STATISTICA, anno LXXIV, n. 3, 2014

MODELING LIFETIME DATA WITH MULTIPLE CAUSES USING CAUSE SPECIFIC REVERSED HAZARD RATES

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1. Introduction

In survival studies, the failure (death) of subjects may be attributed to one of several causes or types. In such situations, the subject is exposed to two or more causes of failure, but its eventual death can be due to exactly one of these causes. In this context, for each subject, we observe a random vector (T, J), where T is possibly a censored survival time and J represents cause of death (exactly one of say k possible causes). J takes the values on the set $\{1, 2, ..., k\}$. Modeling and analysis of such lifetime data under right censoring using various concepts are extensively discussed in statistical literature (see Kalbfleisch and Prentice (2002), Lawless (2003), Peng and Fine (2007)and Jeong and Fine (2009)).

The popular approach employed for the analysis of lifetime data with multiple causes subject to right censoring is based on cause specific hazard rates, $\lambda_j(t)$ defined by

$$\lambda_j(t) = \lim_{\Delta t \to 0} \frac{P[T < t + \Delta t, J = j | T \geq t]}{\Delta t} \qquad j = 1, 2, ...k. \tag{1}$$

Note that $\lambda_j(t)\Delta t$ is the approximate probability of failure of a subject in $(t, t+\Delta t)$ due to cause j given that it has survived up to time t. The analysis of lifetime data using (1) is studied in literature by various authors. Crowder (2001), Kalbfleisch and Prentice (2002), and Lawless (2003) provide reviews on this topic.

There are many occasions in survival studies, where the lifetime data are left censored. For example, Baboons in the Amboseli Reserve, Kenya, sleep in the trees and descend for foraging at some time of the day. Observers often arrive later in the day than this descent and for such days they can only ascertain that descent took place before a particular time, so that the descent times are left censored (Andersen

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et al. (1993)). In early childhood learning centres, interest often focuses upon testing children to determine when a child learns to accomplish certain specified tasks. The age at which a child learns the task would be considered as lifetime. Often, some children can already perform the task when they enter to the study. Such lifetimes are considered as left censored. The reversed hazard rate $h(t)$, defined by

$$h(t) = \lim_{\Delta t \to 0} \frac{P[t - \Delta t < T \leq t | T \leq t]}{\Delta t}, \tag{2}$$

facilitates the analysis of such left censored data. The function $h(t)$ specifies the instantaneous rate of failure of a subject at time t given that it failed before time t. Introduced by Barlow *et al.* (1963), (2) has been used in various contexts, such as, estimation of distribution function under left censoring (Lawless (2003)), analysis of lifetime data arising in parallel systems (Marshall and Olkin (2007)), definition of new stochastic orders (Keilson and Sumita (1982)) and evolving repair and maintenance strategies (Marshall and Olkin (2007)). Recently, Gupta and Gupta (2007) have discussed monotonic behaviour of hazard rate and reversed hazard rate of proportional reversed hazards model. Sengupta and Nanda (2010) introduced a semiparametric regression model using the reversed hazard rate, analogous to well known Cox proportional hazards model. For various properties and applications of (2), one could refer to Andersen *et al.* (1993), Gürler (1996), Block *et al.* (1998), Gupta *et al.* (1998), Finkelstein (2002), Lawless (2003) and Nair *et al.* (2005).

Duffy *et al.* (1990) considered the Australian twin data which consists of information on the age at which appendectomy of monozygotic (MZ) and dizygotic (DZ) twins. There were 21 pairs with missing age at onset and therefore the data contains left censored observations. This data can be viewed in the form of left censored lifetime data with multiple causes. The details of the data are given in Section 6. Duffy *et al.* (1990) excluded these left censored observations in the analysis. It is therefore appropriate to model the data by including these left censored observations, which can be done by developing models using reversed hazard rate. Motivated by this, in this paper, we introduce cause specific reversed hazard rates, which are useful for the analysis of left censored lifetime data with multiple causes.

The rest of the article is arranged as follows. In Section 2, we introduce cause specific reversed hazard rates and study their properties. Nonparametric estimation of cumulative cause specific reversed hazard rates and cumulative incidence functions are discussed in Section 3. We present asymptotic properties of the estimators in Section 4. Simulation studies are conducted in Section 5 to asses the efficiency of the proposed estimators. We, in Section 6 apply the proposed method to two real life data sets. Section 7 provides major conclusions of the study.

2. The Model

Let (T, J) be a pair of random variables as described in Section 1. Let $F(t)$ be the distribution function of T. We assume that the k failures are mutually exclusive and exhaustive so that a subject can have at most one realized failure time with an identifiable cause. The cause specific reversed hazard rate of T is defined as

$$h_j(t) = \lim_{\Delta t \to 0} \frac{P[t - \Delta t \leq T \leq t, J = j | T \leq t]}{\Delta t} \qquad j = 1, 2, ..., k. \tag{3}$$

The $h_j(t)$ specifies the instantaneous rate of failure of a subject at time t due to cause j given that it failed before time t. Denote $F_j(t) = P[T \leq t, J = j]$ as the cumulative incidence function of T. We can write (3) as

$$h_j(t) = \frac{f_j(t)}{F(t)} \qquad j = 1, 2, ..., k \tag{4}$$

where $f_j(t) = \frac{dF_j(t)}{dt}$ is the cause specific density of T and $F(t) = \sum_{j=1}^{k} F_j(t)$. The marginal reversed hazard rate for T is given by

$$h(t) = \sum_{j=1}^{k} h_j(t).$$

Then the distribution function for T is obtained as

$$F(t) = exp[-H(t)] = exp[-\sum_{j=1}^{k} H_j(t)], \tag{5}$$

where $H(t) = \int_t^\infty h(u)du$ is the cumulative reversed hazard rate for T and $H_j(t) = \int_t^\infty h_j(u)du$ is the cumulative cause specific reversed hazard rate.

Now from (4), we obtain the cumulative incidence function as

$$F_j(t) = \int_0^t h_j(u)F(u)du = -\int_0^t F(u)dH_j(u). \tag{6}$$

The function $h_j(t)$ fully describe the distribution of (T, J) in multiple failure mode settings.

