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# Forecasting Remission Time of a Treatment Method for Leukemia as an Application to Statistical Inference Approach

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**Abstract:** In this paper, Weibull-Linear Exponential distribution (WLED) has been investigated whether being it is a well - fit distribution to a clinical real data. These data represent the duration of remission achieved by a certain drug used in the treatment of leukemia for a group of patients. The statistical inference approach is used to estimate the parameters of the WLED through the set of the fitted data. The estimated parameters are utilized to evaluate the survival and hazard functions and hence assessing the treatment method through forecasting the duration of remission times of patients. A two-sample prediction approach has been applied to obtain a predictive sample based on the Bayes estimates of the parameters. The statistical inference approach is applied to the case of censored data namely Type-II hybrid censoring scheme, which is common in clinical studies.

**Keywords:** Statistical inference; censored data; Bayesian estimation; clinical data; assessing treatment methods.

## 1 Introduction

The remission time of patients is an important factor that indicates the effectiveness of the treatment method or the used drug. The remission times of a group of patients, that took the same dose of a drug, are random times. These random times can be registered from the time of taking the drug to a certain time that indicates the remission, which can be determined by the researcher. However, some patients may be left the treatment program for unknown causes and hence we have censored (non-complete) data. The issue here is how to judge the efficiency of the used drug through censored random data. Methods of statistical inferences can give a reliable conclusion for cases like our issue in this paper.

In this paper, the Weibull Linear Exponential Distribution (WLED) is considered as a parametric model to fit the remission random times under study. Due to the interest in the censored scenario, the inference process about the parameters of WLED will be implemented based on the hybrid Type -II censored scheme.

Collecting data based on hybrid censoring scheme can be described as follows: the remission times will be registered until prefixed time by the researcher, say  $T$  and he wishes to terminate the registration process at time  $T$  or at the time of occurring the event whose registration number is  $T_R$ , which is prefixed too by the researcher before starting the registration process. The hybrid Type-II censoring scheme holds when the researcher ends the registration process at time equals  $\max\{T, T_R\}$ , for more details about hybrid Type-II censoring scheme, see Epstein [1] and Mahmoud et al. [2], Mansour and Ramadan [3], Mansoura and Aboshady [4], and Ramadan et al. [5]. Let  $n$  identical units be tested, and the test will be terminated either when a pre-determined time  $T$  is reached or when a pre specified number  $R$  out of  $n$  units are failed. Instance for, if  $Y_{i:n}$  representing the  $i^{th}$  ordered of failure times. In this case the test may be terminated either at time  $T_1 = \min\{Y_{R:n}, T\}$  or at time  $T_2 = \max\{Y_{R:n}, T\}$ . The time  $T_1$  is the termination time of an experiment for testing units under Type-I hybrid censoring scheme (HCS), while,  $T_2$  is the termination time of an experiment for testing units under Type-II HCS.

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Several authors have studied on Type-I HCS; see for example Balakrishnan and Kundu [6] provides a detailed review of hybrid censoring schemes with its generalizations and application in competing risks and step stress modeling. Childs et al. [7] introduced the Type-II HCS, which guarantees at least  $R$  failures will occur. For more details about the merits and the flexibility of Type-II HCS see, Childs et al. [7] and Banerjee and Kundu [8]

A random variable  $X$  is said to have WLED, if its PDF is given by:

$$g(x) = \left(\frac{c}{\gamma^c}\right) (\lambda + \theta x) \left(\lambda x + \frac{\theta}{2} x^2\right)^{c-1} \exp\left[-\left(\frac{\lambda x + \frac{\theta}{2} x^2}{\gamma}\right)^c\right], \theta, \gamma, c, \lambda > 0. \quad (1)$$

and the CDF is

$$G(x) = 1 - \exp\left[-\left(\frac{\lambda x + \frac{\theta}{2} x^2}{\gamma}\right)^c\right], \theta, \gamma, c, \lambda > 0, \quad (2)$$

where  $c, \lambda$  are the shape parameters and  $\theta, \gamma$  are the scale parameters, while the reliability  $S(x)$  and hazared  $h(x)$  functions respectively are given by:

$$S(x) = \exp\left[-\left(\frac{\lambda x + \frac{\theta}{2} x^2}{\gamma}\right)^c\right], \quad x \geq 0, \gamma > 0, \theta > 0, c > 0, \lambda > 0, \quad (3)$$

$$h(x) = \left(\frac{c}{\gamma^c}\right) (\lambda + \theta x) \left(\lambda x + \frac{\theta}{2} x^2\right)^{c-1}, \quad x \geq 0, \gamma > 0, \theta > 0, c > 0, \lambda > 0. \quad (4)$$

The layout of this paper is organized as follows: In Section 2 the maximum likelihood estimates (MLEs) of the parameters under consideration are obtained in addition to the corresponding approximate confidence intervals (ACIs). In Section 3 the Bayesian estimation and Markov chain Monte Carlo (MCMC) approach are derived, in addition two - sample prediction approach has been investigated in this section too. A real data set is analyzed in section 4 to illustrate the importance of the proposed methods. Conclusion remarks are summarized in section 5.

