

BAYESIAN SURVIVAL ANALYSIS BASED ON THE RAYLEIGH MODEL

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SUMMARY

In this paper, the Bayesian analysis of the survival data arising from a Rayleigh model is carried out under the assumption that the clinical study based on n patients is terminated at the d^{th} death, for some preassigned $d(0 < d \leq n)$, resulting in the survival times $t_1 \leq t_2 \leq \dots \leq t_d$, and $(n - d)$ survivors. For the prior knowledge about the Rayleigh parameter, the gamma density, the inverted gamma density, and the beta density of the second kind are respectively assumed, and for each of these prior densities, the Bayes estimators of the mean survival time, the hazard function, and the survival function are obtained by assuming the usual squared error loss function. Finally, the analysis is extended to situations wherein the exact survival time is not available for any patient but only the deaths in given time intervals are recorded. The computations are illustrated by a numerical example.

Key words: Bayesian posterior density; Closure property of the natural conjugate prior; Confluent hypergeometric function; Hazard function; Mean survival time; Modified Bessel function; Rayleigh survival model; Squared error loss function; Survival function; Total squared survival time.

1. INTRODUCTION

It has been observed in some clinical studies dealing with cancer patients that the survival pattern follows the Rayleigh or the so-called linear hazard rate survival distribution (cf. Gross and Clark, 1975; Lee, 1980), for which the survival time X is specified by the *pdf*

$$f(x | \mathcal{G}) = 2\mathcal{G}xe^{-\mathcal{G}x^2} \quad (0 \leq x < \infty; \mathcal{G} > 0). \quad (1.1)$$

Corresponding to this death density function (DDF), the mean survival time (MST), the hazard function (HF), and the survival function (SF) are respectively given by

$$\mu = 2^{-1}\pi^{1/2}\mathcal{G}^{-1/2}, \quad (1.2)$$

$$h = h(t | \mathcal{G}) = 2\mathcal{G}t, \quad (1.3)$$

and

$$S = S(t | \mathcal{G}) = e^{-\mathcal{G}t^2} \quad (t > 0). \quad (1.4)$$

The object of the present paper is to obtain the Bayesian estimators of μ , h , and S on the basis of the survival data recorded on n patients, each with the DDF (1.1). Suppose these patients are followed-up in a clinical study till d deaths occur, for some preassigned d ($0 < d \leq n$). The survival times recorded for the d deaths are denoted by $t_1 \leq t_2 \leq \dots \leq t_d$. Naturally the $(n - d)$ surviving patients are lost to follow-up and the observations are censored at time t_d . This is sometimes done on account of high cost required for follow-up, or else, in order to avoid the inordinate delay (in taking decisions) that may be inevitable if one has to wait till all the patients included in the study die. It is also assumed here that there is available some prior knowledge about the parameter \mathcal{G} of the Rayleigh model based on our past experience with similar survival data, and that this prior knowledge can be mathematically translated into a suitable prior density $g(\mathcal{G})$ defined on the parameter space of \mathcal{G} . The Bayes estimators $\hat{\mu}$, \hat{h} , and \hat{S} are then worked out under the assumption of the squared error loss function and the prior densities g_i , $i = 1, 2, 3$ respectively, specified under the following three cases:

Case I. Beta prior density of the second kind:

$$g_1(\mathcal{G}) = \frac{b^{-p} \mathcal{G}^{p-1}}{B(p, q) [1 + b^{-1}\mathcal{G}]^{p+q}} \quad (0 < \mathcal{G} < \infty; b, p, q > 0). \quad (1.5)$$

Case II. Inverted gamma prior density:

$$g_2(\vartheta) = \frac{a^{v-1}}{\Gamma(v-1)} \vartheta^{-v} e^{-a/\vartheta} \quad (0 < \vartheta < \infty; a > 0, v > 1). \quad (1.6)$$

Case III. Gamma prior density:

$$g_3(\vartheta) = \frac{\tau^\lambda}{\Gamma(\lambda)} \vartheta^{\lambda-1} e^{-\tau\vartheta} \quad (0 < \vartheta < \infty; \tau, \lambda > 0). \quad (1.7)$$

Finally, the situation when only the deaths are recorded and the survival times are not available, is discussed and the Bayes estimators of the SF corresponding to the prior densities $g_i (i = 1, 2, 3)$ are derived. The computations are illustrated by a numerical example.