Consider a parallel system with k physical components, each of which is liable to fail and let T_j denote the lifetime or failure time of component j ($j = 1, 2, ...k$). The system fails when the last component fails so that the lifetime is $T = max(T_1, T_2, ...T_k)$. In this set up, if $h_j(t)$ is the reversed hazard rate of the component j, then the reversed hazard rate of the system is $h(t) = \sum_{j=1}^{k} h_j(t)$.

3. Nonparametric Estimation

In this section, we discuss nonparametric estimation of $H_j(t)$ and $F_j(t)$, $j = 1, 2, ...k$ under left censoring. Suppose that the lifetime random variable T is left censored by the random variable C. Let $G(t)$ be the distribution function of C. We assume that T and C are independent. Under left censoring we observe random vector $(X, \delta, J\delta)$ where $X = max(T, C)$ and $\delta = I(T = X)$ with $I(.)$ as the usual indicator function of X. The independence of T and C implies that

$$L(t) = F(t)G(t) \tag{7}$$

where $L(t)$ is the distribution function of X. Let $(X_i, \delta_i, J_i\delta_i)$ be independent and identically distributed copies of $(X, \delta, J\delta)$, $i = 1, 2...n$.

We now employ the counting process approach for the nonparametric estimation of $H_j(t)$ and $F_j(t)$, $j = 1, 2, ...k$. Suppose that event of interest occur in forward time; but the point of reference, τ is far away from the time span of interest. Let $N_j(t)$ be the number of observed events occurring in $[t, \tau)$ due to cause j. If there are n individuals, define $N_{ij}(t) = I(X_i \geq t, \delta_i = 1, J_i = j) \quad i = 1, 2, ...n, j = 1, 2, ..k$, and $Y_i(t) = I(X_i \leq t)$. Define the sigma field $\mathcal{F}_t = \sigma\{N_{ij}(s), N^c{}_{ij}(s); t \leq s \leq \tau\}$ where $N^c{}_{ij}(t) = I(X_i \geq t, \delta_i = 0, J_i = j) \quad i = 1, 2, ...n, j = 1, 2, ..k$. $\mathcal{F}_t$ represents a filtration such that $\mathcal{F}_t \subseteq \mathcal{F}_s$ whenever $s \leq t$. We denote history at an instant just after to time t by $\mathcal{F}_{t+}$. The process $N_{ij}(.)$ is assumed to be a counting process such that $N_{ij}(t)$ is measurable with respect to the sigma field $\{\mathcal{F}_t\}_{0 \leq t \leq \tau}$. Let $dN_{ij}(t)$ denote the increment of $N_{ij}(t)$ from the right to left of the infinitesimal interval $[t - dt, t]$.

For left censored data, under the assumption of independent censoring, we have

$$\begin{aligned} P\left(X_i \in (t-dt, t), \delta_i = 1, J_i = j | \mathcal{F}_{t+}\right) = &\ h_j(t)dt \qquad\qquad if\ \ X_i \leq t \\ = &\ 0 \qquad\qquad\qquad\ \ if\ \ X_i > t \end{aligned} \tag{8}$$

which leads to the fact that,

$$E[dN_{ij}(t)|\mathcal{F}_{t+}] = Y_i(t)h_j(t)dt \tag{9}$$

where $dN_{ij}(t) = I(X_i = t, \delta_i = 1, J_i = j)$.

Denote $N_j(t) = \sum\limits_{i=1}^{n} N_{ij}(t)$, and $Y(t) = \sum\limits_{i=1}^{n} I(X_i \leq t)$. Now we consider the counting process martingale,

$$M_j(t) = N_j(t) - A_j(t) \tag{10}$$

where $A_j(t) = \sum\limits_{i=1}^{n} \int_t^{t_0} I(X_i \leq u)h_j(u)du$ and $t_0 = \sup(t; F(t) < 1)$. We also have

$$E[N_j(t)|\mathcal{F}_{t+}] = E[A_j(t)|\mathcal{F}_{t+}] = A_j(t). \tag{11}$$

and

$$E[dA_j(s)|\mathcal{F}_{s+}] = E[-I(X \leq s)|\mathcal{F}_{s+}] = dA_j(s). \tag{12}$$

From (10), (11), and (12), we have

$$E[dM_j(t)|\mathcal{F}_{t+}] = E[dN_j(t) - dA_j(t)|\mathcal{F}_{t+}] = 0. \tag{13}$$

Because $E[dM_j(t)|\mathcal{F}_{t+}] = 0$, then for all $t \le s$

$$\begin{aligned} E[M_j(t)|\mathcal{F}_s] - M_j(s) &= E[M_j(t) - M_j(s)|\mathcal{F}_s] \\ &= E\left[\int_t^s dM_j(u)|\mathcal{F}_s\right] \\ &= \int_t^s E[E[dM_j(u)|\mathcal{F}_{u+}]|\mathcal{F}_s] = 0. \end{aligned}$$

From (10) we can write

$$dN_j(t) = Y(t)h_j(t)dt + dM_j(t). \tag{14}$$

If $Y(t) > 0$, then we have,

$$\frac{dN_j(t)}{Y(t)} = h_j(t)dt + \frac{dM_j(t)}{Y(t)}. \tag{15}$$

If $dM_j(t)$ is noise, then so is $\frac{dM_j(t)}{Y(t)}$, because the value of $Y(t)$ at time t are known at time $t+$. We have $E[\frac{dM_j(t)}{Y(t)}|\mathcal{F}_{t+}] = 0$.
Let $K(t) = I(Y(t) > 0)$. Integrating both sides of (15) we get

$$\int_t^{t_0} \frac{K(u)dN_j(u)}{Y(u)} = \int_t^{t_0} K(u)h_j(u)du + \int_t^{t_0} \frac{K(u)dM_j(u)}{Y(u)}. \tag{16}$$

