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On the Estimation of Parametric Cause Specific Hazard Function with Bayesian Approach under Informative Priors

Navin Chandra[a], Habbiburr Rehman[b]

Dedicated to Professor Hari Mohan Srivastava on the occasion of his 80th Birthday

[a]*Department of Statistics, Ramanujan School of Mathematical Sciences, Pondicherry University, Puducherry-605 014, India*
[b]*Department of Statistics, Ramanujan School of Mathematical Sciences, Pondicherry University, Puducherry-605 014, India*

Abstract

In this article we analysed the competing risks data using cause specific hazard approach. We proposed the Cox proportional hazards regression technique of analysing the survival data in the presence of competing risks setting using baseline modified Weibull distribution. For estimating the cumulative cause specific hazard function we used maximum likelihood as well Bayesian methods of estimation. Under Bayesian scenario, we used three types of informative priors such as gamma, Weibull and log-normal for baseline parameters and standard normal prior for regression parameters. The Comparison of Bayes estimates is made based on two different loss functions like, squared error and LINEX loss functions. Simulation study shows the appropriate convergence and identifiability of the proposed model. The bladder cancer data is utilized for the validation of proposed study.

Keywords: Competing risks, Modified Weibull distribution, Informative priors, Squared error loss function, LINEX loss function, Makov Chain Monte Carlo simulation

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1. Introduction

It is relatively common in clinical trial experiments an individual can experience p (≥ 2) mutually exclusive type of events, this situation is known as competing risks analysis. Since, occurrence of one event precludes the occurrence of other events. The situation of competing risks is commonly encountered in public health, demography, actuarial science and engineering applications. In biomedical sciences, when a clinical trial is conducted, the individuals are associated with various risks of death, for instance, in bladder cancer clinical trial, individual can die due to bladder cancer and other causes. Another example is bone marrow transplantation, where death of a patient from different kinds of infections (bacterial, viral, fungal), death due to relapse and chronic graft-versus-host disease is possible.

If the competing risks are present in time to event analysis then Kaplan-Meier survival estimation method is not adequate to use, because competing events are treated as censored events . Therefore, analysis of lifetime data in the presence of competing risks utilizes the two classical approaches known as latent failure times approach [6] and cause specific quantities such as cumulative incidence function (CIF) and cause specific hazard function (CSHF) [18, 8]. Latent failure time approach is inappropriate due to the independence assumption of hypothetical failure times in real

†*Article ID:* MTJPAM-D-20-00025
Email addresses: nc.stat@gmail.com (Navin Chandra), rehmanh79@gmail.com (Habbiburr Rehman)
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⋆*Corresponding Author:* Navin Chandra

life problems [28], but cause specific quantities get considerable amount of attention in survival analysis since 1970s [4, 12]. These quantities are useful for comparison of different treatments as well as observing the effects of other explanatory variables on survival of population under clinical trial study.

Nonparametric and semiparametric methods have been received considerable attention for the estimation of cause specific quantities in literature, but parametric modelling for that is still sparse. If the model is correctly specified then parametric mthod is more robust than nonparametric and semiparametric methods [20]. Bryant and Dignam [5] proposed the parametric inference of CIF by parameterizing the CSHF and overall survival function is estimated nonparametrically. Benichou and Gail [3] assumed piece-wise exponential or exponential distribution for estimating the CIF through CSHF. Jeong and Fine [15] estimated the CIF through parametric CSHF and compared with direct parameterized CIF. Later, the idea of direct parametrization was extended by Jeong and Fine [16]. Further, Anjana and Sankaran [2] considered the idea of parametric reverse CSHF by assuming inverse-Weibull distribution in the presence of left censored survival data. Median statistic is frequently used in medical research, so, idea of parametric quantile inferences in the competing risks setting with adjustment of covariates are proposed by Lee [21].

Above literature studies mainly focused on exponential and Weibull distributions which are restrict to accommodate monotone behaviour of hazard rate rather than nonmonotone behaviour. Hence, in this paper, we considered the modified Weibull distribution (MWD) [19] as a baseline model to describe the circumstance of nonmonotone failure rates using Cox proportional hazards model [7]. We estimate the cumulative CSHF as a quantity of interest because it is uniquely determine by the CSHF.

Moreover, Bayesian method has not received much attention for analysing competing risks survival data through cause specific hazard approach. Bayesian analysis of competing risk with masked causes through CSHF attempted by Sen et al. [25]. Huang et al. [14] considered the Bayesian competing risks survival modelling in the presence of heterogeneous random effect. Sreedevi and Sankaran [27] provided the semiparametric inference on CSHF by using the gamma process prior. Ge and Chen [9] provided the Bayesian inference for fully specified subdistribution model for lifetime data with competing risks.

The aim of this paper is to utilize the classical and Bayesian methods of estimation in the framework of parametric cause specific hazard approach under competing risks set up. For the purpose of comprehensive comparison, we proposed a class of informative priors viz., gamma, Weibull and lognormal for baseline hazard parameters and normal prior for regression parameters for Bayes estimation of parametric cause specific hazard approach. Also, the Bayes estimates are obtained under squared error loss function (SELF) [26] and LINEX loss function (LLF) [11], where SELF and LLF are the symmetric and asymmetric loss functions respectively.

Rest of the paper has organised in the following sections. Section 2 provides the parametric mathematical formulation of CSHF. Maximum likelihood estimator and variance covariance matrix obtained in Section 3. In Section 4, Bayes estimates have been provided for a class of informative priors under SELF as well as LLF. The finite sample behaviour of the model is observed through simulation study in Section 5. The applicability of the model has been checked with real data in Section 6. Finally, Section 7 provides the concluding remarks of the paper.

2. Model assumption

Prentice et al. [24] defined the CSHF of competing risks data $(T, C, \mathbf{X})$ as limiting conditional probability that an individual experience an event $C = j$, $j \in \{1, 2, \ldots, p\}$ at time t in the presence of remaining $p-1$ causes. It is obvious that the population in clinical trials may not be homogeneous, so to represent heterogeneity among the individuals the well known Cox proportional hazard model can be extend in competing risks setting.

