CURE FRACTION MODELS BASED ON A LOMAX-EXPONENTIAL DISTRIBUTION WITH APPLICATIONS.

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Abstract:

Research has proven that due to the development of new drugs, some patients in a cohort of cancer patients are cured permanently, and some are not cured. The patients who are cured permanently are called cured or long-term survivors while patients who experience the recurrence of the disease are termed as susceptible or uncured. Cure fraction models are usually used to model lifetime time data with long-term survivors. This paper presents a maximum likelihood estimation and analysis of a three-parameter Lomax-exponential distribution (LED) involving a cure fraction parameter with application to censored dataset. In order to capture the proportion of cured patients, a mixture and a non-mixture cure models formulation methods are employed. To assess the usefulness of these models in real life applications, the paper used a real-life dataset on acute lymphoblastic leukaemia (ALL) data. The results revealed that the estimates of the cured proportion based on LED are higher for treatment group I than group II which implies a higher probability survival for patients receiving treatment I than those receiving treatment II. It is also revealed that the estimates of the cured proportion are higher for the mixture cure model than the non-mixture cure model. Furthermore, the study revealed that the mixture cure model based on LED has lower values of AIC and BIC than the non-mixture cure model and LED, meaning that the mixture cure model fits the data better than the non-mixture cure model.

Keywords: Cure fraction, Cure model, mixture, non-mixture, LED, Estimation and application.

1. Introduction

Acute lymphoblastic leukaemia (ALL) is a biologically heterogenous malignant disease of early lymphoid precursors characterized by arrest of maturation, proliferation of blasts in the marrow leading to replacement of normal haemopoietic cells and eventual spillage into peripheral blood. ALL is the most common childhood leukaemia diagnosed in children aged 2 to 5 years as well as in young adults (Fleming *et al*., 1993; Akang, 1996; Molyneux *et al*., 2017), with an estimated 5-year survival of about 72% in the

United States (Sasaki *et al*., 2021). While ALL represents 80% of children leukemia, it is uncommon in grown-ups (20% of cases). In the United States, the incidence of ALL is estimated at 1.64 per 100,000 persons (National Cancer Institute, 2020). According to the American Cancer Society database (2019), an estimated 5930 new cases were diagnosed, with 1,500 deaths due to ALL in 2019. The formulation of treatment for grown-ups ALL has been adjusted from pediatric conventions. Shockingly, while cure tends to be 90% for standard-hazard pediatric ALL, the long-term survival rate is humbler in grown-ups (Terwilliger and Abdul-Hay, 2017). ALL treatment outcome has improved significantly in developed countries with remission rate reaching up to 80% (Björkholm *et al*., 2019) unlike in resource constraint nations like Nigeria where rates are mostly less than 50%. The improved outcome witnessed results from better understanding of the disease pathogenesis arising from advances in molecular methodology, development of targeted therapy with less toxicity protocols, as well as availability of other supportive interventions.

The main treatment of ALL is chemotherapy, which comprises of induction, intensification, and long-term maintenance, with the central nervous system (CNS) prophylaxis provided at different times during the therapy. Induction therapy aims to accomplish total remission and to re-establish ordinary hematopoiesis. Following the induction treatment, patients underwent three cycles of consolidation treatment of methotrexate with leucovorin rescue and L-asparaginase. Registered individuals as high-risk disease and a corresponded donor, then received allogeneic stem cell transplantation (allo-SCT). The rest were randomly assigned to standard intensification/ maintenance or autologous bone marrow transplants. The prognostic factors affecting clinical outcome in ALL patients include age, leukocytes count, tumour genetic factors and response to chemotherapy. Cytogenetic characteristic of patients in Nigeria is still not available due to dearth of infrastructure. Several studies have been done and documented the dismal survival rate of ALL patients, but a few have looked at the clinical and laboratory predictors of outcome in these patients in Nigeria (Okpala *et al*., 1990; Abdelmabood *et al*., 2020).