The integral $\int_t^{t_0} \frac{K(u)dM_j(u)}{Y(u)}$ in (16) can be considered as random noise in our estimate. The random quantity $H_j^*(t) = \int_t^{t_0} K(u)h_j(u)du$ is essentially $H_j(t)$ itself in the range where we have data. Ignoring the statistical uncertainty in $\int_t^{t_0} \frac{K(u)dM_j(u)}{Y(u)}$, $\hat{H}_j(t)$ is the nonparametric estimator of $H_j(t)$ given by

$$\hat{H}_j(t) = \int_t^{t_0} \frac{K(u)dN_j(u)}{Y(u)}. \tag{17}$$

From (17), it is easy to see that

$$\hat{H}_j(t) = \sum_{i:X_i>t} \frac{\delta_{ij}}{n_i} \qquad j = 1, 2, ...k$$

where n_i, number of subjects failed just prior to time t_i and $\delta_{ij} = I(J_i = j)$ $j = 1, 2, ...k$, $i = 1, 2, ...n$. The cumulative reversed hazard rate can be easily estimated as

$$\hat{H}(t) = \sum_{j=1}^{k} \hat{H}_j(t) = \int_t^{t_0} \frac{K(u)dN(u)}{Y(u)} \tag{18}$$

where $N(t) = \sum_{j=1}^{k} N_j(t)$. The non-parametric estimator of $F_j(t)$ is given by

$$\hat{F}_j(t) = -\int_0^t \hat{F}(u)d\hat{H}_j(u) \tag{19}$$

where
$$\hat{F}(t) = exp[-\hat{H}(t)]. \tag{20}$$
It may be noted that (19) can be written as

$$\hat{F}_j(t) = \sum_{i:X_i \le t} \hat{F}(t_i)\frac{\delta_{ij}}{n_i} \quad j = 1, 2, ..., k.$$

In the absence of censoring, $F_j(t)$ equals the fraction of subjects with $X_i \le t$ and $J_i = j$ which is the empirical sub distribution function for cause j.

4. Asymptotic Properties

To study asymptotic properties of the nonparametric estimator of $H_j(t)$, we consider the identity (16). First we consider $\hat{H}_j(t) - H_j^*(t)$. From (16),

$$\begin{aligned} \hat{H}_j(t) - H_j^*(t) &= \int_t^{t_0} \frac{K(u)}{Y(u)}[dN_j(u) - Y(u)h_j(u)du] \\ &= \int_t^{t_0} \frac{K(u)}{Y(u)} dM_j(u). \end{aligned} \tag{21}$$

From (21), we immediately obtain $E(\hat{H}_j(t) - H_j^*(t)) = 0$ and

$$\begin{aligned} E(\hat{H}_j(t) - H_j(t)) &= E(H_j^*(t)) - H_j(t)) \\ &= -\int_t^{t_0} P(Y(u) = 0)h_j(u)du. \end{aligned}$$

Note that $\frac{Y(t)}{n}$, $\frac{N_j(t)}{n}$ are sample averages and that, for large n, the random variation in both should be small. Suppose that $\frac{Y(t)}{n}$ converges to a deterministic function $p(t)$ for large n. The process $\sqrt{n}(\hat{H}_j(t) - H_j^*(t))$ is asymptotically equal to $\sqrt{(}n)(\hat{H}_j(t) - H_j(t))$, since $H_j^*(t)$ is very close to $H_j(t)$ for large n.

Now we can prove the consistency of the estimator $H_j(t)$.

Theorem 1. *For fixed j, if $t \in [0, \infty)$ is such that*

$$Y(t) \xrightarrow{p} \infty \ as\ n \to \infty \tag{22}$$

then $\sup_{s\in[t,t_0]} \left|\hat{H}_j(s) - H_j(s)\right| \xrightarrow{p} 0 \ as\ n \to \infty$.

Proof.

$$\begin{aligned} \left|\hat{H}_j(s) - H_j(s)\right| &\le \left|\int_t^{t_0} \frac{K(u)dN_j(u)}{Y(u)} - \int_t^{t_0} K(u)h_j(u)du\right| + \left|\int_t^{t_0} I(Y(u) = 0)h_j(u)du\right| \\ &\le \left|\int_t^{t_0} \frac{K(u)dM_j(u)}{Y(u)}\right| + I(Y(t) = 0)H_j(t) \end{aligned}$$

Since (22) hold, $I(Y(t)=0)H_j(t) \xrightarrow{p} 0$. To prove $\sup_{s\in[t,t_0]} \left|\hat{H}_j(s) - H_j(s)\right| \xrightarrow{p} 0$, it is enough to show that $\sup_{s\in[t,t_0]} \left[\int_t^{t_0} \frac{K(u)dM_j(u)}{Y(u)}\right]^2 \xrightarrow{p} 0$.
Then by Lenglart's inequality and Corollary 3.4.1 of Fleming and Harrington (1991), we get for any $\epsilon, \eta > 0$,

$$P\left[\sup_{s\in[t,t_0]} \left[\int_t^{t_0} \frac{K(u)dM_j(u)}{Y(u)}\right]^2 \geq \epsilon\right] \leq \frac{\eta}{\epsilon} + P\left[\int_t^{t_0} \frac{K(u)h_j(u)du}{Y(u)} \geq \eta\right]. \quad (23)$$

Condition (22) imply that the second term on the right hand side of (23) become zero and it follows that $\sup_{s\in[t,t_0]} \left|\hat{H}_j(s) - H_j(s)\right| \xrightarrow{p} 0$. □

Corollary 2. *Under the assumptions of Theorem 4.1,* $\sup_{s\in[t,t_0]} \left|\hat{F}(s) - F(s)\right| \xrightarrow{p} 0$.

Proof. Proof follows from Theorem 4.1 using the relation between $H_j(t)$ and $F(t)$ given in (5). □

Corollary 3. *Under the assumptions of Theorem 4.1, for fixed* j, $\sup_{s\in[t,t_0]} \left|\hat{F}_j(s) - F_j(s)\right| \xrightarrow{p} 0$.

