JOURNAL OF MULTIVARIATE ANALYSIS 54, 163–174 (1995)

Likelihood Based Inference for Cause Specific Hazard Rates under Order Restrictions

RICHARD DYKSTRA

University of Iowa

SUBHASH KOCHAR

Indian Statistical Institute, New Delhi, India

AND

TIM ROBERTSON

University of Iowa

We consider the competing risks model with grouped data or with discrete failure times where a unit is exposed to several risks, but its eventual failure is due to exactly one of the causes. Nonparametric maximum likelihood estimates of the cause specific hazard rates are obtained under the restriction that these risks are uniformly ordered. We allow for random censoring. Unlike most papers on this topic, no assumption is made about the independence of the various risks, although we do assume that the censoring mechanism is acting independently of the life distribution. We derive the likelihood ratio statistic for testing the null hypothesis of equality of cause specific hazard rates against ordered alternatives. The asymptotic null distribution of the test statistic is seen to be of the chi-bar squared ($\bar{\chi}^2$) type. The procedures developed here are illustrated with the help of an example involving survival rates for mice exposed to radiation.

1. INTRODUCTION

In the standard competing risks model, an experimental unit or subject is exposed to several risks but the actual failure (or death) is attributed to exactly one cause. In this paper, we let T denote the time of failure of an experimental unit and C denote the cause of failure. For convenience, we

Received March 15, 1993; revised May 11, 1995.

AMS 1980 subject classifications: primary 62G10, 62G05, secondary, 62E20, 62N06.

Some key words and phrases: isotonic regression, cause specific hazard rates, competing risks, random censoring, delta method, multinomial distribution.

0047-259X/95 $12.00

label the causes of failure 1, 2, ..., k. Thus, the observed data is in the form of (T, C) for each observed item.

The ordinary concept of hazard (failure) rate has been generalized in the competing risks model to the notion of cause specific hazard rates. In the continuous case the ith cause specific hazard rate is defined as

$$h_i(t) = \lim_{\Delta t \to 0} \frac{1}{\Delta t} pr[t \leqslant T < t + \Delta t,\ C = i \mid T \geqslant t], \tag{1.1}$$

$i = 1, 2, ..., k$. If T is discrete, the ith cause specific hazard rate is given by $pr[T = t,\ C = i \mid T \geqslant t]$. In either case the overall hazard rate for time to failure is then given by

$$h(t) = \sum_{i=1}^{k} h_i(t).$$

In models where the various causes of failure are independent, $h_i(t)$ reduces to the (ordinary) hazard rate corresponding to the marginal distribution of failure from the ith cause.

In some problems the investigator may wish to confirm or deny a hypothesis that some causes of failure are more serious than others. One way to do this is to consider the problem of testing the null hypotheis,

$$H_0\colon h_1(t) = h_2(t) = \cdots = h_k(t) \qquad \text{for all } t \tag{1.2}$$

against the alternative $H_1 - H_0$ (H_1 but not H_0), where H_1 imposes an appropriate order restriction on the values $h_1(t), h_2(t), ..., h_k(t)$. In order to be specific, we consider the case where

$$H_1\colon h_1(t) \leqslant h_2(t) \cdots \leqslant h_k(t) \qquad \text{for all } t. \tag{1.3}$$

Note that there may be no reason to expect *a priori* that the cause specific hazard rates are equal (except, say, when they represent identical components in a series system), but this is a natural choice of null hypothesis for the ordered alternative H_1. Other partial orders on the hazard rates in the alternative hypothesis would lead to similar results. After the linear order restriction given in (1.3), the most extensively studied partial order restriction is the simple tree, $h_1(t) \leqslant h_i(t)$, $i = 2, 3, ..., k$.

Besides applications in the health sciences, our procedure has applications in industrial accelerated life tests. When comparing the quality of k different brands of a component, several components may be tested in series. The components are functioning in the same environment and their times to failure are generally dependent. The system fails as soon as one

of the components fails. This experimental design identifies weak components early in the experiment thus saving valuable time. On the basis of such data, one might like to test whether components supplied by different suppliers are of the same quality against an ordered alternative. This type of testing gives rise to the above type of data.

