ON BURR X NON-MIXTURE LONG-TERM SURVIVAL MODEL WITH APPLICATIONS TO MEDICAL DATA

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ABSTRACT

In the analysis of lifetime data, it is usually assumed that each and every subject in the study population will experience the event of interest if followed for a long period of time. However, due to improvement in the field of medicine, some subjects stay longer than expected. These subjects are termed long-term survivors. Hence, this study introduces a long-term survivor model based on Burr X distribution. The parameters of the model were estimated the Bayesian estimation procedure. To illustrate the applicability of the introduced methodology, a medical dataset was used fitted and the result compared with that of the model without the proportion of long-term survivors.

Keywords: Survival model, Long-term survivor model, non-mixture long-term survivor model, Burr X distribution.

1. Introduction

In the analysis of survival time data, accelerated failure time (AFT) models and proportional hazard (PH) models are frequently used. These models usually assumed that, the subjects in the study population would eventually encounter the event of interest if followed for a long time. However, studies have shown that, some patients would not actually experience the event of interest even if followed for a long period of time (Maller and Zhou, 1996). Therefore, to model this kind of data, the long-term survivor models are used. The long-term survivor models are frequently used when analyzing data from a population that consists of both long-term survivors and those who are at risk for the event of interest (Usman, *et al*., 2022). That is, the long-term survivor models are used for analyzing survival time data in the literature when the study population consists of two types of individuals: individuals who are long-term survivors and those who experienced the event of interest. Basically, there are two types of long-term survivor models: mixture and non-mixture long-term survivor models.

The mixture long-term survivor model was initially introduced by Boag (1949) and further developed by Berkson and Gage (1952) and later extensively studied by other authors such as: exponentiated mixture cure rate model by Kannan (2010), frechet mixture model by Ramos (2017), Nadarah-Haghighi mixture cure rate model by Usman *et al.*, (2021), Weibull exponentiated exponential mixture cure rate model by Usman *et al.*, (2022) and many more. The second model is the non-mixture long-term survival model introduced by Yakovlev *et al.*, (1993) and was further discussed by Chen et al. (1999). According to Chen *et al.*, (1999), the non-mixture long-term survival model is motivated by the underlying biological mechanism and is developed based on the assumption that the number of cancer cells that remain active after cancer treatment follows poison distribution. The model is shown to have some advantages over the mixture long-term

survival model. For example, it is easy to compute due to its simple structure for the survival function which provides certain technical advantage when developing maximum likelihood estimation procedures, it has proportional hazard model structure and it presents a much more biologically meaningful interpretation of the results of the data analysis (see Chen et al. (1999); Uddin et al. (2006) for more details). It is important to note that, the non-mixture model has a mathematical relationship with the standard long-term survival model. That is, the non-mixture model can be written as the standard long-term survival model Uddin *et al.*, (2006).

The rest of the paper is organized as follows: in section 2, we introduced the model, some statistical properties of the model are discussed in section 3 while estimation of the model parameters are given in section 4. Section 5 discusses on the applicability of the introduced methodology and we finally conclude in section 6.

2. Model

2.1. Burr X distribution

Burr (1949) presented twelve different distributions that are used in analyzing lifetime data in different fields including biology, agriculture, and health. These distributions were developed using the differential equation method. Burr X distribution is among these distributions. The probability density function (*pdf*), cumulative distribution function (*cdf*), Survival and hazard functions of the Burr X distribution are respectively given as:

$$f\left(\mathrm{t},\,\theta\right)=2\theta t\exp\left(-t^{2}\right)\left[1-\exp\left(-t^{2}\right)\right]^{\theta-1} \tag{1}$$

$$F\left(\mathrm{t},\,\theta\right)=\left[1-\exp\left(-t^{2}\right)\right]^{\theta}\ ,\mathrm{t}>0,\theta>0 \tag{2}$$

$$S\left(\mathrm{t},\theta\right)=1-\left(1-\exp\left(-t^{2}\right)\right)^{\theta} \tag{3}$$

and,

$$h\left(\mathrm{t},\theta\right)=2\theta t\exp\left(-t^{2}\right)\left(1-\exp\left(-t^{2}\right)\right)^{\theta-1}\left[1-\left(1-\exp\left(-t^{2}\right)\right)^{\theta}\right]^{-1} \tag{4}$$

where, θ is shape parameter. The distribution have been studied by many researchers, for instance, it has been extended to the generalized Rayleigh distribution by Surles and Padgett (2001), beta Burr X by Merovci *et al.*, (2016), Weibull Burr X by Ibrahim *et al.*, (2017) and exponentiated Burr X by Khaleel *et al.*, (2018). The parameter of the distribution was estimated using both the classical and Bayesian methods of estimation. For example, (Kundu and Raqab, 2005) estimated the parameter using some classical method of estimations, (Aliyu and Yahaya, 2016, 2017) and (Yahaya and Aliyu, 2017) estimated the parameters of the distribution using both the classical and non-classical method of estimations, Esemen, and Gürler, (2018) estimated the parameter of the distribution based on rank set sample. The distribution is used quite effectively in modeling strength data and also in modeling general lifetime data.