## 2 Maximum Likelihood Estimation

The log-likelihood functions are the basis for deriving estimators of parameters, given data. ML estimators enjoy with different advantages such as asymptotically normally distributed, asymptotically minimum variance, asymptotically unbiased and satisfy the invariant property, by Royall [9], Aliyu et al. [10] and Azzalini [11], more information on likelihood theory. Under T-II HCS, one of the following two types of censored data can be observed:

Case I:  $\{Y_{1:n} < \dots < Y_{R:n}\}$  if  $T < Y_{R:n}$ .

Case II:  $\{Y_{1:n} < \dots < Y_{R:n} < Y_{R+1:n} < \dots < Y_{m:n} < T\}$  if  $T > Y_{R:n}$  and the  $m$ -th failure took place before  $T, R \leq m \leq n$ . The likelihood function for the Case I is

$$L_1(\gamma, \theta, \lambda, c | \text{data}) = c_1 \frac{c^R}{\gamma^c} e^{-\left(\frac{\lambda y_i + \frac{\theta}{2} y_i^2}{\gamma}\right)^{c(n-R)}} \prod_{i=1}^R (\lambda + \theta y_i) \left(\lambda y_i + \frac{\theta}{2} y_i^2\right)^{c-1} e^{-\sum_{i=1}^R \left(\frac{\lambda y_i + \frac{\theta}{2} y_i^2}{\gamma}\right)^c}, T < Y_{R:n}$$

where  $c_1 = \frac{n!}{(n-R)!}$ , while the likelihood function for the Case II is

$$L_2(\gamma, \theta, \lambda, c | \text{data}) = c_2 \frac{c^m}{\gamma^c} \prod_{i=1}^m (\lambda + \theta y_i) \left(\lambda y_i + \frac{\theta}{2} y_i^2\right)^{c-1} e^{-\sum_{i=1}^m \left(\frac{\lambda y_i + \frac{\theta}{2} y_i^2}{\gamma}\right)^c} e^{-\left(\frac{\lambda y_i + \frac{\theta}{2} y_i^2}{\gamma}\right)^{c(n-m)}}, T < Y_{m:n}$$

where  $c_2 = \frac{n!}{(n-m)!}$ . The two likelihood functions can be combined, and can be written as

$$L(\gamma, \theta, \lambda, c | \text{data}) = c \frac{c^H}{\gamma^c} \prod_{i=1}^H (\lambda + \theta y_i) \left( \lambda y_i + \frac{\theta}{2} y_i^2 \right)^{c-1} e^{-\sum_{i=1}^H \left( \frac{\lambda y_i + \frac{\theta}{2} y_i^2}{\gamma} \right)^c} e^{-\left( \frac{\lambda T + \frac{\theta}{2} T^2}{\gamma} \right)^{c(n-H)}}, \tag{5}$$

where  $c = \frac{n!}{(n-H)!}$  and  $H$  stands for the number of failures;  $u = y_{R:n}$  if  $H = R$  and  $y = T$  if  $H > R$ . The log-likelihood function may then be written as

$$\begin{aligned} \log L(\gamma, \theta, \lambda, c | \text{data}) &= \log \frac{n!}{(n-H)!} + H \log \frac{c}{\gamma^c} + \sum_{i=1}^H \log (\lambda + \theta x_i) \\ &+ \sum_{i=1}^H (c-1) \log \left( \lambda x_i + \frac{\theta}{2} x_i^2 \right) - \sum_{i=1}^H \left( \frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma} \right)^c \\ &- \left( \frac{\lambda T + \frac{\theta}{2} T^2}{\gamma} \right)^{c(n-H)}, \end{aligned}$$

and thus we have the likelihood equations for  $\gamma, \theta, \lambda$  and  $c$  respectively, as

$$-\frac{Hc^2}{\gamma} + \frac{c}{\gamma^{1-c}} \sum_{i=1}^H \left( \lambda x_i + \frac{\theta}{2} x_i^2 \right)^c + \frac{c(n-H)}{\gamma^{1-c(n-H)}} \left( \lambda T + \frac{\theta}{2} T^2 \right)^{c(n-H)} = 0. \tag{6}$$

$$\begin{aligned} \left( \theta + \frac{\lambda}{x_i} \right)^{-1} + (c-1) \sum_{i=1}^H \left( \theta + \frac{2\lambda}{x_i} \right)^{-1} - \frac{c}{(2\gamma)^c} \sum_{i=1}^H x_i^{c+1} (2\lambda + \theta x_i)^{c-1} \\ - \frac{c(n-H)T^{c(c-H)+1}}{2\gamma^{c(n-H)}} (2\lambda + \theta T)^{c(n-H)-1} = 0. \end{aligned} \tag{7}$$

