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Multiprocess Discount Survival Models with Survival Times

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ABSTRACT

For the analysis of survival data including covariates whose effects vary in time, the multiprocess discount survival model is proposed. The parameter vector modeling the time-varying effects of covariates is to vary between time intervals and its evolution between time intervals depends on the perturbation of the next time interval. The recursive estimation of the parameter vector can be obtained at the end of each time interval. The retrospective estimation of the survival function and the forecasting of the survival function of individuals of the specific covariates also can be obtained based on the information gathered until the end of the time interval.

Key Words : Multiprocess dynamic generalized linear model; Discount Bayesian model; Survival data; Proportional hazards model; Covariate; Recursive estimation.

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1. INTRODUCTION

Bolstad(1988) developed the multiprocess dynamic generalized linear model by incorporating the multiprocess dynamic model(Harrison and Stevens,1976) into the dynamic generalized linear model(West et al.,1985). Ameen and Harrison(1985) developed the normal discount Bayesian model to overcome some practical disadvantages of dynamic linear model, where the discount factor d_i ($0 < d_i < 1$) is introduced for an increase of $100(1\text{-}d_i)/d_i$ percent in the variance of the time interval I_i. Cox(1972) proposed the proportional hazards model for the analysis of survival data by introducing time-fixed parameters modeling effects of covariates into the hazard rate under the assumption that covariates have fixed effects on the survival pattern. Gamerman(1991) proposed the dynamic Bayesian model for the analysis of survival data with a hazard rate which is a function of time-varying parameters. It is assumed that the time-variation of the parameter vector is determined through the additive evolution of parameter vector between time intervals.

The multiprocess discount survival model is proposed by incorporating the proportional hazards model into the multiprocess dynamic generalized linear model. The parameter vector modeling time-varying effects of the covariates evolves through the division of the variance of each element by a discount factor of the current time interval, which depends on the perturbation of the current time interval. This model is used for the estimation and forecasting even with the censored and tied survival data. Further it provides quick response to sudden changes of the time-varying parameter vector, which leads to a faithful representation of survival data via the retrospective estimation and forecasting of survival functions.

The multiprocess discount survival model is described in Section 2. The procedure of recursive estimation of the parameter vector under the multiprocess discount model is provided in Section 3. Also the procedure of retrospective estimations of the survival function and the procedure of forecastings of survival functions are provided in Section 4 and Section 5, respectively. The performance of the proposed model is illustrated via the gastric carcinoma data in Section 6.

2. MODEL DESCRIPTIONS

The survival time is assumed to follow a piecewise exponential distribution which has a constant hazard rate in each time interval,

$$\lambda(t) = \lambda_i \text{ for } t \in I_i = (\tau_{i-1}, \tau_i],$$

where τ_0 is usually set to 0 and $I_s = (\tau_{s-1}, \infty)$. The survival function and the probability function for the current time interval I_i given survival up to the end of previous time interval can be easily calculated due to the lack of memory property of exponential distributions. Thus we obtain the likelihood for λ_i under the assumption that the random censoring time has no relation with the survival time,

$$l(\lambda_i|t) = \lambda_i^\delta \exp(-\lambda_i(t - \tau_{i-1})) \quad \text{for } t \in I_i$$