2.2. Non-mixture long-term survivor model

As mentioned earlier, the non-mixture long-term survival model was first introduced by Yakovlev *et al.*, (1993) and was further discussed by Chen et al. (1999). The survival function of the entire population for the non-mixture long-term survivor model is given as:

$$S(t) = \pi^{F_0(t)} \tag{5}$$

where, π is the proportion of long-term survivors and it lies between $0 < \pi < 1$ and $F_0(t) = 1 - S_0(t)$ is the distribution function for the susceptible individuals. The pdf, cfd and the hazard function for the non-mixture long-term survivor model are respectively given as:

$$f(t) = (-\ln \pi)\, f_0(t) \pi^{F_0(t)} \tag{6}$$

$$F(t) = 1 - \pi^{F_0(t)} \tag{7}$$

and,

$$h(t) = (-\ln \pi)\, f_0(t) \tag{8}$$

Hence, the survival function of the entire population for the Burr X non-mixture long-term survivor model is given as:

$$S(\mathrm{t}/\theta, \pi) = \pi^{\left[1-\exp(-t^2)\right]^{\theta}} \tag{9}$$

where $t > 0$ is the survival time, π is the proportion of long-term survivors and θ is the shape parameter. The cdf, pdf and hazard function for the Burr X non-mixture long-term survivor model are respectively given as:

$$F(\mathrm{t}/\theta, \pi) = 1 - \pi^{\left[1-\exp\left(-t^2\right)\right]^{\theta}} \tag{10}$$

$$f(t/\theta, \pi) = 2(-\ln \pi)\theta t \exp\left(-t^2\right)\left(1 - \exp\left(-t^2\right)\right)^{\theta-1} \pi^{\left(1-\exp\left(-t^2\right)\right)^{\theta}} \tag{11}$$

and

$$h(\mathrm{t}/\theta, \pi) = 2\theta t \ln(-\pi) \exp\left(-t^2\right)\left[1 - \exp\left(-t^2\right)\right]^{\theta-1} \tag{12}$$

3. Statistical Properties of the Models

In this section, some statistical properties such as quantile function and moments of the *BXNMLTS* model were discussed.

3.1. Quantile Function of the *BXNMLTS* model

To obtain random realizations from a given model, the quantile function is employed. The quantile function for the BXNMLTS model is given by:

$$Q(u) = -\left[\ln\left(1 - \left(\frac{\ln(1-u)}{\ln(\pi)}\right)^{1/\theta}\right)\right]^{1/2} \tag{13}$$

where u is a random number generated from uniform distribution with parameters zero and one. That is $u \sim U(0, 1)$. The quantile function can be used in obtaining the first, second and third quantiles of the BXNMLTS model. This is done by letting $u = 1/4, 1/2$ and $3/4$ respectively for the first, second and third quantiles. For instance, the second quantile (median) is obtained as:

$$median = -\left[\ln\left(1-\left(\frac{\ln(0.5)}{\ln(\pi)}\right)^{1/\theta}\right)\right]^{1/2} \tag{14}$$

3.2. Moments of the BXNMLTS Model

To obtain the r[th] moment of the Burr X Non-mixture long-term survivor model, we use the *pdf* of the Burr X Non-mixture Long-term survivor Model:

$$f(t) = 2\ln(-\pi)\theta t\exp\left(-t^2\right)\left(1-\exp\left(-t^2\right)\right)^{\theta-1}\pi^{\left(1-\exp\left(-t^2\right)\right)^{\theta}}$$

expanding the *pdf* using binomial series expansion gives:

$$f(t) = 2\ln(-\pi)\theta t\sum_{k,m=0}^{\infty}(-1)^{k+m}\frac{1}{k}\binom{\theta(1+k)-1}{m}\left(\exp\left(-t^2\right)\right)^{m+1}$$