It is common in the literature to assume that the various competing risks are acting independently. However, as noted by Gail [7], among others, this assumption is often unrealistic since the risks usually act under the same environment. For example, the heart condition of a patient may very well depend on the condition of his other organs. It is well known that there are inherent identifiability problems when the competing risks are not assumed to be independent. The problem is confounded by the fact that the assumption of independent risks cannot be tested from competing risks data. However, as emphasized by Prentice *et al.* [13], only those quantities which are expressible in terms of the cause specific hazard rates are estimable and can be estimated from the competing risks data even if the risks are dependent. In this paper, our hypotheses are phrased in terms of the cause specific hazard rates and hence identifiability is not a problem.

Assuming that the underlying risks are independent and the lifetimes are continuous, various authors have proposed nonparametric tests for testing the equality of two or more hazard rates against ordered alternatives. Bagai, Deshpandé, and Kochar [3, 4] developed distribution-free rank tests for testing the equality of two hazard rates against stochastic ordering and hazard rate ordering alternatives. Neuhaus [12] has proposed asymptotically optimal rank tests for comparing several independent competing risks differing in their location or scale parameters. Yip and Lam [16] suggested a class of weighted logrank type statistics. Gray [8], generalizing the approach of Harrington and Fleming [9], has proposed a class of c-sample tests for comparing the crude incidence function, $S_1(t) = pr[T \leqslant t, C = 1]$ of the first risk over c different populations. The case of two *dependent risks* has been considered only recently by Aras and Deshpandé [2] and by Aly, Kochar, and McKeague [1]. Whereas Aras and Deshpandé [2] derived locally most powerful rank tests of H_0 against various parametric alternatives, Aly, Kochar, and McKeague [1] proposed Kolmogrov–Smirnov type tests for testing the equality of two competing risks.

In this paper we assume a discrete time framework and allow for independent random censoring on the right. We obtain maximum likelihood estimates (MLEs) of the cause specific hazard rates under the various alternatives. The restricted maximum likelihood estimators of the cause specific hazard rates under H_1 can be computed by finding the isotonic regression of the usual estimates across risks. This will be discussed in Section 2. In Section 3 we derive a likelihood ratio test for testing H_0 versus $H_1 - H_0$

and obtain the asymptotic null distribution of the test statistic. This asymptotic test is distribution-free and its null distribution is found to be of the chi-bar squared type (see Robertson, Wright, and Dykstra [14]; henceforth abbreviated RWD). Finally, in the last section, the procedures developed in this article are illustrated with the help of a data set involving survival rates for mice exposed to radiation.

2. Maximum Likelihood Estimation

Suppose that we have n individuals exposed to k competing risks and assume that the times and causes of failure represent a random sample from (T, C). As noted earlier, we make no assumptions about the independence of the nominal lifetimes associated with the various risks. We allow the observations to be right censored but assume that the censoring mechanism is independent of actual time to failure.

In this section, we obtain nonparametric maximum likelihood estimates of the cause specific hazard functions in preparation towards constructing the likelihood ratio statistic for testing H_0 against H_1. The maximum likelihood estimates of the cause specific hazard rates under the order restriction imposed by H_1 are of particular interest.

We assume that times to failure have discrete distributions and for convenience we assume that the support points are known. If the failure times are continuous, we assume that the data has been grouped and that t_i is representative of the ith interval. Thus we assume that failures occur on a subset of the times $t_1 < t_2 < \cdots < t_m$ $(t_0 = -\infty, t_{m+1} = \infty)$. For $i = 1, 2, \ldots, k$; $j = 1, 2, \ldots, m$, we let

p_{ij} = probability of failure from cause i at time t_j
$p_{\cdot j} = \sum_{i=1}^{k} p_{ij} = pr[T = t_j]$
n = total number of items on test (sample size)
d_{ij} = number of failures from cause i at time t_j
l_j = number of observations censored between times t_j and t_{j+1}
$n_j = \sum_{r=j}^{m} \{(\sum_{i=1}^{k} d_{ir}) + l_r\}$ = number of items at risk just before time t_j
$d_{\cdot j} = \sum_{i=1}^{k} d_{ij}$ = total number of failures at time t_j.