In this article, we proposed parametric CSHF competing risks analysis using Cox proportional hazard model. The cause specific proportional hazard model under MWD baseline hazard function is given by

$$h_j(t|\mathbf{X}) = a_j(\alpha_j + \lambda_j t)t^{\alpha_j - 1} e^{\beta_j' \mathbf{X}}. \tag{2.1}$$

The corresponding survival function $S(t|\mathbf{X})$ and cumulative CSHF $H_j(t|\mathbf{X})$ are obtained as follows

$$S(t|\mathbf{X}) = e^{(-\sum_{j=1}^{p} H_j(t|\mathbf{X}))}, \tag{2.2}$$

$$H_j(t|\mathbf{X}) = a_j t^{\alpha_j} e^{\lambda_j t} e^{\beta_j' \mathbf{X}} \tag{2.3}$$

where $\mathbf{X} \in \mathbb{R}^d$ is a $m \times 1$ vector of covariates and $\boldsymbol{\beta}_j \in \mathbb{R}^d$ is a vector of constants and $a_j(> 0), \alpha_j(\geq 0), \lambda_j(> 0)$ are the scale, shape 1 and shape 2 parameters of MWD respectively.

Due to the characteristics of MWD, it is flexibile to accommodate survival data sets of nonmonotonic nature of hazard. The hazard function of MWD takes the bathtub shape when $\alpha < 1$ and increasing when $\alpha \geq 1$. The comprehensive study of MWD in the presence of progressively type-II censored data is discussed in [23]. Jiang et al. [17] and Upadhyay and Gupta [29] discusses the Bayes estimates of MWD using Gibbs sampling algorithm via Markov Chain Monte Carlo (MCMC) techniques.

3. Maximum likelihood estimation

In this section we provide the maximum likelihood (ML) estimates of model parameters and cumulative CSHF. Let $T_1, T_2, \ldots, T_n$ be the $n \in \mathbb{N}$ observed independent identically distributed random samples which comes from the MWD i.e. $T_i \sim \mathcal{MWD}(a, \alpha, \lambda)$. Assumed that T^* and D are the failure and censoring time (random right censoring) which are assumed to be independent, then the observed failure time is obtained as $T_i = min(T_i^*, D_i)$. The causes of failure $C = j$ and associated information vector $\mathbf{X}$ related to individual i also observed.

Let we define the indicator variable δ as follows

$$\delta_i = \begin{cases} 1; & C_i = j \text{ i.e. individual experience the death due to jth cause} \\ 0; & \text{when the individual is right censored,} \end{cases}$$

for $j = 1, 2, \ldots, p$. Then the likelihood function based on the observed data $t_i, j_i, \delta_i, \mathbf{X}_i$, $i = 1, 2, \ldots, n$ is given as

$$L(\boldsymbol{\Theta}; t_i, \mathbf{X}_i) = \prod_{i=1}^{n} \Big(\prod_{j=1}^{p} (h_j(t_i|\mathbf{X}_i))^{\delta_i} S(t_i|\mathbf{X}_i) \Big). \tag{3.1}$$

Where $\boldsymbol{\Theta} = (\boldsymbol{\Theta}_1, \boldsymbol{\Theta}_2, \ldots, \boldsymbol{\Theta}_p)$, $j = 1, 2, \ldots, p$ and $\boldsymbol{\Theta}_j = (a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j)$ is the vector of parameters of the model. Therefore, the likelihood function under MWD CSHF using equations (2.1) and (2.2) is provided by the following equation

$$L(\boldsymbol{\Theta}; t_i, \mathbf{X}_i) = \prod_{i=1}^{n} \Big(\prod_{j=1}^{p} (a_j(\alpha_j + \lambda_j t_i) t_i^{\alpha_j - 1} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i})^{\delta_i} e^{(-\sum_{j=1}^{p} a_j t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i})} \Big). \tag{3.2}$$

It will reduce in the following form

$$\begin{aligned} L(\boldsymbol{\Theta}; t_i, \mathbf{X}_i) = \prod_{j=1}^{p} \Big\{ a_j^{n_j} \prod_{i=1}^{n_j} (\alpha_j + \lambda_j t_i) t_i^{\alpha_j - 1} e^{\lambda_j t_i} \Big\} e^{\left(\sum_{j=1}^{p} \sum_{i=1}^{n_j} \boldsymbol{\beta}_j' \mathbf{X}_i \right)} \\ \times e^{\left(-\sum_{j=1}^{p} \sum_{i=1}^{n} a_j t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i} \right)}. \end{aligned} \tag{3.3}$$

Therefore, log-likelihood function is,

$$\begin{aligned} \ell = \sum_{j=1}^{p} n_j \log a_j + \sum_{j=1}^{p} \sum_{i=1}^{n_j} \log(\alpha_j + \lambda_j t_i) + \sum_{j=1}^{p} \sum_{i=1}^{n_j} (\alpha_j - 1) \log t_i \\ + \sum_{j=1}^{p} \lambda_j \sum_{i=1}^{n_j} t_i + \sum_{j=1}^{p} \sum_{i=1}^{n_j} \boldsymbol{\beta}_j' \mathbf{X}_i - \sum_{j=1}^{p} \sum_{i=1}^{n} a_j t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i}. \end{aligned} \tag{3.4}$$

Normal equations of likelihood function are obtained as follows

$$\frac{\partial \ell}{\partial a_j} = \frac{n_j}{a_j} - \sum_{i=1}^{n} t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i} = 0, \tag{3.5}$$

$$\frac{\partial \ell}{\partial \alpha_j} = \sum_{i=1}^{n_j} \frac{1}{(\alpha_j + \lambda_j t_i)} + \sum_{i=1}^{n_j} \log t_i - \sum_{i=1}^{n} a_j t_i^{\alpha_j} \log t_i e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i} = 0, \tag{3.6}$$

$$\frac{\partial \ell}{\partial \lambda_j} = \sum_{i=1}^{n_j} \frac{t_i}{(\alpha_j + \lambda_j t_i)} + \sum_{i=1}^{n_j} t_i - \sum_{i=1}^{n} a_j t_i^{\alpha_j+1} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i} = 0, \tag{3.7}$$

$$\frac{\partial \ell}{\partial \boldsymbol{\beta}_j} = \sum_{i=1}^{n_j} \mathbf{X}_i - \sum_{i=1}^{n} a_j t_i^{\alpha_j} e^{\lambda_j t_i} \mathbf{X}_i e^{\boldsymbol{\beta}_j' \mathbf{X}_i} = 0. \tag{3.8}$$

