Int. J. Nonlinear Anal. Appl. 14 (2023) 4, 15–36
ISSN: 2008-6822 (electronic)
http://dx.doi.org/10.22075/ijnaa.2023.31047.4194

Parametric proportional hazard models using th Bayesian approach with applications to healthcare data

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(Communicated by Asadollah Aghajani)

Abstract

The aim of this study is on using Bayesian inference to analyze right-censored healthcare data using Frechet and exponential baseline proportional hazard (PH) models. For the baseline hazard parameters, a gamma prior was used, and for the regression coefficients, normal priors were used. The exact form of the joint posterior distribution was obtained. Bayes estimators of the parameters are obtained using the Markov chain Monte Carlo (MCMC) simulation technique. Two real-survival data applications were analyzed by the Frechet PH model and the exponential PH model. The convergence diagnostic tests are presented. We found that the Frechet PH model was better than the exponential PH model because it is flexible and could be beneficial in analyzing survival data.

Keywords: Proportional hazards model, Frechet distribution, exponential distribution, Bayesian inference, MCMC
2020 MSC: Primary 90C33; Secondary 26B25

1 Introduction

Survival analysis is one of the most important fields of statistics in medicine and biological sciences. In medical and healthcare studies, doctors are interested in determining the type of treatment and reaching recovery in the shortest possible period of time. We used the proportional hazard (PH) models Frechet and exponential are baseline hazard functions that are affected by covariates. It is one of the most common methods in dealing with parametric regression models for the analysis of survival data. In addition, the computational advances in the last decades have favored the use of Bayesian methods in this context, providing a flexible and powerful alternative to the traditional frequentist approach.

In a recent study, a flexible Bayesian parametric PH model has been explored. Bayesian estimates of the baseline hazard parameters and the regression coefficients were derived with the generalized log-logistic baseline hazard. The proposed model was applied to real-world applications involving two well-known right-censored survival data sets using the MCMC approach [16].

Noraslinda, Zarina, and Norhaiza [11] explored the proportional hazards model (PH) for right-censored data from a Bayesian perspective. The MCMC approach was used to estimate the background distributions for model parameters and was applied to Leukemia data.

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Received: November 2022 *Accepted:* February 2023

A study of the mortality rate of children under the age of five in Bangladesh was carried out using the cox proportional hazard model under both classical and Bayesian methods. Almost similar results were reached using these methods, except for one key finding. Under Bayesian analysis, a child's size at birth appeared as a potential determinant of under-five mortality, whereas it has an insignificant effect on child survival when the classical Cox model has been applied [17].

The researchers (Samuel and Eren) concentrated only on the functioning of the article, Bayesian Survival Analysis. A broad variety of Bayesian survival models may be fitted using the rstanarm R package, which includes typical parametric (exponential, Weibull, and Gompertz) models. The rstanarm package for Bayesian regression modeling has a simple way to get back-end estimates [3].

A model of proportional hazard Bayesian analysis using left truncated and right-censored data. As part of a process that's neutral to the right, they used a survival function with a limited number of dimensions as the "background" for the baseline survival function. The regression coefficient is given precedence over other variables. After that, they had the information you need it. This is exactly what the joint posterior distribution of regression coefficients should look like. And the hazard function at the beginning of the baseline data. As a byproduct, they come up with it to demonstrate the validity of our findings. The accuracy of the regression model's posterior distribution [12].

A study on patients with COVID-19 was developed to see what characteristics influence their length of hospital stay. The time between a patient's admission and discharge served as a response variable and a time-to-event analysis were carried out to identify the factors that could affect this time. Hospitalization duration predictors were identified using the Cox proportional hazard model. The study declared that Patients with more than two chronic diseases tended to stay in the hospital for longer than those without [21].

This paper is concerned with Bayesian inference of the proportional hazard model when observations are right-censored with applications on two distinct right-censored survival data sets. The first data concerns (98 patients with COVID-19 disease, and the second data set concerns (46) patients with leukemia disease. It is also concerned with knowing the risk of the treatments applied for these two diseases. The two data sets were analyzed to demonstrate the flexibility and applicability of the proposed Frechet PH model and the exponential PH model in modeling different survival data sets with different hazard rate shapes. All computations are performed in Bayesian analysis using MCMCpack with the function MCMCmetrop1R, an R package from the R software.

2 Hazard, Cumulative hazard, and Survival Functions

There are three key quantities of interest in standard survival analysis: the hazard rate function, the cumulative hazard function, and the survival function. These quantities are used to form the likelihood function for the survival models described in later sections.

The hazard is the instantaneous rate of occurrence for the event at time t. mathematically, it is

$$h(t) = \frac{P(t \leq T < t + \Delta t \mid T \geq t)}{\Delta t} = \frac{P(t \leq T < t + \Delta t)}{\Delta t P(T \geq t)} = -\frac{d}{dt} \log \log S(t)$$

The cumulative hazard function is defined as

$$H(t) = \int_0^t h(u)du, \quad t > 0$$

and the survival function is defined as

$$S(t) = \exp \exp\{-H(t)\} = \exp\left(-\int_0^t h(u)du\right).$$

It can be seen here that in the standard survival analysis setting where there is one event type of interest (i.e., no competing events) there is a one-to-one relationship between each of the hazard, the cumulative hazard, and the survival probability.

3 Parametric Proportional Hazard (PH) Model

The Cox PH model is most commonly used for analyzing censored survival data where the distribution of lifetime is considered unknown or unspecified. The parametric proportional hazards model is the parametric version of the

Cox proportional hazards model. According to Cox (1972) [6], the hazard function for the lifetime T in presence of a set of covariates $(\mathrm{X}_1, \mathrm{X}_2 \ldots \mathrm{X}_k)$ takes the form

$$h(x) = h_0(t) \exp \exp (x'\beta) = h_0(t) \exp (x_1\beta_1 + x_2\beta_2 + \cdots + x_k\beta_k) \tag{3.1}$$

where h_0(t) denotes the baseline hazard function at time t, X denotes the $k \times 1$ covariate vector for an arbitrary individual in the population, and β denotes a $k \times 1$ vector of regression coefficients.

The key difference between the two kinds of models is that the baseline hazard function is assumed to follow a specific distribution when a fully parametric PH model is fitted to the data, whereas the Cox model has no such constraint. The coefficients are estimated by partial likelihood in the Cox model but maximum likelihood in the parametric PH model. Other than this, the two types of models are equivalent. Hazard ratios have the same interpretation and the proportionality of hazards is still assumed. A number of different parametric PH models may be derived by choosing different hazard functions. The commonly applied models are exponential, and the proposed Frechet model in this study.

3.1 Exponential PH Model

The exponential distribution is a continuous probability distribution with only one unknown parameter λ. It is the simplest distribution for lifetime distribution models. The distribution is not flexible enough to describe commonly encountered hazard rate shapes for survival data. The pdf, cdf, sf, hrf, and chf of the exponential random variable are, respectively, as follows [2] and [5]. Let $X \sim$ exponential (λ),

$$f(t) = \lambda e^{-\lambda t} \tag{3.2}$$

$$F(t) = 1 - e^{-\lambda t} \tag{3.3}$$

$$S(t) = e^{-H(t)} = e^{-\lambda t} \tag{3.4}$$

$$h(t) = \lambda \tag{3.5}$$

$$H(t) = -\log \log S(t) = -\log \log \left(e^{-\lambda t}\right) = \lambda t \tag{3.6}$$

where $\lambda > 0$ is the scale parameter and $t \geq 0$. A short value of k shows low risk and long survival, whereas a large value shows high risk and short survival. For the PH model, the exponential baseline hazard is $h(t) = \lambda$. So, according to the formulation of the PH framework, the hazard rate for an individual with covariate vector X and link function $\eta(x)$ is

$$h(t) = h_0(t)\eta(x) = \lambda\eta(x).$$

Applying the log-linear function $\eta(x) = \exp (x'\beta)$, we can simplify into

$$h_{EPH}(t) = \lambda \exp \exp (x'\beta) = \lambda \exp (x_1\beta_1 + x_2\beta_2 + \cdots + x_k\beta_k)\,. \tag{3.7}$$

The exponential distribution of the hrf in this equation, with scale parameter λ, satisfies the PH assumption, as shown by the expression $(x'\beta)$. It is important to note that several studies have demonstrated that the exponential distribution is insufficient to characterize survival data. This limits the range of applications for this distribution.

The following are the alternative lifespan distributions of the exponential PH model. The survival function of the exponential PH model is

$$S_{EPH}(t) = [\exp(-\lambda t)]^{(x'\beta)}. \tag{3.8}$$

The pdf of the exponential PH model is

$$f_{EPH}(t) = \lambda \cdot \exp \exp(-\lambda t)\,(x'\beta)\,[\exp \exp(-\lambda t)]^{(x'\beta)-1}. \tag{3.9}$$

The cdf of the exponential PH model is

$$F_{EPH}(t) = 1 - [\exp(-\lambda t)]^{(x'\beta)}. \tag{3.10}$$

The chf of the exponential PH model is

$$H_{EPH}(t) = \lambda t\,(x'\beta)\,. \tag{3.11}$$

3.2 The Frechet PH Model

Frechet distribution was presented for the first time by the French mathematics scientist Maurice Frechet (1878-1973) who determined the distribution of his largest statistics in the year (1927). Frechet distribution is one of the continuous probability distributions and is one of the distributions with heavy tails. The distribution of Frechet is a special case of the distribution of generalized extremist values when the location parameter is equal to zero. It has uses in the life sciences, studying the statistical behavior of material properties in the engineering fields, and analyzing many extreme events, including rains, wind speed, floods, earthquakes, and life tests, and it is also used to model failure rates, which are commonly used in reliability and analysis of light signals [1] and [9].