Since we assume the discrete case, the cause specific hazard rate due to the ith cause at time t_j is

$$h_i(t_j) = pr[T = t_j,\ C = i \mid T \geq t_j] = p_{ij} / \sum_{r=j}^{m} p_{\cdot r}. \tag{2.1}$$

Assuming that the censoring mechanism is acting independently of the failure mechanism, it follows from Davies and Lawrence [5] that the

likelihood function can be expressed entirely in terms of the cause specific hazard rates as

$$L \propto \prod_{j=1}^{m} \left\{ \prod_{i=1}^{k} h_i^{d_{ij}}(t_j) \left[1 - \sum_{l=1}^{k} h_l(t_j) \right]^{n_j - d_{\cdot j}} \right\}. \tag{2.2}$$

From this it is easy to see that the unrestricted MLE of $h_i(t_j)$ is

$$\hat{h}_i(t_j) = \frac{d_{ij}}{n_j}, \qquad i = 1, 2, ..., k; \; j = 1, 2, ..., m. \tag{2.3}$$

Under H_0, the MLE of the common cause specific hazard rate is

$$h_i^0(t_j) = \frac{d_{\cdot j}}{k n_j}, \qquad i = 1, 2, ..., k; \; j = 1, 2, ..., m. \tag{2.4}$$

The constraints under H_1 do not constrain $h_i(t_j)$ and $h_{i'}(t_{j'})$ for $j \neq j'$ so that the products inside the parentheses in (2.2) can be maximized individually. Each such problem is a version of the multinomial problem discussed in RWD [14]. The solution vector, $\mathbf{h}^*(t_j) = (h_1^*(t_j), h_2^*(t_j), ..., h_k^*(t_j))$, is the equal weights isotonic regression of the unconstrained maximum likelihood estimator $\hat{\mathbf{h}}(t_j) = (\hat{h}_1(t_j), \hat{h}_2(t_j), ..., \hat{h}_k(t_j))$. If we let $\hat{\theta}_{ij} = d_{ij}/d_{\cdot j}$ and $\boldsymbol{\theta}_j^* = (\theta_{1j}^*, \theta_{2j}^*, ..., \theta_{kj}^*)$, be the equal weights isotonic regression of $\hat{\boldsymbol{\theta}}_j = (\hat{\theta}_{1j}, \hat{\theta}_{2j}, ..., \hat{\theta}_{kj})$, it can be seen that

$$h_i^*(t_j) = \theta_{ij}^* d_{\cdot j}/n_j. \tag{2.5}$$

We will later find it convenient to write $\boldsymbol{\theta}_j^* = P(\hat{\boldsymbol{\theta}}_j \mid \mathscr{L})$ since its components are $\theta_{ij}^* = P(\hat{\boldsymbol{\theta}}_j \mid \mathscr{L})_i$, where $P(\mathbf{y} \mid C)$ denotes the qual weights least squares projection of $\mathbf{y}$ onto the convex cone C. In our setting, $\mathscr{L}$ denotes the set of nondecreasing vectors. If H_1 imposes an order restriction other than the linear order restriction given in (1.3) then the estimates under H_1 can be found by selecting the appropriate set $\mathscr{L}$. For example, if H_1 imposes the tree order restriction then $\mathscr{L} = \{(x_1, x_2, ..., x_k); \; x_1 \leqslant x_i; \; i = 1, ..., k\}$.

3. Hypothesis Testing

We now consider the problem of testing the null hypthesis H_0 against the alternative H_1. In our asymptotic theory, the number, m, of support points for T is fixed and the sample size n increases to ∞.

The likelihood ratio statistic is given as

$$\begin{aligned}\Lambda &= \frac{\sup_{\mathbf{h}\in H_0} L(\mathbf{h})}{\sup_{\mathbf{h}\in H_1} L(\mathbf{h})} = \frac{L(\mathbf{h}^0)}{L(\mathbf{h}^*)} \\ &= \frac{\prod_{j=1}^m \{\prod_{i=1}^k h^{0d_{ij}}(t_j)[1-\sum_{l=1}^k h^0{}_l(t_j)]^{n_j-d_{\cdot j}}\}}{\prod_{j=1}^m \{\prod_{i=1}^k h^{*d_{ij}}(t_j)[1-\sum_{l=1}^k h^*{}_l(t_j)]^{n_j-d_{\cdot j}}\}} \\ &= \frac{\prod_{i=1}^k \prod_{j=1}^m (d_{\cdot j}/kn_j)^{d_{ij}}}{\prod_{i=1}^k \prod_{j=1}^m (\theta_{ij}^*(d_{\cdot j}/n_j))^{d_{ij}}} \\ &= \frac{\prod_{i=1}^k \prod_{j=1}^m (1/k)^{d_{ij}}}{\prod_{i=1}^k \prod_{j=1}^m (\theta_{ij}^*)^{d_{ij}}}.\end{aligned}$$