where δ is the indicator function of a death of the individual in time interval I_i. We denote the hazard rate for the *j-th* individual alive at the beginning of time interval I_i by $\lambda_{i(j)}$, $j = 1, \cdots, n_i$, where n_i is the number of individuals used to be alive at the beginning of time interval I_i. n_i hazard rates $\lambda_{i(j)}$'s can be classified into p different hazard rates which have constant means in each time interval I_i, where p is the number of covariate vectors. Let T_{ij} be the survival time of the *j-th* individual alive at the beginning of time interval I_i. Also let t_{ij} be an observed failure time corresponding to T_{ij}, which can be interpreted as the minimum of survival time of the *j-th* individual and the corresponding censoring time. We define the information of the survival time of the *j-th* individual alive at the beginning of time interval I_i, which is obtained at time t_{ij}, consists of 3 possible events; i) the *j-th* individual dies at t_{ij} ii) the *j-th* individual is censored at t_{ij} iii) the *j-th* individual is alive at $t_{ij} = \tau_i$ so that $T_{ij} > \tau_i$. No further information on the survival time of the *j-th* individual is not provided in first two cases. Let D_i be a set of information from all observations of each time interval, $I_1, \cdots, I_i$, and let $D_{i-1(j)}$ be a set containing D_{i-1} and information from first j observations of time interval I_i so that $D_{i-1(0)} = D_{i-1}$ and $D_{i-1(n_i)} = D_i$.

We assume a model selection probability of time interval I_i, $\pi_i^{(\cdot)}$, which depends on the perturbation of the time interval I_i, is fixed prior to obtaining information from observation in the time interval I_i. Let α_i be the perturbation index variable of parameters in the time interval I_i then

$$\pi_i^{(k)} = P(\alpha_i = k|D_l) \quad \text{for } k = 1, \cdots, K, \quad l = 0, \cdots, i-1.$$

When the perturbation of the time interval I_i is specified by its index value, the evolution of parameter vector is determined by multiplying the variance-covariance vector by a diagonal matrix $B_i^{(l)}$, whose diagonal element $1/\sqrt{d_i^{(l)}}$ depends on the perturbation index value l for $l = 1, \cdots, K$, where $d_i^{(l)}$ is a discount factor of a perturbation index value l of the time interval I_i.

Then the multiprocess discount survival model in the time interval I_i is defined by, for $j = 1, \cdots, n_i, i = 1, \cdots, s$,

i) observation equation; $T_{ij} \sim exp(\lambda_{i(j)})$

ii) guide relationship; $\lambda_{i(j)} = \exp(Z'_{ij}\beta_i)$

iii) evolution equation; $E(\beta_i|\alpha_{i-1} = k, \alpha_i = l, D_{i-1}) = E(\beta_{i-1}|\alpha_{i-1} = k, D_{i-1})$,

$$V(\beta_i|\alpha_{i-1} = k, \alpha_i = l, D_{i-1}) = B_i^{(l)} V(\beta_i|\alpha_{i-1} = k, D_{i-1}) B_i^{(l)}$$

The parametric evolution of the parameter vector β occurs via the evolution equation when passing from one time interval to next time interval.

3. RECURSIVE ESTIMATION OF A PARAMETER VECTOR

The initial distribution of β_0 is specified by mean vector $\widehat{\beta}_0$ and variance-covariance matrix V_0, where $\widehat{\beta}_0$ and V_0 are given prior to time interval I_1.

At the beginning of each time interval I_i, K prior distributions of β_i given D_{i-1} is obtained from each of K posterior distribution of β_{i-1} given D_{i-1} via the evolution equation as

$$(\beta_i|\alpha_{i-1} = k, \alpha_i = l, D_{i-1}) \sim [a_i^{(kl)}, R_i^{(kl)}],$$

where

$$a_i^{(kl)} = \widehat{\beta}_{i-1}^{(k)}, \; R_i^{(kl)} = B_i^{(l)} V_{i-1}^{(k)} B_i^{(l)}.$$

With information from first (j-1) observations, the joint prior distribution of β_i and $\log\lambda_{i(j)}$ is obtained by the guide relationship,

$$\left(\begin{array}{c} \beta_i \\ \log\lambda_{i(j)} \end{array} \;\middle|\; \alpha_{i-1} = k, \alpha_i = l, D_{i-1(j-1)} \right) \sim \left[\left(\begin{array}{c} a_{ij}^{(kl)} \\ f_{ij}^{(kl)} \end{array} \right), \left(\begin{array}{cc} R_{ij}^{(kl)} & S_{ij}^{(kl)} \\ S_{ij}^{(kl)'} & q_{ij}^{(kl)} \end{array} \right) \right],$$