2. PRELIMINARIES

On the basis of the survival times $t_1 \leq t_2 \leq \dots \leq t_d$, and the $(n - d)$ survivors, the joint *pdf* can be written as

$$f(t_1, t_2, \dots, t_d | \vartheta) = \frac{n!}{(n-d)!} \left[\prod_{i=1}^d f(t_i | \vartheta) \right] [S(t_d | \vartheta)]^{n-d} \quad (0 \leq t_1 \leq \dots \leq t_d < \infty). \quad (2.1)$$

Let us define the statistic

$$T_d^* = \left[\sum_{i=1}^d t_i^2 \right] + (n-d)t_d^2, \quad (2.2)$$

which can be referred to as the total squared survival time (TSST) in the clinical study. Then, it follows from (1.1), (1.4) and (2.1) that the kernel of the likelihood function (LF) for the observed survival data is given by

$$l(\vartheta) \propto \vartheta^d e^{-\vartheta T_d^*} \quad (0 < \vartheta < \infty). \quad (2.3)$$

This LF will be used repeatedly in the subsequent sections as also the following two integral representations for the confluent hypergeometric function $\psi(., .; .)$ introduced by Tricomi (cf. Erdélyi, 1953a, Ch. VI) and the modified Bessel function of the third kind $K_x(.)$ (cf. Erdélyi, 1953b,

Ch. VII) respectively. The first formula (cf. Erdélyi, 1953a, p. 255, formula 2) is given by

$$\int_0^\infty y^{A-1}(1+y)^{B-A-1}e^{-Zy} dy = \Gamma(A)\psi(A, B; Z) \quad (\text{Re } A > 0), \quad (2.4)$$

and the second formula (cf. Gradshteyn and Ryzhik, 1965, p. 340, fórmula 9) is given by

$$\int_0^\infty y^{\alpha-1}e^{-\frac{\beta}{y}-\gamma y} dy = 2\left(\frac{\beta}{\gamma}\right)^{\frac{\alpha}{2}}K_\alpha(2\sqrt{\beta\gamma})(\text{Re } \beta, \text{Re } \gamma > 0). \quad (2.5)$$

It may be mentioned here that the special functions $K_\alpha(\cdot)$ and $\psi(\cdot, \cdot; \cdot)$ are tabulated in Abramowitz and Stegun (1972). Thus, the desired numerical computations are possible with the help of the results obtained in this paper. We shall also need the formula

$$K_{-\alpha}(Z) = K_\alpha(Z) \quad (2.6)$$

in the sequel.

3. BAYESIAN ESTIMATION FOR THE CASE I

The LF (2.3) is combined with the prior density (1.5), via Bayes theorem, to obtain the posterior density function

$$g_1^*(g) = C_1^{-1} \frac{g^{p+d-1}e^{-gT_d^*}}{[1+b^{-1}g]^{p+q}} \quad (0 < g < \infty), \quad (3.1)$$

where C_1 is a normalization constant, which can be evaluated by using (2.4). We obtain

$$C_1 = b^{p+d}\Gamma(p+d)\psi(p+d, d-q+1; bT_d^*). \quad (3.2)$$

Hence, under the assumption of the squared error loss function, the Bayes estimator of the MST is obtained as

$$\begin{aligned} \hat{\mu} &= 2^{-1} \int_0^\infty \pi^{1/2} g^{-1/2} g_1^*(g) dg \\ &= \frac{\sqrt{\pi} \Gamma(p+d-1/2) \psi(p+d-1/2, d-q+1/2; bT_d^*)}{2 b^{1/2} \Gamma(p+d) \psi(p+d, d-q+1; bT_d^*)}, \end{aligned} \quad (3.3)$$

by using (2.4), (3.1) and (3.2). In a similar manner, the variance of the posterior distribution of μ is computed as

$$V_1 = \frac{\pi}{4b(p+d-1)} \frac{\psi(p+d-1, d-q; bT_d^*)}{\psi(p+d, d-q+1; bT_d^*)} - (\hat{\mu})^2. \quad (3.4)$$