The LRT is equivalent to a test that rejects H_0 in favor of $H_1 - H_0$ for large values of

$$\begin{aligned}T &= -2\ln\Lambda \\ &= 2\sum_{i=1}^k \sum_{j=1}^m d_{ij}\left\{\ln(\theta_{ij}^*) - \ln\left(\frac{1}{k}\right)\right\}.\end{aligned} \tag{3.1}$$

Expand $\ln(\theta_{ij}^*)$ and $\ln(1/k)$ about $\ln(\hat\theta_{ij})$ in a second degree Taylor's expansion. The linear terms add to zero using Theorem 1.3.3 of RWD, so that T can be rewritten as

$$\begin{aligned}T &= \sum_{j=1}^m \sum_{i=1}^k \left\{(d_{ij}/\beta_{ij}^2)\left(\hat\theta_{ij}-\frac{1}{k}\right)^2 - (d_{ij}/\alpha_{ij}^2)(\theta_{ij}^*-\hat\theta_{ij})^2\right\} \\ &= \sum_{j=1}^m \sum_{i=1}^k \left[\frac{d_{ij}}{n\beta_{ij}^2}\left\{\sqrt{n}\left(\hat\theta_{ij}-\frac{1}{k}\right)\right\}^2\right. \\ &\quad \left. -\left(\frac{d_{ij}}{n\alpha_{ij}^2}\right)\left\{P\left(\sqrt{n}\left(\hat{\boldsymbol\theta}_j-\frac{1}{k}\right)\middle|\mathscr{L}\right)_i - \sqrt{n}\left(\hat\theta_{ij}-\frac{1}{k}\right)\right\}^2\right],\end{aligned} \tag{3.2}$$

where the α_{ij}'s and β_{ij}'s come from Taylor's expansion, α_{ij} is between θ_{ij}^* and $\hat\theta_{ij}$ and β_{ij} is between $\hat\theta_{ij}$ and $1/k$. The factor $\sqrt{n}$ and the term $1/k$ can be brought inside the isotonic regression operator by the corollary to Theorem 8.2.4 and Corollary C to Theorem 8.2.7 of RWD.

By the central limit theorem for multinomial variables, the random matrix $\sqrt{n}(\tilde{\mathbf{P}}-\mathbf{P})$ has a limiting normal distribution, where $\mathbf{P}$ is the $(k\times m)$ matrix of p_{ij}'s and the (ij)th element of $\tilde{\mathbf{P}}$ is $\tilde p_{ij} = d_{ij}/n$. Then, using the multivariate delta method (cf. Serfling [15, p. 122]), it follows that the random matrix whose entry in the ith row and jth column is $\sqrt{n}(\hat\theta_{ij}-1/k)$ has an asymptotic normal distribution with mean zero under H_0. The

variance–covariance matrix of the asymptotic distribution is found by computing a tedious but straightforward matrix product. The asymptotic variance corresponding to $\sqrt{n}(\hat{\theta}_{ij} - 1/k)$ is $p_{ij}(\sum_{l=2}^{k} p_{lj})/(\sum_{l=1}^{k} p_{lj})^3$. The asymptotic covariance of $\sqrt{n}(\hat{\theta}_{ij} - 1/k)$ and $\sqrt{n}(\hat{\theta}_{i'j'} - 1/k)$ is zero if $j \neq j'$ and is $-p_{ij}p_{i'j'}/(\sum_{l=1}^{k} p_{lj})^3$ if $j = j'$ but $i \neq i'$.