Proof. Proof follows from Theorem 4.1 and Corollary 4.1 using the identity connecting $H_j(t)$, $F(t)$ and $F_j(t)$ given in (6). □

Now we obtain the asymptotic variance of $\sqrt{n}(d\hat{H}_j(t) - dH_j(t))$ as

$$\begin{aligned} Asvar[\sqrt{n}(d\hat{H}_j(t) - dH_j(t))] &= nVar\left[\frac{dM_j(t)}{Y(t)}|\mathcal{F}_{t+}\right] \\ &= n\frac{\langle dM_j(t)\rangle}{Y(t)^2} \\ &= n\frac{Y(t)h_j(t)dt}{Y(t)^2} \\ &= \frac{h_j(t)dt}{Y(t)/n}, \end{aligned} \quad (24)$$

which converges to $\frac{h_j(t)dt}{p(t)}$ for large n. Note that $\langle dM_j(t)\rangle$ is the predictable variation process of $dM_j(t)$. Thus, the asymptotic variance of $\sqrt{n}(\hat{H}_j(t) - H_j(t))$ is obtained as,

$$\sigma_j{}^2(t) = \int_t^{t_0} \frac{h_j(u)du}{p(u)}, \quad (25)$$

which can be consistently estimated by

$$\hat{\sigma}_j^2(t) = n \sum_{i:x_i \geq t} \frac{\delta_{ij}}{n_i{}^2}. \quad (26)$$

Theorem 4. *For fixed t and j, $\sqrt{n}(\hat{H}_j(t)-H_j(t))$ is asymptotically distributed as normal with mean zero and variance ${\sigma_j}^2(t)$.*

Proof. From (21) we can write,

$$\sqrt{n}(\hat{H}_j(t) - H_j^*(t)) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \int_t^{t_0} \frac{nK(u)}{Y(u)} dM_{ij}(u).$$

Then by martingale central limit theorem, for fixed t and j, $\sqrt{n}(\hat{H}_j(t) - H_j(t))$ is asymptotically distributed as normal with mean zero and variance ${\sigma_j}^2(t)$ (Fleming and Harrington (1991), page 92-93). □

Corollary 5. *For fixed t, $\sqrt{n}(\hat{H}(t) - H(t))$ has a limiting distribution as normal with mean zero and variance $\sigma^2(t) = \int_t^{t_0} \frac{h(u)du}{p(u)}$.*

Proof. Proof follows from Theorem 4.2. To find asymptotic variance of $\hat{H}(t)$, consider $dM_i(t) = dN_i(t) - Y_i(t)dH(t)$, where $dM_i(t) = \sum\limits_j dM_{ij}(t)$, $dN_i(t) = \sum\limits_j dN_{ij}(t)$ and $dH(t) = \sum\limits_j dH_j(t)$. The rest of the derivations follows directly from the steps for finding the asymptotic variance of $\hat{H}_j(t)$. □

Corollary 6. *For fixed t, $\sqrt{n}(\hat{F}(t) - F(t))$ has a limiting distribution as normal with mean zero and variance $\sigma^{2*}(t)$ given in* (27).

Proof. Since $\hat{F}(t) = exp[-\hat{H}(t)]$, the asymptotic normality of $\hat{H}(t)$ carries over to the asymptotic normality of the estimator $\hat{F}(t)$, by functional delta method (Andersen *et al.* (1993)). Thus for fixed t, $\sqrt{n}(\hat{F}(t) - F(t))$ has a limiting distribution as normal with mean zero. From Appendix B of Lawless (2003)(page 539), the asymptotic variance $\sigma^{2*}(t)$ is obtained as

$$\sigma^{2*}(t) = F^2(t)\,\mathrm{Asvar}(\hat{H}(t)). \tag{27}$$

□

Corollary 7. *For fixed t and j, $\sqrt{n}(\hat{F}_j(t) - F_j(t))$ is asymptotically normal with mean zero and variance given in* (29).

Proof. From (19) we have

$$\begin{aligned}\sqrt{n}\left(\hat{F}_j(t) - F_j(t)\right) &= \sqrt{n}\left[\int_0^t \hat{F}(u)d\hat{H}_j(u) - \int_0^t F(u)dH_j(u)\right] \\ &= \sqrt{n}\left[\int_0^t \left[\hat{F}(u)\left(d\hat{H}_j(u) - dH_j(u)\right)\right] + \int_0^t \left(\hat{F}(u) - F(u)\right) d\hat{H}_j(u)\right]\end{aligned} \tag{28}$$

Since for fixed t and j, $\sqrt{n}(d\hat{H}_j(t) - dH_j(t))$ and $\sqrt{n}(\hat{F}(t) - F(t))$ are asymptotically normal with mean zero, $\sqrt{n}(\hat{F}_j(t) - F_j(t))$ is also asymptotically normal with mean zero and variance $\sigma_j^{2*}(t)$, which can be consistently estimated by

$$\hat{v}ar(\hat{F}_j(t)) = \int_0^t (\hat{F}(u))^2 \frac{dN_j(u)}{Y(u)^2}. \tag{29}$$

□

5. Simulation Studies

Simulation studies are carried out to assess the performance of the proposed estimators. Suppose there are two risks of failure. We generate random samples from the following parametric family of sub-distribution functions proposed by Dewan and Kulathinal (2007). Let,

$$F_1(t) = P[T \le t, J = 1) = \phi F^a(t) \quad and \quad F_2(t) = P[T \le t, J = 2] = F(t) - \phi F^a(t) \tag{30}$$

where $1 \le a \le 2$, $0 \le \phi \le 0.5$ and $F(t)$ is the distribution function of failure time T. Note that $\phi = P[J = 1]$ and when $a = 1$, T and J are independent. For the other choices of a, the two variables T and J are dependent. The restriction on the parameters are imposed due to nonnegativity condition of cause specific density function of T.

Let the failure time distribution be $F(t) = 1 - exp[-\lambda t]$. Censored observations are generated from $U(0, b)$ where b is chosen such a way that approximately 20% or 40% of the observations are censored. We simulated 1000 replications of random samples of size $n = 50$, 100 and 250 by considering different combinations for values of λ, a and ϕ. To study the effect of censoring, we consider three different censoring scenarios viz no censoring , mild censoring (20% of the observations are censored) and heavy censoring (40% of the observations are censored). We compute $\hat{H}_1(t)$ and $\hat{H}_2(t)$ for each sample at different time points of t under different censoring percentages.