$$\begin{aligned} \sum_{i=0}^H \frac{1 + \theta x_i}{\lambda + \theta x_i} + (c-1) \sum_{i=1}^H \left( \lambda + \frac{\theta}{2} x_i \right)^{-1} - \frac{c}{\gamma^c} \sum_{i=1}^H \left( \lambda + \frac{\theta}{2} x_i \right)^{c-1} x_i^c \\ - c(c-H) \left( \frac{T}{\gamma} \right)^{c(n-H)} \left( \lambda + \frac{\theta}{2} T \right)^{c(n-H)-1} = 0. \end{aligned} \tag{8}$$

and

$$\frac{H(1-c^2\gamma^{-1})}{c} + \frac{c}{\gamma^{1-c}} \sum_{i=1}^H \left( \lambda x_i + \frac{\theta}{2} x_i^2 \right)^c + \frac{c(n-H)}{\gamma^{1-c(n-H)}} \left( \lambda T + \frac{\theta}{2} T^2 \right)^{c(n-H)} = 0. \tag{9}$$

The Equations (6), (7), (8) and (9) are nonlinear simultaneous equations in four unknown variables  $\gamma, \lambda, \theta$  and  $c$ . It is obvious that an exact solution is not easy to get. Therefore, a numerical method such as Newton Raphson can be used to find approximate solution. The steps of Newton Raphson algorithm is described in details in EL-Sagheer [?]. The final estimates of  $\gamma, \lambda, \theta$  and  $c$  are the MLEs of the parameters, denoted as  $\hat{\gamma}, \hat{\lambda}, \hat{\theta}$  and  $\hat{c}$ .

### 2.1 Approximate confidence intervals

The  $(1 - \psi) 100\%$  ACIs for the parameters  $\gamma, \lambda, \theta$  and  $c$  can be written as

$$\left. \begin{aligned} (\hat{\gamma}_L, \hat{\gamma}_U) &= \hat{\gamma} \pm z_{1-\frac{\psi}{2}} \sqrt{\text{var}(\hat{\gamma})} \\ (\hat{\lambda}_L, \hat{\lambda}_U) &= \hat{\lambda} \pm z_{1-\frac{\psi}{2}} \sqrt{\text{var}(\hat{\lambda})} \\ (\hat{\theta}_L, \hat{\theta}_U) &= \hat{\theta} \pm z_{1-\frac{\psi}{2}} \sqrt{\text{var}(\hat{\theta})} \\ (\hat{c}_L, \hat{c}_U) &= \hat{c} \pm z_{1-\frac{\psi}{2}} \sqrt{\text{var}(\hat{c})} \end{aligned} \right\},$$

where  $z_{1-\frac{\psi}{2}}$  is the percentile of the standard normal distribution with left-tail probability  $1 - \frac{\psi}{2}$  and  $var(\hat{\gamma}), var(\hat{\lambda}), var(\hat{\theta})$  and  $var(\hat{c})$  represent the asymptotic variances of MLEs which can be calculated using the inverse of the Fisher information matrix.

$$I = - \left( \frac{\partial^2 \log L}{\partial \varepsilon_i \partial \varepsilon_j} \right), i, j = 1, 2, 3,$$

where  $\varepsilon_1 = \gamma, \varepsilon_2 = \lambda, \varepsilon_3 = \theta$  and  $\varepsilon_4 = c$ .

The asymptotic variance–covariance matrix for the maximum likelihood estimates can be put as follows:

$$I^{-1} = \left[ - \left( \frac{\partial^2 \log L}{\partial \varepsilon_i \partial \varepsilon_j} \right) \right]_{\downarrow(\hat{\varepsilon}_1, \hat{\varepsilon}_2, \hat{\varepsilon}_3, \hat{\varepsilon}_4)}^{-1}. \quad (10)$$

for more details see Cohen [13].

### 3 Bayesian Estimation

In this section, Bayesian estimates of the unknown parameters  $\gamma, \lambda, \theta$  and  $c$  are obtained as well as some lifetime parameters  $S(t)$  and  $h(t)$  against the squared error and LINEX loss functions. The prior knowledge about the parameters are represented by independent informative prior distributions. It is assumed that the parameters  $\gamma, \lambda, \theta$  and  $c$  are independent and follow the gamma prior distributions as follows:

$$\left. \begin{aligned} \pi_1(\gamma) &= \gamma^{-(cH+1)} \exp - \sum_{i=1}^H \left( \frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma} \right)^c \quad \gamma > 0, \\ \pi_2(\lambda) &= \lambda^{-1} \prod_{i=1}^H (\lambda + \theta x_i) \prod_{i=1}^H (\lambda x_i + \frac{\theta}{2} x_i^2)^{c-1} \exp - \sum_{i=1}^H \left( \frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma} \right)^c \quad \lambda > 0, \\ \pi_3(\theta) &= \theta^{-1} \prod_{i=1}^H (\lambda + \theta x_i) \prod_{i=1}^H (\lambda x_i + \frac{\theta}{2} x_i^2)^{c-1} \exp - \sum_{i=1}^H \left( \frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma} \right)^c \quad \theta > 0, \\ \pi_4(c) &= \frac{c^{H-1}}{\gamma^H} \prod_{i=1}^H (\lambda x_i + \frac{\theta}{2} x_i^2)^{c-1} \exp - \sum_{i=1}^H \left( \frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma} \right)^c \quad c > 0, \end{aligned} \right\} \quad (11)$$