The pdf, cdf, sf, hrf, and chf of the Frechet random variable are, respectively, as follows. Let $X \sim \mathrm{Fr}(\alpha, \lambda)$

$$f(t) = \alpha\lambda^{\alpha} t^{-(\alpha-1)} e^{-\left(\frac{\lambda}{t}\right)^{\alpha}} \tag{3.12}$$

$$F(t) = e^{-\left(\frac{\lambda}{t}\right)^{\alpha}} \tag{3.13}$$

$$S(t) = 1 - F(t) = 1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}} \tag{3.14}$$

$$h(t) = \frac{f(t)}{S(t)} = \frac{\alpha\lambda^{\alpha} t^{-(\alpha-1)} e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}}{1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}} \tag{3.15}$$

$$H(t) = -\log\log S(t) = \log\log\left(1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}\right)^{-1} \tag{3.16}$$

where $t, \alpha, \lambda > 0$. The parameter λ is called the scale parameter, and the parameter α is called the shape parameter. So, according to the formulation of the PH framework, the hazard rate for an individual with covariate vector $\mathbf{x}$ and link function $\eta(x)$ is

$$h(t) = h_0(t)\eta(x) = \frac{\alpha\lambda^{\alpha} t^{-(\alpha-1)} e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}}{1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}} \cdot \eta(x).$$

Applying the log-linear function $\eta(x) = \exp(x'\beta)$, we can simplify into

$$h_{FrPH}(t) = \frac{\alpha\lambda^{\alpha} t^{-(\alpha-1)} e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}}{1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}} \exp\exp(x'\beta) = \frac{\alpha\lambda^{\alpha} t^{-(\alpha-1)} e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}}{1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}} \exp\left(x_1\beta_1 + x_2\beta_2 + \cdots + x_k\beta_K\right). \tag{3.17}$$

The Frechet distribution of the hrf in this equation, with scale parameter λ, and shape parameter α. satisfies the PH assumption, as shown by the expression $(x'\beta)$. The following are the alternative lifespan distributions of the Frechet PH model. The survival function of the Frechet PH model is

$$S_{FrPH}(t) = \left[1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}\right]^{(x'\beta)}.$$

The pdf of the Frechet PH model is

$$f_{FrPH}(t) = \alpha\lambda^{\alpha} t^{-(\alpha-1)} e^{-\left(\frac{\lambda}{t}\right)^{\alpha}} (x'\beta) \left[1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}\right]^{(x'\beta)-1}. \tag{3.18}$$

The cdf of the Frechet PH model is

$$F_{FrPH}(t) = \left[e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}\right]^{(x'\beta)}. \tag{3.19}$$

The chf of the Frechet PH model is

$$H_{FrPH}(t) = \log\log\left(1 - e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}\right)^{-1} (x'\beta). \tag{3.20}$$

4 Inferential Procedures

In this section, we discuss the frequentist (via the maximum likelihood estimation) and Bayesian inference (applying independent gamma priors for the baseline hazard parameter and normal prior for the regression coefficients for the proposed Frechet PH model parameters and exponential PH model.

4.1 Maximum Likelihood Estimation (MLE) for the Right-Censored Survival Data

Survival data are often right-censored. That is, survival times are known for only a portion of the individuals under study, and the remainder of the survival times are known only to exceed certain values. Specifically, an observation is said to be right censored at time c, if the exact value of the observation is not known but only that it is greater than or equal to c [10].

In this section, we introduce the proportional hazard model for right censoring data and review prior processes neutral to the right for the baseline survival function. We begin by modeling the complete data censoring mechanisms. The postulates of the proportional hazard model are as follows. Let $T_1, T_2, \ldots, T_n$ be survival times with covariates $x_1, x_2, \ldots, x_n$.

Suppose the distribution $\mathrm{F_i}$ of $\mathrm{t_j}$ with covariate $\mathbf{x_i}$ is given by $1-F_i(t) = (1-F(t))\,(x'\beta)$, where β is the regression coefficient and F is the known baseline distribution function. The survival times are observed due to the censoring variables (W_i, C_i), which are assumed to be independent random vectors independent of the $x_i's$. Let $t_j = \min(Ti, Ci)$ and $W_i = I\,(T_j, C_i)$ which equals 1 if $\mathrm{T_i} \leq C_i$ and 0 otherwise.

Suppose that a right-censored random sample with data $D = (t_j, w_i, x_i)\,, i = 1, \ldots n$, where t_i is the censoring time or survival time according to whether $w_i = 1$ if the event has occurred, $w_i = 0$ if the observation is right censored, respectively and $\mathbf{x}_i = \mathrm{x_1, x_{2\alpha} \ldots, x_n}$ is an $n \times 1$ colomn vector of external covariates for the $\mathrm{i^{th}}$ individual. And suppose that ϑ is the vector of parameters associated with the baseline distribution, and β is the vector of regression coefficients. Then the likelihood function for (ϑ, β) for a set of right censored data on n subjects is given by

$$\begin{aligned}
L(\vartheta, \beta \mid D) &= \prod_{i=1}^{n} \left[f\left(t_i \mid \vartheta, \beta, x\right)\right]^{w_i} \left[S\left(t_i \mid \vartheta, \beta, x\right)\right]^{1-w_i} \\
&= \prod_{i=1}^{n} \left[h(\vartheta, \beta, x) \cdot S\left(t_i \mid \vartheta, \beta, x\right)\right]^{w_i} \left[S\left(t_i \mid \vartheta, \beta, x\right)\right]^{1-w_i} \\
&= \prod_{i=1}^{n} \left[h\left(t_i \mid \vartheta, \beta, x\right)\right]^{w_i} \left[S\left(t_i \mid \vartheta, \beta, x\right)\right] \\
&= \prod_{i=1}^{n} \left[h\left(t_i \mid \vartheta, \beta, x\right)\right]^{w_i} \exp\left[-\int_0^t h(u)du\right] \\
&= \prod_{i=1}^{n} \left[h_0\left(t_i \mid \vartheta\right) \exp\left(x'\beta\right)\right]^{w_i} \left[\exp\left(-\sum_{i=1}^{n} H_0\left(t_i \mid \vartheta\right) \exp\left(x'\beta\right)\right)\right]
\end{aligned} \tag{4.1}$$

An iterative optimization procedure (e.g., Newton-Raphson algorithm) can be used to obtain the maximum likelihood estimation $\hat{\vartheta}$ of ϑ. The natural logarithm of the likelihood function, so called log-likelihood function can be written as follows:

$$l(\vartheta, \beta \mid D) = \sum_{i=1}^{n} w_i \left[\log\log h_0\left(t_i \mid \vartheta\right) + \left(x'\beta\right)\right] - \sum_{i=1}^{n} H_0\left(t_i \mid \vartheta\right) \exp\left(x'\beta\right). \tag{4.2}$$

Note that $S_0(t)$ is the baseline survivor function, which is related to $h_0(.) is the baseline hazard$ function by $S_0(t) = \exp\left(\int_0^t h(u)du\right) = \exp\left(-H_0\left(t_i\right)\right)$ where H_0(t) is the baseline cumulative hazard rate function.

4.2 Bayesian Approach

This subsection sketches a Bayesian approach to a multivariate fixed effects proportional hazards model for right-censored data. The specification of its posterior distribution needs the following ingredients: First, the likelihood of the observed data; second, specific prior distributions for regression parameters, hyper parameters, and baseline hazard; third, a Markov Chain Monte Carlo (MCMC) the algorithm which can be used to sample the posterior distribution of the parameters of interest.

4.2.1 Maximum likelihood estimation

The likelihood function is one of the important ingredients of the formula of Bayes' theorem, we can find the likelihood function of baseline hazard distribution of the models studied in this research as follows.

Maximum likelihood estimation for Frechet PH model

We obtain the whole likelihood function of the Frechet PH model by using equations (3.15) and (3.16) in the likelihood function provided in (4.1). The function may be written as follows:

$$L(\alpha,\lambda \mid t)=\prod_{i=1}^{n} 1\left[\frac{\alpha\lambda^{\alpha}t^{-(\alpha-1)}e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}}{1-e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}}\exp\left(x'\beta\right)\right]^{w_i}\left[\exp\left(-\sum_{i=1}^{n}\log\log(1-e^{-\left(\frac{\lambda}{t}\right)^{\alpha}})^{-1}\exp\left(x'\beta\right)\right)\right] \tag{4.3}$$

and also using equations (3.15) and (3.16) in (4.2) we get a log-likelihood function of the Frechet PH model

$$l(\alpha,\lambda \mid t)=\sum_{i=1}^{n} w_i\left[\log\log\frac{\alpha\lambda^{\alpha}t^{-(\alpha-1)}e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}}{1-e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}}+\left(x'\beta\right)\right]-\sum_{i=1}^{n}\log\log\left(1-e^{-\left(\frac{\lambda}{t}\right)^{\alpha}}\right)^{-1}\exp\left(x'\beta\right) \tag{4.4}$$

Maximum likelihood estimation for exponential PH model

We obtain the whole likelihood function of the exponential PH model by using equations (3.5) and (3.6) in the likelihood function provided in (4.2). The function may be written as follows:

$$L(\vartheta \mid t)=\prod_{i=1}^{n} 1\left[\lambda\exp\left(x'\beta\right)\right]^{w_i}\left[\exp\left(-\sum_{i=1}^{n}\lambda t\exp\left(x'\beta\right)\right)\right] \tag{4.5}$$

and also using equations (3.5) and (3.6) in (4.2) we get a log-likelihood function of the exponential PH model

$$l(\vartheta \mid t)=\sum_{i=1}^{n} w_i\left[\log\log\lambda+\left(x'\beta\right)\right]-\sum_{i=1}^{n}\lambda t\exp\left(x'\beta\right). \tag{4.6}$$

4.2.2 Prior Distribution

For each of the parameters, a number of prior distributions are available. Default choices exist, but the user can explicitly specify the priors if they wish. We have assumed normal priors for the covariates and independent gamma priors for the baseline parameters of the Frechet PH model and exponential PH model.