Based on 1000 replications, we compute average absolute bias and average mean squared error (MSE) of the estimates. Tables 1-4 provide average absolute bias and average MSE of estimates for different censoring percentages. As the results for various parametric values are comparable, we present the results for $a = 1.5$, $\lambda = 0.5$ and 2, and $\phi = 0.2$ and 0.4. From the tables, it may be noted that both bias and MSE of the estimates decreases as sample size increases and those slightly increase as censoring percentage increases. As lifetime increases, both bias and MSE of the estimator of $H_j(t)$, $j = 1, 2$ decreases. This may be due to the fact that the influence of left censored observations will be more at the left tail of observations. It is also noted that when ϕ takes small values, there is a tendency of greater bias for $\hat{H}_1(t)$ compared to $\hat{H}_2(t)$. This could be due to the fact that number of observed failures due to cause 1 is less in such contexts.

6. Data Analysis

The proposed method is applied to two real life data sets. The purpose here is to illustrate a possible application of the proposed method rather than provide

TABLE 1

Bias and MSE of the estimates of $H_1(t)$ and $H_2(t)$ for $a = 1.5$, $\phi = 0.2$ and $\lambda = 0.5$

n	t	Uncensored				20%Censored				40%Censored			
		$\hat{H}_1(t)$		$\hat{H}_2(t)$		$\hat{H}_1(t)$		$\hat{H}_2(t)$		$\hat{H}_1(t)$		$\hat{H}_2(t)$	
		Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE
50	0.2	0.0098	0.0053	0.0082	0.0056	0.1923	0.1072	0.0849	0.0279	0.1983	0.1093	0.0898	0.0282
	0.5	0.0082	0.0034	0.0081	0.0056	0.1825	0.1019	0.0557	0.0144	0.1915	0.1051	0.0653	0.0199
	1	0.0068	0.0022	0.0079	0.0045	0.1366	0.0390	0.0372	0.0072	0.1383	0.0419	0.0510	0.0081
	1.5	0.0032	0.0013	0.0073	0.0036	0.0935	0.0192	0.0274	0.0044	0.0982	0.0199	0.0341	0.0053
	2	0.0031	0.0011	0.0064	0.0008	0.0683	0.0115	0.0198	0.0029	0.0941	0.0125	0.0262	0.0034
100	0.2	0.0074	0.0042	0.0073	0.0043	0.1841	0.1221	0.0792	0.0170	0.1882	0.1365	0.0818	0.0127
	0.5	0.0071	0.0021	0.0074	0.0042	0.1388	0.0798	0.0537	0.0095	0.1426	0.1248	0.0609	0.0094
	1	0.0065	0.0007	0.0053	0.0034	0.1241	0.0295	0.0331	0.0046	0.1376	0.0408	0.0413	0.0099
	1.5	0.0021	0.0004	0.0031	0.0042	0.0832	0.0141	0.0314	0.0028	0.0919	0.0342	0.0324	0.0052
	2	0.0020	0.0003	0.0003	0.0003	0.0671	0.0081	0.0142	0.0018	0.0606	0.0095	0.0266	0.0031
250	0.2	0.0073	0.0025	0.0052	0.0032	0.1814	0.1181	0.0740	0.0115	0.1827	0.1955	0.0744	0.0037
	0.5	0.0069	0.0021	0.0049	0.0025	0.1331	0.0677	0.0458	0.0064	0.1418	0.0993	0.0566	0.0081
	1	0.0065	0.0031	0.0048	0.0005	0.1215	0.0253	0.0301	0.0032	0.1235	0.0910	0.0441	0.0041
	1.5	0.0003	0.0001	0.0022	0.0003	0.0767	0.0114	0.0237	0.0019	0.0835	0.0312	0.0334	0.0027
	2	0.0002	0.0001	0.0002	0.0002	0.0583	0.0059	0.0139	0.0011	0.0615	0.0071	0.0241	0.0011

TABLE 2

Bias and MSE of the estimates of $H_1(t)$ and $H_2(t)$ for $a = 1.5$, $\phi = 0.2$ and $\lambda = 2$

n	t	Uncensored				20% censored				40%censored			
		$\hat{H}_1(t)$		$\hat{H}_2(t)$		$\hat{H}_1(t)$		$\hat{H}_2(t)$		$\hat{H}_1(t)$		$\hat{H}_2(t)$	
		Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE
	0.2	0.0072	0.0023	0.0065	0.0044	0.1767	0.0576	0.0534	0.0179	0.1932	0.0432	0.0964	0.0232
	0.5	0.0061	0.0020	0.0057	0.0023	0.0697	0.0121	0.0238	0.0032	0.0779	0.0111	0.0314	0.0112
50	1	0.0052	0.0021	0.0041	0.0007	0.0212	0.0022	0.0083	0.0008	0.0432	0.0032	0.0142	0.0072
	1.5	0.0035	0.0005	0.0013	0.0003	0.0057	0.0006	0.0018	0.0003	0.0214	0.0021	0.0098	0.0014
	2	0.0034	0.0002	0.0033	0.0001	0.0021	0.0002	0.0013	0.0001	0.0096	0.0002	0.0054	0.0004
	0.2	0.0057	0.0032	0.0043	0.0041	0.1673	0.0410	0.0532	0.0065	0.1732	0.0114	0.0662	0.072
	0.5	0.0051	0.0029	0.0041	0.0015	0.0656	0.0079	0.0216	0.0019	0.0745	0.0092	0.0412	0.0054
100	1	0.0033	0.0007	0.0034	0.0003	0.0184	0.0013	0.0078	0.0004	0.0413	0.0062	0.0311	0.0032
	1.5	0.0022	0.0004	0.0011	0.0002	0.0048	0.0004	0.0014	0.0002	0.0102	0.0041	0.0092	0.0011
	2	0.0018	0.0001	0.0012	0.0001	0.0021	0.0001	0.0008	0.0001	0.0092	0.0031	0.0034	0.0004
	0.2	0.0041	0.0013	0.0039	0.0012	0.1610	0.0340	0.0516	0.0042	0.1669	0.0445	0.0412	0.0018
	0.5	0.0033	0.0009	0.0012	0.0006	0.0571	0.0059	0.0215	0.0011	0.0789	0.0092	0.0112	0.0051
250	1	0.0021	0.0004	0.0008	0.0002	0.0107	0.0008	0.0074	0.0002	0.0532	0.0052	0.0099	0.0015
	1.5	0.0012	0.0003	0.0007	0.0002	0.0035	0.0002	0.0011	0.0001	0.0114	0.0031	0.0032	0.0006
	2	0.0015	0.0001	0.0007	0.0001	0.0016	0.0001	0.0009	0.0001	0.0094	0.0003	0.0031	0.0002