where

$$f_{ij}^{(kl)} = Z'_{ij} a_{ij}^{(kl)}, \quad S_{ij}^{(kl)} = R_{ij}^{(kl)} Z_{ij} \quad \text{and} \quad q_{ij}^{(kl)} = Z'_{ij} S_{ij}^{(kl)},$$

with $a_{i1}^{(kl)} = a_i^{(kl)}$ and $R_{i1}^{(kl)} = R_i^{(kl)}$. Here the prior distribution of $\lambda_{i(j)}$ is assumed to be a conjugate gamma distribution $(b_{ij}^{(kl)}, r_{ij}^{(kl)})$, where $b_{ij}^{(kl)}$ and $r_{ij}^{(kl)}$ are estimated in terms of the mean and the variance of the distribution of $\log\lambda_{i(j)}$, such as, respectively, $q_{ij}^{(kl)^{-1}}$ and $q_{ij}^{(kl)^{-1}} \exp(-f_{ij}^{(kl)})$.

With information from the j-th observation, the posterior distribution of $\lambda_{i(j)}$ is obtained as

$$(\lambda_{i(j)}|\alpha_{i-1} = k, \alpha_i = l, D_{i-1(j)}) \sim Ga(b_{ij} + \delta_{ij}, r_{ij} + t_{ij} - \tau_{i-1}). \qquad (3.1)$$

Using (3.1) and applying the linear Bayes estimation on the joint prior distribution of β_i and $\log\lambda_{i(j)}$, the updated distribution of β_i given $D_{i-1(j)}$ is estimated as

$$(\beta_i|\alpha_{i-1}=k,\alpha_i=l,D_{i-1(j)})\sim[\widehat{\beta}^{(kl)}_{ij},V^{(kl)}_{ij}],$$

where

$$\begin{aligned}\widehat{\beta}^{(kl)}_{ij} &= a^{(kl)}_{ij}+S^{(kl)}_{ij}q^{(kl)^{-1}}_{ij}\log(\frac{1+q^{(kl)}_{ij}\delta_{ij}}{1+q^{(kl)}_{ij}(t_{ij}-\tau_{i-1})\exp(f^{(kl)}_{ij})}),\\ V^{(kl)}_{ij} &= R^{(kl)}_{ij}-S^{(kl)}_{ij}S^{(kl)'}_{ij}(\frac{\delta_{ij}}{1+q^{(kl)}_{ij}}).\end{aligned}$$

Since there is no parametric evolution within each time interval, the joint prior distribution of β_i and $\log\lambda_{i(j+1)}$ is given as

$$\left(\begin{array}{c}\beta_i\\ \log\lambda_{i(j+1)}\end{array}\Big|\,\alpha_{i-1}=k,\alpha_i=l,D_{i-1(j)}\right)\sim\left[\left(\begin{array}{c}a^{(kl)}_{i,j+1}\\ f^{(kl)}_{i,j+1}\end{array}\right),\left(\begin{array}{cc}R^{(kl)}_{i,j+1} & S^{(kl)}_{i,j+1}\\ S^{(kl)'}_{i,j+1} & q^{(kl)}_{i,j+1}\end{array}\right)\right]$$

where

$$\begin{aligned}a^{(kl)}_{i,j+1} &= \widehat{\beta}^{(kl)}_{ij},\ f^{(kl)}_{i,j+1}=Z'_{i,j+1}a^{(kl)}_{i,j+1}\\ R^{(kl)}_{i,j+1} &= V^{(kl)}_{ij},\ S^{(kl)}_{i,j+1}=R^{(kl)}_{i,j+1}Z_{i,j+1}\\ q^{(kl)}_{i,j+1} &= Z'_{i,j+1}S^{(kl)}_{i,j+1}.\end{aligned}$$