where  $\gamma, \lambda, \theta$  and  $c$  are independent random variables. Many authors like Kundu and Howlader [14], Dey and Dey [15], Dey et. al. [16], Dey et. al. [17], Antony M. et. al. [18], Aliyu et. al. [10], and Tahani et. al. [19] established the Bayesian estimation for their parameter models based on informative gamma priors. Tierney [20] has studied Markov chains for exploring posterior distributions. The posterior distribution of the parameters  $\gamma, \lambda, \theta$  and  $c$  denoted by  $\pi(\gamma, \lambda, \theta, c | data)$  can be obtained by combining the likelihood function (5) with the prior (11) via Bayes theorem and it can be written as

$$\pi^*(\gamma, \lambda, \theta, c | data) = \frac{L(\gamma, \lambda, \theta, c | data) \times \pi(\gamma, \lambda, \theta, c)}{\int_0^\infty \int_0^\infty \int_0^\infty \int_0^\infty L(\gamma, \lambda, \theta, c | data) \times \pi(\gamma, \lambda, \theta, c) d\gamma d\lambda d\theta dc}. \quad (12)$$

A commonly used loss function is the squared error loss (SEL) function which is a symmetrical loss function that assigns equal losses to over estimation and underestimation. If  $\phi$  is the parameter to be estimated by an estimator  $\hat{\phi}$ , then the SEL function is defined as

$$L(\phi, \hat{\phi}) = (\hat{\phi} - \phi)^2. \quad (13)$$

Therefore, the Bayes estimate of any function of  $\gamma, \lambda, \theta$  and  $c$ , say  $g(\gamma, \lambda, \theta, c)$  under the SEL function is

$$\hat{g}_{BS}(\gamma, \lambda, \theta, c) = E_{\gamma, \lambda, \theta, c | data} [g(\gamma, \lambda, \theta, c)], \quad (14)$$

where

$$E_{\gamma, \lambda, \theta, c | data} [g(\gamma, \lambda, \theta, c)] = \frac{\int_0^\infty \int_0^\infty \int_0^\infty \int_0^\infty g(\gamma, \lambda, \theta, c) \times L(\gamma, \lambda, \theta, c) \times \pi(\gamma, \lambda, \theta, c) d\gamma d\lambda d\theta dc}{\int_0^\infty \int_0^\infty \int_0^\infty \int_0^\infty L(\gamma, \lambda, \theta, c) \times \pi(\gamma, \lambda, \theta, c) d\gamma d\lambda d\theta dc}. \quad (15)$$

Varian [21] considered a LINEX (linear-exponential) loss function  $L(\Delta)$  for a parameter  $\phi$  as follows:

$$L(\Delta) = \left( e^{\varepsilon \Delta} - \varepsilon \Delta - 1 \right), \varepsilon \neq 0, \Delta = \hat{\phi} - \phi, \quad (16)$$

where  $\varepsilon$  is a scale parameter of the loss function. For small values of  $\varepsilon$  (near to zero), the LINEX loss function is almost the same as the SEL function.

Hence, under LINEX loss function, the Bayes estimate of a function  $g(\gamma, \lambda, \theta, c)$  is

$$\hat{g}_{BL}(\gamma, \lambda, \theta, c) = \frac{-1}{\varepsilon} \log \left[ E_{\gamma, \lambda, \theta, c | \text{data}} \left[ e^{-\varepsilon g(\gamma, \lambda, \theta, c)} \right] \right], \quad \varepsilon \neq 0, \tag{17}$$

where

$$E_{\gamma, \lambda, \theta, c | \text{data}} \left[ e^{-\varepsilon g(\gamma, \lambda, \theta, c)} \right] = \frac{\int_0^\infty \int_0^\infty \int_0^\infty \int_0^\infty e^{-\varepsilon g(\gamma, \lambda, \theta, c)} \times L(\gamma, \lambda, \theta, c) \times \pi(\gamma, \lambda, \theta, c) d\gamma d\lambda d\theta dc}{\int_0^\infty \int_0^\infty \int_0^\infty \int_0^\infty L(\gamma, \lambda, \theta, c) \times \pi(\gamma, \lambda, \theta, c) d\gamma d\lambda d\theta dc}. \tag{18}$$