Also, survival analysis generally utilizes product-limit estimates or log-rank test (Bradburn et al., 2003a), semi-parametrical models (for instance, Cox proportional hazards model), or regular parametrical models considering several well-known distributions in the existence of covariates (Cox, 1972). The Weibull distribution and other distributions with flexible risk functions have been widely used in cancer research (Bradburn *et al*., 2003b). However, data sets of medical studies often necessitate more advanced parametric models. As a consequence, to resolve this problem, several authors in the literature have proposed new classes of parametric distributions such as the exponentiated Weibull distribution (Mudholkar and Srivastava, 1993), the generalized modified Weibull distribution (Carrasco *et al*., 2008), the log-beta Weibull (Ortega *et al*., 2013), the generalized alpha power inverse Weibull distribution (Basheer, 2019), the generalized Gompertz distribution by Swain *et al*. (2016) and the Burr XII distribution by Coelho-Barros et al. (2017). Others include Leão *et al*. (2018), Varshney *et al*. (2018), Barriga *et al*. (2018), Borges (2020) as well as Omer et al. (2021). Another common scenario in survival data analysis, particularly in cancer research, is when a fraction of a population is not exposed to the event of interest. For this situation, patients were divided into two groups: those who were exposed to the event under study, and those who were not exposed to it and, therefore, were not at risk. These patients are viewed as cured or immunized.

The existence of cured subjects in a sample data is commonly proposed by a Kaplan-Meier curve, which displays a tall and a steady level with dense censoring at the right extreme (Corbière et al., 2009). To model the proportion of cured subjects, many authors have proposed several statistical methods. Interested readers can check (Boag, 1949; Berkson and Gage, 1952; Haybittle, 1965; Farewell, 1982; Goldman, 1984; Farewell, 1986; Gamel et al., 1990; Maller and Zhou, 1992; Kuk and Chen, 1992; Taylor, 1995; Peng and Dear, 2000; Peng and Carriere, 2003; Tajuddin et al.,

2006; Lambert et al., 2007; Abubakar et al., 2008; Lu, 2010; López-Cheda et al., 2017; Martinez and Achcar, 2014; Martinez and Achcar, 2018; Naseri *et al*., 2018). Moreover, the maximum likelihood estimation technique has been suggested by some authors such as (Farewell, 1982; Yamaguchi, 1992; Ghitany and Maller, 1992; Peng et al., 1998; Sy and Taylor, 2000) amongst others.

The aim of this paper is to derive and study a mixture and a non-mixture cure fraction models considering the Lomax-exponential distribution (LED) with estimation of parameters and application to acute lymphocytic leukemia (ALL) data.

The remaining parts of this paper will come in the following form: Section 2 covers the methodology under which subsection 2.1 presents LED, 2.2 presents mixture cure models based on LED, and 2.3 gives non-mixture cure models based on LED. Section 4 presents the estimation of the mixture and non-mixture cure models based on the LED. The application of the LED cure fraction models is illustrated in section 5 using acute lymphocytic leukemia (ALL) data while the summary and conclusion of the research is given in section 6.

2. Methodology

2.1 Lomax-Exponential Distribution (LED)

According to Jeren and Kuhe (2018), the proper cumulative distribution function (cdf) and proper probability density function (pdf) of the Lomax-exponential distribution (LED) are defined respectively as given in equation (1) and (2) below:

$$F_o(t) == 1-\beta^{\alpha}\left(\beta+\lambda t\right)^{-\alpha} \tag{1}$$

And

$$f_o(x) = \alpha\beta^{\alpha}\lambda\{\beta+\lambda t\}^{-(\alpha+1)} \quad (2)$$

where α, β and λ, are the parameters of the LED. Relatedly, the corresponding survival function (SF) and hazard function (HF) of LED are given respectively as:

$$S_o(t) = \beta^{\alpha}(\beta+\lambda t)^{-\alpha} \quad (3)$$

And

$$h_o(t) = \frac{f_o(t)}{S_o(t)} = \alpha\lambda\{\beta+\lambda t\}^{-1} \quad (4)$$

2.2 Mixture cure model

The first mixture cure model was initially proposed by Boag (1949) and later by Berkson and Gage (1952). According to Boag (1949), a mixture cure model assumes that the survival function for the entire population can be expressed as a mixture of the cured and the uncured patients (the overall population) and is given by,

$$S(t) = p + (1-p)S_o(t) \quad (5)$$

where p is the proportion of subjects that are cured (long-term survivors), and $1-p$ is the proportion of subjects that are not cured (susceptible), and $S_o(t)$ denotes a proper survival function for the uncured patients assumed to follow a probability distribution. The corresponding density function of T is expressed as;

$$f(t) = (1-p)f_o(t) \quad (6)$$

where $f_o(t)$ is the probability density function of uncured patients assumed to follow a probability

distribution. Also, the cumulative distribution function of the overall population is given as;

$$F(t) = (1-p)F_o(t) \tag{7}$$

where $F_o(t)$ denotes a proper cumulative distribution function for the uncured patients assumed to follow a probability distribution.