The *rth* moment is obtained as follows:

$$E\left(t^r\right) = \int_0^{\infty} t^r f(t)\partial t$$

$$= 2\ln(-\pi)\theta t\sum_{k,m=0}^{\infty}(-1)^{k+m}\binom{1}{k}\binom{\theta(1+k)-1}{m}\int_0^{\infty} t^r\left(\exp\left(-t^2\right)\right)^{m+1}\partial t$$

taking the integral part:

$$\int_0^{\infty} t^r\left(\exp\left(-t^2\right)\right)^{m+1}\partial t$$

let $y = (m+1)t^2$

$$t = \left(\frac{y}{(m+1)}\right)^{1/2}$$

$$dy = (m+1)2tdt$$

$$dt = \frac{dy}{(m+1)2t}$$

$$= \cancel{2}\ln(-\pi)\theta\cancel{t}\sum_{k,m=0}^{\infty}(-1)^{k+m}\binom{1}{k}\binom{\theta(1+k)-1}{m}\int_0^{\infty}\left[\frac{y}{(m+1)}\right]^{r/2}\exp(-y)\frac{dy}{(m+1)\cancel{2t}}$$

$$= \frac{\ln(-\pi)\theta\sum_{k,m=0}^{\infty}(-1)^{k+m}\binom{1}{k}\binom{\theta(1+k)-1}{m}}{(m+1)^{r/2+1}}\int_0^{\infty}[y]^{r/2}\exp(-y)dy$$

where $\int_0^{\infty}[y]^{r/2}\exp(-y)dy = \Gamma\left(\frac{r}{2}+1\right)$ and hence, the *rth* moment is given by:

$$E\left(t^r\right)=\frac{\ln(-\pi)\sum_{k,m=0}^{\infty}(-1)^{k+m}\binom{1}{k}\binom{\theta(1+k)-1}{m}\Gamma\left(\frac{r}{2}+1\right)}{(m+1)^{\frac{r}{2}+1}} \tag{15}$$

4. Estimation Procedure

In this section, Bayesian method of estimation is used in estimating the parameters of the BXNMLTS model. MCMC technique is used to get the approximate posterior summaries of the parameters of the BXNMLTS model.

Consider a random sample (t_i,δ_i) i = 1, . . . , n , where t_i is the time to the occurrence of the event of interest and δ_i is a censoring indicator defined as:

$$\delta_i=\begin{cases} i=1 & \textit{for uncencored lifetime} \\ i=0 & \textit{for censored lifetime} \end{cases}$$

then the likelihood function is defined as:

$$L_i=\prod_{i=1}^{n}\left[h(t_i)\right]^{\delta_i}S(t_i) \tag{16}$$

Substituting the survival and hazard functions in equations (5) and (8) into equation (16) gives:

$$L_i=\prod_{i=1}^{n}\left[\left(-\ln\pi\right)f_0\left(t_i\right)\right]^{\delta_i}\pi^{F_0(t_i)} \tag{17}$$

Hence, the likelihood of the BXNMLTS model is obtained by substituting the survival and hazard functions of the BXNMLTS model in equations (9) and (12) into equation (17). This gives:

$$L_i=\prod_{i=1}^{n}\left[-\ln(\pi)\theta t\exp(-t^2)(1-\exp(-t^2))\right]^{\delta_i}\pi^{(1-\exp(-t^2))^{\theta}} \tag{18}$$

Let Θ be the vector of unknown parameters. For Bayesian method of estimation, let the prior density for the parameters: θ and π respectively be denoted by $\Pi(\theta)$ and $\Pi(\pi)$. A gamma prior for the shape parameter of the proposed model is assumed. That is:

$$\Pi(\theta)=\frac{1}{\Gamma(a)b^{a-1}}\theta^{a-1}e^{-\frac{\theta}{b}} \tag{19}$$

On the other hand, the proportion of long-term survivors (π) is assumed to follow the beta prior. That is:

$$\Pi(\pi)=\frac{1}{B(c,\,d)}\pi^{c-1}(1-\pi)^{d-1} \tag{20}$$

where a, b, c and d are hyper-parameters, $B(c,\,d)$ is referred to as beta function which is defined by $B(c,\,d)=\frac{\Gamma(c)\Gamma(d)}{\Gamma(c+d)}$. We further assumed the hyper-parameters to be specified and non-negative. Prior independence among the parameters is also assumed. Hence, the joint prior distribution is given by:

$$\Pi(\Theta) = \frac{1}{B(c,\, d)\Gamma(a)b^{a-1}}\theta^{a-1}\pi^{c-1}(1-\pi)^{d-1}e^{-\frac{\theta}{b}} \tag{21}$$

To be specific, $\theta \sim gamma(1,1)$ since $\theta > 0$ and $\pi \sim Beta(1,1)$, since $0 < \pi < 1$. The joint posterior distribution is obtained by combining the joint prior distribution of the parameters in equation (26) and the likelihood function in equation (23). This gives:

$$\Pi(\Theta) = \frac{1}{B(c,\, d)\Gamma(a)b^{a-1}}\theta^{a-1}\pi^{c-1}(1-\pi)^{d-1}e^{-\frac{\theta}{b}} \times \prod_{i=1}^{n}\left[-\ln(\pi)\theta t\exp(-t^2)(1-\exp(-t^2))\right]^{\delta_i}\pi^{(1-\exp(-t^2))^{\theta}} \tag{22}$$

A great computational simplification in simulating samples from this posterior density can be achieved using the OpenBUGS software, where only the distribution of the data and the prior distributions of the parameters are required.