It may be noted that, the calculation of the multiple integrals in (15) and (18) cannot be solved analytically, this is due to the complex form of the likelihood function given in (5). For this reason, the MCMC approximation method can be used to generate samples from the joint posterior density function in (14) to compute the Bayes estimate of  $\gamma, \lambda, \theta, c, S(t)$  and  $h(t)$  and also to construct their associated credible intervals. The joint posterior distribution can be written as follows:

$$\begin{aligned} \pi^*(\gamma, \lambda, \theta, c | \text{data}) = & \left(\frac{c}{\gamma}\right)^H \frac{n!(\theta\gamma\lambda c)^{-1}}{(n-1)!} \prod_{i=1}^H (\lambda + \theta x_i) \prod_{i=1}^H \left(\lambda x_i + \frac{\theta}{2} x_i^2\right)^{c-1} \\ & + \exp - \sum_{i=1}^H \left(\frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma}\right)^c \exp - \left(\frac{\lambda T^* + \frac{\theta}{2} T^{*2}}{\gamma}\right)^{c(n-H)}. \end{aligned} \tag{19}$$

### 3.1 MCMC Technique

The main goal of the MCMC technique is to compute an approximate value of integrals in (15) and (18). A lot of papers dealt with MCMC technique such as, EL-Sagheer [?], Mahmoud et al. [22], Ritwik et al [23] and among others. An important sup-class of MCMC methods are Gibbs sampling and more general Metropolis within-Gibbs samplers. The Metropolis algorithm is a random walk that uses an acceptance/rejection rule to converge to the target distribution. The Metropolis algorithm was first proposed in Metropolis et al. [24] and it was then generalized by Hastings in Hastings [25]. From (19), the conditional posterior densities of  $\gamma, \lambda, \theta$  and  $c$  can also be written as:

$$\begin{aligned} \pi_1^*(\gamma | \lambda, \theta, c, \text{data}) \propto & \frac{n! \gamma^{-cH}}{(n-1)!} \prod_{i=1}^H (\lambda + \theta x_i) \prod_{i=1}^H \left(\lambda x_i + \frac{\theta}{2} x_i^2\right)^{c-1} \\ & + \exp - \sum_{i=1}^H \left(\frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma}\right)^c \exp - \left(\frac{\lambda T^* + \frac{\theta}{2} T^{*2}}{\gamma}\right)^{c(n-H)}, \end{aligned} \tag{20}$$

$$\begin{aligned} \pi_2^*(\lambda | \gamma, \theta, c, \text{data}) \propto & \frac{n!}{(n-1)! \lambda} \prod_{i=1}^H (\lambda + \theta x_i) \prod_{i=1}^H \left(\lambda x_i + \frac{\theta}{2} x_i^2\right)^{c-1} \\ & + \exp - \sum_{i=1}^H \left(\frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma}\right)^c \exp - \left(\frac{\lambda T^* + \frac{\theta}{2} T^{*2}}{\gamma}\right)^{c(n-H)}, \end{aligned} \tag{21}$$

$$\begin{aligned} \pi_3^*(\theta | \gamma, \lambda, c, \text{data}) \propto & \frac{n!}{(n-1)! \theta} \prod_{i=1}^H (\lambda + \theta x_i) \prod_{i=1}^H \left(\lambda x_i + \frac{\theta}{2} x_i^2\right)^{c-1} \\ & + \exp - \sum_{i=1}^H \left(\frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma}\right)^c \exp - \left(\frac{\lambda T^* + \frac{\theta}{2} T^{*2}}{\gamma}\right)^{c(n-H)}, \end{aligned} \tag{22}$$

and

$$\begin{aligned} \pi_4^*(c|\gamma, \lambda, \theta, \text{data}) &\propto \left(\frac{c}{\gamma^c}\right)^H \frac{n!}{(n-1)!c} \prod_{i=1}^H (\lambda + \theta x_i) \prod_{i=1}^H \left(\lambda x_i + \frac{\theta}{2} x_i^2\right)^{c-1} \\ &+ \exp - \sum_{i=1}^H \left(\frac{\lambda x_i + \frac{\theta}{2} x_i^2}{\gamma}\right)^c \exp - \left(\frac{\lambda T^* + \frac{\theta}{2} T^{*2}}{\gamma}\right)^{c(n-H)}. \end{aligned} \quad (23)$$

It can be easily seen that the conditional posteriors of  $\gamma, \lambda, \theta$  and  $c$  in Equations (20), (21), (22) and (23) are not known distributions, so Gibbs sampling is not a straightforward option, the use of the Metropolis–Hasting (M–H) sampler is required for the implementations of MCMC approach. Now, the following steps illustrate the process of the Metropolis–Hasting algorithm within Gibbs sampling:

(1) Start with Initial guess  $(\lambda^{(0)} = \hat{\lambda}, \gamma^{(0)} = \hat{\gamma}, \theta^{(0)} = \hat{\theta}, c^{(0)} = \hat{c})$ .