Substituting for the proper $F_o(t)$, $S_o(t)$ and $f_o(t)$ from the proposed LED, the CDF, PDF, SF and HF of the cured patients under mixture form are obtained respectively as;

$$F(t) = (1-p)\left(1-\beta^{\alpha}(\beta+\lambda t)^{-\alpha}\right) \tag{8}$$

$$S(t) = p+(1-p)\left(\beta^{\alpha}(\beta+\lambda t)^{-\alpha}\right) \tag{9}$$

$$f(t) = (1-p)\left(\alpha\beta^{\alpha}\lambda(\beta+\lambda t)^{-(\alpha+1)}\right) \tag{10}$$

and

$$h(t) = \frac{f(t)}{S(t)} = \frac{(1-p)\left(\alpha\beta^{\alpha}\lambda(\beta+\lambda)^{-(\alpha+1)}\right)}{p+(1-p)\left(\beta^{\alpha}(\beta+\lambda t)^{-\alpha}\right)} \tag{11}$$

2.3 Non-mixture cure model

According to Yakovlev *et al*., (1993), this model was developed based on the assumption that the number of cancer cells that remain active after cancer treatment and may grow slowly and produce a detectable cancer, whose growth is assumed to follow a Poisson distribution. The survival function of a non-mixture cured model is given by,

$$S(t) = p^{F_o(t)} \tag{12}$$

where p is the proportion of subjects that are cured (long-term survivors) and $F_o(t)$ denotes a proper cumulative distribution function for the uncured patients assumed to follow a probability distribution. The corresponding density function, cumulative distribution function and hazard function are given respectively as;

$$f(t) = -\ln p f_o(t)\, p^{F_o(t)} \tag{13}$$

$$F(t) = 1 - p^{F_o(t)} \tag{14}$$

And

$$h(t) = -\ln(p)\, f_o(t) \tag{15}$$

Where $f_o(t)$ is the density function of uncured subjects or patients assumed to follow a probability distribution.

Using the proper $F_o(t)$, $S_o(t)$ and $f_o(t)$ from the LED, the CDF, PDF, SF and HF of the cured patients under non-mixture form are obtained respectively as;

$$F(t) = 1 - p^{\left[1-\beta^{\alpha}(\beta+\lambda t)^{-\alpha}\right]} \tag{16}$$

$$S(t) = p^{\left[1-\beta^{\alpha}(\beta+\lambda t)^{-\alpha}\right]} \tag{17}$$

$$f(t) = -\ln(p)\,\alpha\beta^{\alpha}\lambda(\beta+\lambda t)^{-(\alpha+1)}\, p^{\left[1-\beta^{\alpha}(\beta+\lambda t)^{-\alpha}\right]} \tag{18}$$

and

$$h(t) = -\ln(p)\,\alpha\beta^{\alpha}\lambda(\beta+\lambda t)^{-(\alpha+1)} \tag{19}$$

2.4 Estimation of Parameters of the Mixture and Non-mixture Models

Suppose that, for each individual, $i = 1, 2, ..., n$, we have a pair of random variables, (t_i, δ_i). t_i can either represent the failure time, X_i, or (non-informative right-) censoring time, C_i, such that, $t_i = \min(X_i, C_i)$, and $\delta_i = I(X_i < C_i)$ is the censoring indicator, where $\delta_i = 1$, if the individual's failure time is observed, or $\delta_i = 0$ if the individual is right-censored or alive. Therefore, the likelihood function is expressed as,

$$L_i = \prod_{i=1}^{n} f(t_i, \delta_i) = \prod_{i=1}^{n} \left[\left(f(t_i) \right)^{\delta_i} \left(S(t_i) \right)^{1-\delta_i} \right] \quad (20)$$

Intuitively, for example, at the end of a cancer study, if the patient is alive/censored at time t_i $(\delta_i = 0)$, then the i^{th} contribution to the total likelihood is the survival probability, $S(t_i)$. Conversely, if the patient dies during the study, then the i^{th} contribution to the total likelihood is the probability that the patient dies at the observed time, t_i.