5. Applications

In this section, two real life data sets were used in demonstrating the applicability of the proposed non-mixture long-term survivor methodology: the Allogeneic bone marrow transplant data and cervical carcinoma datasets.

The allogeneic bone marrow transplant data consist of 90 observations that was previously analyzed by Shao and Zhou (2004), Kutal and Qian (2018), Usman et al. (2021), Usman *et al.*, (2022) and Aliyu and Usman (2025). The first data was used to fit the non-mixture long-term survivor model studied in previous section and compared its performance with that of Burr X distribution. The data recorded the times to recurrence of leukaemia for patients after one of allogeneic transplant or autologous transplant. Forty-six (46) patients were treated by allogeneic transplant while the remaining forty-four (44) were treated by autologous transplant. However, thirty-three (33) and thirty-five patients treated by allogeneic transplant and autologous transplant respectively suffered a recurrence of leukaemia at different ranges of time. It is also observed that thirteen (13) and nine (9) patients from these respective groups have no record of recurrence. That is they are censored. Bayesian method of estimation discussed in section 4 was used to analyze this data.

In analyzing this data, gamma prior is assumed for θ while beta prior is assumed for the long-term survivor parameter. To be specific, $\theta \sim Gamma(1,\ 1)$ and $\pi \sim Beta(1,\ 1)$. We further assumed prior independence among the parameters included in the model. MCMC technique was applied in obtaining posterior summaries from the joint posterior distribution. We generated 1,050,000 samples for each parameter of interest from the posterior distribution. However, the first 50,000 samples were discarded as burn-in-samples in order to reduce the effect of initial values while to reduce the effect of autocorrelation, samples are taken at every 100th sample. Therefore, all posterior summaries of interest were based on 10,000 samples. The results are given in Table 1.

Table 1 Posterior summaries for models with and without long-term survivor – Allogeneic Bone Marrow Transplant data

Models	Parameter	Median	S.D	95% CrI	DIC
OBX	θ	0.599	0.08729	(0.45,0.79)	153.4
OBXNM	π	0.3045	3.472E-7	(0.19,0.44)	110.9

θ	0.5566	0.08769	(0.41,0.74)

Table 1 gives the posterior summaries for the fitted Burr X models with and without long-term survivor parameter. Standard deviation (S.D) and 95% credible interval (CrI) of the estimates were also given. The Deviance information criteria for the fitted models were also provided. We note that, the Bayesian estimates for the parameter θ for both the Burr X distribution and BXNMLS model are relatively close. However, based on the *DIC* value for these fitted models, it can easily be seen that, the BXNMLS model is more efficient than the Burr X distribution in fitting the data.

The second data set used in this article is the overall survival time extracted from the cervical carcinoma data given in (Brenna et al. 2004). The data consists of a total of 148 women who were diagnosed and treated for invasive cervical carcinoma between 1992 and 2002. A sub-sample of 118 women who received the standard treatment recommended by International Federation of Gynecology and Obstetrics (FIGO) were used. The time from the date of surgery to the first event of disease recurrence is defined as the disease-free survival (DFS). While the time from the date of surgery to death is defined as the overall survival. Similar procedures as in allogeneic bone marrow transplant is followed in analyzing this dataset. However, in this application, the performance of the proposed methodology is compared with that of Rayleigh non-mixture long-term survivor model. The result of this analysis is given in Table 2.

Table 2 Bayesian Estimates for Non-Mixture models – OST data

Models	Parameter	Median	S.D	95% CrI	DIC
BXNMLSM	π	0.371	0.05255	(0.27,0.48)	162.2
	θ	0.6859	0.07899	(0.54,0.86)	
RNMLSM	π	0.3555	0.0530	(0.25-0.46)	170.9
	θ	0.5856	0.0544	(0.50,0.71)	

Table 2 shows the posterior estimates of each parameter as well as the estimates of their standard errors, 95% credible interval and DIC. The table shows that, the BXNMLS model is more efficient in fitting the data compared to the RNMLS since it has the lowest value of DIC.

6. Conclusion

The presence of long-term survivor is usually included in lifetime data analysis, particularly in applications related to medicine. In this research, a non-mixture long-term survival model for right-censored data is introduced by employing Burr *X* distribution in the presence of right-censoring. Bayesian estimation procedure is used to estimate the model parameters. Two datasets are used in demonstrating the applicability of the proposed methodology. It was found that, the model with long-term survivor parameter is more efficient in fitting the data than the model without long-term survivor parameter. In addition, the proposed model is found to be more efficient in fitting the overall survival time (OS) of cervical carcinoma dataset than the Rayleigh long-term non-mixture models.

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