(2) Put  $j = 1$

(3) Using the following M-H algorithm, generate  $\lambda^{(j)}, \gamma^{(j)}, \theta^{(j)}$  and  $c^{(j)}$  from  $\pi_1^*(\gamma^{(j-1)}|\lambda^{(j-1)}, \theta^{(j-1)}, c^{(j-1)}, \text{data}), \pi_2^*(\lambda^{(j-1)}|\gamma^{(j)}, \theta^{(j-1)}, c^{(j-1)}, \text{data}), \pi_3^*(\theta^{(j-1)}|\gamma^{(j)}, \lambda^{(j)}, c^{(j-1)}, \text{data})$  and  $\pi_4^*(c^{(j-1)}|\gamma^{(j)}, \lambda^{(j)}, \theta^{(j)}, \text{data})$  with the normal proposal distributions

$$N(\gamma^{(j-1)}, \text{var}(\gamma)), N(\lambda^{(j-1)}, \text{var}(\lambda)), N(\theta^{(j-1)}, \text{var}(\theta)), N(c^{(j-1)}, \text{var}(c)).$$

i-Generate a proposal  $\gamma^*$  from  $N(\gamma^{(j-1)}, \text{var}(\gamma)), \lambda^*$  from  $N(\lambda^{(j-1)}, \text{var}(\lambda)), \theta^*$  from  $N(\theta^{(j-1)}, \text{var}(\theta))$  and  $c^*$  from  $N(c^{(j-1)}, \text{var}(c))$ .

ii-Evaluate the acceptance probabilities

$$\left. \begin{aligned} \rho_\gamma &= \min \left[ 1, \frac{\pi_1^*(\gamma^*|\lambda^{(j)}, \theta^{(j-1)}, c^{(j-1)}, \text{data})}{\pi_1^*(\gamma^{(j-1)}|\lambda^{(j)}, \theta^{(j-1)}, c^{(j-1)}, \text{data})} \right], \\ \rho_\lambda &= \min \left[ 1, \frac{\pi_2^*(\lambda^*|\gamma^{(j-1)}, \theta^{(j-1)}, c^{(j-1)}, \text{data})}{\pi_2^*(\lambda^{(j-1)}|\gamma^{(j-1)}, \theta^{(j-1)}, c^{(j-1)}, \text{data})} \right], \\ \rho_\theta &= \min \left[ 1, \frac{\pi_3^*(\theta^*|\gamma^{(j)}, \lambda^{(j)}, c^{(j-1)}, \text{data})}{\pi_3^*(\theta^{(j-1)}|\gamma^{(j)}, \lambda^{(j)}, c^{(j-1)}, \text{data})} \right], \\ \rho_c &= \min \left[ 1, \frac{\pi_4^*(c^*|\gamma^{(j)}, \theta^{(j)}, \lambda^{(j)}, \text{data})}{\pi_4^*(c^{(j-1)}|\gamma^{(j)}, \theta^{(j)}, \lambda^{(j)}, \text{data})} \right], \end{aligned} \right\}.$$

iii-Generate a  $u_1, u_2, u_3$  and  $u_4$  from a Uniform (0, 1) distribution.

iv-If  $u_1 < \rho_\gamma$ , accept the proposal and set  $\gamma^{(j)} = \gamma^*$ , else set  $\gamma^{(j-1)} = \gamma^*$ .

v-If  $u_2 < \rho_\lambda$ , accept the proposal and set  $\lambda^{(j)} = \lambda^*$ , else set  $\lambda^{(j-1)} = \lambda^*$ .

vi-If  $u_3 < \rho_\theta$ , accept the proposal and set  $\theta^{(j)} = \theta^*$ , else set  $\theta^{(j-1)} = \theta^*$ .

vii-If  $u_4 < \rho_c$ , accept the proposal and set  $c^{(j)} = c^*$ , else set  $c^{(j-1)} = c^*$ .

(4) Compute the reliability function, hazard function as

$$\left\{ \begin{aligned} S^j(t) &= \exp \left[ - \left( \frac{\lambda^{(j)} t + \frac{\theta}{2(j)} t^2}{\gamma^{(j)}} \right)^c \right]; & t \geq 0 \\ h^j(t) &= \left( \frac{c}{\gamma^{jc(j)}} \right) \left( \lambda^{(j)} + \theta^{(j)} t \right) \left( \lambda^{(j)} t + \frac{\theta}{2(j)} t^2 \right)^{c(j)-1}; & t \geq 0. \end{aligned} \right. \quad (24)$$

(5) Set  $j = j + 1$ .

(6) Repeat Steps (3) – (5),  $N$  times and obtain  $\gamma^{(i)}, \lambda^{(i)}, \theta^{(i)}, c^{(i)}, S^{(i)}(t)$  and  $h^{(i)}(t), i = 1, 2, \dots, N$ .