Substitution of the mixture density in equation (10) and the mixture survival function in equation (9) in the standard likelihood function in Equation (20) yields the likelihood for the long-term survivor mixture model:

$$Li = \left[(1-p)\alpha\beta^{\alpha}\lambda(\beta+\lambda t_i)^{-(\alpha+1)} \right]^{\delta_i} \left[p + (1-p)\beta^{\alpha}(\beta+\lambda t_i)^{-\alpha} \right]^{1-\delta_i} \quad (21)$$

Thus, the log-likelihood considering all observations is given by:

$$l = \sum_{i=1}^{n} \delta_i (1-p) + \sum_{i=1}^{n} \delta_i \log\left[\alpha\beta^{\alpha}\lambda(\beta+\lambda t_i)^{-(\alpha+1)} \right] + \sum_{i=1}^{n} (1-\delta_i) \log\left[p + (1-p)\beta^{\alpha}(\beta+\lambda t_i)^{-\alpha} \right] \quad (22)$$

$$\begin{aligned} l = {} & r\log(1+p) + r\log\alpha + r\alpha\log\beta + r\log\lambda - \\ & (\alpha+1)\sum_{i=1}^{n} \delta_i \log(\beta+\lambda t_i) + \sum_{i=1}^{n} (1-\delta_i) \log\left[p + (1-p)\beta^{\alpha}(\beta+\lambda t_i)^{-\alpha} \right] \end{aligned} \quad (23)$$

where $r=\sum_{i=1}^{n}\delta_i$ is the number of uncensored observations.

Given the observed lifetime data, (t_i,δ_i), $i=1,...,n$, and defining $l=\log L(\theta\mid t,\delta)$, the maximum likelihood estimates for $\theta=(\alpha,\beta,\lambda,p)$ denoted by $\hat{\theta}=(\hat{\alpha},\hat{\beta},\hat{\lambda},\hat{p})$ are obtained by differentiating l partially with respect to α β, λ, and p respectively:

$$\frac{\partial l}{\partial\alpha}=\frac{r}{\alpha}+r\log\beta-\sum\delta_i\log(p+\lambda t_i)+\beta^{\alpha}\sum_{i=1}^{n}(1-\delta_i)\left[\frac{(1-p)(\beta+\lambda t)^{-\alpha}(\ln\beta-\ln(p+\lambda t))}{\left[p+(1-p)\beta^{\alpha}(\beta+\lambda t_i)^{-\alpha}\right]}\right] \quad (24)$$

$$\frac{\partial l}{\partial\beta}=\frac{r\alpha}{\beta}-(\alpha+1)\sum_{i=1}^{n}\delta_i\left[\frac{1}{(\beta+\lambda t_i)}\right]+\alpha\beta^{\alpha}\sum_{i=1}^{n}(1-\delta_i)\left[\frac{(1-p)(\beta+\lambda t)^{-\alpha}\left(\beta^{-1}-(\beta+\lambda t)^{-1}\right)}{p+(1-p)\beta^{\alpha}(\beta+\lambda t_i)^{-\alpha}}\right] \quad (25)$$

$$\frac{\partial l}{\partial\lambda}=\frac{r}{\lambda}-(\alpha-1)\sum_{i=1}^{n}\delta_i\left[\frac{t_i}{(\beta+\lambda t_i)}\right]-\alpha\sum_{i=1}^{n}(1-\delta_i)\left[\frac{(1-p)(\beta+\lambda t_i)^{-\alpha}t_i}{p+(1-p)\beta^{\alpha}(\beta+\lambda t_i)^{\alpha}}\right] \quad (26)$$

$$\frac{\partial l}{\partial p}=-\frac{r}{1-p}+\sum_{i=1}^{n}(1-\delta_i)\left[\frac{1-\beta^{\alpha}(\beta+\lambda t_i)^{-\alpha}}{\left[p+(1-p)\beta^{\alpha}(\beta+\lambda t_i)^{-\alpha}\right]}\right] \quad (27)$$

Equating (24), (25), (26) and (27) to zero (0) and solving for the solution of the non-linear system of equations produce the maximum likelihood estimates of parameters α β, λ, and p. Note that it is difficult to solve the above equations analytically and therefore the Newton-Raphson's iteration method is applied using computer applications such as Python, R, Matlab or any other suitable software.