From equation (3.5) estimate of parameter a_j obtained in closed form in terms of α_j, λ_j and $\boldsymbol{\beta}_j$ as $\hat{a}_j = \frac{n_j}{\sum_{i=1}^{n} t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i}}$. But the estimates of parameters α_j, λ_j and $\boldsymbol{\beta}_j$ are not turned out in explicit form. Therefore, we used iterative method to obtain the parameter estimates numerically. Further, we computed the standard error of the parameters from the variance covariance matrix which is nothing but the inverse of the Fisher information matrix. Whereas, $\boldsymbol{\Theta} \sim \mathcal{N}\big(\boldsymbol{\Theta}, \boldsymbol{I}^{-1}(\boldsymbol{\Theta})\big)$ asymptomatically and Fisher information matrix $\boldsymbol{I}(\boldsymbol{\Theta})$, which is approximated from the observed Fisher information matrix $\boldsymbol{I}_0(\boldsymbol{\Theta})$ (see, remark 3.1). Next, we consider the estimates of cumulative CSHF using the invariance property of likelihood estimates in the following function

$$\hat{H}_j(t|\mathbf{X}) = \hat{a}_j t^{\hat{\alpha}_j} e^{\hat{\lambda}_j t} e^{\hat{\boldsymbol{\beta}}_j' \mathbf{X}}.$$

Remark 3.1. This remark deals with obtaining the observed Fisher information matrix.

$$\boldsymbol{I}_0(\boldsymbol{\Theta}) = \begin{bmatrix} -\frac{\partial^2 \ell}{\partial a_j^2} & -\frac{\partial^2 \ell}{\partial a_j \alpha_j} & -\frac{\partial^2 \ell}{\partial a_j \lambda_j} & -\frac{\partial^2 \ell}{\partial a_j \boldsymbol{\beta}_j'} \\ - & -\frac{\partial^2 \ell}{\partial \alpha_j^2} & -\frac{\partial^2 \ell}{\partial \alpha_j \lambda_j} & -\frac{\partial^2 \ell}{\partial \alpha_j \boldsymbol{\beta}_j'} \\ - & - & -\frac{\partial^2 \ell}{\partial \lambda_j^2} & -\frac{\partial^2 \ell}{\partial \lambda_j \boldsymbol{\beta}_j'} \\ - & - & - & -\frac{\partial^2 \ell}{\partial \boldsymbol{\beta}_j \partial \boldsymbol{\beta}_j'} \end{bmatrix}_{\boldsymbol{\Theta} = \hat{\boldsymbol{\Theta}}}$$

The elements of the observed Fisher information matrix are given below

$$-\frac{\partial^2 \ell}{\partial a_j^2} = \frac{n_j}{a_j^2}, -\frac{\partial^2 \ell}{\partial a_j \alpha_j} = \sum_{i=1}^{n} t_i^{\alpha_j} \log t_i e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i}, -\frac{\partial^2 \ell}{\partial a_j \lambda_j} = \sum_{i=1}^{n} t_i^{\alpha_j+1} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i},$$
$$-\frac{\partial^2 \ell}{\partial a_j \boldsymbol{\beta}_j'} = \sum_{i=1}^{n} t_i^{\alpha_j} e^{\lambda_j t_i} \mathbf{X}_i e^{\boldsymbol{\beta}_j' \mathbf{X}_i}, -\frac{\partial^2 \ell}{\partial \alpha_j^2} = \sum_{i=1}^{n_j} \frac{1}{(\alpha_j + \lambda_j t_i)^2} + \sum_{i=1}^{n} a_j t_i^{\alpha_j} (\log t_i)^2 e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i},$$
$$-\frac{\partial^2 \ell}{\partial \alpha_j \lambda_j} = \sum_{i=1}^{n_j} \frac{t_i}{(\alpha_j + \lambda_j t_i)} + \sum_{i=1}^{n} a_j t_i^{\alpha_j+1} \log t_i e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i},$$
$$-\frac{\partial^2 \ell}{\partial \alpha_j \boldsymbol{\beta}_j} = \sum_{i=1}^{n} a_j t_i^{\alpha_j} \log t_i e^{\lambda_j t_i} \mathbf{X}_i e^{\boldsymbol{\beta}_j' \mathbf{X}_i}, -\frac{\partial^2 \ell}{\partial \lambda_j^2} = \sum_{i=1}^{n_j} \frac{t_i^2}{(\alpha_j + \lambda_j t_i)} + \sum_{i=1}^{n} a_j t_i^{\alpha_j+2} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i},$$

$$-\frac{\partial^2 \ell}{\partial \lambda_j \boldsymbol{\beta}_j'} = \sum_{i=1}^{n} a_j t_i^{\alpha_j+1} e^{\lambda_j t_i} \mathbf{X}_i e^{\boldsymbol{\beta}_j' \mathbf{X}_i}, -\frac{\partial^2 \ell}{\partial \boldsymbol{\beta}_j \partial \boldsymbol{\beta}_j'} = \sum_{i=1}^{n} a_j t_i^{\alpha_j} e^{\lambda_j t_i} \mathbf{X}_i \mathbf{X}_i' e^{\boldsymbol{\beta}_j' \mathbf{X}_i}.$$

The matrix $\boldsymbol{I}_0(\boldsymbol{\Theta})$ obtained by replacing the parameter values with their ML estimates.

4. Bayes estimation

The Bayesian estimates of the model parameters are constructed by specifying the prior distribution for the parameters a_j, α_j, λ_j and $\boldsymbol{\beta}_j$. In this, article we utilized the informative priors for the parameters. In the existing literature on MWD, Upadhyay and Gupta [29] considered the vague and Jiang et al. [17] utilized the uniform priors for a_j, α_j, λ_j. However, we don't have the past information about parameters except that the domain of a_j, α_j and λ_j lies on non-negative real line. Therefore, we proposed a class of informative priors for non-negative random variables a_j, α_j, λ_j

which consist gamma, Weibull and log-normal distributions and standard normal distribution for the random variable $\boldsymbol{\beta}_j$ for dealing Bayesian estimation in this article.

Suppose that random variables $a_j, \alpha_j, \lambda_j \sim \mathcal{G}(q_{uj}, r_{uj}), u = 1, 2, 3$ and the regression parameters $\boldsymbol{\beta}_j \sim \mathcal{N}(0, 1)$. Then, the joint prior density come out to the following form

$$\begin{aligned}\pi_1(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j) \propto a_j^{q_{1j}-1} \alpha_j^{q_{2j}-1} \lambda_j^{q_{3j}-1} e^{-(r_{1j}a_j + r_{2j}\alpha_j + r_{3j}\lambda_j + \frac{1}{2}\boldsymbol{\beta}_j^2)}, t \geq 0;\\ a_j(>0), \alpha_j(\geq 0), \lambda_j(>0); r_{uj}(>0), q_{uj}(>0); -\infty < \boldsymbol{\beta}_j < \infty,\end{aligned} \tag{4.1}$$

whereas, q_{uj} and r_{uj} are the hyper-parameters of the prior distribution which will reflect the belief about the past information.

