

Bayesian Survival Analysis Of Rayleigh-X Family With Time Varying Covariate*

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Abstract

In this paper, the Rayleigh-X family has been extended to a regression model. Based on the Rayleigh-X family, the Rayleigh generalized log-logistic (RGLL) distribution, Rayleigh Rayleigh (RR) distribution, and Rayleigh exponential (RE) distribution have been obtained and used as a baseline hazard function under the extended Cox hazard model. This paper aims to fit the three models, namely, RGLL Cox hazard model, RR Cox hazard model, RE Cox hazard model, to the time-varying covariate survival data under the Bayesian environment in R using the Stan language. Stan is a probabilistic programming language that offers Bayesian inference through the Hamiltonian Monte Carlo algorithm. Posterior predictive density plot is computed to check the performance of models and leave one out cross-validation & Watanabe Akaike information criteria are applied to select the best models. Stancode for the analysis are provided.

1 Introduction

Lord Rayleigh [26] introduced the Rayleigh distribution (RD), which plays a vital role in modeling and analyzing the lifetime data such as life testing experiments, project effort loadings modeling, reliability analysis, survival analysis, communication theory, engineering, physical sciences, medical imaging science, applied statistics, and clinical studies. Due to the importance of Rayleigh distribution in diverse fields, a wide range of extensions of Rayleigh distribution has been derived. Kundu and Raqab [19] introduced a generalized Rayleigh distribution in which different estimation procedures have been used to estimate the unknown parameters. Voda [30] obtained a new generalization of Rayleigh distribution using the conservative technique. Dey [12] studied the Bayesian estimation of Rayleigh distribution parameters using the square error loss function and linex loss function. Merovci [22] developed transmuted Rayleigh distribution using the square ordinal transformation method. Merovci and Elbatal [23] presented a Weibull-Rayleigh distribution. Mahmoud and Ghazal [20] discussed the estimation of the exponentiated Rayleigh parameters based on type II censored data. Ateeq et al. [4] have used the Transformed Transformer technique to derive the Rayleigh-Rayleigh distribution (RRD). El-Sherpieny and Almetwally [14] proposed bivariate generalized Rayleigh distribution based on Clayton copula. Almetwally et al. [2] studied the maximum likelihood and maximum product spacing estimates for generalized Rayleigh distribution based on the adaptive type-II progressive censoring schemes. Al-Babtain [1] derived a new extended Rayleigh distribution with two parameters called type I half logistic Rayleigh distribution. Bhat and Ahmad [6] proposed power Rayleigh distribution using the power transformation technique. Alongy et al. [3] proposed a new extension of the Rayleigh distribution with three parameters called extended odd Weibull Rayleigh distribution.

In this paper, the Rayleigh-X family [4] has been extended to a regression model for the analysis of censored survival data. Based on the Rayleigh-X family, the Rayleigh generalized log-logistic distribution (RGLLD), Rayleigh Rayleigh distribution (RRD), and Rayleigh exponential distribution (RED) are obtained with the base distribution like generalized log-logistic, Rayleigh, and exponential. The above three distributions have been used as the baseline distribution under the extended Cox hazard model to fit the censored

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survival data, which contains time-varying covariate. Cox [11] introduced the Cox proportional hazards (PH) model, which is the most popular survival model in medical applications and plays a vital role in analyzing the time to an event data. In its basic form, it describes the probability of the endpoint as expressed by the baseline hazard function and a set of covariates that have linear effects. A fundamental assumption in the Cox PH model is that the underlying hazard function for any two levels of some covariates is proportional over the period of follow-up time, and the hazard ratio remains constant over time. Although the PH assumption may not hold for one or more covariates over the entire study period, it may hold in shorter time intervals. Therefore, the PH assumption violation could be handled by using time-varying covariates. A time-varying variable is defined as any variable whose value for a given subject may vary over time. The Cox PH model with a time-varying covariate is referred to as the extended Cox hazard model.

The Bayesian approach has been used to model the time-varying covariate survival data, which requires a full likelihood function to estimate all unknown parameters in the model. The models are implemented in R [25] using Stan language [28]. Stan is a probabilistic programming language, which suits to Bayesian framework [8] and it uses No-U-Turn Sampler algorithm [16] that is an extension of Hamiltonian Monte Carlo algorithm [13, 24]. These algorithms are more efficient MCMC algorithm compare to the others algorithm like Metropolis-Hasting and Gibbs sampler, and converge much more quickly, especially for high-dimensional models, regardless of whether the priors are conjugate or not [16]. Posterior predictive check is computed to assess the model adequacy, and Watanabe Akaike information criteria (WAIC) [31] and leave-one-out cross-validation information criteria (LOOIC) [29] are applied to select the best model.

The main objective of this paper is to fit the RGLL Cox hazard model, RR Cox hazard model, and RE Cox hazard model to the same time-varying covariate data under the Bayesian paradigm in R using Stan language and select the best model for the real survival data.

The rest of the paper is organized as follows, Section 2 defines all three Cox hazard models, which are obtained by using the Rayleigh-X family. Section 3 describes the data, in which the data frame is created with R. In Section 4, we have specified priors and posterior distributions and shown fitting with Stan & models comparison with LOOIC & WAIC. The last Section 5 presented conclusions.

2 Rayleigh-X Family Distribution

Based on Ateeq et al. [4], the cumulative distribution function (CDF) of the Rayleigh-X family is given by

$$F(t) = 1 - e^{-\frac{[\log(1-G(t))]^2}{2\sigma^2}}, \quad t > 0, \sigma > 0 \quad (1)$$

and probability density function (PDF) is given by

$$f(t) = \frac{g(t) \{-\log(1-G(t))\}}{\sigma^2 [1-G(t)]} \times e^{-\frac{[\log(1-G(t))]^2}{2\sigma^2}}, \quad t > 0, \sigma > 0, \quad (2)$$

where σ is scale parameter, $G(t)$ and $g(t)$ are the CDF and PDF of baseline distribution.

2.1 Rayleigh Generalized Log-logistic Cox Hazard Model

The four-parameter RGLL distribution is a special model of the Rayleigh-X family with generalized log-logistic as a baseline function. The PDF and CDF of the GLL distribution are given respectively by

$$g(t) = \frac{k\rho(\rho t)^{k-1}}{[1 + (\gamma t)^k]^{\frac{\rho k}{\gamma k} + 1}}, \quad t > 0, \rho > 0, k > 0, \gamma > 0, \quad (3)$$

and

$$G(t) = 1 - [1 + (\gamma t)^k]^{-\frac{\rho k}{\gamma k}}, \quad t > 0, \rho > 0, k > 0, \gamma > 0. \quad (4)$$

Substituting PDF (3) and CDF (4) of GLL distribution into Equation (1) and Equation (2) leads us to the CDF and PDF of the RGLL distribution. The CDF of RGLL distribution is given by

$$F(t) = 1 - e^{-\frac{\rho^{2k}(\log(1+(\gamma t)^k))^2}{2\sigma^2\gamma^{2k}}}, \quad t > 0, \rho > 0, k > 0, \gamma > 0, \sigma > 0, \quad (5)$$

and the respective PDF is expressed as

$$f(t) = k\rho(\rho t)^{k-1} [1 + (\gamma t)^k]^{-1} \times \frac{\rho^k}{\gamma^k} \log(1 + (\gamma t)^k) \times \frac{1}{\sigma^2} \times e^{-\frac{\rho^{2k}(\log(1+(\gamma t)^k))^2}{2\sigma^2\gamma^{2k}}} \quad (6)$$

for $t > 0, \rho > 0, k > 0, \gamma > 0, \sigma > 0$. Therefore, a random variable with PDF(6) is denoted by $T \sim \text{RGLL}(\rho, k, \gamma, \sigma)$.

The survival function of RGLL is given by

$$S(t) = e^{-\frac{\rho^{2k}(\log(1+(\gamma t)^k))^2}{2\sigma^2\gamma^{2k}}}. \quad (7)$$

Hazard function of RGLL is given by

$$h(t) = \frac{k\rho^{2k}t^{k-1}}{\sigma^2\gamma^k [1 + (\gamma t)^k]} \times \log(1 + (\gamma t)^k). \quad (8)$$

The extended Cox hazard model is defined as

$$h(t|X, X(t), b, b_t) = e^{X'b + X(t)b_t} h_o(t). \quad (9)$$

Substituting the hazard function (8) into extended Cox hazard model (9) as a baseline hazard function, we obtained the RGLL Cox hazard model

$$h(t|X, X(t), \Psi) = e^{X'b + X(t)b_t} \frac{k\rho^{2k}t^{k-1}}{\sigma^2\gamma^k [1 + (\gamma t)^k]} \times \log(1 + (\gamma t)^k), \quad (10)$$

where $t > 0, X$ and $X(t)$ are fixed and time-varying covariate, and $\Psi = (\rho, k, \gamma, \sigma, b, b_t)$.