When all individuals alive at the beginning of time interval I_i are observed, K^2 posterior distributions of β_i are estimated as

$$(\beta_i|\alpha_{i-1}=k,\alpha_i=l,D_i)\sim[\widehat{\beta}^{(kl)}_i,V^{(kl)}_i],$$

where

$$D_i=D_{i-1(n_i)},\quad \widehat{\beta}^{(kl)}_i=\widehat{\beta}^{(kl)}_{i,n_i}\quad\text{and}\quad V^{(kl)}_i=V^{(kl)}_{i,n_i}.$$

Here the posterior distribution of $(\beta_i|\alpha_i=l,D_i)$ is represented as the mixture of K posterior distributions of $(\beta_i|\alpha_{i-1}=k,\alpha_i=l,D_i)$ with the posterior index probability $p^{(kl)}_i$. Using that

$$p(t_{i\cdot}|\alpha_{i-1}=k,\alpha_i=l,D_{i-1})=\prod_{j=1}^{n_i}\frac{\Gamma(\delta_{ij}+b^{(kl)}_{ij})}{\Gamma(b^{(kl)}_{ij})}\frac{(r^{(kl)}_{ij})^{b^{(kl)}_{ij}}}{(t_{ij}-\tau_{i-1}+r^{(kl)}_{ij})^{\delta_{ij}+b^{(kl)}_{ij}}}$$

the posterior index probability is obtained as

$$p_i^{(kl)} = P(\alpha_{i-1} = k, \alpha_i = l|D_i) \propto p(t_{i\cdot}|\alpha_{i-1} = k, \alpha_i = l, D_{i-1})p_{i-1}^{(k)}\pi_i^{(l)},$$

where $p_{i-1}^{(k)} = P(\alpha_{i-1} = k|D_{i-1})$. Thus the posterior distribution of β_i given $\alpha_i = l$ and D_i is estimated by mean vector $\widehat{\beta}_i^{(l)}$ and variance-covariance matrix $V_i^{(l)}$, where

$$\begin{aligned} \widehat{\beta}_i^{(l)} &= \sum_{k=1}^{K} \widehat{\beta}_i^{(kl)} p_i^{(kl)} / p_i^{(l)}, \\ V_i^{(l)} &= \sum_{k=1}^{K} [V_i^{(kl)} + (\widehat{\beta}_i^{(l)} - \widehat{\beta}_i^{(kl)})(\widehat{\beta}_i^{(l)} - \widehat{\beta}_i^{(kl)})'] p_i^{(kl)} / p_i^{(l)}. \end{aligned}$$

And the distribution of β_i given D_i is estimated by mean vector $\widehat{\beta}_i$ and variance-covariance matrix V_i , where

$$\widehat{\beta}_i = \sum_{k=1}^{K} \widehat{\beta}_i^{(l)} p_i^{(l)}, \quad V_i = \sum_{k=1}^{K} [V_i^{(l)} + (\widehat{\beta}_i - \widehat{\beta}_i^{(l)})(\widehat{\beta}_i - \widehat{\beta}_i^{(l)})'] p_i^{(l)}.$$

4. ESTIMATION OF THE SURVIVAL FUNCTION

In this section, under the assumption of the conjugate gamma distribution of the corresponding hazard rate, the estimated survival function of individuals of a covariate vector Z_h is obtained with information gathered until the end of time interval I_N. Using smoothed distribution of β_i given D_N, the distribution of the corresponding hazard rate given D_N is obtained by the guide relationship, which leads to the estimation of the survival function.