Similarly, we assume Weibull and log-normal distributions as the priors for baseline parameters i.e. $a_j, \alpha_j, \lambda_j \sim \mathcal{W}(k_{uj}, \theta_{uj})$ and $a_j, \alpha_j, \lambda_j \sim \mathcal{LN}(\mu_{uj}, \sigma_{uj})$. Then the joint prior distributions of the random variables are obtained as follows

$$\pi_2(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j) \propto a_j^{k_{1j}-1} \alpha_j^{k_{2j}-1} \lambda_j^{k_{3j}-1} e^{-\left((\theta_{1j}a_j)^{k_{1j}} + (\theta_{2j}\alpha_j)^{k_{2j}} + (\theta_{3j}\lambda_j)^{k_{3j}} + \frac{1}{2}\boldsymbol{\beta}_j^2\right)}, \tag{4.2}$$

$$\pi_3(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j) \propto \frac{1}{a_j\alpha_j\lambda_j} e^{-\frac{1}{2}\left(\left(\frac{\log a_j - \mu_{1j}}{\sigma_{1j}}\right)^2 + \left(\frac{\log \alpha_j - \mu_{2j}}{\sigma_{2j}}\right)^2 + \left(\frac{\log \lambda_j - \mu_{3j}}{\sigma_{3j}}\right)^2 + \boldsymbol{\beta}_j^2\right)}, \tag{4.3}$$

where $k_{uj}(>0), \theta_{uj}(>0), -\infty < \mu_{uj} < \infty$ and $\sigma_{uj}(>0), u = 1, 2, 3$ are the hyper-parameters.

Now, the joint posterior densities of the random variables a_j, α_j, λ_j and $\boldsymbol{\beta}_j$ is obtained by combining observed information with past information through the Bayes theorem as follows

$$p(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j | \mathbf{t}_i, \mathbf{X}_i) = \frac{L(\boldsymbol{\Theta}; t_i, \mathbf{X}_i)\pi(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j)}{\int_0^\infty \int_0^\infty \int_0^\infty \int_{-\infty}^\infty L(\boldsymbol{\Theta}; t_i, \mathbf{X}_i)\pi(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j) da_j d\alpha_j d\lambda_j d\boldsymbol{\beta}_j}.$$

4.1. Posterior densities under a class of informative priors

The joint posterior density function of the random variables a_j, α_j, λ_j and $\boldsymbol{\beta}_j$ using joint prior density in (4.1) given the observed data in (3.3) obtained as follows

$$\begin{aligned}p_1(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j | \mathbf{t}_i, \mathbf{X}_i) \propto a_j^{n_j + q_{1j} - 1} \alpha_j^{q_{2j}-1} \lambda_j^{q_{3j}-1} \prod_{i=1}^{n_j} \left\{(\alpha_j + \lambda_j t_i) t_i^{\alpha_j - 1} e^{\lambda_j t_i}\right\}\\ \times e^{\left(\sum_{j=1}^p \sum_{i=1}^{n_j} \boldsymbol{\beta}_j' \mathbf{X}_i\right)} e^{\left(-\sum_{i=1}^n \sum_{j=1}^p a_j t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i}\right)}\\ \times e^{-\left(r_{1j}a_j + r_{2j}\alpha_j + r_{3j}\lambda_j + \frac{1}{2}\boldsymbol{\beta}_j^2\right)}.\end{aligned} \tag{4.4}$$

Where the joint posterior density is the product of marginal posterior densities of random variables a_j, α_j, λ_j and $\boldsymbol{\beta}_j$ i.e.,

$$\begin{aligned}p_1(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j | \mathbf{t}_i, \mathbf{X}_i) \propto p_{11}(a_j | \alpha_j, \lambda_j, \boldsymbol{\beta}_j, \mathbf{t}_i, \mathbf{X}_i) \times p_{12}(\alpha_j | a_j, \lambda_j, \boldsymbol{\beta}_j, \mathbf{t}_i, \mathbf{X}_i)\\ \times p_{13}(\lambda_j | a_j, \alpha_j, \boldsymbol{\beta}_j, \mathbf{t}_i, \mathbf{X}_i) \times p_{14}(\boldsymbol{\beta}_j | a_j, \alpha_j, \lambda_j, \mathbf{t}_i, \mathbf{X}_i)\end{aligned}$$

Remark 4.1. From equation (4.4), it is seen that the marginal posterior $p_{11}(a_j | \alpha_j, \lambda_j, \boldsymbol{\beta}_j, \mathbf{t}_i, \mathbf{X}_i)$ can be easily generated from a gamma density i.e.

$$p_{11}(a_j | \alpha_j, \lambda_j, \boldsymbol{\beta}_j, \mathbf{t}_i, \mathbf{X}_i) \sim \mathcal{G}\Big(n_j + q_{1j}, r_{1j} + \sum_{i=1}^n a_j t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i}\Big).$$

Marginal posteriors $p_{12}(\alpha_j | a_j, \lambda_j, \boldsymbol{\beta}_j, \mathbf{t}_i, \mathbf{X}_i)$ and $p_{13}(\lambda_j | a_j, \alpha_j, \boldsymbol{\beta}_j, \mathbf{t}_i, \mathbf{X}_i)$ are log-concave if $q_{2j} > 1$ and $q_{3j} > 1$, also, $p_{14}(\boldsymbol{\beta}_j | a_j, \alpha_j, \lambda_j, \mathbf{t}_i, \mathbf{X}_i)$ is log-concave.

Now, we obtain the joint posterior densities of the random variables a_j, α_j, λ_j and $\boldsymbol{\beta}_j$ under the Weibull and log-normal priors as follows

$$\begin{aligned} p_2(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j | \mathbf{t}_i, \mathbf{X}_i) \propto\, & a_j^{n_j+k_{1j}-1} \alpha_j^{k_{2j}-1} \lambda_j^{k_{3j}-1} \prod_{i=1}^{n_j} \left\{ (\alpha_j + \lambda_j t_i) t_i^{\alpha_j - 1} e^{\lambda_j t_i} \right\} \\ & \times e^{\left(\sum_{j=1}^{p} \sum_{i=1}^{n_j} \boldsymbol{\beta}_j' \mathbf{X}_i \right)} e^{\left(-\sum_{i=1}^{n} \sum_{j=1}^{p} a_j t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i} \right)} \\ & \times e^{-\left((\theta_{1j} a_j)^{k_{1j}} + (\theta_{2j}\alpha_j)^{k_{2j}} + (\theta_{3j}\lambda_j)^{k_{3j}} + \frac{1}{2}\boldsymbol{\beta}_j^2 \right)}, \end{aligned} \tag{4.5}$$