Now the Bayes estimator of the HF, under the assumption of the squared error loss function, is given by

$$\begin{aligned} \hat{h} &= 2t \int_0^\infty \vartheta g_1^*(\vartheta) d\vartheta \\ &= 2t b(p+d) \frac{\psi(p+d+1, d-q+2; bT_d^*)}{\psi(p+d, d-q+1; bT_d^*)}, \end{aligned} \quad (3.5)$$

by using (2.4), (3.1) and (3.2). Similarly, the variance of the posterior distribution of h is obtained as

$$V_1' = 4t^2 b^2 (p+d)(p+d-1) \frac{\psi(p+d+2, d-q+3; bT_d^*)}{\psi(p+d, d-q+1; bT_d^*)} - (\hat{h})^2. \quad (3.6)$$

The Bayes estimator of the SF is computed as

$$\begin{aligned} \hat{S} &= \int_0^\infty e^{-\vartheta t^2} g_1^*(\vartheta) d\vartheta \\ &= \frac{\psi(p+d, d-q+1; b[t^2 + T_d^*])}{\psi(p+d, d-q+1; bT_d^*)}. \end{aligned} \quad (3.7)$$

The variance of the posterior distribution of the SF is given by

$$V_1^* = \frac{\psi(p+d, d-q+1; b[2t^2 + T_d^*])}{\psi(p+d, d-q+1; bT_d^*)} - (\hat{S})^2. \quad (3.8)$$

4. BAYESIAN ESTIMATION FOR THE CASE II

The LF (2.3) is combined with the prior density (1.6) to obtain the Bayesian posterior density

$$g_2^*(\vartheta) = C_2^{-1} \vartheta^{d-\nu} e^{-\vartheta T_d^* - a/\vartheta} \quad (0 < \vartheta < \infty), \quad (4.1)$$

where C_2 is a normalization constant, which can be evaluated by using (2.5). We obtain

$$C_2 = 2(a/T_d^*)^{(d-\nu+1)/2} \cdot K_{d-\nu+1}(2\sqrt{aT_d^*}). \quad (4.2)$$

Hence, the Bayes estimator of the MST is given by

$$\begin{aligned} \hat{\mu} &= 2^{-1}\pi^{1/2} \int_0^\infty \vartheta^{-1/2} g_2^*(\vartheta) d\vartheta \\ &= \frac{\pi^{1/2}}{2} \left(\frac{T_d^*}{a}\right)^{1/4} \frac{K_{d-\nu+1/2}(2\sqrt{aT_d^*})}{K_{d-\nu+1}(2\sqrt{aT_d^*})}, \end{aligned} \quad (4.3)$$

by using (2.5), (4.1) and (4.2). In a similar manner, the variance of the posterior distribution of μ is computed as

$$V_2 = (\pi/4)[T_d^*/a]^{1/2} \frac{K_{d-\nu}(2\sqrt{aT_d^*})}{K_{d-\nu+1}(2\sqrt{aT_d^*})} - (\hat{\mu})^2. \quad (4.4)$$

In the same way, the Bayes estimator of the HF and its posterior variance are respectively given by

$$\hat{h} = 2t(a/T_d^*)^{1/2} \frac{K_{d-\nu+2}(2\sqrt{aT_d^*})}{K_{d-\nu+1}(2\sqrt{aT_d^*})}. \quad (4.5)$$

and

$$V'_2 = 4t^2(a/T_d^*) \frac{K_{d-\nu+3}(2\sqrt{aT_d^*})}{K_{d-\nu+1}(2\sqrt{aT_d^*})} - (\hat{h})^2. \quad (4.6)$$