Suppose now that $\mathbf{U}$ is a $k \times m$ matrix of random variables having a multivariate normal distribution with mean zero and the above dispersion matrix. Then, under H_0, T must converge in law to

$$T' = \sum_{j=1}^{m} \sum_{i=1}^{k} [(p_{ij}/\theta_{ij}^2)\, U_{ij}^2 - (p_{ij}/\theta_{ij}^2)\{P(\mathbf{U}_j \mid \mathscr{L})_i - U_{ij}\}^2].$$

If we let

$$V_{ij} = (\sqrt{p_{ij}}/\theta_{ij})\, U_{ij},$$

we may use H_0 and the corollary to Theorem 8.2.4 of RWD to write T' as

$$T' = \sum_{j=1}^{m} \sum_{i=1}^{k} \{V_{ij}^2 - [P(\mathbf{V}_j \mid \mathscr{L})_i - V_{ij}]^2\}. \tag{3.3}$$

The matrix $\mathbf{V}$ has a multivariate normal distribution with mean matrix $\mathbf{0}$. The common variance of V_{ij} is $(k-1)/k$. If $j \neq j'$, the covariance between V_{ij} and $V_{i'j'}$ is zero and if $j = j'$ but $i \neq i'$, the covariance between V_{ij} and $V_{i'j}$ is $-(1/k)$.

If we let $\mathbf{X}$ be a $k \times m$ matrix of independent standard normal variables and we let

$$Y_{ij} = X_{ij} - (1/k) \sum_{l=1}^{k} X_{lj},$$

then $\mathbf{Y}$ is distributed as $\mathbf{V}$. Thus, T' has the same distribution (under H_0) as

$$\begin{aligned} &\sum_{j=1}^{m} \sum_{i=1}^{k} \left[\left\{ Y_{ij} - \frac{1}{k} \sum_{l=1}^{k} Y_{lj} \right\}^2 - \{P(\mathbf{Y}_j \mid \mathscr{L})_i - Y_{ij}\}^2 \right] \\ &\quad = \sum_{j=1}^{m} \sum_{i=1}^{k} \left[P(\mathbf{Y}_j \mid \mathscr{L})_i - \frac{1}{k} \sum_{l=1}^{k} Y_{lj} \right]^2 \\ &\quad = \sum_{j=1}^{m} \sum_{i=1}^{k} \left[P(\mathbf{X}_j \mid \mathscr{L})_i - \frac{1}{k} \sum_{l=1}^{k} X_{lj} \right]^2; \end{aligned} \tag{3.4}$$

the first equality follows as in (2.2.3) and (2.2.4) of RWD. Now by Theorem 2.3.1 of RWD, the sum

$$\sum_{i=1}^{k}\left[P(\mathbf{X}_j \mid \mathscr{L})_i - \frac{1}{k}\sum_{l=1}^{k} X_{lj}\right]^2 \tag{3.5}$$

has a $\bar{\chi}^2$ distribution. Since these sums for different values of j in (3.4) are independent, it follows as in Dykstra, Kochar, and Robertson [6] that the distribution of $-2\ln\Lambda$ will have a $\bar{\chi}^2$ distribution. The results are summarized in the following theorem.

THEOREM 3.1. *Under H_0, the test statistic $-2\ln\Lambda$ converges in law to*

$$T^* = \sum_{j=1}^{m}\sum_{i=1}^{k}\left[P(\mathbf{X}_j \mid \mathscr{L})_i - \frac{1}{k}\sum_{l=1}^{k} X_{lj}\right]^2 \tag{3.6}$$

as the sample size, n, goes to infinity where $\mathbf{X} = (X_{ij})$ is a $k \times m$ matrix of independent standard normal variables. For every j, the distribution of

$$T_j^* = \sum_{i=1}^{k}\left[P(\mathbf{X}_j \mid \mathscr{L})_i - \frac{1}{k}\sum_{l=1}^{k} X_{lj}\right]^2 \tag{3.7}$$

is a chi-bar squared distribution and its survival function is given by

$$pr[T_j^* \geq t] = \sum_{l=1}^{k} p(l,k)\, pr[\chi^2_{l-1} \geq t], \tag{3.8}$$

for any $t > 0$, where the $p(l,k)$ are the equal weight level probabilities discussed in Section 2.4 of RWD. It follows that T^* has a $\bar{\chi}^2$ distribution of the form

$$pr[T^* \geq t] = \sum_{l=m}^{km} C(l,k,m)\, pr[\chi^2_{l-m} \geq t], \tag{3.9}$$

where the sequence $\{C(l,k,m)\}_{l=m}^{mk}$ is the m-fold convolution of the sequence $\{p(l,k)\}_{l=1}^{k}$.