Prior Distribution of the Frechet PH model

We assume the independent gamma priors for $\alpha \backsim G\left(a_1,b_1\right)$ and $\lambda \backsim G\left(a_2,b_2\right)$ as

$$p(\alpha) \backsim G\left(a_1,b_1\right)=\frac{b_1^{a_1}}{\Gamma\left(a_1\right)}\alpha^{a_1-1}e^{-b_1\alpha}, a_1,b_1,\alpha>0 \tag{4.7}$$

$$p(\lambda) \backsim G\left(a_2,b_2\right)=\frac{{b_2}^{a_2}}{\Gamma\left(a_2\right)}\lambda^{a_2-1}e^{-b_2\lambda}, a_2,b_2,\lambda>0. \tag{4.8}$$

Prior to that, we had the regression coefficients (assuming a normal distribution).

$$p\left(\beta'\right) \backsim N\left(a_3,b_3\right)$$

The density function of the combined prior distribution of all unknown parameters and the regression coefficients of the Frechet PH model is given as

$$p\left(\alpha,\lambda,\beta'\right)=P(\alpha)p(\lambda)p\left(\beta'\right) \tag{4.9}$$

Prior Distribution of the exponential PH model

We assume the independent gamma priors for $\lambda \backsim G\left(a_2,b_2\right)$ as

$$p(\lambda) \backsim G\left(a_2,b_2\right)=\frac{b_2a_2}{\Gamma\left(a_2\right)}\lambda^{a_2-1}e^{-b_2\lambda}, a_2,b_2,\lambda>0.$$

Prior to that, we had the regression coefficients (assuming a normal distribution)

$$p\left(\beta'\right) \backsim N\left(a_3,b_3\right).$$

The density function of the combined prior distribution of all unknown parameters and the regression coefficients of the exponential PH model is given as

$$p\left(\lambda,\beta'\right)=p(\lambda)p\left(\beta'\right). \tag{4.10}$$

4.2.3 The Posterior Distribution

The joint posterior density function is equal to the multiplication of the prior distribution and the likelihood function.

The Posterior Distribution of the Frechet PH model

The joint posterior density function of the parameters α, λ, and β' of the Frechet PH model given the data can be expressed using Bayes' theorem as

$$p(\alpha, \lambda, \beta' \mid x) \propto p(\alpha, \lambda, \beta')\, L(\alpha, \lambda, \beta')$$

or

$$p(\alpha, \lambda, \beta' \mid x) \propto p(\alpha) p(\lambda) p(\beta')\, L(\alpha, \lambda, \beta') \tag{4.11}$$

where the first two terms represent the prior specification for the unknown parameters and are assumed to be independent and $L(\alpha, \lambda, \beta')$ is the likelihood function from Equation (4.3)

$$p(\alpha, \lambda, \beta' \mid x) \propto \left\{ \prod_{j=1}^{p} \beta_j \right\} \alpha^{a_1+n-1} e^{-b_1\alpha} \lambda^{a_2+n-1} e^{-b_2\lambda} L(\alpha, \lambda, \beta'). \tag{4.12}$$

The Posterior Distribution of the exponential PH model

The joint posterior density function of the parameters λ and β' of the exponential PH model given the data can be expressed using Bayes' theorem as

$$p(\lambda, \beta' \mid x) \propto p(\lambda, \beta')\, L(\lambda, \beta')$$

or

$$p(\lambda, \beta' \mid x) \propto p(\lambda) p(\beta')\, L(\lambda, \beta') \tag{4.13}$$

where the first two terms represent the prior specification for the unknown parameters and are assumed to be independent and $L(\lambda, \beta')$ is the likelihood function from Equation (4.5)

$$p(\lambda, \beta' \mid x) \propto \left\{ \prod_{j=1}^{p} \beta_j \right\} \lambda^{a_2+n-1} e^{-b_2\lambda} L(\lambda, \beta'). \tag{4.14}$$

The marginal distribution of the model parameters and the normalizing joint posterior density function is difficult to calculate analytically, requiring high-dimensional integration and no closed form inferences. To obtain estimates, we use MCMC simulation methods, which involve sampling from the posterior distribution using the Metropolis-Hastings Algorithm.

5 A model for the comparison of two groups

An alternative way of expressing the model in Equation (36) leads to a model that can more easily be generalized. We assume that survival data are available on n individuals and denote the hazard function for the ith of these by $h_i(t), i = 1, 2, \ldots, n$. Also, write $h_0(t)$ for the hazard function for an individual on the standard treatment. The hazard function for an individual on the new treatment is then HR $\mathrm{h_0(t)}$. The relative hazard HR cannot be negative, so it is convenient to set $HR = \exp(\beta)$. The parameter β is then the logarithm of the hazard ratio, that is, $\beta = \log HR$, and any value of β in the range $(-\infty, \infty)$ will lead to a positive value of HR. Note that positive values of β are obtained when the hazard ratio, HR, is greater than unity, that is when the new treatment is inferior to the standard.

If x_i is the value of indicator variable X for the $\mathrm{i^{th}}$ individual in the study, $i = 1, 2, \ldots, n$, the hazard function for this individual can be written as

$$h_i(t) = h_0(t) e^{\beta x_i}$$

where $x_i = 0$ if the i^{th} individual is on the new treatment and $x_i = 1$ otherwise. This is the proportional hazards model for the comparison of two treatment groups [5] and [14].

6 Application to Real Data

In this section, two applications were considered on real-life survival data. The first application concerns a data set of (96) infected patients with COVID-19 disease. The second application concern a data set of (42) patients with leukemia disease. The two data sets were right-censored, which is the most common type of censoring in the analysis of survival data.

6.1 Data Set I: COVID-19 Survival Data

Coronavirus disease (COVID-19) has become a global pandemic that has affected millions of people worldwide. The presence of multiple risk factors for COVID-19 makes it difficult to plan treatment and optimize the use of medical resources. In this study, we are interested to determine the hazard ratio of the new therapy (Favipiravir) compared to the typical therapy. A sample of 96 positive cases of COVID-19 from Al-Diwaniyah Teaching Hospital is monitored from the 1^{st} to the 30^{th} of January 2022. Out of those 96 cases, 49 patients were treated with the new therapy and 48 patients were treated with the typical therapy. We will apply this data to two Frechet PH and exponential PH models. Table 1 describes the variables applied in the study

In checking the proportionality assumption for our problem, a widely used method for assessing the PH assumption is based on the TTT plot. As a result, we anticipate that the Frechet PH model will provide a good fit when compared to the exponential PH model employed in this study.

Figure 1 shows the TTT plot, box plot, and the histogram for the survival times of the COVID-19 data set. Based on the TTT plot, the hazard rate function is an increasing hazard. The data could be analyzed using a model such as the Frechet distribution, which would be represented by the PH framework. Posterior Analysis of Frechet distribution. In this study, we assume the noninformative independent framework with a normal prior N(0, 1000) for β' (regression coefficients) and an independent gamma prior for the baseline parameter for $\alpha \backsim G(a_1, b_1)$ and $\lambda \backsim G(a_2, b_2)$ with hyper-parameter values ($a_1 = b_1 = a_2 = b_2 = 0.0001$).

We started the parallel chain for a sufficiently large number of iterations until convergence was achieved. The convergence was achieved at 110,000 replication with a burn-in of 10000 . We use MCMCpack, an R package that contains functions to perform Bayesian inference using posterior simulation for a number of statistical models.

The MCMCmetrop1R function allows users to sample from a user-defined continuous density using a random walk Metropolis algorithm with a multivariate normal proposal distribution. This can be used to explore a posterior (or log-posterior) distribution, as well as any other target distribution of interest [7] and [18]. The sampler itself is coded in C + +, so the iterations run quite fast. Users only have to provide the target density as an R function [15].

Numerical Summary

Different quantities of interest are introduced to investigate posterior properties. Numerical values for these posterior properties of the Frechet PH model using an MCMC sample are presented. The Naive standard error (SE) is defined as the mean standard error that incorporates simulation error rather than posterior uncertainty.

$$\text{Naive } SE = \frac{\text{posterior } SD}{\sqrt{n}}.$$

The time series SE adjusts the Naive SE for autocorrelation. Trace plots and autocorrelation plots are the most common ways to judge the convergence of an MCMC simulation graphically [8].

The posterior mean, posterior standard deviation, Naive standard error SE, time series standard error, 95% credible interval $(2.5\%, 97.5\%)$ and the highest posterior density (HPD) interval for the model parameters in Table 2. Table 3 showed the basic statistics for Frechet PH model via MCMC sample. These statistics include the minimum, Quartiles, maximum, mode, skewness, and kurtosis.

Table (2) shows that the Naive SE is smaller than the standard deviations (SD) for all of the distributional parameters and regression coefficients, as expected, indicating that the MCMC algorithm has converged to the posterior distribution.