Also, substitution of the non-mixture density in equation (18) and the non-mixture survival function in equation (17) in the standard likelihood function in Equation (20) produces the likelihood for the long-term survivor non-mixture model as follows:

$$L_i = \left[-ln(p)\alpha\beta^{\alpha}\lambda\left(\beta+\lambda t_i\right)^{-(\alpha+1)}\ p^{\left[1-\beta^{\alpha}\left(\beta+\lambda t_i\right)^{-\alpha}\right]} \right]^{\delta_i} \left[p^{\left[1-\beta^{\alpha}\left(\beta+\lambda t_i\right)^{-\alpha}\right]} \right]^{1-\delta_i} \quad (28)$$

Hence, the log-likelihood considering all observations for the non-mixture approach is given by:

$$l = \sum_{i=1}^{n}\delta_i \log\left[-\log(p)\right] + \sum_{i=1}^{n}\delta_i \log\left[\alpha\beta^{\alpha}\lambda\left(\beta+\lambda t_i\right)^{-(\alpha+1)}\right] + \log(p)\sum_{i=1}^{n}\left[1-\beta^{\alpha}\left(\beta+\lambda t_i\right)^{-\alpha}\right]$$

$$l = r\log\left[-\log(p)\right] + r\log\alpha + r\log + r\alpha\log\beta + r\log\lambda - (\alpha+1)\sum_{i=1}^{n}\delta_i\log\left(\beta+\lambda t_i\right) + \log(p)\sum_{i=1}^{n}\left[1-\beta^{\alpha}\left(\beta+\lambda t_i\right)^{-\alpha}\right] \quad (30)$$

where $r = \sum_{i=1}^{n}\delta_i$ is the number of uncensored observations.

Differentiating the log-likelihood function in equation (30) above partially with respect to α β, λ, and p respectively and setting the results equal to zero produces the maximum likelihood estimates $\hat{\alpha}$ $\hat{\beta}$, $\hat{\lambda}$, and $\hat{p}$ as follows:

$$\frac{\partial l}{\partial\alpha} = \frac{r}{\alpha} + r\log\beta - \sum_{i=1}^{n}\delta_i\log\left(\beta+\lambda t_i\right) - \log(p)\beta^{\alpha}\sum\left[\left(\beta^{\alpha}+\lambda t_i\right)^{-\alpha}\left(\ln\beta+\ln\left(\beta+\lambda t_i\right)\right)\right] \quad (31)$$

$$\frac{\partial l}{\partial\beta} = \frac{r\alpha}{\beta} - (\alpha+1)\sum\delta_i\frac{1}{\left(\beta+\lambda t_i\right)} - \log(p)\alpha\beta^{\alpha}\sum_{i=1}^{n}\left[\left(\beta+\lambda t\right)^{-\alpha}\left(\frac{1}{\beta}+\beta+\lambda t\right)^{-1}\right] \quad (32)$$

$$\frac{\partial l}{\partial\lambda} = \frac{r}{\lambda} - (\alpha+1)\sum\delta_i\left[\frac{t_i}{\beta+\lambda t_i}\right] + \log(p)\alpha\beta^{\alpha}\sum\left[t_i\left(\beta+\lambda t_i\right)^{-\alpha-1}\right] \quad (33)$$

$$\frac{\partial l}{\partial p} = \frac{r}{p\log(p)} + \frac{1}{p}\sum_{i=1}^{n}\left[1-\beta^{\alpha}\left(\beta+\lambda t_i\right)^{-\alpha}\right] \quad (34)$$

Again, equating (31), (32), (33) and (34) to zero (0) and solving for the solution of the non-linear system of equations produces the maximum likelihood estimates of parameters α β, λ, and p.

Solving Equation (34) algebraically, the maximum likelihood estimator of the cure proportion $\hat{p}$ is obtained as:

$$\hat{p} = \exp\left\{-\sum_{i=1}^{n}\left[\frac{\delta_i}{\left[1-\beta^{\alpha}\left(\beta+\lambda t_i\right)^{-\alpha}\right]}\right]\right\} \tag{35}$$

Equation (35) is useful for calculating $\hat{p}$ with available data and other necessary parameters and also useful for finding the estimates of $\hat{\alpha}$ $\hat{\beta}$ and $\hat{\lambda}$ by substituting for $\hat{p}$ into the Equations (31), (32) and (33) respectively and solving with numerical methods.