TABLE 3

Bias and MSE of the estimates of $H_1(t)$ and $H_2(t)$ for $a = 1.5$, $\phi = 0.4$ and $\lambda = 0.5$

n	t	Uncensored				20% Censored				40% Censored			
		$\hat{H}_1(t)$		$\hat{H}_2(t)$		$\hat{H}_1(t)$		$\hat{H}_2(t)$		$\hat{H}_1(t)$		$\hat{H}_2(t)$	
		Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE
50	0.2	0.0098	0.0072	0.0097	0.0089	0.2430	0.1813	0.1936	0.1063	0.2486	0.1891	0.1962	0.1171
	0.5	0.0084	0.0052	0.0079	0.0082	0.1305	0.0508	0.1488	0.0535	0.1407	0.0539	0.1493	0.0723
	1	0.0064	0.0032	0.0091	0.0053	0.0707	0.0171	0.1032	0.0257	0.1009	0.0174	0.1094	0.0354
	1.5	0.0047	0.0031	0.0058	0.0046	0.0447	0.0076	0.0771	0.0155	0.0588	0.0092	0.0832	0.0167
	2	0.0032	0.0015	0.0052	0.0035	0.0302	0.0043	0.0555	0.0095	0.0393	0.0054	0.0574	0.0094
100	0.2	0.0085	0.0066	0.0096	0.0064	0.2258	0.1249	0.1112	0.0716	0.2264	0.1619	0.1475	0.0809
	0.5	0.0081	0.0046	0.0075	0.0056	0.1263	0.0369	0.1276	0.0383	0.1361	0.0382	0.1294	0.0715
	1	0.0061	0.0032	0.0062	0.0032	0.0704	0.0108	0.0916	0.0194	0.0982	0.0285	0.0973	0.0432
	1.5	0.0034	0.0013	0.0059	0.0028	0.0439	0.0048	0.0632	0.0116	0.0515	0.0082	0.0665	0.0097
	2	0.0012	0.0009	0.0003	0.0002	0.0212	0.0025	0.0432	0.0071	0.0312	0.0032	0.0532	0.0032
250	0.2	0.0102	0.0093	0.0033	0.0009	0.2213	0.0897	0.1072	0.0537	0.2221	0.0912	0.1289	0.0794
	0.5	0.0094	0.0034	0.0029	0.0007	0.1201	0.0259	0.0985	0.0303	0.1314	0.0313	0.0114	0.0652
	1	0.0073	0.0009	0.0014	0.0007	0.0645	0.0076	0.0820	0.0153	0.0651	0.0094	0.0886	0.0173
	1.5	0.0053	0.0007	0.0001	0.0003	0.0353	0.0031	0.0627	0.0087	0.0494	0.0037	0.0713	0.0092
	2	0.0032	0.0003	0.0001	0.0001	0.0203	0.0015	0.0329	0.0051	0.0324	0.0022	0.0399	0.0032

TABLE 4

Bias and MSE of the estimates of $H_1(t)$ and $H_2(t)$ for $a = 1.5$, $\phi = 0.4$ and $\lambda = 2$

n	t	Uncensored				20% Censored				40% Censored			
		$\hat{H}_1(t)$		$\hat{H}_2(t)$		$\hat{H}_1(t)$		$\hat{H}_2(t)$		$\hat{H}_1(t)$		$\hat{H}_2(t)$	
		Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE	Bias	MSE
	0.2	0.0095	0.0049	0.0077	0.0066	0.0951	0.0235	0.1398	0.0374	0.1086	0.0271	0.1440	0.0193
	0.5	0.0093	0.0012	0.0062	0.0054	0.0302	0.0042	0.0631	0.0102	0.0966	0.0045	0.0680	0.0141
50	1	0.0083	0.0011	0.0057	0.0032	0.0083	0.0007	0.0240	0.0022	0.0149	0.0096	0.0272	0.0038
	1.5	0.0007	0.0002	0.0039	0.0015	0.0029	0.0002	0.0083	0.0006	0.0091	0.0004	0.0098	0.0009
	2	0.0001	0.0002	0.0011	0.0009	0.0001	0.0001	0.0031	0.0002	0.0041	0.0004	0.0029	0.0002
	0.2	0.0062	0.0019	0.0075	0.0041	0.0949	0.0159	0.1246	0.0244	0.1065	0.0193	0.1313	0.0254
	0.5	0.0061	0.0014	0.0064	0.0026	0.0300	0.0024	0.0615	0.0069	0.0404	0.0023	0.0677	0.0073
100	1	0.0014	0.0009	0.0041	0.0016	0.0081	0.0004	0.0212	0.0013	0.0108	0.0051	0.0394	0.0012
	1.5	0.0005	0.0007	0.0042	0.0011	0.0028	0.0002	0.0080	0.0004	0.0023	0.0013	0.0093	0.0007
	2	0.0003	0.0005	0.0023	0.0015	0.0009	0.0001	0.0028	0.0001	0.0003	0.0001	0.0023	0.0005
	0.2	0.0024	0.0009	0.0033	0.0009	0.0891	0.0121	0.1299	0.0205	0.0900	0.0137	0.1048	0.0238
	0.5	0.0014	0.0006	0.0008	0.0007	0.0207	0.0016	0.0614	0.0050	0.0394	0.0058	0.0633	0.0057
250	1	0.0011	0.0003	0.0003	0.0002	0.0080	0.0003	0.0194	0.0007	0.0107	0.0012	0.0199	0.0021
	1.5	0.0003	0.0002	0.0002	0.0001	0.0022	0.0001	0.0065	0.0002	0.0039	0.0009	0.0072	0.0009
	2	0.0002	0.0001	0.0002	0.0001	0.0012	0.0001	0.0023	0.0001	0.0015	0.0006	0.0022	0.0003