Visual Summary

The convergence diagnostics of an MCMC algorithm can be examined by some graphical techniques. These techniques include the trace plots, the density plots and the autocorrelation plots. We looked at these diagnostic

Table 1: Description of the variables of patients with COVID-19 disease

Variable	Description
ti	the time until relapse occurs (in days)
Wi	the logical anticipation variable, equal to 1 when the relapse has occurred and 0 when you are still in anticipation for this component.
Sex	the gender (value 0: female, value 1: male)
RX	the therapy type variable where new therapy (Favipiravir) is encoded as 0 and typical therapy is encoded as 1
WBC	the variable number of total white blood cells }granulocytes (neutrophils, eosinophils, and basophils), monocytes, and lymphocytes}per microliter of blood
Lym%	Lymphocytes Percentage: It determines the level of lymphocytes in relation to other WBC types. The lymphocyte: It is one of the types of white blood cells found in the blood. This test can be used to detect a disease that affects the lymphocytes and immune system, such as Viral infections, cancer, etc.
Gran%	The percentage of Granulocyte in relation to other WBC types. Gran is short for granulocyte (neutrophils, eosinophils, and basophils). An elevated level of granulocytes is indicative of infection, especially bacterial cause and leukemia
Mid%	(MID) cells its WBC other than lymphocyte and Granulocyte include less frequently occurring and rare cells correlating to monocytes, eosinophils, basophils, blasts, and other precursor white cells that fall in a particular size range
Lym#	that identifies the amount of lymphocytes in a microliter of blood it value in COVID-19 patients to differentiate disease severity and to predict mortality
Gran#	It is an indication of the white blood cell type of granulocytes, which are known as granulocytes referred to It indicates the presence of some health problems, such as bacterial infections. Bacterial or viral infection. Autoimmune diseases.
Mid#	mid in the blood test stands for Mid-range absolute count, and the mid-test means the combined value of types of white blood cells such as lymphocytes.
RBC	Red Blood Cell Count: An RBC test analysis measures the number of red blood cells present in a blood sample and is often used to assess an individual's health
HGB	Hemoglobin is a protein in red blood cells that carries oxygen throughout the body
HCT	Hematocrit test measures the proportion of red blood cells in your blood.
MCV	Mean corpuscular volume measures the average size of red blood cells.

plots to get a visual description of the posterior properties. These plots and graphs provide a nearly comprehensive representation of the parameter's posterior uncertainty for the application of the COVID-19 data set.

A time series plot (also known as a trace plot) is among the most widely used MCMC simulation diagnostics [8]. Figure 2 shows that the MCMC sampling process converges to the joint posterior distribution with no periodicity. As a result, we can say that the chains have converged. The basic forms of standard analytic distribution may be compared to density through density plots. Density charts can show the behavior in the tails, skewness, and other characteristics.

The density graphs for the Frechet PH model parameters are shown in Figure (2). It appears that data outliers and multimodal behavior are both present.

Although the autocorrelation plot is not strictly a convergence diagnostic tool, it does aid in indirectly assessing the convergence of the MCMC simulation process [19]. Figure (3) shows the autocorrelation plots for Frechet baseline parameter and the regression coefficients. Table 4 show all the variables have converged of the Frechet PH model

according to Geweke diagnostic.

Hazard Ratio (HR).

The hazard ratio is concerned with the application of the therapy type variable represented by Rx from table 1 for patients with COVID-19. From table 2, the Bayes estimate of the coefficient of the therapy type variable, Rx is $\beta 2 = -1.11931$ with a standard error SE = 0.00144. From section 6 , the hazard ratio becomes $e^{\hat{\beta}2} = 0.3265$, and since we have coded this therapy l Favipiravir) as 0 and the typical therapy as 1 , this means that using the typical therapy will increase the risk by 0.3265 times compared to using the new therapy.

Table 2: Numerical summaries of posterior characteristics based on the Frechet PH model via MCMC sample for the COVID-19 data sets.

Node	Mean	SD	Naive SE	Time-series SE	95% credible interval	HPD interval (95%)
β0	0.09219	28.73451	0.08664	1.85647	(-52.88996, 2.20624)	(-55.81047, 0.94856)
β1	-0.9336	0.39588	0.00119	0.02795	(-1.76352,-0.20061)	(-1.68965, -0.17429)
β2	-1.11931	0.47612	0.00144	0.0348	(-2.08094, -0.12583)	(-2.04715, -0.23335)
β3	0.87603	0.73404	0.00221	0.07518	(-0.16816, 2.62714)	(-0.30111, 2.2447)
β4	-0.69436	0.76923	0.00232	0.05618	(-2.28832, 0.87517)	(-2.21592, 0.95068)
β5	-0.62822	0.78046	0.00235	0.05745	(-2.23902, 0.94855)	(-2.19672, 1.01229)
β6	-0.48368	0.81023	0.00244	0.05948	(-2.13808, 1.03696)	(-2.10628, 1.24996)
β7	-0.40038	0.85665	0.00258	0.08454	(-2.22767, 0.96704)	(-1.88658, 1.35391)
β8	-1.19331	0.74708	0.00225	0.07453	(-2.88972, -0.01613)	(-2.6045, -0.0049)
β9	-2.11015	1.68809	0.00509	0.12981	(-5.64583, 0.88027)	(-5.73752, 0.81674)
β10	2.53733	2.25851	0.00681	0.18599	(-1.75805, 0.88027)	(-1.3456, 6.57655)
β11	2.96114	2.59053	0.00781	0.19437	(-1.55457, 8.29601)	(-2.22106, 7.52863)
β12	-1.15459	0.92886	0.0028	0.07131	(-3.06022, 0.49704)	(-3.01505, 0.41729)
β13	1.30967	0.79882	0.00241	0.05986	(-0.21149, 2.84499)	(-0.28383, 2.90254)
β14	-3.78414	2.40552	0.00725	0.17907	(-8.61465, 0.77841)	(-8.4969, 1.24689)
β15	1.95942	2.29628	0.00692	0.17285	(-2.50977, 6.63951)	(-2.73779, 6.04265)
β16	-0.32711	0.1817	0.00055	0.01184	(-0.70785, 0.05024)	(-0.69341, 0.07066)
β17	0.00062	0.00212	0.00001	0.00015	(-0.00349, 0.00471)	(-0.00319, 0.00526)
α	0.89277	0.06501	0.0002	0.00836	(0.79835, 1.06773)	(0.64804, 0.90048)
λ	112.0631	18.5206	0.05584	4.91788	(66.61264, 139.56594)	(96.21888, 299.34375)

Table 4. Show all the variables have converged of the Frechet PH model according to Geweke diagnostic.

Posterior Analysis of exponential distribution

In this study, we assume the noninformative independent framework with a normal prior N(0, 1000) for β' 's (regression coefficients) and an independent gamma prior for the baseline parameter for $\lambda \backsim G(a_2, b_2)$ with hyper-parameter values ($a_2 = b_2 = 0.0001$).

We started the parallel chain for a sufficiently large number of iterations until convergence was achieved. The convergence was achieved at 51,000 replication with a burn-in of 1000 . We use MCMCpack, an R package that contains functions to perform Bayesian inference using posterior simulation for a number of statistical models.

Numerical Summary

Different quantities of interest are introduced to investigate posterior properties. Numerical values for these posterior properties of the exponential PH model using an MCMC sample are presented.

The posterior mean, posterior standard deviation, Naive standard error SE, time series standard error, 95% credible interval $(2.5\%, 97.5\%)$, and the highest posterior density (HPD) interval for the model parameters are in Table 5. Table 6 showed the basic statistics for the exponential PH model via the MCMC sample. These statistics include the minimum, Quartiles, maximum, mode, skewness, and kurtosis.

Table 5 shows that the Naive SE is smaller than the standard deviations (SD) for the distributional parameter and regression coefficients, as expected, indicating that the MCMC algorithm has converged to the posterior distribution.

Visual Summary

Table 3: Some basic statistics for the Frechet PH model via MCMC sample for the COVID-19 data sets.

Node	Minimum	Q1	Median(Q2)	Q3	Maximum	Mode	Skewness	Kurtosis
β0	-93.45437	-9.93495	-1.93714	18.99365	117.89278	-1.98363	0.24174	2.87549
β1	-2.20542	-1.1877	-0.93816	-0.64403	0.23872	-0.81559	-0.13806	2.90803
β2	-2.75601	-1.4164	-1.11392	-0.82505	0.45461	-1.0739	-0.21425	3.43439
β3	-0.55101	0.31838	0.77902	1.2751	3.90211	1.20581	0.79627	3.45918
β4	-2.92075	-1.21508	-0.69233	-0.17313	1.86673	-1.11304	-0.0086	2.81526
β5	-2.94017	-1.15342	-0.63595	-0.10698	1.95988	-1.0766	0.0052	2.8172
β6	-2.98232	-0.99467	-0.5075	0.03924	2.07247	-0.89245	-0.06385	2.84258
β7	-3.6366	-0.93475	-0.31462	0.1997	1.51252	-0.93475	-0.59689	3.49351
β8	-4.37341	-1.65139	-1.09994	-0.60981	0.39315	-1.38511	-0.77929	3.44638
β9	-8.07469	-3.3019	-1.91921	-0.85089	2.41593	-1.46139	-0.36899	2.8734
β10	-3.69181	1.02194	2.38664	3.98541	9.77333	0.502	0.34137	3.05962
β11	-5.13083	1.08471	2.8577	4.64984	12.92809	0.02002	0.28477	3.12993
β12	-4.75981	-1.74251	-1.10616	-0.4849	1.72719	-0.03431	-0.3131	3.24383
β13	-1.14415	0.75977	1.30818	1.8879	3.88256	1.61509	0.09526	2.87551
β14	-11.26719	-5.32084	-3.86968	-2.05313	3.11543	-4.97804	-0.10185	2.85738
β15	-5.27679	0.50227	1.9605	3.53476	9.19491	3.99217	0.07234	3.08222
β16	-0.97812	-0.43179	-0.32809	-0.21156	0.30823	-0.33099	-0.10656	3.45317
β17	-0.00564	-0.00075	0.00051	0.00216	0.00784	-0.00058	0.07361	2.73578
α	0.75195	0.84733	0.88598	0.92429	1.41349	0.85113	1.64602	8.70074
λ	36.14755	101.08019	111.9775	127.38016	145.99857	127.38016	-0.69213	3.45299