One can use the fact that the $p(l,k)$ satisfy the recurrence relation

$$p(l,k) = \frac{1}{k}\,p(l-1,k-1) + \frac{k-1}{k}\,p(l,k-1)$$

(Miles [11]) to establish that the $C(l,k,m)$ satisfy the recurrence relation,

$$C(l,k,m) = \sum_{j=0}^{m}\binom{m}{j}\left(\frac{1}{k}\right)^j\left(\frac{k-1}{k}\right)^{m-j} C(l-j,k-1,m), \tag{3.10}$$

TABLE I

Critical Points for LRT of Linearly Ordered Cause Specific Hazard Rates, at Respective Levels 0.01, 0.05, and 0.10

	k								
m	2	3	4	5	6	7	8	9	10
	5.41	6.82	7.71	8.36	8.87	9.28	9.64	9.95	10.22
2	2.71	3.82	4.53	5.05	5.46	5.80	6.09	6.34	6.56
	1.64	2.58	3.19	3.64	3.99	4.29	4.54	4.76	4.96
	7.29	9.30	10.61	11.59	12.38	13.03	13.58	14.07	14.50
3	4.23	5.86	6.94	7.76	8.41	8.95	9.42	9.83	10.19
	2.95	4.37	5.33	6.05	6.63	7.12	7.53	7.90	8.22
	8.75	11.31	13.02	14.31	15.35	16.22	16.95	17.60	18.18
4	5.44	7.55	8.99	10.08	10.96	11.69	1 2.32	12.88	13.37
	4.01	5.88	7.17	8.15	8.94	9.61	10.18	10.69	11.14
	10.02	13.11	15.20	16.79	18.07	19.14	20.06	20.86	21.57
5	6.50	9.08	10.86	12.21	13.31	14.23	15.03	15.72	16.34
	4.96	7.27	8.87	10.10	11.10	11.94	12.67	13.31	13.8 8
	11.19	14.78	17.24	19.11	20.62	21.89	22.98	23.93	24.78
6	7.48	10.52	12.63	14.24	15.55	16.65	17.61	18.44	19.19
	5.84	8.57	10.49	11.97	13.17	14.18	15.06	15.84	16.53
	12.27	16.37	19.18	21.33	23.07	24.53	25.78	26.88	27.86
7	8.41	11.90	14.32	16.19	17.71	18.99	20.10	21.07	21.94
	6.67	9.83	12.05	13.77	15.17	16.36	17.39	18.29	19.10
	13.31	17.89	21.05	23.47	25.43	27.08	28.49	29.74	30.85
8	9.30	13.22	15.97	18.09	19.81	21.27	22.52	23.63	24.62
	7.48	11.05	13.57	15.53	17.13	18.48	19.66	20.69	21.61
	14.31	19.36	22.86	25.55	27.73	29.56	31.14	32.53	33.76
9	10.15	14.51	17.57	19.94	21.86	23.49	24.90	26.14	27.24
	8.26	12.24	15.06	17.26	19.05	20.57	21.89	23.05	24.09
	15.27	20.79	24.63	27.57	29.97	31.99	33.73	35.25	36.61
10	10.99	15.77	19.14	21.75	23.88	25.68	27.23	28.60	29.83
	9.02	13.41	16.53	18.96	20.94	22.63	24.09	25.37	26.53
	16.21	22.19	26.36	29.57	32.17	34.37	36.26	37.93	39.41
11	11.80	17.01	20.68	23.53	25.86	27.83	29.53	31.03	32.38
	9.76	14.56	17.97	20.63	22.81	24.66	26.26	27.67	28.94
	17.13	23.56	28.05	31.52	34.33	36.71	38.76	40.57	42.17
12	12.60	18.22	22.20	25.29	27.82	29.95	31.80	33.43	34.89
	10.50	15.69	19.39	22.28	24.66	26.67	28.41	29.95	31.33
	18.02	24.90	29.72	33.44	36.46	39.01	41.22	43.16	44.89
13	13.38	19.42	23.70	27.03	29.75	32.05	34.05	35.81	37.38
	11.22	16.80	20.80	23.92	26.48	28.65	30.54	32.20	33.69
	18.90	26.22	31.36	35.33	38.57	41.29	43.65	45.72	47.57
14	14.15	20.60	25.18	28.74	31.66	34.13	36.27	38.16	39.85
	11.93	17.91	22.19	25.54	28.29	30.63	32.65	34.44	36.04
	19.76	27.53	32.98	37.21	40.65	43.55	46.05	48.26	50.24
15	14.91	21.77	26.64	30.45	33.56	36.19	38.48	40.49	42.29
	12.63	19.00	23.58	27.15	30.09	32.58	34.75	36.66	38.37
	20.61	28.81	34.58	39.05	42.70	45.77	48.44	50.77	52.87
16	15.66	22.92	28.10	32.13	35.44	38.24	40.66	42.81	44.72
	13.33	20.09	24.95	28.75	31.88	34.53	36.83	38.87	40.69
	21.45	30.08	36.17	40.98	44.73	47.98	50.79	53.27	55.48
17	16.40	24.07	29.54	33.80	37.30	40.27	42.83	45.10	47.13
	14.02	21.16	26.31	30.34	33.65	36.46	38.90	41.06	42.99
	22.27	31.34	37.74	42.70	46.75	50.17	53.13	55.73	58.06
18	17.13	25.20	30.96	35.46	39.15	42.28	44.99	47.39	49.53
	14.70	22.23	27.66	31.91	35.41	38.38	40.96	43.25	45.29
	23.09	32.58	39.29	44.50	48.75	52.34	55.44	58.19	60.63
19	17.86	26.32	32.38	37.11	40.99	44.28	47.14	49.65	51.91
	15.37	23.29	29.00	33.48	37.17	40.29	43.01	45.41	47.57
	23.90	33.81	40.84	46.28	50.73	54.49	57.75	60.62	63.18
20	18.57	27.44	33.79	38.75	42.82	46.27	49.27	51.91	54.28
	16.05	24.35	30.34	35.04	38.91	42.20	45.05	47.58	49.84