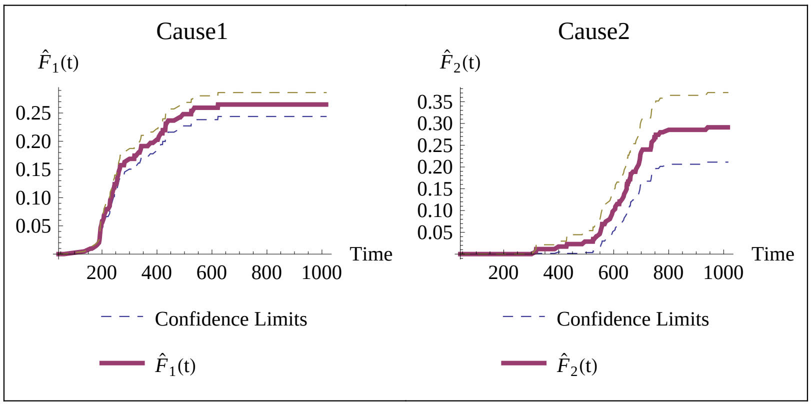

Figure 1 – Plot of estimate of $F_j(t)$; $j = 1, 2$ for mice mortality data

a definite analysis of the data. The first data give the survival times of mice, kept in a conventional germ-free environment, all of which were exposed to a fixed dose of radiation at an age of 5 to 6 weeks (Hoel (1972)). There are 3 causes of death viz thymic lymphoma (cause 1), reticulam cell sacroma (cause 2), and other causes (cause 3). This data were analysed by different researchers in various contexts (See Lawless (2003)). We treat other failures due to cause 3 as left censored observations. The estimates of $H_j(t)$ and $F_j(t)$ $j = 1, 2$, are computed at different time points. For $j = 1, 2$ the estimates of $H_j(t)$ and its standard error (written in parenthesis) are given in Table 5. Plots of $\hat{F}_j(t), j = 1, 2$ along with 95% confidence limits are given in Figure 1. From Figure 1 it can be seen that $\hat{F}_1(t)$ predominates over $\hat{F}_2(t)$, which means that most of the initial failures are due to cause 1.

Now we consider the Australian twin data given in Duffy *et al.* (1990) which consists of information on the age at which appendectomy of monozygotic (MZ) and dizygotic (DZ) twins. The data are given in Table 6. Individuals having age less than 11 are considered as left censored observations. The data were analyzed in various contexts by different researchers (See Kalbfleisch and Prentice (2002), and Sankaran and Gleeja (2011)). We consider only the information on age of twin one from each pair. The types MZ male, MZ female, DZ male and DZ female pairs are considered as four different causes. Now the data are in the form of left censored lifetime data with multiple causes. It is therefore, more appropriate to model the data using cause specific reversed hazard rates, by including left censored observations.

The estimates of $H_j(t)$ and $F_j(t)$, $j = 1, ...4$ are computed. The plots of estimates of cumulative cause specific reversed hazard rates and cumulative incidence functions along with 95% confidence limits are given in Figures 2 and 3 respectively. From Figure 3, it follows that the chance of appendectomy for DZ female is high compared to other types.

TABLE 5
Estimate of $H_j(t)$

Time	$\hat{H}_1(t)$	$\hat{H}_2(t)$
158	1.8832 (0.3261)	0.4801 (0.0703)
192	1.3828 (0.1987)	0.4801 (0.0703)
212	0.8575 (0.1528)	0.4801 (0.0703)
317	0.2567 (0.0602)	0.4801 (0.0703)
430	0.1003 (0.0339)	0.4214 (0.0569)
529	0.0325 (0.0194)	0.3818 (0.0506)
586	0.009 (0.01)	0.3033 (0.0451)
747	0 (0)	0.0519 (0.0196)
821	0 (0)	0.012 (0.0092)
986	0 (0)	0.0057 (0.0065)

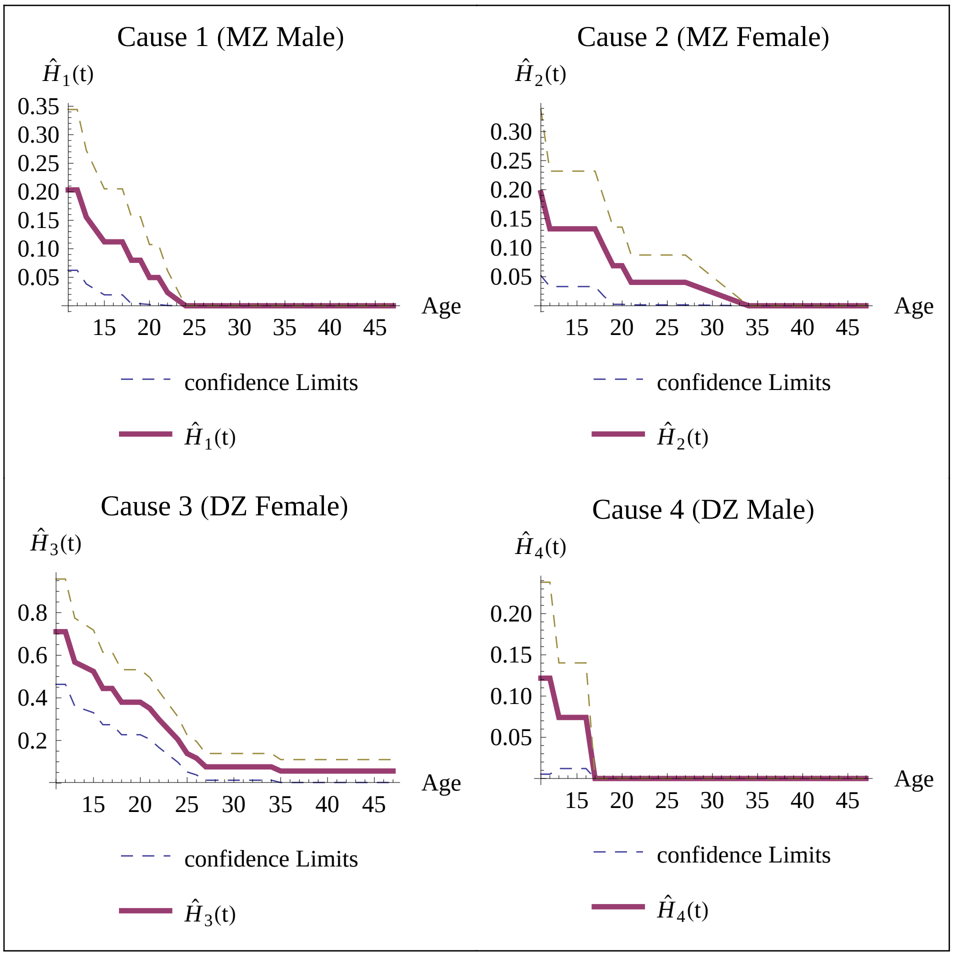

Figure 2 – Plot of estimate of $H_j(t)$; $j = 1, 2, 3, 4$ for Australian twin data