Through the evolution equation, the joint distribution of β_i and β_{i+1} given D_i is obtained as

$$\left(\begin{array}{c} \beta_i \\ \beta_{i+1} \end{array} | \, \alpha_i = k, \alpha_{i+1} = l, D_i \right) \sim \left[\left(\begin{array}{c} \widehat{\beta}_i^{(k)} \\ a_{i+1}^{(kl)} \end{array} \right), \left(\begin{array}{cc} V_i^{(k)} & V_i^{(k)} B_{i+1}^{(l)} \\ B_{i+1}^{(l)} V_i^{(k)} & R_{i+1}^{(kl)} \end{array} \right) \right],$$

Starting with $(\beta_N|\alpha_N = k, \alpha_{N+1} = l, D_N) = (\beta_N|\alpha_N = k, D_N)$ and applying the linear Bayes estimation on the joint distribution of β_i and β_{i+1}, the distribution of β_i given D_N is estimated in terms of

$$\begin{aligned} \widehat{\beta}_{i:N}^{(kl)} &= E[\beta_i|\alpha_i = k, \alpha_{i+1} = l, D_N] \\ &= \widehat{\beta}_i^{(k)} + V_i^{(k)} B_{i+1}^{(l)} R_{i+1}^{(kl)^{-1}} (\widehat{\beta}_{i+1:N}^{(kl)} - a_{i+1}^{(kl)}), \\ V_{i:N}^{(kl)} &= V[\beta_i|\alpha_i = k, \alpha_{i+1} = l, D_N] \end{aligned}$$

$$= V_i^{(k)} - V_i^{(k)} B_{i+1}^{(l)} R_{i+1}^{(kl)^{-1}} (R_{i+1}^{(kl)} - V_{i+1:N}^{(kl)}) R_{i+1}^{(kl)^{-1}} B_{i+1}^{(l)} V_i^{(k)}.$$

Thus the smoothed distribution of β_i given D_N is estimated as

$$(\beta_i | D_N) \sim [\widehat{\beta}_{i:N}, V_{i:N}], \tag{4.1}$$

where

$$\widehat{\beta}_{i:N} = \sum_{k,l}^{K} \widehat{\beta}_{i:N}^{(kl)} p_{i+1}^{(kl)}, \quad V_{i:N} = \sum_{k,l}^{K} [V_{i:N}^{(kl)} + (\widehat{\beta}_{i:N} - \widehat{\beta}_{i:N}^{(kl)})(\widehat{\beta}_{i:N} - \widehat{\beta}_{i:N}^{(kl)})'] p_{i+1}^{(kl)}.$$

Applying the guide relationship on (4.1), estimates of the defining parameters of the assumed distribution of $\lambda_{i(h)}$, $\mathrm{Ga}(b_i, r_i)$ are obtained as, respectively, $(Z_h V_{i:N} Z_h')^{-1}$ and $\exp(-Z_h \widehat{\beta}_{i:N})(Z_h V_{i:N} Z_h')^{-1}$. By integration

$$P(T_h > t | T_h > \tau_{i-1}, D_N) = (1 + \frac{t - \tau_{i-1}}{r_i})^{-b_i}.$$

Thus, at the end of time interval I_N, the survival function for individuals of the covariate vector Z_h by Bayes rule is obtained as, for $t \in I_i$,

$$P(T_h > t | D_N) = (1 + \frac{t - \tau_{i-1}}{r_i})^{-b_i} \prod_{k=1}^{i-1} (1 + \frac{\tau_k - \tau_{k-1}}{r_k})^{-b_k}$$

5. FORECASTING OF THE SURVIVAL FUNCTION

The survival function of individuals of the specific covariate vector Z_h alive at the end of time interval I_i is forecasted based on information gathered until the end of time interval I_i.

At the end of a specific time interval I_i, through which individuals of the covariate vector Z_h has been observed alive, posterior distributions of β_i which are equivalent to distributions of β_i given $T_h > \tau_i$ and D_i are estimated as

$$(\beta_i | \alpha_i = k, T_h > \tau_i, D_i) \sim [\widehat{\beta}_i^{(k)}, V_i^{(k)}].$$