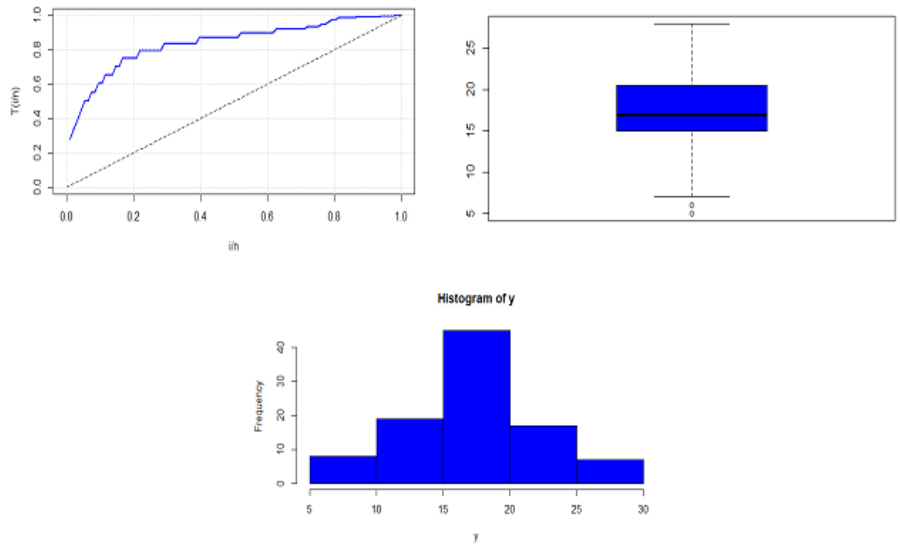

Figure 1: The TTT plot, box plot, and histogram for the survival times of the COVID-19 data set.

The convergence diagnostics of an MCMC algorithm can be examined by some graphical techniques. These techniques include trace plots, density plots, and autocorrelation plots. We looked at these diagnostic plots to get a visual description of the posterior properties. These plots and graphs provide a nearly comprehensive representation of the parameter's posterior uncertainty for the application of the COVID-19 data set.

Figure 5 shows that the MCMC sampling process converges to the joint posterior distribution with no periodicity. As a result, we can say that the chains have converged. The basic forms of standard analytic distribution may be compared to density through density plots. Density charts can show the behavior in the tails, skewness, and other characteristics. The density graphs for the exponential PH model parameters are shown in Figure 5 . It appears that data outliers and multimodal behavior are both present. Although the autocorrelation plot is not strictly a convergence diagnostic tool, it does aid in indirectly assessing the convergence of the MCMC simulation process [19].

Figure 2: Trace plots and Density distribution for Frechet baseline hazard parameters and the regression coefficients for the COVID-19 data sets.

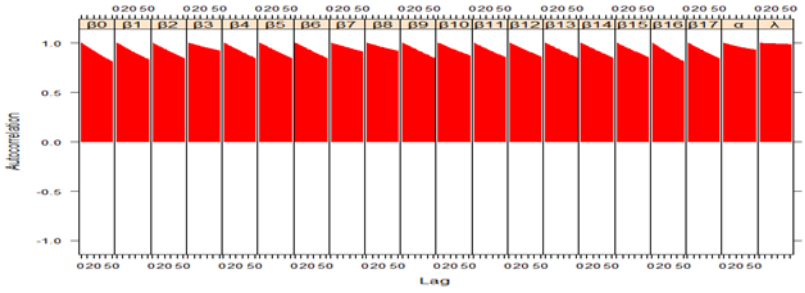

Figure 3: Autocorrelation plots for Frechet baseline parameters and all regression coefficients for the COVID-19 data set

Figure 6 shows the autocorrelation plots for the exponential baseline parameter and the regression coefficients.

Hazard Ratio (HR)

The hazard ratio is concerned with the application of the therapy type variable represented by Rx from table 1 for patients with COVID-19. From table 5, the Bayes estimate of the coefficient of the therapy type variable, Rx is $\hat{\beta}2 = -0.39286$ with a standard error SE $= 0.0019$. From section 6 , the hazard ratio becomes $e^{\hat{\beta}2} = 0.67512$, and since we have coded this therapy (Favipiravir) as 0 and the typical therapy as 1 , this means that using the typical

Table 4: Geweke diagnostic of the Frechet PH model parameters for the COVID-19 data sets.

Parameter	Geweke diagnostic Pr > |z|
β0	-1.08024
β1	-0.0230
β2	0.53332
β3	-0.59451
β4	1.94725
β5	1.99652
β6	1.93691
β7	1.24267
β8	0.08828
β9	-0.27783
β10	0.25511
β11	1.22276
β12	-0.90002
β13	-1.22675
β14	1.26191
β15	-1.66808
β16	-0.3652
β17	0.68502
α	-3.68747
λ	1.3347

therapy will increase the risk by 0.67512 times compared to using the new therapy.

Table 5: Numerical summaries of posterior characteristics based on exponential PH model via MCMC sample for the COVID-19 data sets.

Node	Mean	SD	Naive SE	Time-series SE	95% credible interval	HPD interval (95%)
β0	-0.89458	29.58176	0.13099	1.62419	(-58.801, 55.32675)	(-60.1906, 52.9614)
β1	-0.59398	0.38386	0.0017	0.02245	(-1.4207, 0.16299)	(-1.36985, 0.18039)
β2	-0.39286	0.42903	0.0019	0.02422	(-1.31014, 0.41485)	(-1.33051, 0.3409)
β3	0.75365	0.67981	0.00301	0.05531	(-0.18879, 2.36844)	(-0.26539, 2.15298)
β4	-0.54202	0.73877	0.00327	0.04331	(-2.04868, 0.85983)	(-2.02799, 0.87489)
β5	-0.50614	0.74583	0.0033	0.04388	(-2.02975, 0.94082)	(-1.93243, 0.98338)
β6	-0.47032	0.78427	0.00347	0.0469	(-2.05094, 1.05526)	(-1.85564, 1.18655)
β7	-0.48201	0.78231	0.00346	0.06124	(-2.34816, 0.72638)	(-2.14995, 0.81129)
β8	-0.99506	0.70802	0.00314	0.05725	(-2.69528, 0.03793)	(-2.42236, 0.14403)
β9	-1.40254	1.66668	0.00738	0.10338	(-5.11998, 1.45464)	(-4.51469, 1.67045)
β10	1.51207	2.167	0.0096	0.12783	(-2.60529, 5.65292)	(-2.54055, 5.6888)
β11	1.87958	2.63272	0.01166	0.16654	(-3.37972, 7.31401)	(-3.51968, 6.86063)
β12	-0.70315	0.9175	0.00406	0.05832	(-2.60101, 1.05649)	(-2.62527, 1.0068)
β13	0.91535	0.71999	0.00319	0.04239	(-0.44864, 2.38801)	(-0.5636, 2.20207)
β14	-2.7058	2.20076	0.00975	0.12824	(-7.13623, 1.41348)	(-6.65195, 1.6917)
β15	1.48249	2.04898	0.00907	0.12013	(-2.57847, 5.63987)	(-2.67861, 5.22875)
β16	-0.16794	0.19594	0.00087	0.01186	(-0.58596, 0.20523)	(-0.55385, 0.2201)
β17	0.00112	0.00214	0.00001	0.00012	(-0.00305, 0.00555)	(-0.00273, 0.00568)
λ	0.10197	0.00676	0.00003	0.00341	(0.09138, 0.11359)	(0.09122, 0.11309)

Table 6: Some basic statistics for exponential PH model via MCMC sample for the COVID-19 data sets.

Node	Minimum	Q1	Median(Q2)	Q3	Maximum	Mode	Skewness	Kurtosis
β0	-107.58965	-21.81257	-0.51454	20.26522	114.83106	-10.60055	0.02288	-107.58965
β1	-1.91367	-0.83562	-0.60019	-0.34945	0.70135	-0.25671	-0.12273	-1.91367
β2	-1.91604	-0.64859	-0.39302	-0.08165	1.00938	-0.64859	-0.1644	-1.91604
β3	-0.60337	0.20391	0.62894	1.13926	3.46104	0.12911	0.96333	-0.60337
β4	-3.64883	-0.99201	-0.53751	-0.07373	1.9085	-0.13078	-0.08244	-3.64883
β5	-3.64829	-0.95728	-0.4976	-0.03067	1.9372	-0.10485	-0.08729	-3.64829
β6	-3.69119	-0.9801	-0.47304	0.0414	1.92824	-0.04906	-0.14159	-3.69119
β7	-3.67359	-0.93466	-0.34032	0.06253	1.28254	0.06045	-0.81584	-3.67359
β8	-3.74727	-1.39354	-0.86716	-0.46819	0.40125	-0.25025	-0.91321	-3.74727
β9	-8.49269	-2.45185	-1.15087	-0.22406	3.32334	0.25844	-0.51903	-8.49269
β10	-5.6213	0.04974	1.5764	3.05895	9.15638	2.12142	0.08389	-5.6213
β11	-6.59058	0.13829	1.75542	3.47012	11.70996	1.28238	0.18484	-6.59058
β12	-4.06886	-1.2428	-0.67528	-0.0738	2.21355	-0.56719	-0.21304	-4.06886
β13	-1.44639	0.38995	0.93959	1.39191	3.74936	0.5277	0.10818	-1.44639
β14	-11.20896	-4.14139	-2.75417	-1.07049	4.2258	-1.34745	-0.10205	-11.20896
β15	-5.30994	0.06435	1.46072	2.97345	8.91524	0.41621	0.07277	-5.30994
β16	-0.8903	-0.29027	-0.17016	-0.03713	0.52959	-0.27923	-0.13032	-0.8903
β17	-0.00606	-0.00031	0.00101	0.00255	0.00874	-0.00075	0.14675	-0.00606
λ	0.09001	0.09667	0.10003	0.10878	0.11542	0.09549	0.21234	0.09001