In order to guarantee the convergence and to remove the affection of the selection of initial values, the first  $M$  simulated varieties are discarded. The previous algorithm is implemented via the notation of parallel computing through the Mathematica software, for more details see Mansour and Aboshady [26]. Then the selected samples are

$\gamma^{(j)}, \lambda^{(j)}, \theta^{(j)}, c^{(j)}, S^{(j)}(t)$  and  $h^{(j)}(t), j = M + 1, \dots, N$ , for sufficiently large  $N$ , forms an approximate posterior samples which can be used to develop the Bayesian inferences. Based on SEL, the approximate Bayes estimates of  $\phi = \gamma, \lambda, \theta, c, S(t)$  or  $h(t)$  is given by

$$\hat{\zeta}_{BS} = \frac{1}{N - M} \sum_{j=M+1}^N \zeta^{(j)},$$

and the approximate Bayes estimates for  $\zeta$ , under LINEX loss function are

$$\hat{\zeta}_{BS} = \frac{-1}{\epsilon} \log \left[ \frac{1}{N - M} \sum_{j=M+1}^N e^{-\epsilon \zeta^{(j)}} \right],$$

To compute the credible intervals of  $\gamma, \lambda, \theta, c, S(t)$  and  $h(t)$  order  $\gamma^{(i)}, \lambda^{(i)}, \theta^{(i)}, c^{(i)}, S^{(i)}(t)$  and  $h^{(i)}(t), i = M + 1, \dots, N$ . Then the  $100(1 - \nu)\%$  credible intervals of  $\zeta = \gamma, \lambda, \theta, c, S(t)$  or  $h(t)$  become  $(\zeta(N - \frac{\nu}{2}), \zeta(N - 1 - \frac{\nu}{2}))$ .

### 3.2 Two - sample prediction

Let  $Y_{1:m} \geq Y_{2:m} \dots \geq Y_{m:m}$  be the order statistics from a future random sample of size  $m$  from the same population for more details Arnold et al. [27]. In this section a general procedure is developed for deriving the interval predictions, for  $Y_{s:m}, 1 \leq s \leq m$  for WLED based on Type-II HCS. It is well known that the marginal density function of the  $s$ th order statistic from a sample of size  $m$  from a continuous distribution with CDF  $F(x)$  and PDF  $f(x)$  is given by

$$\begin{aligned} f_{Y_{s:m}}(y_s | \kappa) &= \frac{m!}{(s-1)!(m-s)!} [F(y_s)]^{s-1} [1 - F(y_s)]^{m-s} f(y_s). \\ &= \sum_{q=0}^{m-s} \frac{(-1)^q \binom{m-s}{q} m!}{(s-1)!(m-s)!} [F(y_s)]^{s+q-1} f(y_s), \end{aligned} \tag{25}$$

where  $y_s \geq 0$  and  $\kappa = (\gamma, \theta, \lambda, c)$  see Arnold et al. [21]. Upon substituting (1) and (2) in (25), the marginal density function of  $Y_{s:m}$  becomes

$$\begin{aligned} f_{Y_{s:m}}(y_s | \gamma, \theta, \lambda, c) &= \left(\frac{c}{\gamma^c}\right) \left(\lambda + \theta y_s\right) \left(\lambda y_s + \frac{\theta}{2} y_s^2\right)^{c-1} \exp \left[ -\left(\frac{\lambda y_s + \frac{\theta}{2} y_s^2}{\gamma}\right)^c \right] \\ &\sum_{q=0}^{m-s} \frac{(-1)^q \binom{m-s}{q} m!}{(s-1)!(m-s)!} \left[ 1 - \exp \left[ -\left(\frac{\lambda y_s + \frac{\theta}{2} y_s^2}{\gamma}\right)^c \right] \right]^{s+q-1}. \end{aligned} \tag{26}$$

From (19) and (26), the Bayesian predictive density function of  $Y_{s:m}$  can be given as follows:

$$\begin{aligned} f^*(y_s | x) &= \int_0^\infty \int_0^\infty \int_0^\infty \int_0^\infty f_{Y_{s:m}}(y_s | x) \pi^*(\gamma, \theta, \lambda, c | x) d\gamma d\theta d\lambda dc. \\ f^*(y_s | x) &= \sum_{q=0}^{m-s} \frac{(-1)^q \binom{m-s}{q} m!}{(s-1)!(m-s)!} \int_0^\infty \int_0^\infty \int_0^\infty \int_0^\infty \left(\frac{c}{\gamma^c}\right)^{H+1} \frac{n!(\theta\gamma\lambda c)^{-1}}{(n-1)!} \left(\lambda + \theta y_s\right) \left(\lambda y_s + \frac{\theta}{2} y_s^2\right)^{c-1} \\ &\prod_{i=1}^H \left(\lambda + \theta x_{i:n}\right) \prod_{i=1}^H \left(\lambda x_i + \frac{\theta}{2} x_{i:n}^2\right)^{c-1} + \exp \left[ -\sum_{i=1}^H \left(\frac{\lambda x_{i:n} + \frac{\theta}{2} x_{i:n}^2}{\gamma}\right)^c \right] \\ &\exp \left[ -\left(\frac{\lambda T^* + \frac{\theta}{2} T^{*2}}{\gamma}\right)^{c(n-H)} \right] \exp \left[ -\left(\frac{\lambda y_s + \frac{\theta}{2} y_s^2}{\gamma}\right)^c \right] \\ &\left[ 1 - \exp \left[ -\left(\frac{\lambda y_s + \frac{\theta}{2} y_s^2}{\gamma}\right)^c \right] \right]^{s+q-1} d\gamma d\theta d\lambda dc. \end{aligned} \tag{27}$$