Let t_0 denote the time at which the time-varying covariate changes from unexposed ($X = 0$) to exposed ($X = 1$). Thus, $X(t) = 0$ for $t < t_0$, while $X(t) = 1$ for $t \geq t_0$. We have determined the associated survival function corresponding to hazard function (10) for $t < t_0$ and for $t \geq t_0$, and it is given by

$$S(t|X, X(t), \Psi) = \begin{cases} \exp\left(-e^{Xb + X(t)b_t} \times \frac{\rho^{2k}(\log(1+(\gamma t)^k))^2}{2\sigma^2\gamma^{2k}}\right), & t < t_0, \\ \exp\left(-\frac{e^{Xb} \rho^{2k}}{2\sigma^2\gamma^{2k}} \left[(1 - e^{b_t}) (\log(1 + (\gamma t_0)^k))^2 + e^{b_t} (\log(1 + (\gamma t_0)^k))^2\right]\right), & t \geq t_0. \end{cases} \quad (11)$$

Because the survival function has a different functional form over these two domains, therefore the cumulative hazard function will also have a different functional form over these two domains, and the definition of the inverse of the cumulative hazard function will have a piece-wise definition [5]. Using the technique given by Austin [5] for generating survival time from the Cox hazard model with a time-varying covariate, we have derived the function for generating time variable from the RGLL Cox hazard model as

$$t = \begin{cases} \frac{1}{\gamma} \left[\exp\left(\frac{2\gamma^{2k}\sigma^2(-\log(u))}{\rho^{2k}e^{Xb}}\right)^{\frac{1}{2}} - 1 \right]^{\frac{1}{k}}, & t < t_0, \\ \frac{1}{\gamma} \left[\exp\left(\frac{2\sigma^2\gamma^{2k}(-\log(u))}{\rho^{2k}e^{Xb+b_t}} - \frac{1-e^{b_t}}{e^{b_t}} (\log(1 + (\gamma t_0)^k))^2\right)^{\frac{1}{2}} - 1 \right]^{\frac{1}{k}}, & t \geq t_0, \end{cases} \quad (12)$$

where u is the random sample simulated from standard uniform distribution ($U \sim \text{Uniform}(0, 1)$).

Following Collett [9], the joint likelihood function of the RGLL Cox model based on right-censored event times is defined as

$$L(\Psi|D) = \prod_{i=1}^n h(t_i|X, X(t_i), \Psi)^{\delta_i} S(t_i|X, X(t_i), \Psi), \quad (13)$$

where δ_i is an indicator variable, which takes value 0 for censored event times and 1 for observed event times, and $D = (t, X, X(t), \delta_i)$.

Substituting Equation (10) and Equation (11) into Equation (13) to obtain the likelihood function for $t < t_o$ and $t \geq t_o$ respectively, where

$$L(\Psi|D) = \begin{cases} \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \frac{k\rho^{2k}t^{k-1}}{\sigma^2\gamma^k[1+(\gamma t)^k]} \times \log(1+(\gamma t)^k) \right\}^{\delta_i} & t < t_o, \\ \times \left\{ \exp\left(-e^{Xb+X(t)b_t} \times \frac{\rho^{2k}(\log(1+(\gamma t)^k))^2}{2\sigma^2\gamma^{2k}}\right) \right\}, & \\ \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \frac{k\rho^{2k}t^{k-1}}{\sigma^2\gamma^k[1+(\gamma t)^k]} \times \log(1+(\gamma t)^k) \right\}^{\delta_i} & t \geq t_o. \\ \times \left\{ \exp\left(-\frac{e^{Xb}\rho^{2k}}{2\sigma^2\rho^{2k}} \left[(1-e^{b_t}) (\log(1+(\gamma t_o)^k))^2 + e^{b_t} (\log(1+(\gamma t_o)^k))^2 \right] \right) \right\}, & \end{cases} \quad (14)$$

2.2 Rayleigh Rayleigh Cox Hazard Model

The PDF and CDF of Rayleigh distribution are given respectively by

$$g(t) = \frac{t}{\beta^2} e^{-\frac{t^2}{2\beta^2}}, \quad t > 0, \beta > 0 \quad (15)$$

and

$$G(t) = 1 - e^{-\frac{t^2}{2\beta^2}}, \quad t > 0, \beta > 0. \quad (16)$$

The two parameters Rayleigh-Rayleigh distribution is obtained by substituting PDF (15) and CDF (16) into Equation (1) and Equation (2). The CDF and PDF of RR distribution takes the following form

$$F(t) = 1 - e^{-\frac{t^4}{8\beta^4\sigma^2}}, \quad t > 0, \beta > 0, \sigma > 0 \quad (17)$$

and

$$f(t) = \frac{t^3}{2\beta^4\sigma^2} e^{-\frac{t^4}{8\beta^4\sigma^2}}, \quad t > 0, \beta > 0, \sigma > 0. \quad (18)$$

Therefore, a random variable with PDF (20) is denoted by $T \sim \text{RR}(\beta, \sigma)$.

The survival function and hazard rate function of RR distribution are respectively given by

$$S(t) = e^{-\frac{t^4}{8\beta^4\sigma^2}}, \quad (19)$$

and

$$h(t) = \frac{t^3}{2\beta^4\sigma^2}. \quad (20)$$

Using Equation (20) as a baseline hazard function into Equation (9) yields the RR Cox hazard model

$$h(t|X, X(t), \Psi) = e^{Xb+X(t)b_t} \times \frac{t^3}{2\beta^4\sigma^2}, \quad (21)$$

where $\Psi = (\beta, \sigma, b, b_t)$.

Survival function for $t < t_o$, and $t \geq t_o$ corresponding to Equation (21) is given by

$$S(t|X, X(t), \Psi) = \begin{cases} \exp\left(-e^{Xb+X(t)b_t} \times \frac{t^4}{8\beta^4\sigma^2}\right), & t < t_o, \\ \exp\left(-\frac{e^{Xb}}{8\beta^4\sigma^2} \left[(1-e^{b_t})t_o^4 + e^{b_t}t^4 \right] \right), & t \geq t_o. \end{cases} \quad (22)$$

The function for generating survival time variable from the RR Cox hazard model is given by

$$t = \begin{cases} \left[\frac{8\beta^4\sigma^2}{e^{b_t/x}} \right]^{\frac{1}{4}}, & t < t_o, \\ \left[\frac{8\beta^4\sigma^2(-\log(u))}{e^{(b_t/x+b_t)}} - \frac{1-e^{b_t}}{e^{b_t}} t_o^4 \right]^{\frac{1}{4}}, & t \geq t_o. \end{cases} \quad (23)$$

Substituting Equation (21), and Equation (22) into Equation (13), the joint likelihood function of the RR Cox hazard model based on right-censored data is written as

$$L(\Psi|D) = \begin{cases} \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \times \frac{t^3}{2\beta^4\sigma^2} \right\}^{\delta_i} \left\{ \exp \left(-e^{Xb+X(t)b_t} \frac{t^4}{8\beta^4\sigma^2} \right) \right\}, & t < t_o, \\ \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \times \frac{t^3}{2\beta^4\sigma^2} \right\}^{\delta_i} \left\{ \exp \left(-\frac{e^{Xb}}{8\beta^4\sigma^2} [(1 - e^{b_t})t_o^4 + e^{b_t}t^4] \right) \right\}, & t \geq t_o. \end{cases} \quad (24)$$

2.3 Rayleigh Exponential Cox Hazard Model

Let $g(t)$ and $G(t)$ be the PDF and CDF of exponential distribution with scale parameter θ . The PDF of exponential distribution is expressed as

$$g(t) = \frac{1}{\theta} e^{-\frac{t}{\theta}}, \quad t > 0, \theta > 0, \quad (25)$$

and respective CDF is given by

$$G(t) = 1 - e^{-\frac{t}{\theta}}, \quad t > 0, \theta > 0. \quad (26)$$

The CDF of RE distribution is derived by substituting Equation (25) and Equation (26) into Equation (1) and it is written as

$$F(t) = 1 - e^{-\frac{t^2}{2\theta^2\sigma^2}}, \quad t > 0, \theta > 0, \sigma > 0. \quad (27)$$

The PDF corresponding to CDF (27) is derived by substituting Equation (25) and Equation (26) into Equation (2) and it is given by

$$f(t) = \frac{t}{\theta^2\sigma^2} e^{-\frac{t^2}{2\theta^2\sigma^2}}, \quad t > 0, \theta > 0, \sigma > 0. \quad (28)$$

Therefore, a random variable with PDF (28) is denoted by $T \sim \text{RE}(\theta, \sigma)$.