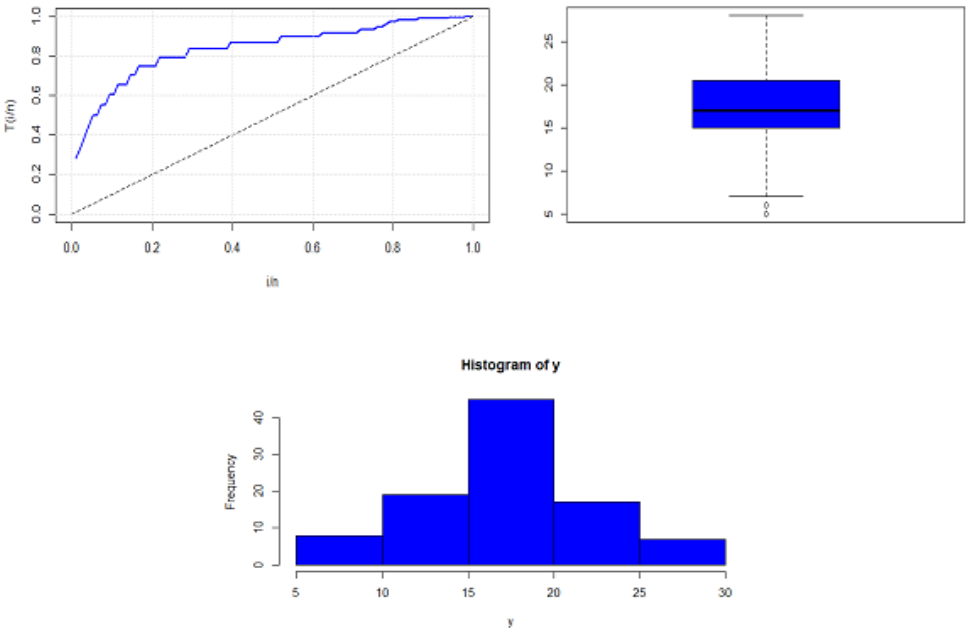

Figure 4: The TTT plot, box plot, and histogram for the survival times of the COVID-19 data set

6.2 Data Set II: Leukemia Survival Data

In a medical study conducted by Caplehorn [4] on a group of (46) leukemia patients, a new treatment different from the usual standard treatment was experimented. The effect of this treatment was monitored after recovery on the occurrence of relapse (the event under study) for a period of 35 months. We will apply this data to two Frechet PH and exponential PH models. The response and exploratory factors (variables) used in this clinical trial are shown in Table 8.

Posterior Analysis of Frechet distribution

In this study, we assume the noninformative independent framework with a normal prior $N(0, 1000)$ for β' s

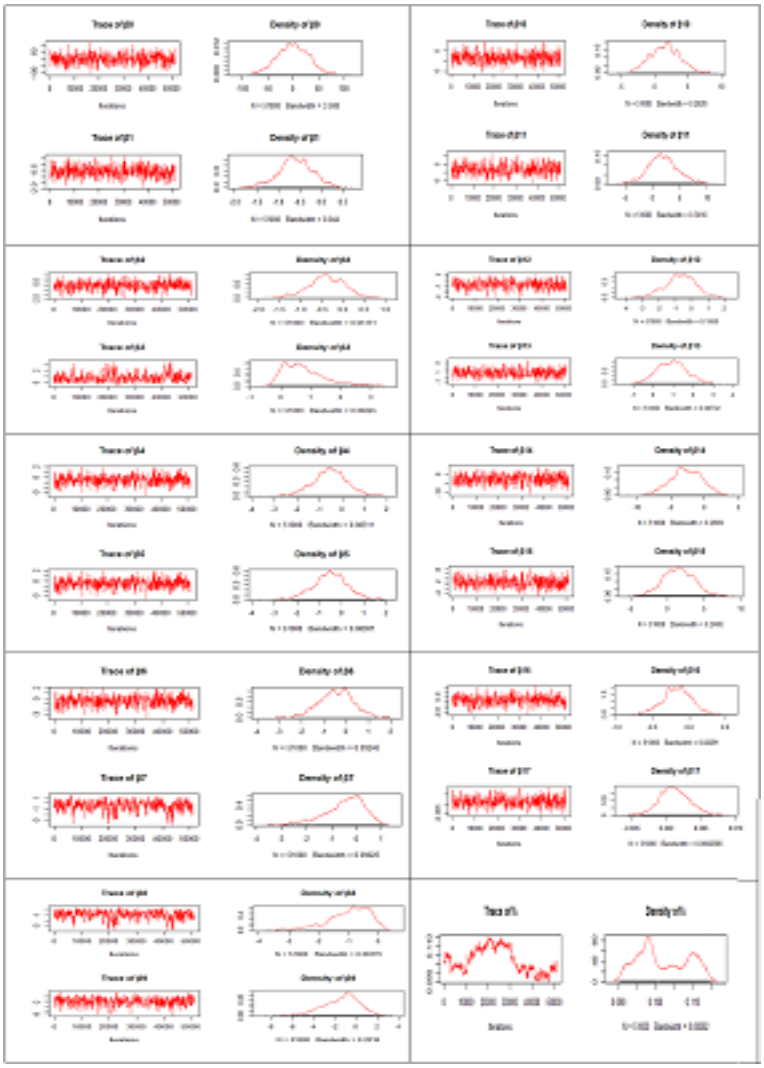

Figure 5: Trace plots and Density distribution for exponential baseline hazard parameter and the regression coefficients for the COVID-19 data sets.

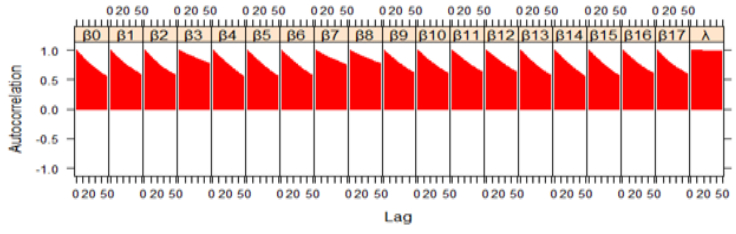

Figure 6: Autocorrelation plots for exponential baseline parameter and all regression coefficients for the COVID-19 data set.

(regression coefficients) and an independent gamma prior for the baseline parameter for $\alpha \backsim G(a_1, b_1)$ and $\lambda \backsim G(a_2, b_2)$ with hyper-parameter values $(a_1 = b_1 = a_2 = b_2 = 0.0001)$.

Using the same data, we continue our analysis with the Bayesian approach using MCMCpack, an R package The choice of hyperparameters and initial values are not sensitive to the estimation of the parameters. one chain with the starting values was carried out simultaneously. 110,000 iterations are performed for the chain after 10000 iterations for burn-in To obtain the algorithm's affinity for the target distribution.

Table 7: Geweke diagnostic of the exponential PH model parameters for the COVID-19 data sets.

Parameter	Geweke diagnostic Pr > |z|
β0	1.07669
β1	0.00594
β2	-0.4063
β3	-1.33789
β4	-1.18726
β5	-1.19669
β6	-1.33463
β7	0.74013
β8	1.24806
β9	0.87899
β10	-1.23373
β11	-0.24041
β12	0.5624
β13	0.83273
β14	-1.13958
β15	1.30166
β16	0.00502
β17	-0.52439
λ	0.61875

Table 8: Description of the variables of patients with leukemia disease

Variable	**Description**
t	the time until relapse occurs (in months)
Censor	the logical anticipation variable, equal to 1 when the relapse has occurred and 0 when are still in anticipation for this component.
Sex	the gender (value 0: female, value 1: male)
WBC	the variable number of total white blood cells} granulocytes (neutrophils, eosinophils, and basophils), monocytes, and lymphocytes} per microliter of blood
RX	the therapy type variable where new therapy is encoded as 0 and typical therapy is encoded as 1

MCMC Algorithm Convergence

For the leukemia data set, using the MCMC method, the complex posterior distribution is sampled. A convergence diagnostics test of the MCMC algorithm is performed using the Geweke diagnostics test. Table .8 indicates the Geweke diagnostics statistic for the Frechet PH model parameters. It shows that all the variables have converged for the Frechet PH model.

Hazard Ratio (HR)

The hazard ratio is concerned with the application of the therapy type variable represented by Rx from table 8 for patients with leukemia. From table 9 the Bayes estimate of the coefficient of the therapy type variable, Rx is $\hat{\beta}3 = 1.73452$ with a Naive standard error (0.0015), and the hazard ratio is $e^{\widehat{\beta 3}} = 5.66621$ and since we coded the new therapy as 0 and the typical therapy as 1 , this means that using the typical therapy will increase the risk by 5.66621 times compared to using the new therapy.