By the evolution equation and the guide relationship, the joint prior distribution of β_{i+1} and $\log \lambda_{i+1(h)}$ is obtained as

$$\left(\begin{array}{c} \beta_i \\ \log \lambda_{i+1(h)} \end{array} \Big| \ \alpha_i = k, \alpha_{i+1} = l, T_h > \tau_i, D_i \right) \sim \left[\begin{pmatrix} a_{i+1}^{(kl)} \\ f_{i+1}^{(kl)} \end{pmatrix}, \begin{pmatrix} R_{i+1}^{(kl)} & S_{i+1}^{(kl)} \\ S_{i+1}^{(kl)'} & q_{i+1}^{(kl)} \end{pmatrix} \right]$$

Here the prior distribution of $\lambda_{i+1(h)}$ is assumed to be a conjugate gamma distribution $(b_{i+1}^{(kl)}, r_{i+1}^{(kl)})$, where $b_{i+1}^{(kl)}$ and $r_{i+1}^{(kl)}$ are estimated to be expressed as, respectively, $q_{i+1}^{(kl)^{-1}}$ and $q_{i+1}^{(kl)^{-1}} \exp(-f_{i+1}^{(kl)})$. For $t \in I_{i+1}$,

$$\begin{aligned}
&P(T_h > t | l, T_h > \tau_i, D_i) \\
&= \sum_{k,l=1}^{K} P(T_h > t | \alpha_i = k, \alpha_{i+1} = l, T_h > \tau_i, D_i) p_i(k) \pi_{i+1}^{(l)} \\
&= \sum_{k,l=1}^{K} (1 + \frac{t - \tau_i}{r_{i+1}^{(kl)}})^{-b_{i+1}^{(kl)}}.
\end{aligned}$$

The distribution of $\lambda_{i+1(h)}$ given $T_h > \tau_{i+1}$ and D_i is

$$(\lambda_{i+1(h)} | \alpha_i = k, \alpha_{i+1} = l, T_h > \tau_{i+1}, D_i) \sim Ga(b_{i+1}^{(kl)}, r_{i+1}^{(kl)} + \tau_{i+1} - \tau_i). \quad (5.1)$$

Using (5.1) and applying the linear Bayes estimation on the joint prior distribution of β_i and $\log \lambda_{i(h)}$, the distribution of β_{i+1} given $T_h > \tau_{i+1}$ and D_i is estimated as

$$(\beta_{i+1} | \alpha_i = k, \alpha_{i+1} = l, T_h > \tau_{i+1}, D_i) \sim [\widehat{\beta}_{i+1}^{(kl)}, V_{i+1}^{(kl)}]. \quad (5.2)$$

By collapsing on (5.2),

$$(\beta_{i+1} | \alpha_{i+1} = l, T_h > \tau_{i+1}, D_i) \sim [\widehat{\beta}_{i+1}^{(l)}, V_{i+1}^{(l)}],$$

which is used to obtain the prior distribution β_{i+2} and the forecasted survival function $P(T_h > t | T_h > \tau_{i+1}, D_i), t \in I_{i+2}$ in the time interval I_{i+2}.

Thus the survival function of individuals of the covariate vector Z_h based on $(T_h > \tau_i)$ and D_i is forecasted as, for $t \in I_{i+v}, v > 1$,

$$P(T_h > t | T_h > \tau_i, D_i) = P(T_h > t | T_h > \tau_{i+v-1}, D_i) \prod_{k=i}^{i+v-2} P(T_h > \tau_{k+1} | T_h > \tau_k, D_i)$$

6. ILLUSTRATIONS

Via the data in Table 1, which consist of survival times of 90 gastric carcinoma patients equally divided into two groups with respect to the type of treatments, the chemotherapy and the combination of chemotherapy and radiation therapy, the performances of the estimation and forecasting proposed in previous sections are illustrated.