Survival function and hazard rate function are respectively given by

$$S(t) = e^{-\frac{t^2}{2\theta^2\sigma^2}}, \quad (29)$$

and

$$h(t) = \frac{t}{\theta^2\sigma^2}. \quad (30)$$

The RE Cox hazard model is obtained by using Equation (30) as a baseline hazard function into Equation (9), that takes the following form

$$h(t|X, X(t), \Psi) = e^{Xb+X(t)b_t} \times \frac{t}{\theta^2\sigma^2}, \quad (31)$$

where $\Psi = (\theta, \sigma, b, b_t)$.

Survival function corresponding to Equation (31) for $t < t_o$ and $t \geq t_o$ is defined as

$$S(t|X, X(t), \Psi) = \begin{cases} \exp \left(-e^{Xb+X(t)b_t} \frac{t^2}{2\theta^2\sigma^2} \right), & t < t_o, \\ \exp \left(-\frac{e^{Xb}}{2\theta^2\sigma^2} \{ (1 - e^{b_t})t_o^2 + e^{b_t}t^2 \} \right), & t \geq t_o. \end{cases} \quad (32)$$

The generation of survival time from the RE Cox hazard model is defined as

$$t = \begin{cases} \left[\frac{2\theta^2\sigma^2(-\log(u))}{e^{Xb}} \right]^{\frac{1}{2}}, & t < t_o, \\ \left[\frac{2\theta^2\sigma^2(-\log(u))}{e^{Xb+X(t)b_t}} - \frac{(1 - e^{b_t})t_o^2}{e^{b_t}} \right]^{\frac{1}{2}}, & t \geq t_o. \end{cases} \quad (33)$$

Substituting Equation (31) and Equation (32) into Equation (13), the joint likelihood function of the RE Cox hazard model based on right-censored data is obtained as

$$L(\Psi|D) = \begin{cases} \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \times \frac{t}{\theta^2\sigma^2} \right\}^{\delta_i} \left\{ \exp \left(-e^{Xb+X(t)b_t} \frac{t^2}{2\theta^2\sigma^2} \right) \right\}, & t < t_o, \\ \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \times \frac{t}{\theta^2\sigma^2} \right\}^{\delta_i} \left\{ \exp \left(-\frac{e^{Xb}}{2\theta^2\sigma^2} \{ (1 - e^{b_t})t_o^2 + e^{b_t}t^2 \} \right) \right\}, & t \geq t_o. \end{cases} \quad (34)$$

3 Bone Marrow Transplant Data

We have considered bone marrow transplant data for illustration, which is first discussed by Copelan et al. [10] and then Klein and Moeschberger [18] and Collett [9]. `KMsurv` [7] package of R is required to access the data. The data set is concerned with 137 patients, who have acute lymphoblastic leukemia (ALL) and acute myelocytic leukemia (AML). Further, AML is divided into low and high risk, and several potential risk factors were measured at the time of transplantation. The observed survival time of each patient was recorded in days. The prognostic variables to be used in this example concern the disease group, an indicator variable that denotes whether the platelet count returned to a normal level and the time taken to return to normal level. To examine the effect of a time-dependent variable ($\text{Plate}(t)$) on patient survival, that is, the time taken for platelets to return to their normal level is defined as

$$\text{Plate}(t) = \begin{cases} 0 & \text{if } t < \text{time at which platelets returned to normal,} \\ 1 & \text{if } t \geq \text{time at which platelets returned to normal.} \end{cases}$$

3.1 Creation of Data Frame in R

Stan language requires data in a listed form. For that, data frame `dbmt` is created in R using the `list()` function.

```
>require(KMsurv)
>data(bmt)
#Survival time in days
>time<-bmt$t1
# 0= censored, 1=observed
>status<-bmt$d1
# Disease group, 1= ALL, 2= AML (low risk), and 3= AML (high risk),
are converted into two categorical variable
# 0= ALL, and 1= AML (low risk)
>low<-as.numeric(bmt$group==2)
# 0= ALL, and 1= AML (high risk)
>high<-as.numeric(bmt$group==3)
#Platelet recovery indicator (0 = no, 1 = yes)
>precovery<-bmt$dp
#Time in days to return of platelets to normal level (if precovery = 1)
>ptime<-bmt$tp
## Model matrix
# fixed covariate
>xf<-cbind(1,low,high)
# time varying covariate
>xv<-matrix(precovery)
# data frame
>dbmt<-list(y=time,yp=ptime,xf=xf,xv=xv,N=nrow(xf),M=ncol(xf),event=status)
```

4 Bayesian Analysis of Rayleigh-X Family

4.1 Prior Specification

In this paper, we have used regularizing prior for the regression coefficient that is normal distribution with mean=0 and sd=5, which is recommended by McElreath [21] and half-Cauchy distribution with scale =25 for shape and scale parameter. Regularizing prior prevents a model from getting too excited by the data and slows the rate of learning from the data. Notably, it reduces the over-fitting of the model to the data.

The half-Cauchy with scale = 25 is nearly flat prior, which provides enough information for the numerical approximation algorithm to continue to explore the target density, the posterior distribution [17].

4.2 Model Specification

Using Bayes theorem, the joint posterior density can be written as

$$P(\Psi|D) \propto L(\Psi|D) \times P(\Psi). \quad (35)$$

$$\text{Posterior} \propto \text{Likelihood} \times \text{Prior}$$

4.2.1 Posterior Density of RGLL Cox Hazard Model

For $t < t_o$,

$$\begin{aligned} P(\Psi|D) &\propto \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \frac{k\rho^{2k}t^{k-1}}{\sigma^2\gamma^k [1+(\gamma t)^k]} \times \log(1+(\gamma t)^k) \right\}^{\delta_i} \\ &\quad \times \left\{ e^{-\frac{\rho^{2k}(\log(1+(\gamma t)^k))^2}{2\sigma^2\gamma^{2k}}} \right\}^{e^{Xb+X(t)b_t}} \times \frac{2 \times 25}{\pi(k^2 + 25^2)} \times \frac{2 \times 25}{\pi(\rho^2 + 25^2)} \\ &\quad \times \frac{2 \times 25}{\pi(\gamma^2 + 25^2)} \times \frac{2 \times 25}{\pi(\sigma^2 + 25^2)} \times \prod_{j=0}^J \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_j^2}{2 \times 25}\right)} \times \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_t^2}{2 \times 25}\right)}, \end{aligned}$$

where $\Psi = (\rho, k, \gamma\sigma, b, b_t)$. For $t \geq t_o$,

$$\begin{aligned} P(\Psi|D) &\propto \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \frac{k\rho^{2k}t^{k-1}}{\sigma^2\gamma^k [1+(\gamma t)^k]} \times \log(1+(\gamma t)^k) \right\}^{\delta_i} \\ &\quad \times \left\{ \exp\left(-\frac{e^{Xb}\rho^{2k}}{2\sigma^2\rho^{2k}} \left[(1-e^{b_t}) (\log(1+(\gamma t_o)^k))^2 + e^{b_t} (\log(1+(\gamma t_o)^k))^2 \right] \right) \right\} \\ &\quad \times \frac{2 \times 25}{\pi(k^2 + 25^2)} \times \frac{2 \times 25}{\pi(\rho^2 + 25^2)} \times \frac{2 \times 25}{\pi(\gamma^2 + 25^2)} \times \frac{2 \times 25}{\pi(\sigma^2 + 25^2)} \\ &\quad \times \prod_{j=0}^J \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_j^2}{2 \times 25}\right)} \times \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_t^2}{2 \times 25}\right)}. \end{aligned}$$

4.2.2 Posterior Density of RR Cox Hazard Model

For $t < t_o$,

$$\begin{aligned} P(\Psi|D) &\propto \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \times \frac{t^3}{2\beta^4\sigma^2} \right\}^{\delta_i} \times \left\{ e^{-\frac{t^4}{8\beta^4\sigma^2}} \right\}^{e^{Xb+X(t)b_t}} \\ &\quad \times \frac{2 \times 25}{\pi(\beta^2 + 25^2)} \times \frac{2 \times 25}{\pi(\sigma^2 + 25^2)} \times \prod_{j=0}^J \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_j^2}{2 \times 25}\right)} \times \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_t^2}{2 \times 25}\right)}, \end{aligned}$$

where $\Psi = (\beta, \sigma, b, b_t)$. For $t \geq t_o$,

$$\begin{aligned} P(\Psi|D) &\propto \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \times \frac{t^3}{2\beta^4\sigma^2} \right\}^{\delta_i} \times \exp\left(-\frac{e^{Xb}}{8\beta^4\sigma^2} [(1-e^{b_t})t_o^4 + e^{b_t}t^4]\right) \\ &\quad \times \frac{2 \times 25}{\pi(\beta^2 + 25^2)} \times \frac{2 \times 25}{\pi(\sigma^2 + 25^2)} \times \prod_{j=0}^J \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_j^2}{2 \times 25}\right)} \times \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_t^2}{2 \times 25}\right)}. \end{aligned}$$