Table 11. Show all the variables have converged of the Frechet PH model according to Geweke diagnostic.

Posterior Analysis of exponential distribution

As in the first application in section (6.1), we assume the noninformative independent framework with a normal prior $N(0, 1000)$ for β' ((regression coefficients) and an independent gamma prior for the distributional parameter

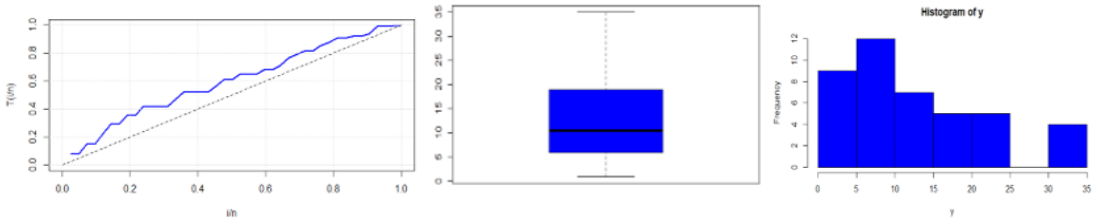

Figure 7: The TTT plot, box plot, and histogram for the survival times of the leukemia data set.

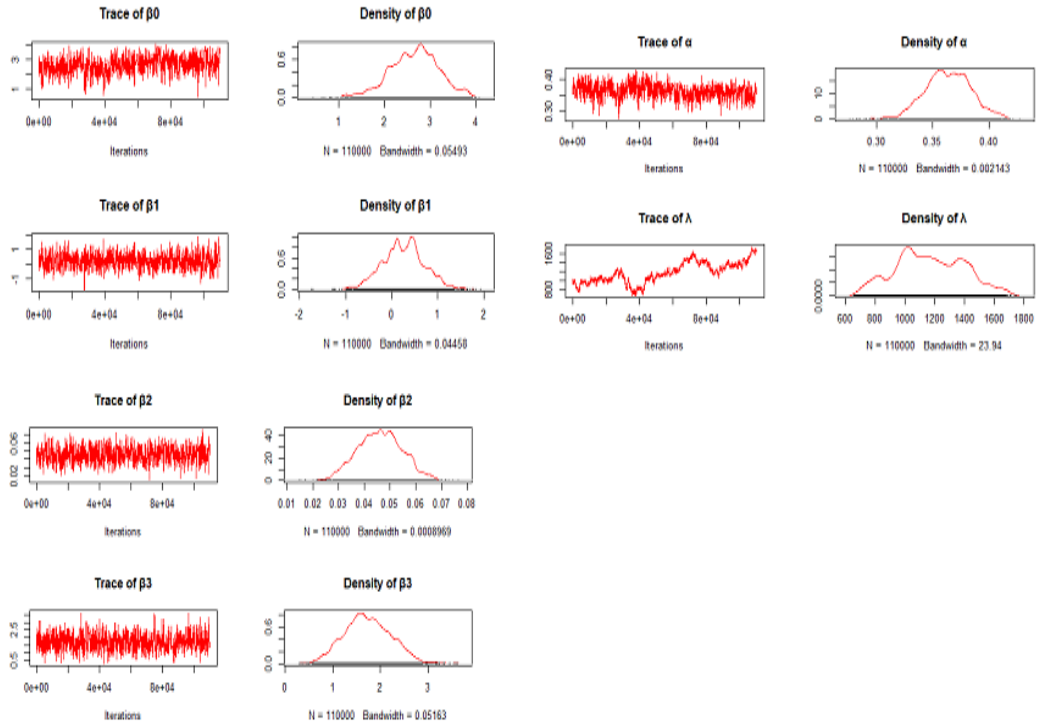

Figure 8: Trace plots and Density distribution for Frechet baseline hazard parameters and the regression coefficients for the leukemia data sets.

Table 9: Numerical summaries of posterior characteristics based on Frechet PH model via MCMC sample for the leukemia data sets.

Node	Mean	SD	Naive SE	Time-series SE	95% credible interval	HPD interval (95%)
β0	2.65325	0.52817	0.00159	0.02755	(1.56643, 3.69445)	(1.64952, 3.74999)
β1	0.25726	0.45745	0.00138	0.02139	(-0.61565, 1.15152)	(-0.63685, 1.11478)
β2	0.04608	0.00862	0.00003	0.0004	(0.02971, 0.0632)	(0.02829, 0.06135)
β3	1.73452	0.49644	0.0015	0.02378	(0.8031, 2.70396)	(0.76542, 2.63906)
α	0.36336	0.02061	0.00006	0.00112	(0.32353, 0.40428)	(0.3224, 0.40249)
λ	1169.26498	230.2423	0.69421	85.77063	(746.06628,1617.0168)	(724.56102,1582.59647)

Table 10: Some basic statistics for the Frechet PH model via MCMC sample for the leukemia data sets.

Node	Minimum	Q1	Median(Q2)	Q3	Maximum	Mode	Skewness	Kurtosis
β0	0.44118	2.30527	2.69119	3.01751	4.06731	2.83169	-0.28127	3.26251
β1	-1.73828	-0.03535	0.26332	0.5390	1.92811	0.16202	0.02751	3.05339
β2	0.01437	0.04008	0.04617	0.05189	0.07645	0.0489	0.01323	2.73183
β3	0.28513	1.38697	1.70903	2.07047	3.62471	1.41651	0.19883	2.9468
α	0.27649	0.34994	0.36346	0.37803	0.42708	0.35624	-0.13075	3.10884
λ	654.50743	1002.24738	1158.21782	1352.02039	1749.33906	1214.71824	0.07982	2.33019

$\lambda \backsim G(a_2, b_2)$ with hyper-parameter values $(a_2 = b_2 = 0.0001)$. The convergence was achieved at 51000 replication with a burn-in of 1000 through the posterior simulation.

Numerical Summary

The posterior mean, posterior standard deviation, Naive standard error SE, time series standard error, 95% credible

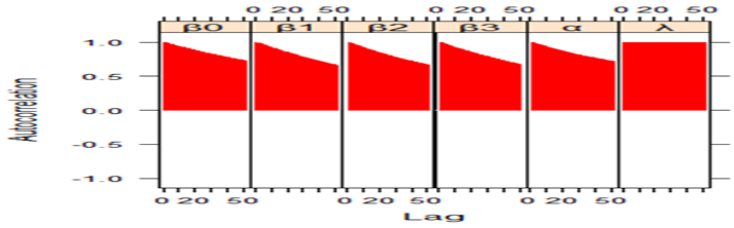

Figure 9: Autocorrelation plots for Frechet baseline parameters and all regression coefficients for the leukemia data set.

Table 11: Geweke diagnostic of the Frechet PH model parameters for the leukemia data sets.

Parameter	Geweke diagnostic Pr > |z|
β0	-5.07506
β1	-0.4845
β2	-0.40953
β3	0.86171
α	5.06115
λ	-8.36206

interval $(2.5\%, 97.5\%)$, and the highest posterior density (HPD) interval for the model parameters are in Table 12. Table 13 showed the basic statistics for the exponential PH model via the MCMC sample. These statistics include the minimum, Quartiles, maximum, mode, skewness, and kurtosis.

Table 12 shows that the Naive SE is smaller than the standard deviations (SD) for the exponential baseline parameter and all of the regression coefficients, as expected, indicating that the MCMC algorithm has converged to the posterior distribution.

As in the first application in section (8.1), we assume the noninformative independent framework with a normal prior $\mathrm{N}(0, 1000)$ for β' (regression coefficients) and an independent gamma prior for the distributional parameter $\lambda \sim G(a_2, b_2)$ with hyper-parameter values $(a_2 = b_2 = 0.0001)$. The convergence was achieved at 51000 replication with a burn-in of 1000 through the posterior simulation.

Visual Summary

The density graphs for the exponential PH model parameters are shown in Figure 11. It appears that data outliers and multimodal behavior are also present. Figure 11 also shows that the MCMC sampling process converges to the joint posterior distribution with no periodicity. Figure 10 shows the ITT plot, box plot, and histogram for the survival times of the leukemia data set. Based on the TTT plot, the hazard rate function is an increasing hazard. The data could be analyzed using a model such as the exponential distribution, which would be represented by the PH framework. As a result, we can say that the chains have converged. Figure 12 shows the autocorrelation plots for the exponential baseline parameter and the regression coefficients.

MCMC Algorithm Convergence

For the leukemia data set, using the MCMC method, the complex posterior distribution is sampled. A convergence diagnostics test of the MCMC algorithm is performed using the Geweke diagnostics test. Table 14 indicates the Geweke diagnostics statistic for the exponential PH model parameters. It shows that all the variables have converged for the exponential PH model.

Hazard Ratio (HR)

The hazard ratio is concerned with the application of the therapy type variable represented by Rx from table 8 for patients with leukemia. From table 12 the Bayes estimate of the coefficient of the therapy type variable, Rx is $\hat{\beta}3 = 1.22032$ with a standard error (0.00203), and the hazard ratio is $e^{\widehat{\beta 3}} = 3.38827$ and since we coded the new therapy as 0 and the typical therapy as 1 , this means that using the typical therapy will increase the risk by 3.38827 times compared to using the new therapy.