Table 1. Survival Times in Days

Chemotherapy	1,63,105,129,182,216,250,262,301,301,342, 354,356,358,380,381c,383,383,388,394,408, 460,489,499,524,529c,535,562,675,676,748, 748,778,786,797,945c,955,968,1180c,1245, 1271,1277c,1397c,1512c,1519c
Chemotherapy and Radiation	17,42,44,48,60,72,74,95,103,108,122,144, 167,170,183,185,193,195,197,208,234,235, 254,307,315,401,445,464,484,528,542,567, 577,580,795,855,882c,892c,1031c,1033c, 1306c,1335c,1366,1452c,1472c

c: censored, source: Stablein et al.(1981)

In the model, the survival time of the the *j-th* individual alive at the beginning of time interval I_i is assumed to have the exponential distribution with a hazard rate such as $\lambda_{i(j)} = \exp(Z'_{ij}\beta_i)$ with $Z'_{ij} = (1, z_{ij})$ and $\beta_i = (\beta_{0i}, \beta_{1i})'$, where $z_{ij} = 0$ for the chemotherapy and $z_{ij} = 1$ for the combined therapy of the *j-th* individual alive at the beginning of time interval I_i. End point of each time interval is taken as the multiple of 30 days. We assume that there are two perturbations for the parameter β_{1i} in each time interval, steady state and sudden slope change, numbered by 1 and 2, respectively. The model selection probability in each time interval I_i, $i = 1, \cdots$,s, is assumed by $\pi_i^{(1)} = 0.95$, $\pi_i^{(2)} = 0.05$. We start the analysis with the initial distribution $(\beta_0 \mid D_0) \sim [0,\ 10^2 I_2]$ reflecting lack of information at time $t = 0$. The diagonal matrix $B_i^{(l)}$, $l = 1, 2$, is assumed by

$$B_i^{(1)} = \begin{pmatrix} 1 & 0 \\ 0 & \sqrt{0.75} \end{pmatrix}, \qquad B_i^{(2)} = \begin{pmatrix} 1 & 0 \\ 0 & 1/\sqrt{0.45} \end{pmatrix}$$

Figure 1 shows the time variation of the mean of the parameter β_{1i} for the difference of the combined therapy from the chemotherapy. It changes from a positive contribution to the hazard rate in the early time to a negative contribution as time elapses. The smoothed estimate of the mean generally retains the same pattern as the on-line estimate but values are more concentrated around zero.