$$\begin{aligned} p_3(a_j, \alpha_j, \lambda_j, \boldsymbol{\beta}_j | \mathbf{t}_i, \mathbf{X}_i) \propto\, & \frac{a_j^{n_j-1}}{\alpha_j \lambda_j} \prod_{i=1}^{n_j} \left\{ (\alpha_j + \lambda_j t_i) t_i^{\alpha_j - 1} e^{\lambda_j t_i} \right\} \\ & \times e^{\left(\sum_{j=1}^{p} \sum_{i=1}^{n_j} \boldsymbol{\beta}_j' \mathbf{X}_i \right)} e^{\left(-\sum_{i=1}^{n} \sum_{j=1}^{p} a_j t_i^{\alpha_j} e^{\lambda_j t_i} e^{\boldsymbol{\beta}_j' \mathbf{X}_i} \right)} \\ & \times e^{-\frac{1}{2}\left(\left(\frac{\log a_j - \mu_{1j}}{\sigma_{1j}} \right)^2 + \left(\frac{\log \alpha_j - \mu_{2j}}{\sigma_{2j}} \right)^2 + \left(\frac{\log \lambda_j - \mu_{3j}}{\sigma_{3j}} \right)^2 + \boldsymbol{\beta}_j^2 \right)}. \end{aligned} \tag{4.6}$$

It is clear from the joint posterior density (4.5) that the marginal densities of random variables a_j, α_j, λ_j are log-concave if $k_{uj} > 1, u = 1, 2, 3$ and marginal density of $\boldsymbol{\beta}_j$ also log-concave. But, it is difficult to reveal this characteristics under joint posterior density (4.6).

Further, as mention earlier in Section 1 we consider two loss functions known as SELF and LLF. The SELF given by $L(\boldsymbol{\Theta}, \hat{\boldsymbol{\Theta}}) = (\boldsymbol{\Theta} - \hat{\boldsymbol{\Theta}})^2$ for a parameter $\boldsymbol{\Theta}$ is a symmetric loss function and it is not appropriate in the situation when over estimation is more serious than under estimation and vis-versa. To overcome this limitation of SELF, asymmetric loss function i.e. LLF is considered which is given by $L(\boldsymbol{\Theta}, \hat{\boldsymbol{\Theta}}) = e^{p(\hat{\boldsymbol{\Theta}} - \boldsymbol{\Theta})} - p(\hat{\boldsymbol{\Theta}} - \boldsymbol{\Theta}) - 1, p \neq 0$. Under these loss functions the Bayes estimates of cumulative CSHF are obtained as follows

$$\hat{H}_j^{self}(t|\mathbf{X}) = \frac{1}{N} \sum_{l=1}^{N} \left[H_j(t|\mathbf{X}) \right]_{a_j = a_l, \alpha_j = \alpha_l, \lambda_j = \lambda_l, \boldsymbol{\beta}_j = \boldsymbol{\beta}_l},$$

$$\hat{H}_j^{llf}(t|\mathbf{X}) = -\frac{1}{p} \log \left(\frac{1}{N} e^{-p \left[H_j(t|\mathbf{X}) \right]_{a_j = a_l, \alpha_j = \alpha_l, \lambda_j = \lambda_l, \boldsymbol{\beta}_j = \boldsymbol{\beta}_l}} \right),$$

where $l = 1, 2, \ldots, N$ are the posterior samples. Notice, that p is the hyper parameter of the LLF, which reflect the degree of asymmetry i.e. $p < 0$ providing the information that underestimation is more serious than the overestimation and vise-versa for $p > 0$ and when p approaches to zero then LLF approximately a symmetric function. Unfortunately, the joint posterior densities in equations (4.4-4.6) are not any known distributional form. Because, due to the multiple integration it is difficult to obtain analytical expressions of the corresponding marginal posteriors of the parameters a_j, α_j, λ_j and $\boldsymbol{\beta}_j$. But, based on their distributional characteristics an appropriate simulation algorithm of MCMC methods are utilized for drawing the posterior samples of a_j, α_j, λ_j and $\boldsymbol{\beta}_j$.

5. Simulation study

In this Section, we validate the proposed methods of estimation for assumed model via Monte Carlo simulation study. Here, we considered the two causes of failure i.e. $j = 1, 2$ and a single covariate X which is generated from standard normal distribution. The simulation study is carried out for choosen values of model parameters as $a_1 = 0.5, \alpha_1 = 0.7, \lambda_1 = 0.1$ and $\beta_1 = 0.1$ for cause 1 and $a_2 = 0.4, \alpha_2 = 0.5, \lambda_2 = 0.1$ and $\beta_2 = 0.1$ for cause 2, where λ_j is assumed to be known for mathematically convenient.We choose four different size of samples i.e. $n = 20, 50, 100, 200$. For generating the survival times we applied the inverse transformation method and causes of failure based on survival time are obtained from the binomial distribution [4]. The censoring time D_i is generated from $\mathcal{U}(0, d_i)$, where d_i imposing the percentage of censoring around 20%. The comparison of the estimators (ML and Bayes) are made on based on average estimate and empirical mean square error (MSE) over 500 replications.

In Section 4, we mentioned that the posterior samples will be generated using the MCMC procedure, since posterior densities are not in closed form and it will escape the problem of multiple integrals. MCMC procedure is a broad class of computational algorithms such as Metropolis–Hastings algorithm [13] and Gibbs sampling [10] etc. In order to generate the posterior sample we used BUGS package in `R software` through OpenBugs interface [22]. BUGS software has the flexibility to incorporate the MCMC algorithms based on the characteristics of posterior densities. Further, for computing the hyper-parameters we utilized empirical Bayes method by using the ML estimates and empirical variance of a_j, α_j and λ_j. First, we generate the 1000 random sample of size 25 and obtained the ML estimates and variance then compared with mean and variance of priors of the a_j, α_j and λ_j. Calculated hyper-parameters of gamma, Weibull and log-normal priors given in Table 1.

Table 1. hyper-parameters of gamma, Weibull and log-normal priors.

