac{1}{2}$.

Proof. $V$ can be expressed in the form

$$
V=\sum_{i=1}^{m} a_{i} Y_{i}, \quad a_{i} \geq 0
$$

where $Y_{i}=W_{i}-W_{i}^{*}$ and $m=\left[\frac{n+1}{2}\right]$ and $\left(W_{i}, W_{i}^{*}\right)$ are independent and identically distributed Bernoulli trials with parameter $\theta$.

The distribution of $Y_{i}$ is

$$
\begin{gathered}
P\left(Y_{i}=1\right)=P\left(Y_{i}=-1\right)=\theta(1-\theta) \\
P\left(Y_{i}=0\right)=1-\theta(1-\theta) .
\end{gathered}
$$

Since the maximum value of $\theta(1-\theta)$ which is $\frac{1}{4}$ occurs at $\theta=\frac{1}{2}$, it follows that the distribution of each $Y_{i}$ is symmetric and unimodal about the origin.

Also,

$$
Y_{i}^{*} \stackrel{p}{\leq} Y_{i}, \quad i=1,2, \ldots, m
$$

where $Y_{i}^{*}$ corresponds to the distribution of $Y_{i}$ with $\theta=\frac{1}{2}$. Since $a_{1}, \ldots, a_{m}$ are nonnegative, it follows that each $a_{i} Y_{i}$ is symmetric and unimodal with

$$
a_{i} Y_{i}^{*} \stackrel{p}{\leq} a_{i} Y_{i}, \quad i=1,2, \ldots, m
$$

It follows from Theorem 7.6 (p. 165) of Dharmadhikari and Joag-Dev [10] that

$$
\sum_{i=1}^{m} a_{i} Y_{i}^{*} \stackrel{p}{\leq} \sum_{i=1}^{m} a_{i} Y_{i}
$$

proving that the distribution of $V$ under $H_{0}$ is least favorable when $\theta=\frac{1}{2}$.

## Acknowledgements

We are thankful to the referee for his helpful comments on an earlier version of the paper which helped in clarifying some aspects of the problem. This work was partly done when Subhash Kochar was visiting the University of Iowa.

## References

[1] Aly, E., Kochar, S. and McKeague, I. (1994). Some tests for comparing cause specific hazard rates. J. Amer. Stat. Assoc. 89, 994-999.
[2] Bagai, I., Deshpandé, J. V. and Kochar, S. C. (1989). Distribution-free tests for the stochastic ordering alternatives under the competing risk model. Biometrika 76, 75-81.
[3] Bhapkar, V.P. (1989). Conditioning on ancillary statistics and loss of information in the presence of nuisance parameters. J. Statist. Plan. Inf. 21, 139-160.
[4] Block, H. W. and Basu, A. P. (1974). A continuous bivariate exponential distribution. J. Amer. Stat. Assoc. 69, 1031-1037.
[5] Chiang, C.L. (1961). On the probability of death from specific causes in the presence of competing risks. Proc. Fourth Berkeley Symposium in Math. Statist. IV (L. M. LeCam et al. eds.) Berkeley : University of California Press, 169-180.
[6] Chiang, C. L. (1968). Introduction to Stochastic Processes in Biostatistics. Wiley, New York.
[7] Chiang, C. L. (1970). Competing risks and conditional probabilities. Biometrics 26, 767-776.
[8] Cox, D. R. (1959). The analysis of exponentially distributed lifetimes with two types of failures. J.R. Statist. Soc. 21, 411-421.
[9] Csörgö, S. (1989). Testing for the proportional hazards model of random censorship. Proceedings of the Fourth Prague Symposium on Asymptotic Statistics, 41-53. Charles University, Prague.
[10] Dharmadhikari, S. and Joag-Dev, K. (1987). Unimodality, Convexity and Applications. Academic Press, Inc.
[11] Dykstra, R., Kochar, S. and Robertson, T. (1995). Likelihood based inference for cause specific hazard rates under order restrictions. J. Mult. Anal. 54, 263-274.
[12] Gail, M. (1975). A review and critique of some models used in competing risk analysis. Biometrics 31, 209-222.
[13] Gumbel, E. J. (1960). Bivariate exponential distribution. J. Amer. Stat. Assoc. 75, 454-459.
[14] Hoel, D. G. (1972). A representation of mortality data by competing risks. Biometrics 28, 475-488.
[15] Holt, J. D. (1978). Competing risk analysis with special reference to matched pair experiments. Biometrika 65,159-166.
[16] Kalbfleisch, J. D. and Prentice, R. L. (1980). The Statistical Analysis of Failure Time Data, Wiley : New York.
[17] Kochar, S.C. and Proschan, F. (1991). Independence of time and cause of failure in the dependent competing risks model. Statistica Sinica 1, 295-299.
[18] Lehmann, E. L. (1966). Some concepts of dependence. Ann. Math. Statist. 37, 1137-1153.
[19] Prentice, R. L., Kalbfleisch, J. D., Peterson, A. V., Flourney, N., Farewell, V. T. and Breslow, N. E. (1978). The analysis of failure times in the presence of competing risks. Biometrics 34, 541-554.
[20] Rye, K. (1993). An extension of Marshall and Olkin's bivariate exponential distribution. J. Amer. Stat. Assoc. 88, 1458-1465.
[21] Sen, P. K. (1979). Nonparametric tests for interchangeability under competing risks. Contributions to Statistics-J. Hajek Memorial Volume, (ed. J. Jureckova), Reidel, Dordrecht, 211-228.
[22] Shorack, G. and Wellner, J. (1986). Empirical Processes with Applications to Statistics. Wiley: New York.

## Richard Dykstra

Department of Statistics and Actuarial Science

University of Iowa
Iowa City, IA 52242
USA

## Tim Robertson

Department of Statistics and Actuarial Science

University of Iowa
Iowa City, IA 52242
USA

Subhash Kochar
Indian Statistical Institute
7, SJS Sansanwal Marg
New Delhi, 110016
INDIA