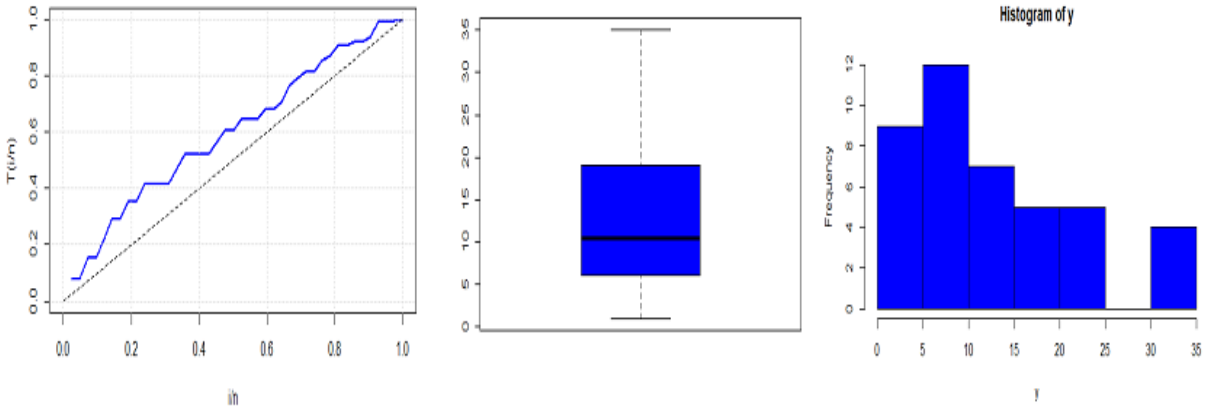

Figure 10: The TTT plot, box plot, and histogram for the survival times of the leukemia data set

Table 12: Numerical summaries of posterior characteristics based on exponential PH model via MCMC sample for the leukemia data sets.

Node	Mean	SD	Naive SE	Time-series SE	95% credible interval	HPD interval (95%)
β0	-1.49681	0.45235	0.002	0.01378	(-2.39664, -0.64239)	(-2.39853, -0.64692)
β1	-0.13395	0.45461	0.00201	0.00912	(-1.02361, 0.74491)	(-1.02426, 0.7405)
β2	0.02001	0.00555	0.00002	0.00011	(0.00869, 0.03052)	(0.00922, 0.03081)
β3	1.22032	0.45856	0.00203	0.00927	(0.35255, 2.14288)	(0.36423, 2.14899)
λ	0.08103	0.01466	0.00006	0.00676	(0.05617, 0.10609)	(0.05698, 0.10664)

Table 13: Some basic statistics for exponential PH model via MCMC sample for the leukemia data sets.

Node	Minimum	Q1	Median(Q2)	Q3	Maximum	Mode	Skewness	Kurtosis
β0	-3.2024	-1.79815	-1.49017	-1.18111	0.01915	-1.87004	-0.1475	3.00635
β1	-2.07883	-0.44002	-0.13751	0.17542	1.55301	0.16951	-0.00554	2.99515
β2	-0.00736	0.0164	0.02015	0.02381	0.03841	0.01924	-0.17031	3.12082
β3	-0.36527	0.90103	1.21036	1.5248	3.09429	1.38497	0.14508	2.95385
λ	0.04941	0.06953	0.07905	0.09442	0.11133	0.10629	0.11046	1.91948

Table 14: Geweke diagnostic of the exponential PH model parameters for the leukemia data sets.

Parameter	Geweke diagnostic Pr > |z|
β0	-8.26446
β1	1.07099
β2	0.07161
β3	0.07941
λ	2.00676

Table 14. Show all the variables have converged of the exponential PH model according to Geweke diagnostic.

7 Bayesian Model Selection

In this study, we will use deviation information criteria (DIC) is a metric used to compare Bayesian models. This criterion is available in most MCMC packages. It is closely related to the Akaike information criteria (AIC) which are defined as

$$AIC = -2\log\log p(\hat{\theta}) + 2p = D(\hat{\theta}) + 2p$$

where p is the number of parameters in a model (dimension of θ), and $\hat{\theta}$ is the maximum likelihood (minimum deviance) estimate. The DIC makes some changes to this formula. Firstly by replacing a maximised log-likelihood with the log-likelihood evaluated at the Bayes estimate $\hat{\theta}$ and by replacing p with an alternative correction

$$DIC = -2\log\log p(\hat{\theta}) + 2p_{DIC} = D(\underline{\theta}) + 2p_{DIC}.$$

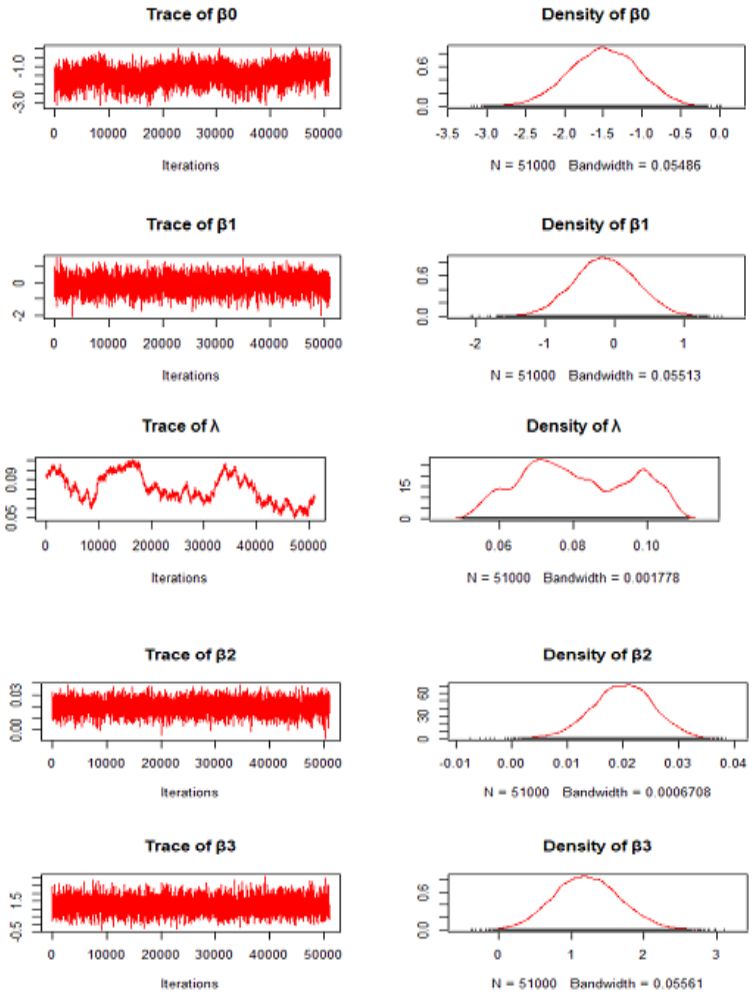

Figure 11: Trace plots and Density distribution for exponential baseline hazard parameter and the regression coefficients for the leukemia data sets.

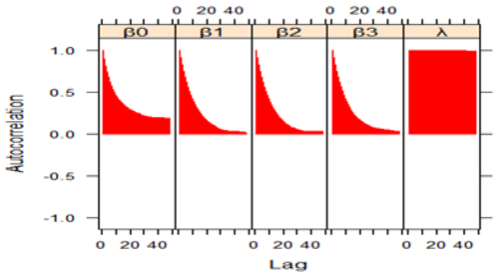

Figure 12: Autocorrelation plots for exponential baseline parameter and all regression coefficients for the leukemia data set.

Spiegelhalter et al. [20] use an informal information-theoretic argument to suggest a measure p_{DIC} defined by

$$p_{DIC} = E_{\theta|y}[-2\log\log p(\theta)] + 2\log\log p(\hat{\theta}) = \underline{D} - D(\hat{\theta})$$

where $\underline{D}$ = measure of fit and $\hat{\theta}$ is a "good" plug-in estimate of θ. If we take $\hat{\theta} = E[\theta \mid y] = \underline{\theta}$, then p_{DIC} = "posterior mean deviance - deviance of posterior means.

These changes make it more suitable for a Bayesian model. [13]. In general, the best-fitting model has the lowest DIC values.

Table 15: Homograft study. DIC for two Bayesian PH models for the COVID-19 data set

Model	DIC
Frechet	399.9583
exponential	524.5553

The values of DIC for the fitted models are reported in Table 15. They again confirm their preference for the proposed Frechet model

Table 16: Homograft study. DIC for two Bayesian PH models for the leukemia data sets.

Model	DIC
Frechet	191.2807
exponential	212.7492

The values of DIC for the fitted models are reported in Table 16. They again confirm their preference for the proposed Frechet model

8 Conclusions

In this study, we have discussed the Bayesian estimates of the parameters of two proportional hazard models. The first model includes a Frechet baseline hazard parameters and the second includes the exponential baseline hazard with the regression coefficients of the parametric proportional hazard model. The Markov chain Monte Carlo (MCMC) method was applied. This approach provides an adaptable method for estimating the parameters of the proposed model. A variety of priors were used in the Bayesian inference process, and several diagnostic techniques were applied to look into the convergence pattern. Both PH models are found simple and flexible and can be used in the analysis of parametric survival data. Computational aspects were performed using MCMCpack with the function MCMCmetrop1R, an R package from the R software.

According to our results, we have shown using the DIC criteria that the PH model using Frechet baseline hazard is better than the PH model using exponential baseline.

Two survival right-censored data sets were carried out. The first data set concerns data of patients infected with COVID-19 disease. The second data set concerns patients with leukemia disease. Results of the COVID-19 patients showed that all variables were significant for both the Frechet PH model and the exponential PH model according to Geweke diagnostic test. Results of the leukemia patients showed that all variables were significant for the Frechet PH model and exponential PH model according to Geweke diagnostic test. Finally, we conclude that the application of the indicated therapies for both COVID-19 and leukemia patients would reduce the hazard of the patient's relapse.

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