Note. "k" denotes the number of risks and "m" denotes the number of support points.

for $l = m, ..., km$. Elsewhere, $C(l, k, m) = 0$. Since $C(m, 1, m) = 1$ for $m \geqslant 1$, it is reasonably easy to compute $C(l, k, m)$ by our recurrence relationship for all values of l, k, and m. If $k = 2$, it easily follows that the $C(l, 2, m)$ are binomial probabilities with parameters m and $\frac{1}{2}$.

See Dykstra, Kochar, and Robertson [6] for more details regarding the convolution of independent $\bar{\chi}^2$ distributions. Critical points for the linear order case, at levels 0.01, 0.05, and 0.10 are given in Table I for $k \leqslant 10$ and $m \leqslant 20$.

As noted in Section 1, similar results may be obtained for order restrictions other than the linear order restriction specified by (1.3). For example, for the tree order restriction, $h_1(t) \leqslant h_i(t)$, $i = 2, 3, ..., k$, as noted in Section 2, the form of the test statistic would change through the set $\mathscr{L}$ associated with the projection $\boldsymbol{\theta}^*$. The asymptotic distribution given in Theorem 3.1 would be chi-bar-squared, where the level probabilities $p(l, k)$ would be the ones associated with the tree order (cf. Section 2.4 of RWD).

We note that the asymptotic null distribution of our test statistic is independent of the $p_{\cdot j}$ (as long as they are not zero) and, hence, the test will fortuitously be an asymptotically similar test. Many testing problems involving inequality constraints do not have this desirable property.