3 Results and discussion

Dataset: This paper considered a leukemia dataset on the bone marrow transplant study for the refractory acute lymphoblastic leukemia (ALL) patients, which was first analyzed by Kersey et al. (1987) and is available in smcure package in R software (Cai *et al*., 2012). It has also been used by Cai (2013) and Omer *et al*. (2021). This dataset consists of 91 patients with high-risk ALL and is divided into two subsets; the first subset (Group 1) contains 46 patients who were exposed to allogeneic bone marrow transplants and the second subset (Group 2) includes 45 patients who received autologous bone marrow transplants. The event of interest is time to death.

The Kaplan–Meier estimate of the survival/hazard functions for the acute lymphoblastic leukemia (ALL) data is given in Figure 1 below:

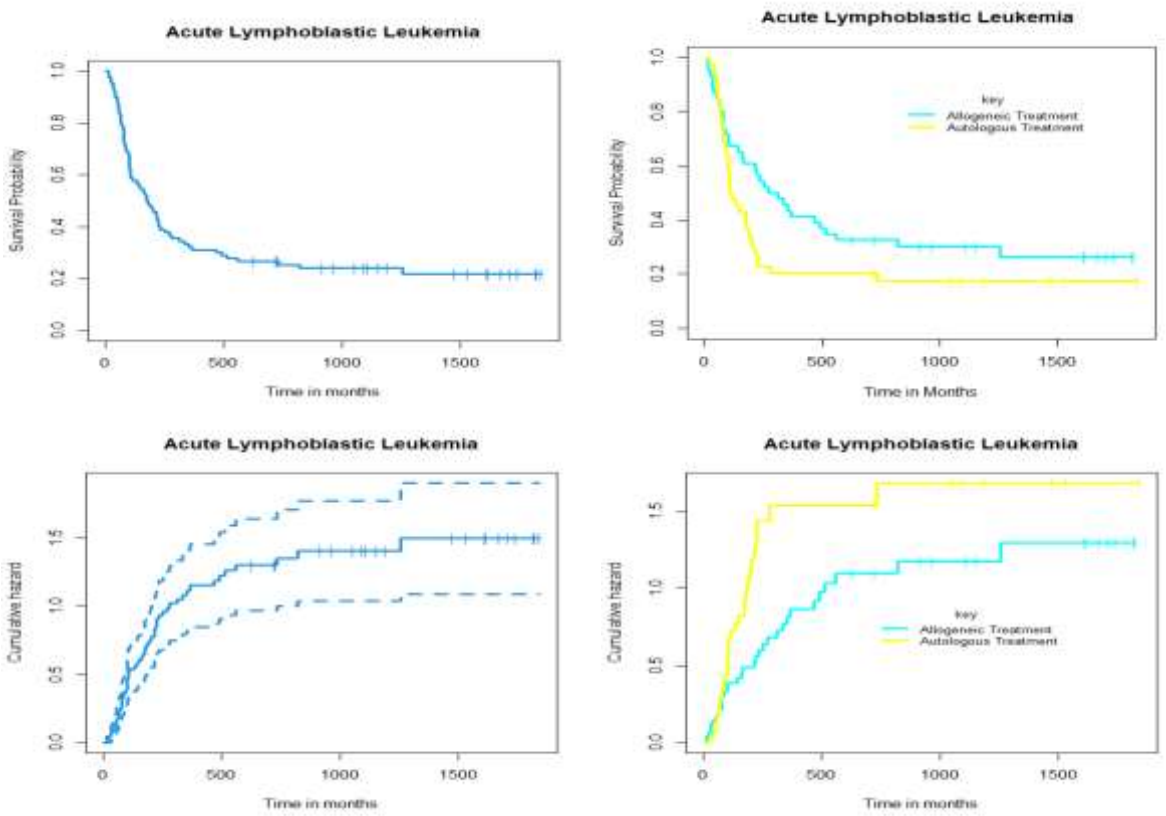

Figure 1: Kaplan-Meier estimates of overall survival/hazard & for each type of Treatment

The Kaplan–Meier estimate of the survival/hazard function for the ALL data is presented in Figure 1, the flat cure or a plateau in the survival curve suggests the presence of a cured fraction for both treatment methods (allogeneic and autologous). It shows that models without cured proportion, p of long-term survivors cannot appropriately model this data. The right side of the graph in Figure 1 shows the survival functions for each treatment and the survival probability is higher for allogeneic method compared to the autologous method, this implies that patients who received allogeneic method have higher chances of survival than those who received autologous and vice versa.