Priors	Hyper-parameters
Gamma	$q_{11} = 8.48, r_{11} = 16.53, q_{21} = 11.88, r_{21} = 15.26, q_{21} = 7.43, r_{21} = 18.14, q_{22} = 8.83, r_{22} = 15.08$
Weibull	$k_{11} = 3.2, \theta_{11} = 5.94, k_{21} = 3.85, \theta_{21} = 1.78, k_{21} = 2.97, \theta_{21} = 10.1, k_{22} = 3.27, \theta_{22} = 4.02$
Log-normal	$\mu_{11} = -0.72, \sigma_{11} = 0.11, \mu_{12} = -0.29, \sigma_{12} = 0.08, \mu_{21} = -0.96, \sigma_{21} = 0.13, \mu_{22} = -0.59, \sigma_{22} = 0.11$

We generated the 10,000 MCMC samples of marginal posteriors of the parameters a_j, α_j, λ_j and $\boldsymbol{\beta}_j$. The first 4,000 samples have been discard in burn in period of Markov chain for reducing the effect of initial values. We used every second equally spaced outcome i.e. thin=2 for minimizing the autocorrelation state of Markov chain. By the visualization of the convergence diagnostics plots it is realized that chains are converging nicely.

The numerical findings of the simulation study are presented in the following Tables 4, 5, 6 and 7 which are containing the average estimate and MSEs of both the ML and Bayes estimates of cumulative CSHF at each of time points 0.5, 0.8 and 1 for both the competing causes.

- It is observed that the sample size n and MSEs have inverse relationship i.e. sample size is increasing and MSEs are decreasing.
- Results in Table 4 and 5 shows that Bayes estimates are more efficient compared to ML estimate. The Bayes estimates under SELF are more precise in gamma prior for cause 1 and in log-normal prior for cause 2. Under LLF at $p = \pm 1.5$ gamma prior work well for cause 1 and log-normal prior for cause 2.
- It is observed that the applicability of the Bayesian method is observed for sample size 100 and 200 in terms of magnitude of MSEs of cumulative CSHF.
- For large sample size Bayes estimates based on gamma and Weibull prior are close for both causes and based on log-normal prior are close to ML estimate for cause 1.
- The performance of Weibull prior more or less lies in between gamma and log-normal prior.
- As expected, it is seen that for higher value of scale parameter of LLF i.e. p=1.5, Bayes estimates leads to smaller estimates as compared to smaller value of LLF i.e. p=-1.5.

6. Real life application

In this section we illustrate proposed estimation procedures of cause specific hazard analysis with bladder cancer tumour data [30]. This study was conducted by the Veterans Administration Co-operative Urological Research Group (VACURG). All the patients had a sign of superficial bladder tumours at time of entering in the trial. For all patients three types of treatments: placebo, pyridoxine and thiotepa were randomly assigned after removing the tumours. In the study 118 patient entered in the trial and each patient have different characteristics such as number of recurrences of tumour, initial number of tumours and initial size of tumour. The follow-up time were measured in months for each patient. The major cause of death are bladder cancer and other causes , yielding two competing risks and remaining patients were right censored. We introduced pyridoxine treatment and initial size of the tumour as covariates for investigating the effect on death due to bladder cancer and other causes. The detail description of the data available in [1].

First, we characterize the shape of the cause specific hazard of other causes by nonparametrically and compared with proposed model. We found that shape of the cause specific hazard of other causes under both procedures are very close and looks like bathtub shape, see Figure 1. We therefore, compared the goodness of fit of the model with Weibull, log-normal and gamma distributions on the basis of Akaike information criterion (AIC), and Bayesian information criterion (BIC). The baseline fitting summary of the other causes are reported in Table 2. It is also clear from the goodness of fit statistics i.e. MWD have least AIC and BIC among the counter distributions. The graph of the empirical and fitted models are shown in Figure 2. Figure 2 clearly shows that under baseline model for other causes gives best fit for MWD as compared to Weibull, log-normal, and gamma distributions.

Table 2. Baseline parameter estimate and goodness of fit statistics for other causes.

Model	**MLE**	**Loglikelihood**	**AIC**	**BIC**
MWD	$a = 0.0237, \alpha = 0.4375, \lambda = 0.0229$	-166.305	338.6102	346.9222
Weibull	Shape=0.8265, Scale=166.0449	-168.988	341.9766	347.5179
Log-normal	Meanlog=5.6463, Sdlog=2.8459	-174.678	353.3568	358.8982
Gamma	Shape=0.7810, Rate=0.0046	-168.753	341.564	347.0478

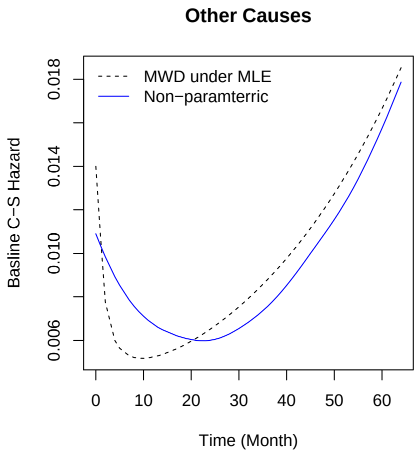

Figure 1. Non-parametric and MWD cause specific hazard plotting for other causes.

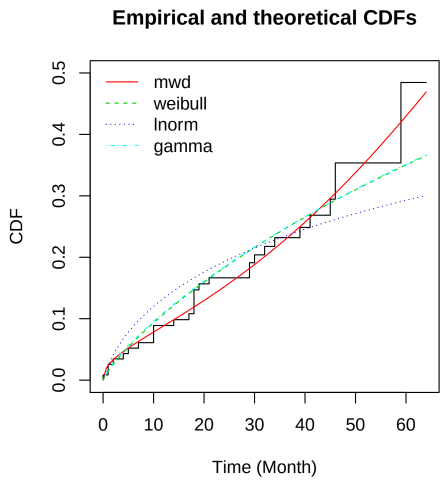

Figure 2. Fitted and empirical CDFs plot of other causes.

Further, we also analyse the proposed model for competing events (i.e. death due to bladder cancer and other event) by applying both the proposed estimation procedures. It is observed from the data 22 patients died due to other causes, only 2 patients died due to bladder cancer and 88 patients are right censored. Since, very few patients died due to bladder cancer, then we randomly convert some right censored observations as failure by bladder cancer for observing the effect of treatments and tumour size on competing events. The estimates of baseline parameters and regression parameters with standard deviation are given in Table 3.

Table 3. ML and Bayes parameter estimates with standard for both causes.