4.2.3 Posterior Density of RE Cox Hazard Model

For $t < t_o$,

$$P(\Psi|D) \propto \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \times \frac{t}{\theta^2 \sigma^2} \right\}^{\delta_i} \times \left\{ e^{-\frac{t^2}{2\theta^2 \sigma^2}} \right\} e^{-Xb+X(t)b_t} \\ \times \frac{2 \times 25}{\pi(\theta^2 + 25^2)} \times \frac{2 \times 25}{\pi(\sigma^2 + 25^2)} \times \prod_{j=0}^J \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_j^2}{2 \times 25}\right)} \times \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_j^2}{2 \times 25}\right)},$$

where $\Psi = (\theta, \sigma, b, b_t)$. For $t \geq t_o$,

$$P(\Psi|D) \propto \prod_{i=1}^n \left\{ e^{Xb+X(t)b_t} \times \frac{t}{\theta^2 \sigma^2} \right\}^{\delta_i} \times \exp\left(-\frac{e^{-Xb}}{2\theta^2 \sigma^2} \{(1 - r^{b_t})t_o^2 + e^{b_t} t^2\}\right) \\ \times \frac{2 \times 25}{\pi(\theta^2 + 25^2)} \times \frac{2 \times 25}{\pi(\sigma^2 + 25^2)} \times \prod_{j=0}^J \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_j^2}{2 \times 25}\right)} \times \frac{1}{5\sqrt{2\pi}} e^{-\left(\frac{b_j^2}{2 \times 25}\right)}.$$

4.3 Implementation using Stan

Modeling the parametric survival model in **Stan** is straightforward. The object `model_RGLL`, `model_RR`, and `model_RE` in Section 4.3.1, Section 4.3.2, and Section 4.3.3 are the **Stan** model code for the RGLL Cox hazard model, RR Cox hazard model, and RE Cox hazard model, where the models are specified directly as a string in **R**. These model code consists several blocks: functions block, data block, transformed data block, parameters block, transformed parameters block, model block, and generated quantities block. These blocks are the set of statements surrounded by brackets and preceded by the block name. The first is the function block, in which user can define their own function. Next is the data block, which contains the declaration of the variables in the data object `dbmt`. Proceed to the parameter block, where parameters are defined, and the model block specifies the prior distribution and the likelihood. The final block is generated quantities block. This block can be used to perform the posterior predictive check.

4.3.1 Stancode for RGLL Cox Hazard Model

```
model_RGLL="functions{
vector log_sgll(vector t,vector tp, real k,real rho,real gamma,real sigma,matrix xf,
vector bf, matrix xv,real bv){
vector[num_elements(t)]log_sgll;
for(i in 1:num_elements(t)){for(j in 1:cols(xf)){
if (xv[i,1]==1){
log_sgll[i]=(-1)*exp(xf[i,j]*bf[j])*rho^(2*k)/(2*gamma^(2*k)*sigma^2)*(exp(bv)*
(log(1+(gamma*t[i]^k))^2+(1-exp(bv))*(log(1+(gamma*tp[i]^k))^2);
}
else if (xv[i,1]==0){
log_sgll[i]=exp(xf[i,j]*bf[j])*(-rho^(2*k)*1/(2*gamma^(2*k)*sigma^2)*
(log(1+(gamma*t[i]^k))^2);
}}}
return log_sgll;
}
vector log_hgll(vector t, real k,real rho,real gamma,real sigma,matrix xf,vector bf,
matrix xv,real bv){
vector[num_elements(t)]log_hgll;
for(i in 1:num_elements(t)){for(j in 1:cols(xf)){
```



```

log_hgll[i]=(xf[i,j]*bf[j]+bv*xv[i,1])+log(k)+2*k*log(rho)+(k-1)*log(t[i])
-2*log(sigma)-k*log(gamma)-log(1+(gamma*t[i])^k)+log(log(1+(gamma*t[i])^k));
}}
return log_hgll;
}
real surv_gll_cox_lpdf(vector t,vector tp,vector d, real k,real rho,real gamma,
real sigma,matrix xf, vector bf, matrix xv,real bv){
vector[num_elements(t)]llikgll;
real prob;
llikgll=d .* log_hgll(t,k,rho,gamma,sigma,xf,bf,xv,bv)+
log_sgll(t,tp,k,rho,gamma,sigma,xf,bf,xv,bv);
prob=sum(llikgll);
return prob;
}}
data{
int N;
vector<lower=0>[N]y;
vector<lower=0>[N]yp;
vector<lower=0,upper=1>[N]event;
int M;
matrix[N,M]xf;
matrix[N,1]xv;
}
parameters{
vector[M]bf;
real bv;
real<lower=0>k;
real<lower=0>rho;
real<lower=0>gamma;
real<lower=0>sigma;
}
model{
target+=cauchy_lpdf(k|0,25)- 1 * cauchy_lccdf(0|0,25);
target+=cauchy_lpdf(rho|0,25)- 1 * cauchy_lccdf(0|0,25);
target+=cauchy_lpdf(gamma|0,25)- 1 * cauchy_lccdf(0|0,25);
target+=cauchy_lpdf(sigma|0,25)- 1 * cauchy_lccdf(0|0,25);
target+=normal_lpdf(bf|0,5);
target+=normal_lpdf(bv|0,5);
target+=surv_gll_cox_lpdf(y|yp,event,k,rho,gamma,sigma,xf,bf,xv,bv);
}
generated quantities{
real log_lik[N];
vector[N] yrepgll1;
for(n in 1:N){for(j in 1:M){
if (xv[n,1]==1){
log_lik[n]=event[n]*((xf[n,j]*bf[j]+bv*xv[n,1])+log(k)+2*k*log(rho)+(k-1)*log(y[n])-
2*log(sigma)-k*log(gamma)-log(1+(gamma*y[n])^k)+log(log(1+(gamma*y[n])^k)))+(-1)*
(exp(xf[n,j]*bf[j])*rho^(2*k)*1/(2*gamma^(2*k)*sigma^2)*(exp(bv)*
(log(1+(gamma*y[n])^k))^2+(1-exp(bv))*(log(1+(gamma*yp[n])^k))^2));
}
else if (xv[n,1]==0){

```

```

log_lik[n]=event[n]*((xf[n,j]*bf[j]+bv*xv[n,1])+log(k)+2*k*log(rho)+(k-1)*log(y[n])
-2*log(sigma)-k*log(gamma)-log(1+(gamma*y[n])^k)+log(log(1+(gamma*y[n])^k)))+
exp(xf[n,j]*bf[j])*(-rho^(2*k)*1/(2*gamma^(2*k)*sigma^2)*(log(1+(gamma*y[n])^k))^2);
}}
{real u ;
u=uniform_rng(0,1);
for(n in 1:N){for(j in 1:M){
if (xv[n,1]==1){
yrep_gll1[n]=1/gamma*(exp((2*sigma^2*gamma^(2*k))*(-log(u))*1/(rho^(2*k))*
exp(xf[n,j]*bf[j]+bv))-(1-exp(bv))/(exp(bv))*
(log(1+(gamma*yp[n])^k)^(1/2))-1)^(1/k);
}
else if (xv[n,1]==0){
yrep_gll1[n]=1/gamma*(exp((2*gamma^(2*k)*sigma^2*(-log(u))*1/(rho^(2*k))*
exp(xf[n,j]*bf[j]))^(1/2))-1)^(1/k);
}}}
}}"