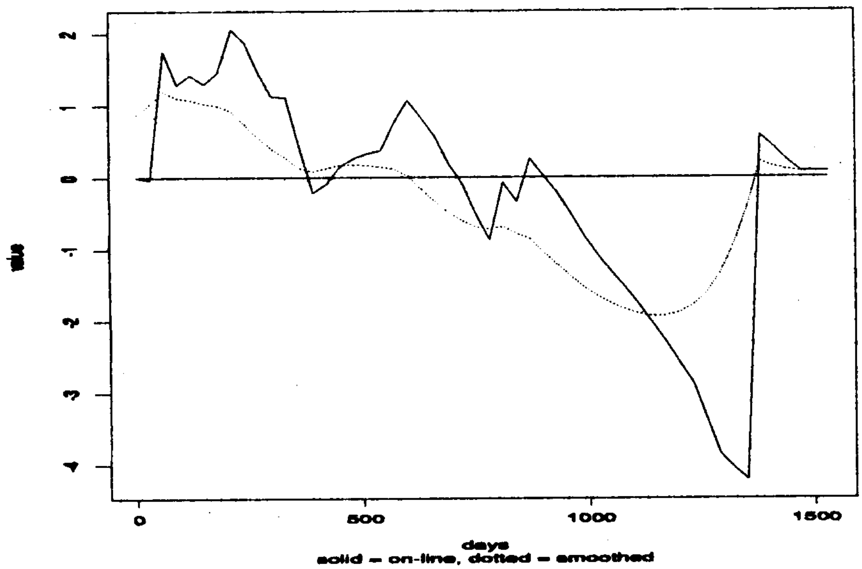

Figure 1. Estimated Mean of the Parameter of Treatment Difference

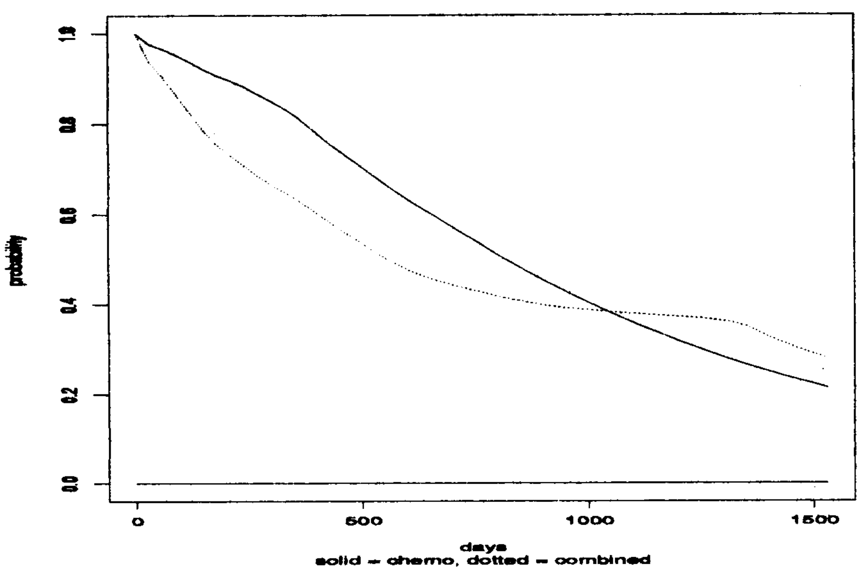

Figure 2. Estimated Survival Functions under the MDSM

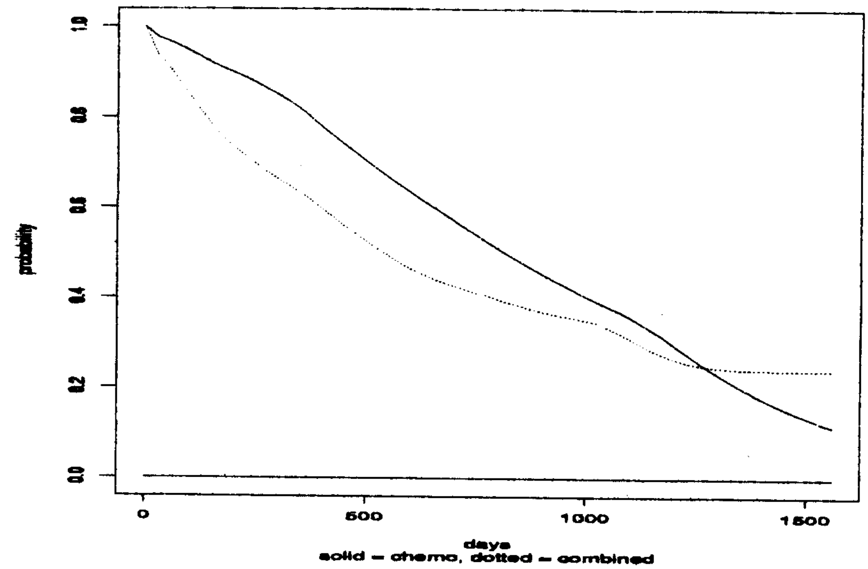

Figure 3. Forecasted Survival Functions Observed Until 990 Days

Figure 2 shows estimated survival functions of two treatment groups under the multiprocess discount survival model. At nearly 1000 days two functions intersect, which does not agrees with estimates of survival functions under the Cox model but PL-estimates(Kaplan and Meier,1958). This implies that the mortality of the combined therapy group is higher in early days, but as time elapse on it becomes lower than the chemotherapy group. Figure 3 shows the survival functions under the assumption that survival times are observed until 990 days, survival functions are estimated and forecasted based on D_{33}, $P(T_h > \tau_i | D_{33}), i = 0, 1, \cdots, 51$. It indicates that the mortality of the combined therapy group is higher until the observed time(990 days) but it is forecasted to change to lower in future time.

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