The Bayes estimator of the SF and its posterior variance are respectively given by

$$\hat{S} = \left(\frac{T_d^*}{T_d^* + t^2}\right)^{(d-\nu+1)/2} \frac{K_{d-\nu+1}(2\sqrt{a[t^2 + T_d^*]})}{K_{d-\nu+1}(2\sqrt{aT_d^*})}, \quad (4.7)$$

and

$$V_2^* = \left(\frac{d}{T_d^* + 2t^2}\right)^{(d-\nu+1)/2} \frac{K_{d-\nu+1}(2\sqrt{a[2t^2 + T_d^*]})}{K_{d-\nu+1}(2\sqrt{aT_d^*})} - (\hat{S})^2. \quad (4.8)$$

5. BAYESIAN ESTIMATION FOR THE CASE III

The LF (2.3) is combined with the prior density (1.7) to obtain the Bayesian posterior density

$$g_3^*(g) = \frac{(\tau + T_d^*)^{d+\lambda}}{\Gamma(d + \lambda)} \cdot g^{d+\lambda-1} e^{-g[\tau + T_d^*]} \quad (0 < g < \infty). \quad (5.1)$$

In this case the, the prior (1.7) and the posterior (5.1) belong to the same family, that is, the so-called ‘closure property’ is satisfied, and this was to be expected because the gamma prior considered here is a natural conjugate (cf. Raiffa and Schlaifer, 1961) for the Rayleigh density (1.1). Hence, the derivations are quite straightforward in this case, and therefore, the results are merely recorded. The Bayes estimators of the MST, the HF and the SF are respectively given by

$$\hat{\mu} = \frac{\pi^{1/2} \Gamma(d + \lambda - 1/2)}{2\Gamma(d + \lambda)} (\tau + T_d^*)^{1/2}, \quad (5.2)$$

$$\hat{h} = \frac{2(d + \lambda)t}{(\tau + T_d^*)}, \quad (5.3)$$

and

$$\hat{S} = \left[1 + \frac{t^2}{(\tau + T_d^*)} \right]^{-(d+\lambda)}. \quad (5.4)$$

The posterior variance of μ , h , and S are respectively given by

$$V_3 = \frac{\pi(\tau + T_d^*)}{4(d + \lambda - 1)} - (\hat{\mu})^2, \quad (5.5)$$

$$V'_3 = \frac{4(d + \lambda)(d + \lambda + 1)t^2}{(\tau + T_d^*)^2} - (\hat{h})^2, \quad (5.6)$$

and

$$V_3^* = \left[1 + \frac{2t^2}{(\tau + T_d^*)} \right]^{-(d+\lambda)} - (\hat{S})^2. \quad (5.7)$$

6. BAYESIAN ESTIMATION OF THE SF BASED ON DEATH RECORDS

In some clinical studies, the situation may be somewhat different in so far as the experimenter decides to terminate the experiment after a preassigned period of time, say $T(>0)$, rather than at the time of the d^{th} death. Here the number of survivors $s(0 \leq s \leq n)$ out of n patients included in the study is recorded after the expiry of the period T , and the exact survival times for the $(n - s)$ deaths also are not available. Thus, only the triple (n, s, T) is recorded. We shall discuss a somewhat more general situation wherein the record of k such triples (n_i, s_i, T_i) are available for $i = 1, 2, \dots, k$. Clearly $0 \leq s_i \leq n_i$ ($i = 1, 2, \dots, k$). The LF corresponding to this sample data is given by

$$l^*(\vartheta) = \left[\prod_{i=1}^k \binom{n_i}{s_i} \right] e^{-\sum_{i=1}^k s_i T_i^2} \left[\prod_{i=1}^k (1 - e^{-\vartheta T_i^2})^{n_i - s_i} \right] \quad (0 < \vartheta < \infty). \quad (6.1)$$