```

4.3.2 Stancode for RR Cox Hazard Model

```

model_RR="functions{
vector log_srr(vector t,vector tp, real beta,real sigma, matrix xf, vector bf,
matrix xv,real bv){
vector[num_elements(t)]log_srr;
for(i in 1:num_elements(t)){for(j in 1:cols(xf)){
if (xv[i,1]==1){
log_srr[i]=exp(xf[i,j]*bf[j])/(8*beta^4*sigma^2)*(exp(bv)*(-t[i]^4)+(1-exp(bv))*
(-tp[i]^4));
}
else if(xv[i,1]==0){
log_srr[i]=exp(xf[i,j]*bf[j])*((-t[i]^4)/(8*beta^4*sigma^2));
}}}
return log_srr;
}
vector log_hrr(vector t,real beta,real sigma,matrix xf,vector bf,matrix xv,real bv){
vector[num_elements(t)]log_hrr;
for(i in 1:num_elements(t)){for(j in 1:cols(xf)){
log_hrr[i]=(xf[i,j]*bf[j]+bv*xv[i,1])+3*log(t[i])-log(2)-4*log(beta)-2*log(sigma);
}}}
return log_hrr;
}
real surv_rr_cox_lpdf(vector t,vector tp,vector d, real beta,real sigma, matrix xf,
vector bf, matrix xv,real bv){
vector[num_elements(t)]llikrr;
real prob;
llikrr=d .* log_hrr(t,beta,sigma,xf,bf,xv,bv)+log_srr(t,tp,beta,sigma,xf,bf,xv,bv);
prob=sum(llikrr);
return prob;
}}
data{
int N;
vector<lower=0>[N]y;

```

```

vector<lower=0>[N] yp;
vector<lower=0,upper=1>[N] event;
int M;
matrix[N,M] xf;
matrix[N,1] xv;
}
parameters{
vector[M] bf;
real bv;
real<lower=0>beta;
real<lower=0>sigma;
}
model{
target+=cauchy_lpdf(beta|0,25)- 1 * cauchy_lccdf(0|0,25);
target+=cauchy_lpdf(sigma|0,25)- 1 * cauchy_lccdf(0|0,25);
target+=normal_lpdf(bf|0,5);
target+=normal_lpdf(bv|0,5);
target+=surv_rr_cox_lpdf(y|yp,event,beta,sigma,xf,bf,xv,bv);
}
generated quantities{
real log_lik[N];
vector[N] yreprr;
for(n in 1:N){for(j in 1:M){
if (xv[n,1]==1){
log_lik[n]=event[n]*((xf[n,j]*bf[j]+bv*xv[n,1])+3*log(y[n])-log(2)-4*log(beta)-
2*log(sigma))+exp(xf[n,j]*bf[j])/(8*beta^4*sigma^2)*(exp(bv)*(-y[n]^4)+
(1-exp(bv))*(-yp[n]^4)));}
else if (xv[n,1]==0){
log_lik[n]=event[n]*((xf[n,j]*bf[j]+bv*xv[n,1])+3*log(y[n])-log(2)-4*log(beta)
-2*log(sigma))+exp(xf[n,j]*bf[j])*((-y[n]^4)/(8*beta^4*sigma^2)));
}}}
{real u ;
u=uniform_rng(0,1);
for(n in 1:N){for(j in 1:M){
if (xv[n,1]==1){
yreprr[n]=((8*beta^4*sigma^2*(-log(u)))/(exp(xf[n,j]*bf[j]+bv))-
((1-exp(bv))/(exp(bv))*yp[n]^4))^(1/4);
}
else if (xv[n,1]==0){
yreprr[n]=(8*beta^4*sigma^2*(1/exp(xf[n,j]*bf[j]))*(-log(u)))^(1/4);
}}}
}}"

```

4.3.3 Stancode for RE Cox Hazard Model

```

model_RE="functions{
vector log_sre(vector t,vector tp, real theta,real sigma, matrix xf,
vector bf, matrix xv,real bv){
vector[num_elements(t)]log_sre;
for(i in 1:num_elements(t)){for(j in 1:cols(xf)){
if (xv[i,1]==1){
log_sre[i]=exp(xf[i,j]*bf[j])/(2*theta^2*sigma^2)*(exp(bv)*(-t[i]^2)+

```

```

(1-exp(bv))*(-tp[i]^2));
}
else if (xv[i,1]==0){
log_sre[i]=exp(xf[i,j]*bf[j])*(-t[i]^2/(2*theta^2*sigma^2));
}}
return log_sre;
}
vector log_hre(vector t, real theta,real sigma,matrix xf,vector bf,matrix xv,
real bv){
vector[num_elements(t)]log_hre;
for(i in 1:num_elements(t)){for(j in 1:cols(xf)){
log_hre[i]=(xf[i,j]*bf[j]+bv*xv[i,1])+log(t[i])-2*log(theta)-2*log(sigma);
}}
return log_hre;
}
real surv_re1_cox_lpdf(vector t,vector tp,vector d,real theta,real sigma,matrix xf,
vector bf, matrix xv,real bv){
vector[num_elements(t)]llikre1;
real prob;
llikre1=d .* log_hre(t,theta,sigma,xf,bf,xv,bv)+log_sre(t,tp,theta,sigma,xf,bf,xv,bv);
prob=sum(llikre1);
return prob;
}}
data{
int N;
vector<lower=0>[N]y;
vector<lower=0>[N]yp;
vector<lower=0,upper=1>[N]event;
int M;
matrix[N,M]xf;
matrix[N,1]xv;
}
parameters{
vector[M]bf;
real bv;
real<lower=0>theta;
real<lower=0>sigma;
}
model{
target+=cauchy_lpdf(theta|0,25)- 1 * cauchy_lccdf(0|0,25);
target+=cauchy_lpdf(sigma|0,25)- 1 * cauchy_lccdf(0|0,25);
target+=normal_lpdf(bf|0,5);
target+=normal_lpdf(bv|0,5);
target+=surv_re1_cox_lpdf(y|yp,event,theta,sigma,xf,bf,xv,bv);
}
generated quantities{
real log_lik[N];
vector[N] yrepre;
for(n in 1:N){for(j in 1:M){
if (xv[n,1]==1){
log_lik[n]=event[n]*((xf[n,j]*bf[j]+bv*xv[n,1])+log(y[n])-2*log(theta)-2*log(sigma))+

```

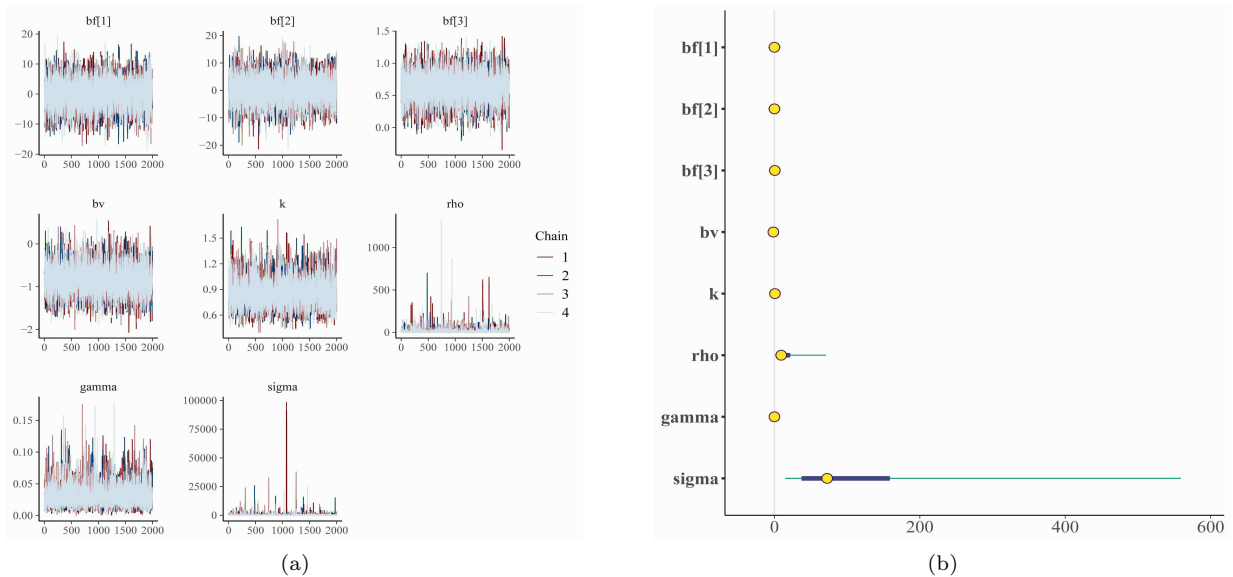


Figure 1: (a) Trace plot of each parameter of RGLL Cox hazard model shows that the Markov chains converge to the target distribution, (b) Caterpillar plot of each RGLL Cox hazard model's parameter.

```

(exp(xf[n,j]*bf[j])/(2*theta^2*sigma^2)*(exp(bv)*(-y[n]^2)+(1-exp(bv))*(-yp[n]^2)));
}
else if (xv[n,1]==0){
log_lik[n]=event[n]*((xf[n,j]*bf[j]+bv*xv[n,1])+log(y[n])-2*log(theta)-2*log(sigma))+
exp(xf[n,j]*bf[j])*(-y[n]^2/(2*theta^2*sigma^2)));
}}
{real u ;
u=uniform_rng(0,1);
for(n in 1:N){for(j in 1:M){
if (xv[n,1]==1){
yrepr1[n]=((2*theta^2*sigma^2*(-log(u)))/(exp(xf[n,j]*bf[j]+bv))-
((1-exp(bv))/(exp(bv))*yp[n]^2))^(1/2);
}
else if (xv[n,1]==0){
yrepr1[n]=(2*theta^2*sigma^2*(1/exp(xf[n,j]*bf[j]))*(-log(u)))^(1/2);
}}}
}"}