Estimates		Other					Bladder				
		a_1	α_1	λ_1	β_{11}	β_{12}	a_2	α_2	λ_2	β_{21}	β_{22}
MLE	Estimate	0.005	0.152	0.064	0.242	0.011	0.021	0.330	0.025	0.365	0.123
	S.E	0.002	0.190	0.016	0.560	0.139	0.011	0.147	0.009	0.395	0.092
Gamma	SELF	0.265	0.416	0.170	0.001	-1.040	0.341	0.265	0.121	0.002	0.157
Prior	LLF p=1.5	0.217	0.354	0.158	-0.741	-1.568	0.272	0.250	0.115	-0.752	-0.116
	LLF p=-1.5	0.367	0.515	0.184	0.754	-0.576	0.531	0.282	0.128	0.759	0.399
	S.D	0.292	0.319	0.129	0.997	0.817	0.364	0.145	0.092	1.003	0.583
Weibull	SELF	0.694	0.444	0.077	0.000	-1.354	0.773	0.315	0.056	-0.003	-0.260
Prior	LLF p=1.5	0.546	0.408	0.073	-0.749	-1.834	0.630	0.302	0.054	-0.747	-0.476
	LLF p=-1.5	0.958	0.485	0.081	0.763	-0.915	1.025	0.330	0.058	0.739	-0.072
	S.D	0.505	0.226	0.072	1.005	0.783	0.494	0.139	0.051	0.994	0.516
Log-normal	SELF	0.388	0.444	0.210	0.000	-1.431	0.560	0.279	0.146	0.002	-0.248
Prior	LLF p=1.5	0.321	0.393	0.201	-0.750	-1.940	0.453	0.267	0.142	-0.742	-0.512
	LLF p=-1.5	0.594	0.523	0.219	0.747	-0.977	0.976	0.293	0.150	0.748	-0.041
	S.D	0.360	0.286	0.108	0.999	0.807	0.466	0.132	0.073	0.996	0.556

β_{j1} regression coefficient of pyridoxine treatment for cause j.
β_{j1} regression coefficient of tumour size for cause j.
$j = 1$ for other causes, $j = 2$ for bladder cancer.

7. Conclusion

The analysis of parametric CSHF is considered through MWD with covariates. Where the parameter estimates and cumulative CSHF estimates are obtained through maximum likelihood and Bayesian methods. The selection of class of informative priors and two loss functions shows their applicability through simulation study. The flexibility and appropriate convergence of the model are observed for ML and Bayes estimates. In real life application, the suitability of parametric model is assessed through goodness of fit statistics and graphical check. It is also observed that pyridoxine treatment and tumour size are not significant.

Acknowledgements

This paper is dedicated to Professor Hari Mohan Srivastava on the occasion of his 80th Birthday.

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Table 4. Average ML and Bayes estimates with MSEs of cumulative CSHF for cause 1 and cause 2 with $n = 20$ at $X = -0.3$ when $a_1 = 0.5, \alpha_1 = 0.7, \lambda_1 = 0.1$ and $\beta_1 = 0.1$ for cause 1 and $a_2 = 0.4, \alpha_2 = 0.5, \lambda_2 = 0.1$ and $\beta_2 = 0.1$ for cause 2.

n=20		**Cause 1**			**Cause 2**		
Time Points		0.5	0.8	1	0.5	0.8	1
True Value		0.314	0.44962	0.53625	0.28856	0.37611	0.429
ML	Estimate	0.30888	0.45978	0.56117	0.29331	0.39948	0.46712
	MSE	2.32194	4.62834	6.81119	2.23275	3.95489	5.4574
Gamma	Estimate	0.30765	0.45087	0.54522	0.28515	0.3827	0.44352
SELF	MSE	0.50087	0.981	1.43874	0.48167	0.82234	1.11368
Gamma	Estimate	0.30156	0.43972	0.52948	0.2795	0.37348	0.43135
LLF p=1.5	MSE	0.48421	0.9153	1.30085	0.46074	0.75707	0.99672
Gamma	Estimate	0.31413	0.4629	0.56247	0.29116	0.39261	0.45675
LLF p=-1.5	MSE	0.52882	1.08876	1.66795	0.51278	0.91748	1.28625
Weibull	Estimate	0.30895	0.45485	0.55126	0.28693	0.38664	0.44895
SELF	MSE	0.51834	1.03092	1.53332	0.48739	0.85105	1.16912
Weibull	Estimate	0.3028	0.44357	0.53525	0.28123	0.3773	0.43657
LLF p=1.5	MSE	0.5078	0.98062	1.41672	0.47341	0.79874	1.06853
Weibull	Estimate	0.3154	0.46672	0.56823	0.29289	0.39645	0.46204
LLF p=-1.5	MSE	0.53797	1.11304	1.71815	0.50939	0.92646	1.31278
Log-normal	Estimate	0.30778	0.45224	0.54758	0.28455	0.38115	0.44134
SELF	MSE	1.70823	3.63404	5.37375	0.47882	0.81139	1.09311
Log-normal	Estimate	0.29671	0.43051	0.51646	0.27893	0.37201	0.42928
LLF p=1.5	MSE	1.54545	3.10235	4.38443	0.4528	0.73525	0.96073
Log-normal	Estimate	0.32025	0.47795	0.58604	0.29059	0.39116	0.45473
LLF p=-1.5	MSE	1.95366	4.56799	7.35256	0.51719	0.92465	1.29498

Table 5. Average ML and Bayes estimates with MSEs of cumulative CSHF for cause 1 and cause 2 with $n = 50$ at $X = -0.3$ when $a_1 = 0.5, \alpha_1 = 0.7, \lambda_1 = 0.1$ and $\beta_1 = 0.1$ for cause 1 and $a_2 = 0.4, \alpha_2 = 0.5, \lambda_2 = 0.1$ and $\beta_2 = 0.1$ for cause 2.