The predictive survival function

$$\bar{F}^*_{y_{s:m}}(t|x) = \int_t^\infty f^*(y_s|x)dy_s, t \geq 0. \tag{28}$$

Then, the Bayesian predictive bounds of a two-sided equi-tailed  $100(1 - \nu)$  interval for  $y_{s:m}, 1 \geq s \geq m$ , can be obtained by solving the following two equations:

$$\bar{F}^*_{y_{s:m}}(L_{y_{s:m}}|x) = 1 - \frac{\nu}{2}. \tag{29}$$

and

$$\bar{F}^*_{y_{s:m}}(U_{y_{s:m}}|x) = \frac{\nu}{2}, \tag{30}$$

where  $L_{y_{s:m}}$  and  $U_{y_{s:m}}$  indicate the lower and upper bounds, respectively. It is evident that is not possible to compute (27) and (28) analytically. Then, the MCMC method is suggested for constructing the Bayesian prediction intervals to the illustrative example in the next section.

### 4 Application to Real Data

In this section, a real data set is presented in Table 1. where these data are remission times of 20 patients suffering from Leukemia after they cured a certain drug, see Lawless [28].

The aim is to assess the efficacy of the used drug through these remission times based on a hybrid Type-II censored scheme.

$T$  and  $r$  are selected to be 2.5 and 10, respectively.

The different point estimates for  $\gamma, \lambda, \theta$  and  $c$  in case of non-Bayesian and Bayesian estimation, are presented in Table 2.

In Table 4. The reliability function,  $S(t)$  was estimated for different values of  $t$ , and it was found that it is rare for the remission periods to exceed around seven months which is a good indicator of the efficacy of the used drug,  $P(X > 0.6) = 0.0000350858$ .

**Table 1:** Remission times in years.

1.013	1.034	1.109	1.169	1.226
1.509	1.533	1.563	1.716	1.929
1.965	2.061	2.344	2.546	2.626
2.778	2.951	3.413	4.118	5.136

**Table 2:** Different point estimates for  $\gamma, \lambda, \theta$  and  $c$ .

	$(\cdot)_{ML}$	$(\cdot)_{BMC-SEL}$	$(\cdot)_{BMC-LINEX}$	
			$c_1 = -2.0$	$c_2 = 2.0$
$\gamma$	0.030	0.030	0.030	0.030
$\lambda$	0.400	0.399	0.399	0.399
$\theta$	0.300	0.299	0.299	0.299
$c$	1.020	1.020	1.020	1.020

**Table 3:** 95% confidence intervals for  $\gamma, \lambda, \theta$  and  $c$ .

	$\gamma$	Length	$\lambda$	Length	$\theta$	Length	$c$	Length
ACI	[0.030, 0.030]	0.030	[-0.413, 1.213]	0.400	[-0.350, 0.950]	0.300	[1.02, 1.02]	1.02
CRI	[0.030, 0.030]	0.036	[1.02, 1.02]	5.06	[0.299, 0.300]	0.022	[1.02, 1.020]	0.992

**Table 4:** 95% Two-sample Bayesian prediction bounds for  $Y_s$ .

s	Lower	Upper	Length
1	0.060025	5.194165	5.25419
2	0.00005	4.27676	4.27681
3	0.09500	3.470785	3.375785
4	0.12000	6.11157	6.23157
5	0.00106	7.02221	7.02327
6	0.21000	7.78127	7.99127
7	0.26000	9.50952	9.76952

## 5 Conclusion

A statistical inference approach has been discussed about the parameters of WLED through clinical data of remission times of some patients suffering from Leukemia. The maximum likelihood method is used for deriving estimators of the model parameters. In addition to using the inverse of the Fisher information matrix to represent the asymptotic variance-covariance matrix of maximum likelihood estimates. The Bayesian estimates are obtained of the unknown parameters as well as some lifetime parameters (reliability and failure rate functions) against the squared error and LINEX loss functions. The MCMC technique is used to compute an approximate value of integrals in the Bayes estimate under the SEL function and the LINEX loss function. Farther more, a general procedure is developed for deriving the interval predictions for WLED based on Type-II HCS. Finally, a real data set is presented and the study showed that the remission times as a result of the used drug did not exceeded 0.6. Therefore it is recommended to use and generalize the drug under study for treating such type of cancer.

## Conflicts of Interest

There are no conflicts of interest declared by the authors for the publication of this paper.

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