This LF is combined with the prior density (1.5) in Case I, to obtain the Bayesian posterior density

$$g_1^{**}(\vartheta) = B_1^{-1} \frac{\vartheta^{p-1} e^{-\vartheta \sum_{i=1}^k s_i T_i^2}}{[1 + b^{-1} \vartheta]^{p+q}} \left[\prod_{i=1}^k (1 - e^{-\vartheta T_i^2})^{n_i - s_i} \right] \quad (0 < \vartheta < \infty), \quad (6.2)$$

where the normalization constant B_1 is given by

$$\begin{aligned} B_1 &= \int_0^\infty \frac{\vartheta^{p-1} e^{-\vartheta \sum_{i=1}^k s_i T_i^2}}{[1 + b^{-1} \vartheta]^{p+q}} \left[\prod_{i=1}^k (1 - e^{-\vartheta T_i^2})^{n_i - s_i} \right] d\vartheta \\ &= b^p \Sigma' \left(\prod_{i=1}^k D_i \right) (-1)^{N-R - \sum_{i=1}^k j_i} \int_0^\infty \frac{y^{p-1} e^{-y \left[\sum_{i=1}^k b(n_i - j_i) T_i^2 \right]}}{(1 + y)^{p+q}} dy, \end{aligned} \quad (6.3)$$

which has been written by using the binomial series expansion for $(1 - e^{-\vartheta T_i^2})^{n_i - s_i}$ ($i = 1, 2, \dots, k$), and the following notations:

$$\left. \begin{aligned} D_1 &= \binom{n_i - s_i}{j_i} \quad (i = 1, 2, \dots, k), \\ \Sigma &= \sum_{j_1=0}^{n_1-s_1} \sum_{j_2=0}^{n_2-s_2} \cdots \sum_{j_k=0}^{n_k-s_k}, \\ N &= \sum_{i=1}^k n_i, \quad R = \sum_{i=1}^k s_i. \end{aligned} \right] \quad (6.4)$$

Now by using (2.4), B_1 is obtained from (6.3) as given below:

$$B_1 = b^p \Gamma(p) \Sigma' \left[\prod_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} \psi(p, 1-q; b \sum_{i=1}^k (n_i - j_i) T_i^2) \quad (6.5)$$

The Bayesian estimator of the SF, under the assumption of the squared error loss function, is given by

$$\hat{S} = \int_0^\infty e^{-\theta t^2} g_1^{**}(\mathcal{G}) \, d\mathcal{G}. \quad (6.6)$$

This integral is computed by using the same procedure as in the evaluation of B_1 . The final result is given below:

$$\hat{S} = \frac{\Sigma' \left[\sum_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} \psi \left(p, 1-q; b \left[t^2 + \sum_{i=1}^k (n_i - j_i) T_i^2 \right] \right)}{\Sigma' \left[\sum_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} \psi \left(p, 1-q; b_i \sum_{i=1}^k (n_i - j_i) T_i^2 \right)}. \quad (6.7)$$

Similarly, for case II, the LF (6.1) is combined with the prior density (1.6) to obtain the Bayesian posterior density

$$g_2^{**}(\mathcal{G}) = B_2^{-1} \mathcal{G}^{-\nu} e^{-a/\mathcal{G} - \mathcal{G} \sum_{i=1}^k s_i T_i^2} \left[\sum_{i=1}^k (1 - e^{-\mathcal{G} T_i^2})^{n_i - s_i} \right] \quad (0 < \mathcal{G} < \infty), \quad (6.8)$$

where the normalization constant B_2 is obtained in the same manner as above. Thus,

$$B_2 = \Sigma' \left[\prod_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} \int_0^\infty \mathcal{G}^{-\nu} e^{-\frac{a}{\mathcal{G}} - \mathcal{G} \left[\sum_{i=1}^k (n_i - j_i) T_i^2 \right]} d\mathcal{G}$$

$$\begin{aligned}
 &= \Sigma' \left[\prod_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} 2 \left(\frac{a}{\sum_{i=1}^k (n_i - j_i) T_i^2} \right)^{-(v-1)/2} \times \\
 &\times K_{v-1} \left(2 \sqrt{a \sum_{i=1}^k (n_i - j_i) T_i^2} \right), \tag{6.9}
 \end{aligned}$$

by using (2.5) and (2.6). Hence, the final result for the Bayes estimator of the SF is obtained as