n=50		**Cause 1**			**Cause 2**		
Time Points		0.5	0.8	1	0.5	0.8	1
True Value		0.314	0.44962	0.53625	0.28856	0.37611	0.429
ML	Estimate	0.32681	0.47382	0.56924	0.28973	0.38521	0.44398
	MSE	0.8821	1.65652	2.34714	0.70081	1.16762	1.54528
Gamma	Estimate	0.31966	0.46372	0.55742	0.28377	0.37742	0.43518
SELF	MSE	0.42547	0.82348	1.18808	0.34649	0.57213	0.75704
Gamma	Estimate	0.31614	0.45749	0.54877	0.28068	0.37248	0.42873
LLF p=1.5	MSE	0.41091	0.77941	1.1061	0.34141	0.55438	0.72422
Gamma	Estimate	0.32329	0.4702	0.56644	0.28696	0.38253	0.44187
LLF p=-1.5	MSE	0.44336	0.87844	1.29188	0.35391	0.59616	0.80095
Weibull	Estimate	0.32149	0.46835	0.56415	0.28644	0.38252	0.44193
SELF	MSE	0.44081	0.86189	1.25657	0.36675	0.61506	0.8237
Weibull	Estimate	0.31795	0.46209	0.55547	0.28326	0.37742	0.43526
LLF p=1.5	MSE	0.42728	0.81982	1.17607	0.36154	0.59599	0.78758
Weibull	Estimate	0.32513	0.47479	0.57312	0.2897	0.38776	0.44882
LLF p=-1.5	MSE	0.45738	0.91353	1.35613	0.37424	0.64017	0.87051
Log-normal	Estimate	0.32064	0.46473	0.55836	0.28237	0.37484	0.4318
SELF	MSE	0.74604	1.49172	2.14681	0.33192	0.543	0.7138
Log-normal	Estimate	0.31606	0.45636	0.54671	0.27933	0.36998	0.42546
LLF p=1.5	MSE	0.71407	1.39797	1.9783	0.32673	0.52548	0.68191
Log-normal	Estimate	0.32541	0.47353	0.57071	0.28552	0.3799	0.43843
LLF p=-1.5	MSE	0.78472	1.60917	2.36376	0.33953	0.56711	0.75737

Table 6. Average ML and Bayes estimates with MSEs of cumulative CSHF for cause 1 and cause 2 with $n = 100$ at $X = -0.3$ when $a_1 = 0.5, \alpha_1 = 0.7, \lambda_1 = 0.1$ and $\beta_1 = 0.1$ for cause 1 and $a_2 = 0.4, \alpha_2 = 0.5, \lambda_2 = 0.1$ and $\beta_2 = 0.1$ for cause 2.

n=100		**Cause 1**			**Cause 2**		
Time Points		0.5	0.8	1	0.5	0.8	1
True Value		0.314	0.44962	0.53625	0.28856	0.37611	0.429
ML	Estimate	0.3219	0.46463	0.55662	0.29102	0.38445	0.44152
	MSE	0.4674	0.87211	1.2218	0.42836	0.71089	0.93349
Gamma	Estimate	0.31862	0.46033	0.55189	0.28603	0.37866	0.43542
SELF	MSE	0.31381	0.59857	0.849	0.28784	0.47599	0.62549
Gamma	Estimate	0.3166	0.45682	0.54708	0.28421	0.37576	0.43165
LLF p=1.5	MSE	0.30733	0.57953	0.81444	0.28456	0.46567	0.60721
Gamma	Estimate	0.32068	0.46391	0.55682	0.28789	0.38162	0.43928
LLF p=-1.5	MSE	0.3213	0.62079	0.88973	0.29191	0.48842	0.64745
Weibull	Estimate	0.32001	0.46379	0.55691	0.28812	0.38247	0.4404
SELF	MSE	0.32643	0.62847	0.89836	0.297	0.49537	0.6557
Weibull	Estimate	0.31795	0.46023	0.55202	0.28627	0.37953	0.43656
LLF p=1.5	MSE	0.32018	0.60929	0.86262	0.29353	0.48417	0.63563
Weibull	Estimate	0.32209	0.46742	0.5619	0.29001	0.38547	0.4443
LLF p=-1.5	MSE	0.33367	0.65069	0.93996	0.30126	0.50861	0.67933
Log-normal	Estimate	0.31828	0.45945	0.55062	0.28459	0.37616	0.43222
SELF	MSE	0.42163	0.81384	1.15011	0.28157	0.4632	0.606
Log-normal	Estimate	0.31596	0.45535	0.54499	0.2828	0.37332	0.42852
LLF p=1.5	MSE	0.41237	0.78738	1.10303	0.27838	0.45338	0.58883
Log-normal	Estimate	0.32064	0.46365	0.55641	0.28642	0.37907	0.436
LLF p=-1.5	MSE	0.43231	0.84491	1.20612	0.28557	0.47516	0.62689

Table 7. Average ML and Bayes estimates with MSEs of cumulative CSHF for cause 1 and cause 2 with $n = 200$ at $X = -0.3$ when $a_1 = 0.5, \alpha_1 = 0.7, \lambda_1 = 0.1$ and $\beta_1 = 0.1$ for cause 1 and $a_2 = 0.4, \alpha_2 = 0.5, \lambda_2 = 0.1$ and $\beta_2 = 0.1$ for cause 2.

n=200		**Cause 1**			**Cause 2**		
Time Points		0.5	0.8	1	0.5	0.8	1
True Value		0.314	0.44962	0.53625	0.28856	0.37611	0.429
ML	Estimate	0.32099	0.46222	0.55294	0.29221	0.38542	0.44221
	MSE	0.27466	0.51	0.71151	0.20756	0.34933	0.46409
Gamma	Estimate	0.31906	0.45979	0.55036	0.2893	0.38211	0.43878
SELF	MSE	0.21614	0.40848	0.57624	0.16378	0.27454	0.36521
Gamma	Estimate	0.31796	0.45791	0.54781	0.2883	0.38054	0.43675
LLF p=1.5	MSE	0.21334	0.40044	0.56191	0.16238	0.27001	0.3572
Gamma	Estimate	0.32016	0.46169	0.55294	0.2903	0.38369	0.44084
LLF p=-1.5	MSE	0.21922	0.41736	0.59218	0.16541	0.27964	0.3742
Weibull	Estimate	0.31994	0.46199	0.55354	0.29091	0.38491	0.44238
SELF	MSE	0.22347	0.42481	0.60196	0.17135	0.29118	0.39052
Weibull	Estimate	0.31883	0.46009	0.55096	0.2899	0.38332	0.44032
LLF p=1.5	MSE	0.22053	0.41619	0.58644	0.16967	0.28586	0.38112
Weibull	Estimate	0.32106	0.46392	0.55615	0.29192	0.38652	0.44447
LLF p=-1.5	MSE	0.2267	0.43429	0.61909	0.17324	0.29708	0.40091
Log-normal	Estimate	0.31874	0.45909	0.5494	0.28835	0.38053	0.43679
SELF	MSE	0.25204	0.47918	0.67422	0.16165	0.26918	0.35658
Log-normal	Estimate	0.31756	0.45706	0.54662	0.28737	0.37898	0.43479
LLF p=1.5	MSE	0.24876	0.46984	0.6577	0.16033	0.26495	0.34911
Log-normal	Estimate	0.31992	0.46115	0.5522	0.28934	0.3821	0.43883
LLF p=-1.5	MSE	0.25565	0.48953	0.69265	0.16319	0.27397	0.365