```

4.3.4 Fitting of RGLL Cox Hazard Model with Stan

In order to run the stancode in R, there is need to require a package `rstan` [27]. `rstan` is an interface of R and Stan through which a Stan model code can be run in R. The `model_RGLL` described in Section 4.3.1 is run through `stan()` function. After running the model, the samples are returned and assigned to the `coxrgll` object. We can obtain summary of the parameter distributions using the `print()` function.

```

require(rstan)
coxrgll = stan(model_code = model_RGLL, data=dbmt, chains = 4, iter=4000)
print(coxrgll,c("bf","bv","k","rho","gamma","sigma"),digit=3)

```

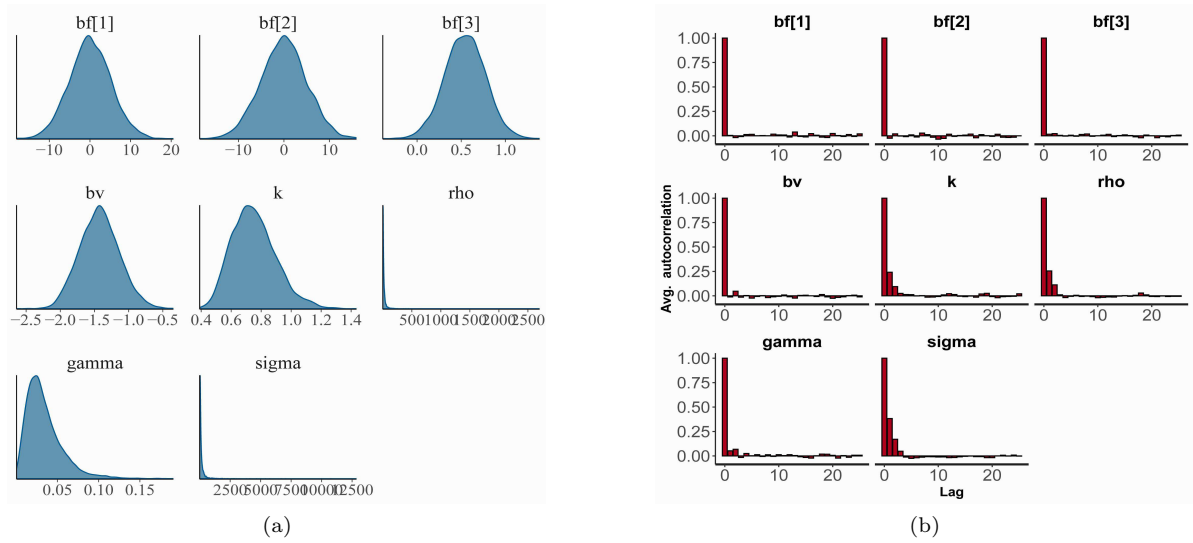


Figure 2: (a) Posterior density plot for each parameter of RGLL Cox hazard model. (b) Autocorrelation plot for each parameter of RGLL Cox hazard model at around 5 is declining towards zero.

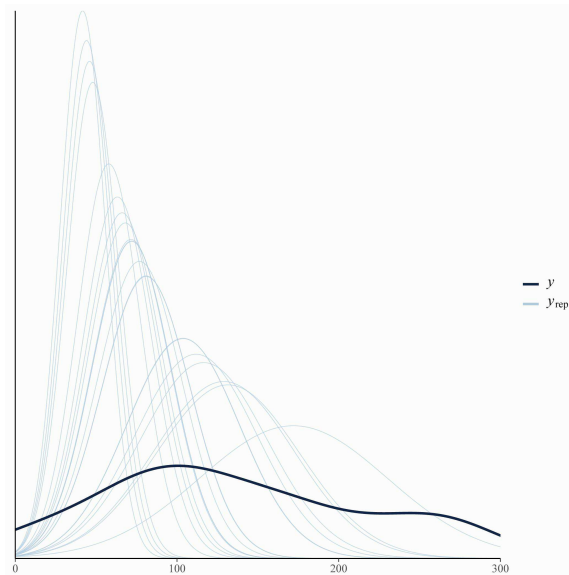


Figure 3: PPD plot of RGLL Cox hazard model shows that the posterior predictive density fits the data well.

Table 1: Posterior summary of RGLL Cox hazard model.

parameters	mean	se_mean	sd	2.5%	50%	97.5%	n_eff	Rhat
bf[1]	-0.014	0.057	4.933	-9.676	0.027	9.572	7482	1.000
bf[2]	-0.008	0.061	5.124	-9.911	-0.074	10.113	7122	1.000
bf[3]	0.626	0.003	0.233	-0.164	0.622	1.074	7571	1.000
bv	-0.840	0.005	0.356	-1.510	-0.848	-0.136	5546	1.000
k	0.856	0.003	0.172	0.565	0.837	1.240	3756	1.001
rho	14.180	0.454	34.127	0.239	5.622	79.288	5642	1.000
gamma	0.030	0.000	0.017	0.007	0.027	0.072	5210	1.000
sigma	440.921	67.050	2584.776	12.779	125.611	2193.639	1486	1.002

Output Summary

After fitting the RGLL Cox hazard model to the bone marrow transplant data with **Stan**, the posterior summary of the RGLL Cox hazard model is given in Table 1. It contains posterior estimate, Monte Carlo error (se_mean), standard deviation, credible interval, effective sample size as n_eff (number of independent samples from the posterior distribution), and Rhat (\hat{R}), which measure the convergence of Markov chains to the posterior distribution. According to Gelman et al. [15], the acceptable limit of effective sample size is > 100 and potential scale reduction factor $\hat{R} < 1.1$. It can be seen from Table 1 that Rhat is close to 1 for all parameters of the RGLL Cox hazard model, which means Markov chains converges to the target distribution (posterior distribution) and n_eff is $\gg 100$, that is enough to get the convergence. Besides \hat{R} , the trace plot also shows the convergence of a model. As we can see in Figure 1a, the different chains are overlaid in a single plot, and they are not distinguishable as different chains, which is the indication of convergence of Markov chains. bf[1], bf[2], and bf[3] are regression coefficients of intercept, covariates AML (low risk), and AML (high risk), respectively. bv is the regression coefficient of covariate Plate(t). It is an evident from Table 1 and the caterpillar plot Figure 1b that the credible interval (-9.911, 10.113) corresponding to regression coefficient bf[2] and (-0.164, 1.074) corresponding to regression coefficient bf[3] include 0, so, covariates AML (low risk) and AML (high risk) are statistically insignificant at 95% credible interval, and covariate plate(t) (platelets recovery) is statistically significant at 95% credible interval because their corresponding credible interval (-1.510,-0.136) does not contain 0. The posterior estimates associated with the disease group show that the hazard of death is much greater for those suffering from ALL and the high-risk group of AML. As we can see in Table 1, the posterior estimate associated with Plate(t) is negative, which indicates that there is a greater risk of death for a patient whose platelets are not at a normal level.

Graphical Analysis

In order to assess the model adequacy in **Stan**, the generated quantities block is used to perform the posterior predictive check. It compares the predicted data set or replicated data set (y_{rep}) with the observed data set (y), where y_{rep} is set of n new observation generated from the posterior distribution. These replicated data set are compares graphically by using the posterior predictive density (PPD) plot. PPD plot is done by plotting the data y and then overlaying the density of the predicted values y_{rep} . In Figure 3, the dark blue line shows the density plot of observed data y , and light blue lines show the density plots of replicated data sets y_{rep} .