4. Examples

We consider some mortality data provided by Dr. H. E. Walburg, Jr. of the Oak Ridge National Laboratory (see Hoel [10]). The data was

TABLE II

Ages at Death for 99 RFM Conventional Male Mice Which Received a Radiation Dose of 300r 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	670	695	697	700	
705	712	713	738	748	753				

TABLE III

No.	Interval	d_{1j}	d_{2j}	$\hat{\theta}_{1j}$	$\hat{\theta}_{2j}$	θ_{1j}^*	θ_{2j}^*
1	40.0–160.5	4	1	4/5	1/5	0.500	0.500
2	160.5–281.0	7	13	7/21	14/21	0.333	0.667
3	281.0–401.5	6	6	6/12	6/12	0.500	0.500
4	401.5–522.0	9	5	9/14	5/14	0.500	0.500
5	522.0–642.5	8	17	8/25	17/25	0.320	0.680
6	642.5–763.0	5	17	5/22	17/22	0.228	0.772

obtained from a laboratory experiment on RFM strain male mice which had received a radiation dose of 300r at an age of 5–6 weeks and were then kept in a conventional environment. We consider only two major risks of death—the first risk is cancer and the second risk is the combination of all other risks. Table II gives autopsy data for 99 such mice.

Let $h_1(t)$ and $h_2(t)$ denote the cause specific hazard rates of death due to other causes and cancer, respectively. We grouped the data based on six equal length intervals. The details are given in Table III. When we compute the value of $T = -2 \ln \Lambda$ as defined in (3.1), we obtain 12.60 which gives a p-value of 0.0087.

These data would appear to strongly support the conclusion that the cause specific hazard rate is larger for the risk of cancer than for all other risks when that hypothesis is compared to equality of cause specific hazard rates.

We are grateful to the Editor and the referees for their thoughtful comments and suggestions which have greatly improved the presentation of the paper.

REFERENCES

[1] ALY, E.-E., KOCHAR, S., AND MCKEAGUE, I. (1994). Some tests for comparing cumulative incidence functions and cause specific hazard rates. *J. Amer. Statist. Assoc.* **89** 994–999.

[2] ARAS, G., AND DESHPANDÉ, J. V. (1992). Statistical analysis of dependent competing risks. *Statist. Decisions* **10** 323–336.

[3] BAGAI, I., DESHPANDÉ, J. V., AND KOCHAR, S. C. (1989). A distribution-free tests for the equality of two failure rates in the presence of competing risks. *Comm. Statist. Theory Methods* **15** 107–120.

[4] 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.

[5] DAVIS, T. P., AND LAWRENCE, A. J. (1989). The likelihood for competing risk survival analysis. *Scand. J. Statist.* **16** 23–28.

[6] DYKSTRA, R., KOCHAR, S., AND ROBERTSON, T. (1991). Statistical inference for uniform stochastic ordering in several populations. *Ann. Statist.* **19** 870–888.

[7] GAIL, M. (1982). Competing risks. In *Encyclopedia in Statist. Sci* (S. Kotz and N. L. Johnson, Eds.), pp. 75–81, Wiley, New York.

[8] GRAY, R. J. (1988). A class of k-sample tests for comparing the cumulative incidence of a competing risk. *Ann. Statist.* **16** 1141–1154.

[9] HARRINGTON, D. P., AND FLEMING, T. R. (1982). A class of rank test procedures for censored survival data. *Biometrika* **69** 553–566.

[10] HOEL, D. G. (1972). A representation of mortality data by competing risks. *Biometrika* **28** 475–488.

[11] MILES, R. E. (1959). The complete amalgamation into blocks, by weighted means, of a finite set of real numbers. *Biometrika* **46** 317–327.

[12] NEUHAUS, G. (1991). Some linear and nonlinear rank tests for competing risks models. *Comm. Statist. Theory Methods* **20** 667–701.

[13] PRENTICE, R. L., KALBFLEISCH, J. D., PETERSON, A. V., FLUORNEY, N., FAREWELL, V. T., AND BRESLOW, N. E. (1978). The analysis of failure times in the presence of competing risks. *Biometrics* **34** 541–554.

[14] ROBERTSON, T., WRIGHT, F. T., AND DYKSTRA, R. L. (1988). *Order Restricted Statistical Inference*. Wiley, Chichester.

[15] SERFLING, R. J. (1980). *Approximation Theorems of Mathematical Statistics*. Wiley, New York.

[16] YIP, P., AND LAM, K. F. (1992). A class of non-parametric tests for the equality of failure rates in a competing risks model. *Comm. Statist. Theory Methods* **21** 2541–2556.