$$\begin{aligned}
 \hat{S} = & \frac{\Sigma' \left[\prod_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} \left(t^2 + \sum_{i=1}^k (n_i - j_i) T_i^2 \right)^{v-1} K_{v-1} \left(2 \sqrt{a \left[t^2 + \sum_{i=1}^k (n_i - j_i) T_i^2 \right]} \right)}{\Sigma' \left[\prod_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} \left(\sum_{i=1}^k (n_i - j_i) T_i^2 \right)^{v-1} K_{v-1} \left(2 \sqrt{a \sum_{i=1}^k (n_i - j_i) T_i^2} \right)} \tag{6.10}
 \end{aligned}$$

Finally, for case III, the Bayes estimator of the SF is recorded below:

$$\begin{aligned}
 \hat{S} = & \frac{\Sigma' \left[\prod_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} \left(\tau + t^2 + \sum_{i=1}^k (n_i - j_i) T_i^2 \right)^{-\lambda}}{\Sigma' \left[\prod_{i=1}^k D_i \right] (-1)^{N-R-\sum_{i=1}^k j_i} \left(\tau + \sum_{i=1}^k (n_i - j_i) T_i^2 \right)^{-\lambda}} \tag{6.11}
 \end{aligned}$$

7. NUMERICAL ILLUSTRATION

In an experiment, suppose there are 15 cancer patients for whom the survival times follow the Rayleigh survival distribution specified by the *pdf* (1.1). Suppose further that these patients are followed-up till $d = 10$ deaths occur. The survival times are recorded and the total squared survival time T_d^* defined at (2.2) is observed as 28.7495. Under the assumption of the squared error loss function and the beta prior, inverted gamma prior and the gamma prior respectively for ϑ , the respective posterior densities, the posterior expectation, of ϑ and the mean survival times are computed numerically and graphics are presented. The details are explained in the following three cases:

Case I: Beta prior density of the second kind:

The beta density given at (1.5) with parameters $p = 4$, $q = 1.15$ and $b = 0.01$ is assumed. Using expressions (3.1) and (3.2) and formula 13.5.6 (Abramowitz and Stegun, 1972), the posterior density of ϑ is obtained as

$$g_1^*(\vartheta) = 5.5246 \times 10^{18} \cdot \vartheta^{13} \cdot (1 + 100\vartheta)^{-5.15} e^{-28.7495\vartheta}. \quad (7.1)$$

The prior and the posterior densities are plotted in Fig. 1. Again using the formula 13.5.6 (op. cit.), the posterior expectations for ϑ and the mean survival time μ are computed as 0.3078 and 1.67 respectively.

Case II: Inverted gamma prior density:

The inverted gamma density, specified by the *pdf* (1.6) with parameters $a = 0.5$ and $v = 4$ is assumed. Using expressions (4.1) and (4.2) and the table 9.9 (op. cit.), the posterior density of ϑ is obtained as

$$g_2^*(\vartheta) = 1.67 \times 10^8 \cdot \vartheta^6 \cdot e^{-(28.7495 + 0.5\vartheta^{-1})}. \quad (7.2)$$

The prior and the posterior densities are plotted in Fig. 2. The posterior expectation of ϑ is computed as 0.296. Using formula 10.2.15 (op. cit.), the Bayes estimator of the mean survival time is worked out as 1.6359.

Case III: Gamma prior density:

The gamma density specified as (1.7) with parameters $\lambda = 2$ and $\tau = 8$ is considered as the prior density. Using expression (5.1), the posterior density of ϑ is (obtained as

$$g_3^*(\vartheta) = 1.5021 \times 10^{11} \cdot \vartheta^{11} \cdot e^{-36.7495\vartheta}. \quad (7.3)$$

The posterior expectation of ϑ and the mean survival time are obtained as 0.3625 and 1.60 respectively. The prior and the posterior densities of ϑ are depicted in Fig. 3.

It would seem from the graphs plotted that in case I, the change in our knowledge of ϑ after the prior knowledge is incorporated into the sample evidence is the maximum. Analogous changes in ϑ can also be read and easily compared from the graphs.

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