4.3.5 Fitting of RR Cox hazard model with Stan

```
require(rstan)
coxrr=stan(model_code = model_RR,data=dbmt,chains = 4,iter=4000)
print(coxrr,c("bf","bv","beta","sigma"),digit=3)
```

Output Summary

Table 2: Posterior summary of RR Cox hazard model.

parameters	mean	se_mean	sd	2.5%	50%	97.5%	n_eff	Rhat
bf[1]	0.060	0.058	4.965	-9.437	0.031	9.694	7277	1.001
bf[2]	-0.087	0.061	5.029	-10.138	-0.136	9.771	6853	1.000
bf[3]	0.190	0.003	0.237	-0.292	0.197	0.643	6700	1.000
bv	-3.321	0.003	0.292	-3.875	-3.324	-2.729	7066	1.000
beta	82.177	1.199	68.034	14.569	67.775	242.085	3219	1.001
sigma	150.791	9.711	489.779	3.552	45.411	969.352	2544	1.001

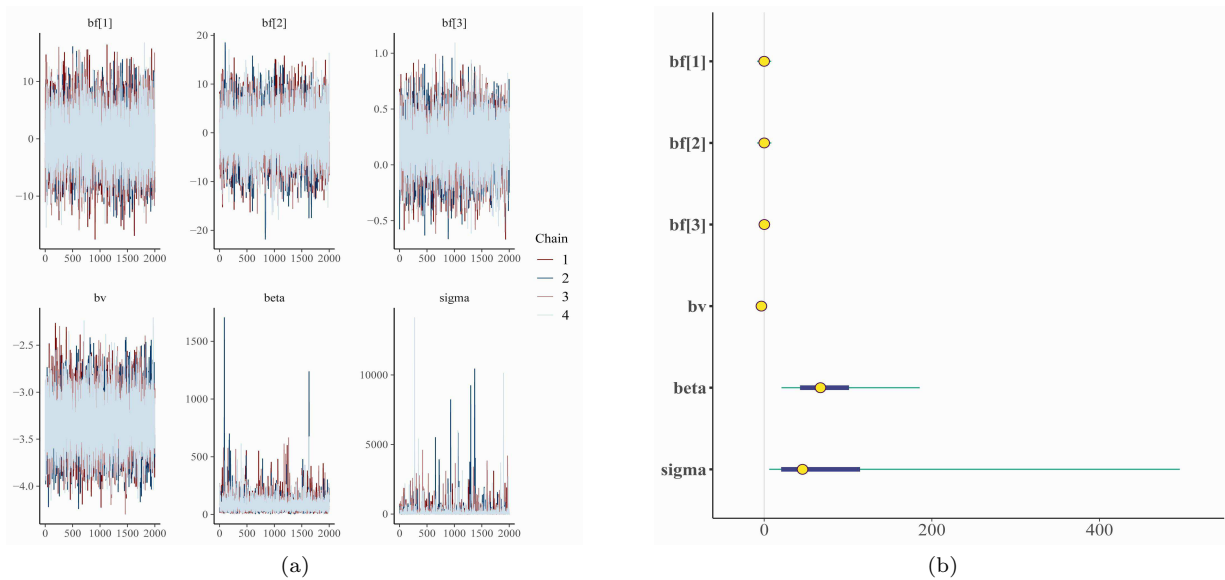


Figure 4: (a) Trace plot for each parameter of RR Cox hazard model shows that Markov chains converges to the posterior distribution, and (b) Caterpillar plot for each parameter of RR Cox hazard model.

It is clearly seen from Table 2, the Rhat for all parameters of the RR Cox hazard model is close to 1, which means the Markov chain converges to the target distribution (posterior distribution), and effective sample size (n_eff) is enough to get the conversion. It is evident from Table 2 and caterpillar plot Figure 4b that the covariates AML (low risk) and AML (high risk) are statistically insignificant and the covariate Plate(t) is statistically significant at 95% credible interval.

Graphical Analysis

4.3.6 Fitting of RE Cox hazard model with Stan

```
require(rstan)
coxre=stan(model_code = model_RE,data=dbmt,chains = 4,iter=4000)
print(coxre,c("bf","bv","lambda","sigma"),digit=3)
```

Output Summary

It is an evident from Table 3 that Rhat is close to 1 for each RE Cox hazard model's parameter that means Markov chains converges to the target distribution and effective sample size (n_eff) is enough to get

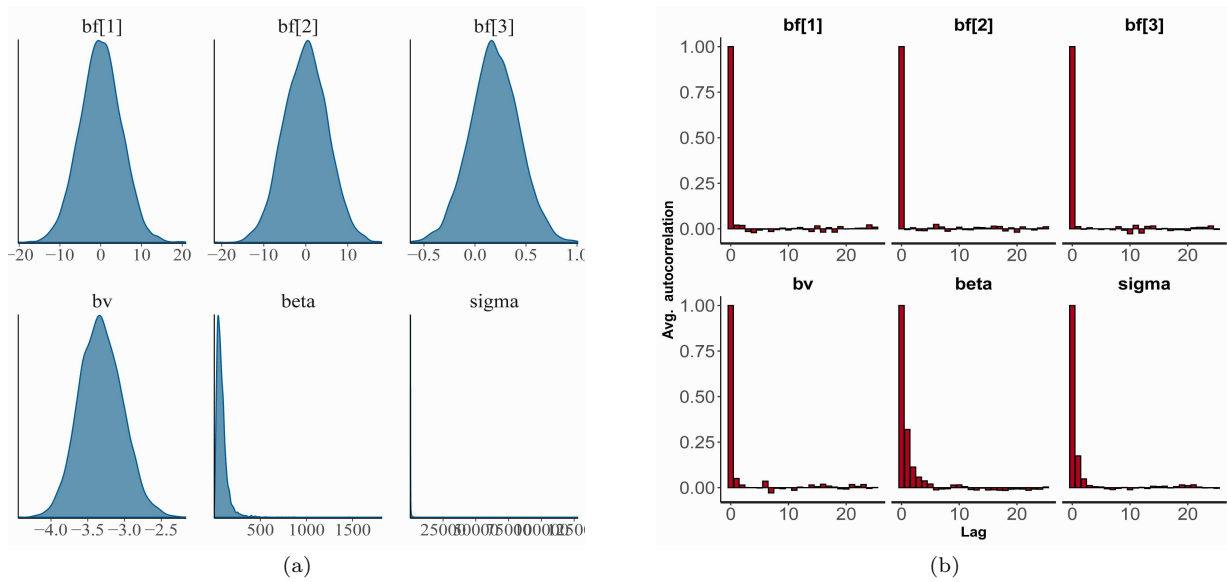


Figure 5: (a) Posterior density for each parameter of RR Cox hazard model, and (b) Autocorrelation plot for each parameter of RR Cox model shows that autocorrelation reduces to zero after 5 lags.

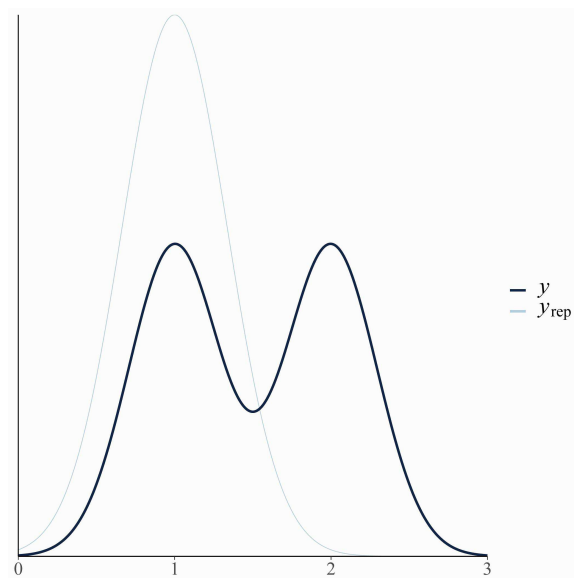


Figure 6: The posterior predictive density plot of the RR Cox hazard model shows that the model is less compatible with the given data.