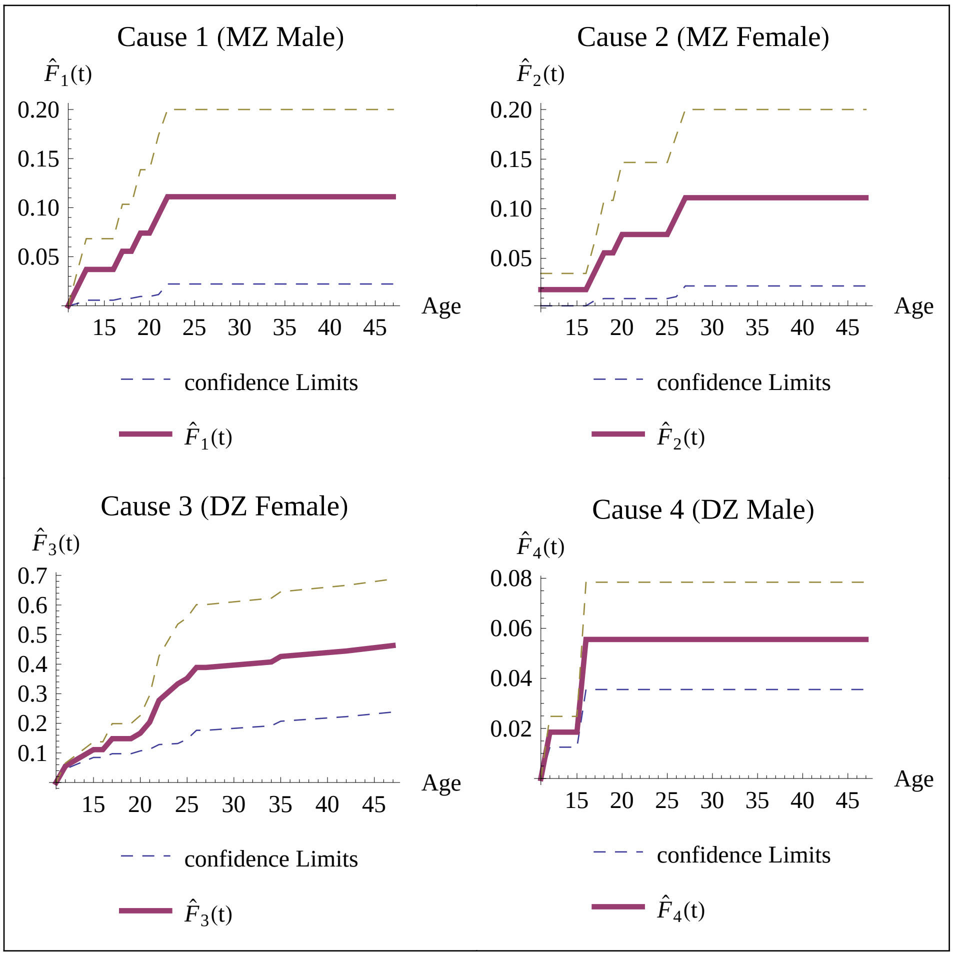

Figure 3 – Plot of estimate of $F_j(t)$; $j = 1, 2, 3, 4$ for Australian twin data

TABLE 6
Australian twin data

Age at onset(T)	Censoring(δ)	Cause(J)	Age at onset (T)	Censoring(δ)	Cause(J)
24	1	3	25	1	3
34	1	3	22	1	3
26	1	2	12	1	4
21	1	1	13	1	3
11	0	3	16	1	4
21	1	3	11	0	4
11	0	1	12	1	1
12	1	3	13	1	1
11	0	3	11	0	1
18	1	2	20	1	2
11	0	3	11	0	2
11	0	3	17	1	2
11	0	4	11	0	3
16	1	4	15	1	3
26	1	3	11	0	3
17	1	3	21	1	3
19	1	1	17	1	3
22	1	3	11	0	4
15	1	3	17	1	1
27	1	2	20	1	3
11	1	2	11	0	3
11	0	2	12	1	3
42	1	3	24	1	3
22	1	3	47	1	3
22	1	1	22	1	3
12	1	3	26	1	3
11	0	1	35	1	3

7. Conclusion

In the present paper, we have introduced a new procedure using cause specific reversed hazard rates for modeling and analysis of left censored lifetime data with multiple causes. We proposed a non parametric estimator for the cumulative cause specific reversed hazard rates. The asymptotic properties of the estimators has been established using counting process method. Simulation studies establishes that the proposed procedure is efficient. The proposed method was applied to two real life data sets. Nonparametric tests for equality of cause specific hazard rates will be useful for comparing several risks. The work in this direction will be reported elsewhere.

ACKNOWLEDGEMENTS

We thank the editor and referee for their valuable comments and suggestions. The second author would like to thank Department of Science and Technology, Government of India for providing financial support for this work under INSPIRE fellowship.

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SUMMARY

Modeling lifetime data with multiple causes using cause specific reversed hazard rates

In this paper we introduce and study cause specific reversed hazard rates in the context of left censored lifetime data with multiple causes. Nonparametric inference procedure for left censored lifetime data with multiple causes using cause specific reversed hazard rate is discussed. Asymptotic properties of the estimators are studied. Simulation studies are conducted to assess the efficiency of the estimators. Further, the proposed method is applied to mice mortality data (Hoel (1972)) and Australian twin data (Duffy *et al.* (1990)).

Keywords: Cause specific reversed hazard rates; Cumulative incidence function; Nonparametric estimation