Table 3: Posterior summary of RE Cox hazard model.

parameters	mean	se_mean	sd	2.5%	50%	97.5%	n_eff	Rhat
bf[1]	0.162	0.062	5.005	-9.806	0.240	9.820	6588	1.000
bf[2]	-0.064	0.065	5.091	-9.903	-0.003	9.919	6145	1.000
bf[3]	0.481	0.003	0.236	-0.010	0.485	0.941	6080	1.000
bv	-2.252	0.004	0.291	-2.799	-2.259	-1.656	5854	1.001
lambda	31.856	0.956	51.855	3.069	20.029	130.674	2941	1.000
sigma	30.644	0.675	43.624	3.070	19.724	130.501	4172	1.000

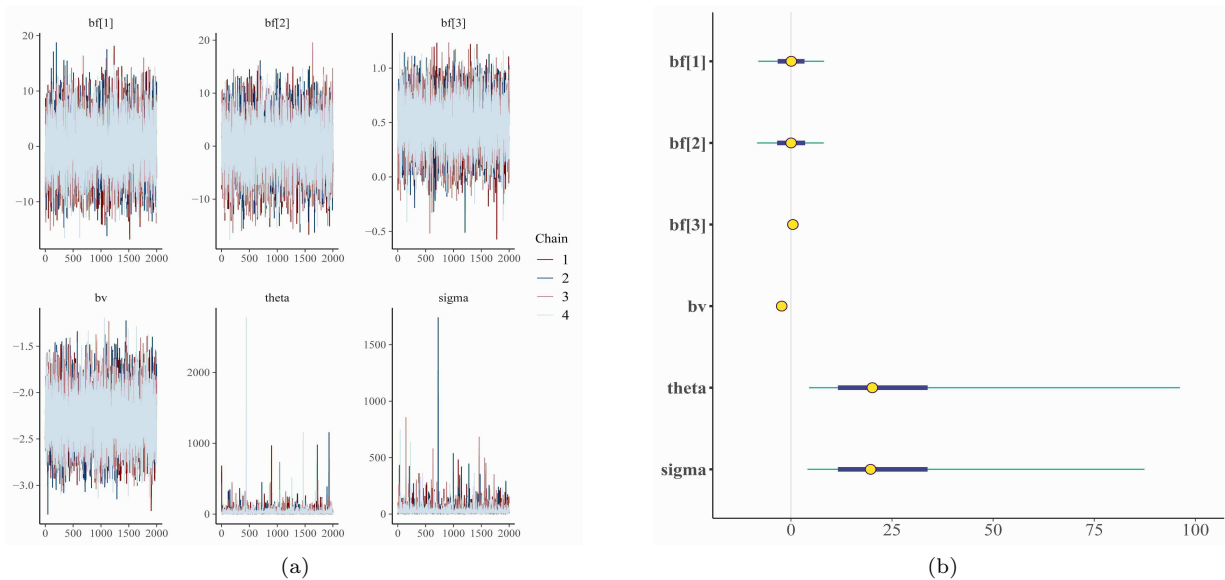


Figure 7: (a) Trace plot for each parameter of RE Cox hazard model shows that Markov chains converges to the target distribution, and (b) Caterpillar plot for each parameter of RE Cox hazard model.

the conversion. The Intercept, covariate AML (low risk) and AML (high risk) are not statistically significant at 95% credible interval, and covariate Plate(t) is statistically significant at 95% credible interval.

Graphical Analysis

4.4 Bayesian Model Comparison

To compare the fitted survival models, we have considered the two fully Bayesian criteria like Watanabe Akaike information criteria (WAIC) and leave-one-out-cross-validation information criteria (LOOIC). These information criteria require pointwise log-likelihood for the computation and that are computed in generated quantities block of `Stan` model code. In finite cases, WAIC and LOOIC often give very similar estimates, but LOOIC is more robust in the finite case with weak prior or influential observation [29]. Lower the value of information criteria better the model fitting. It is clear from Table 4 and Figure 10 that the RGLL cox hazard model has a lower LOOIC value and WAIC value among the others, which means RGLL Cox hazard is the best model for fitting the bone marrow transplant data.

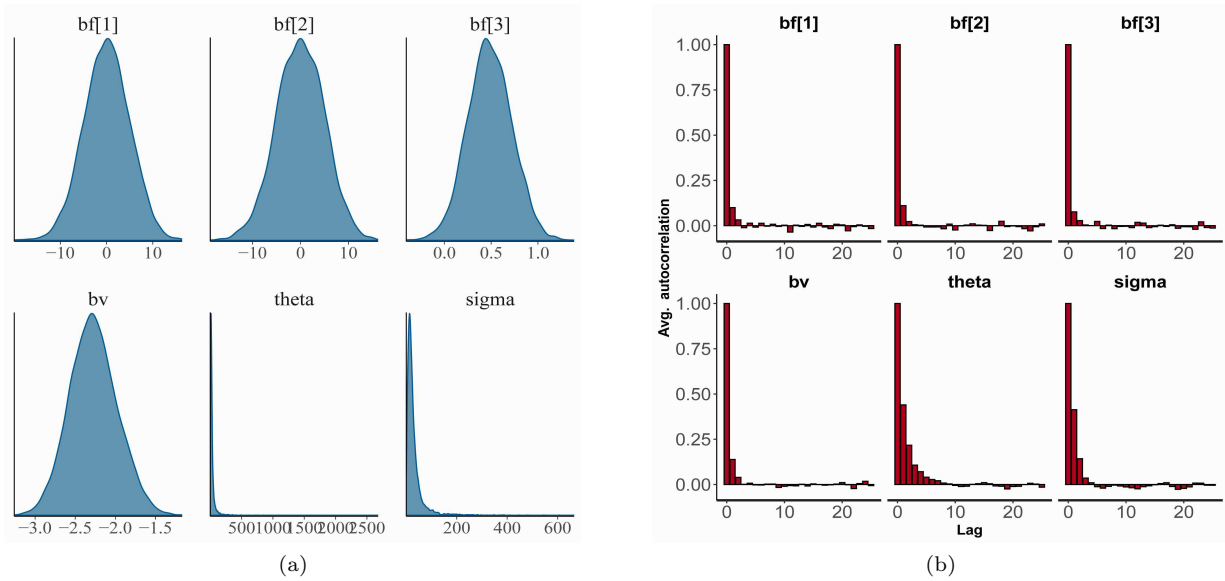


Figure 8: (a) Posterior density for each parameter of RE Cox hazard model, and (b) Autocorrelation plot for each parameter of RE Cox model is declining towards zero at around 5 lags.

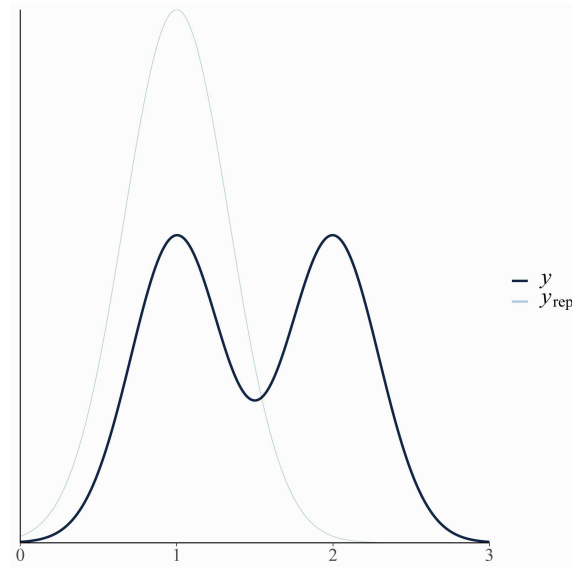


Figure 9: The posterior predictive density plot of the RE Cox hazard model shows that the model is less compatible with the given data.

Table 4: LOOIC and WAIC values for all models

Models	WAIC	LOOIC
RGLL Cox hazard	1295.3	1295.6
RR Cox hazard	2089.3	2091.9
RE Cox hazard	1509.8	1512.3

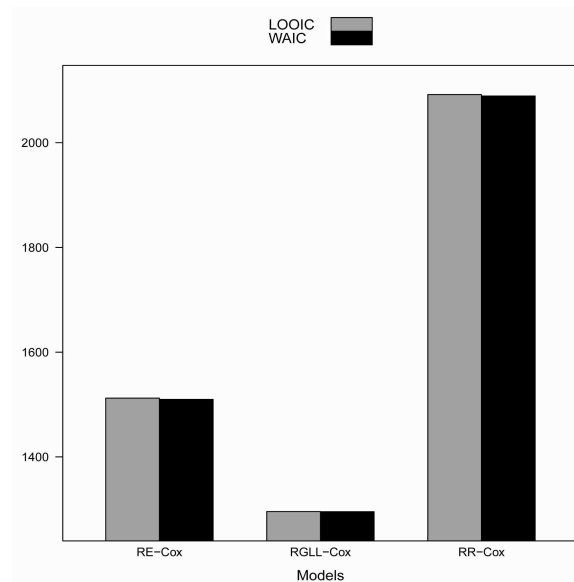


Figure 10: Barplot for LOOIC and WAIC values of the models.

5 Conclusions

The Rayleigh generalized log-logistic Cox hazard model, Rayleigh Rayleigh Cox hazard model, and Rayleigh exponential Cox hazard model are fitted to the bone marrow transplant data. The Bayesian regression fitting approach is used to model the given time-varying covariate data in R using `Stan` language. In fitting of all three models with `Stan`, the MCMC algorithm converges to the target distribution (posterior distribution). The covariate AML (low risk) and AML (high risk) are insignificant, and Plate(t) is significant for all the three models. The hazard of death is high for those suffering from ALL, AML (high risk), and the patient whose platelets are not at normal level. Comparing models based on posterior predictive density plot, WAIC, and LOOIC, we conclude that the RGLL Cox hazard model is the best-suited model for the bone marrow transplant data.

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