Table 1: MLEs of the Parameter with Standard errors, Z-values, P-values, AIC and BIC for Treatment Group I

Parameter	Estimates	Standard Error	Z-value	*P*-value	AIC	BIC
LED	$\hat{\alpha}$ =2.8419089	2.5168104	1.1292	0.2588	678.778	684.264
	$\hat{\beta}$ =5.5031450	0.5268799	10.4448	<2e-16 ***		
	$\hat{\lambda}$ =0.0049797	0.0053680	0.9277	0.3536		
LEDMCM	$\hat{\alpha}$ =3.2124509	4.3841379	0.7327	0.463715	489.1	496.4146
	$\hat{\beta}$ =5.4542130	0.0380806	143.2280	<2.2e-16 ***		
	$\hat{\lambda}$ =0.0080407	0.0122455	0.6566	0.511419		
	$\hat{p}$ =0.2525328	0.0784740	3.2180	0.001291 **		
LEDNMCM	$\hat{\alpha}$ =1.9155017	3.2098506	0.5968	0.55067	489.4366	496.7512
	$\hat{\beta}$ =4.6584552	0.1902664	24.4839	< 2e-16 ***		
	$\hat{\lambda}$ =0.0063866	0.0099547	0.6416	0.52116		
	$\hat{p}$ =0.2268542	0.1073761	2.1127	0.03463 *		

* means significant at 5% level of significance

Table 1 shows the maximum likelihood estimates (MLEs) with standard errors, Z-values, P-values, AIC and BIC of the Lomax-Exponential distribution (LED), LED Mixture cure model (LEDMCM) and LED Non-mixture cure model (LEDNMCM) fitted to the treatment group I of the ALL data. The results from the Table reveal that two of the parameters (β and p) are significant in all the models while two (α and λ) are not significant at the 5% level of significance. The result also reveals that the LEDMCM has slightly lower values of AIC and BIC

than the LEDNMCM and then the LED, so the LEDMCM and LEDNMCM are better than LED due to the presence of cure parameter in the models based on treatment group I dataset.

Table 2: MLEs of the Parameter with Standard errors, Z-values, P-values, AIC and BIC for Treatment Group II

Parameter	Estimates	Standard Error	Z-value	*P*-value	AIC	BIC
LED	$\hat{\alpha} = 2.0729861$	0.9116786	2.2738	0.02298 *	595.4878	600.8403
	$\hat{\beta} = 4.6222790$	0.0062622	738.1181	< 2e-16 ***		
	$\hat{\lambda} = 0.0121023$	0.0073864	1.6384	0.10133		
LEDMCM	$\hat{\alpha} = 1.5942e+01$	4.1455e-06	3.8457e+06	< 2.2e-16 ***	474.0955	481.2322
	$\hat{\beta} = 1.1273e+01$	6.6137e-07	1.7045e+07	< 2.2e-16 ***		
	$\hat{\lambda} = 5.5542e-03$	9.9861e-04	5.5620e+00	2.668e-08 ***		
	$\hat{p} = 1.7994e-01$	5.8287e-02	3.0872e+00	0.00202 **		
LEDNMCM	$\hat{\alpha} = 7.9701e+00$	7.9113e-05	1.0074e+05	< 2.2e-16 ***	478.1091	485.2458
	$\hat{\beta} = 9.0849e+00$	9.6678e-06	9.3971e+05	< 2.2e-16 ***		
	$\hat{\lambda} = 4.5015e-03$	1.2288e-03	3.6634e+00	0.0002489 ***		
	$\hat{p} = 1.7132e-01$	6.3377e-02	2.7033e+00	0.0068661 **		

* means significant at 5% level of significance

Table 2 also shows the MLEs with standard errors, Z-values, P-values, AIC and BIC of the Lomax-Exponential distribution (LED), LED Mixture cure model (LEDMCM) and LED Non-mixture cure model (LEDNMCM) fitted to the treatment group II of the ALL data. The results from Table 2 reveals that all the parameters are significant in the LEDMCM and LEDNMCM and also two of

the parameters (α and β) are significant in LED except one parameter (λ) at the 5% level of significance. It also shows that the LEDMCM has lower values of AIC and BIC than the LEDNMCM and then the LED, so the LEDMCM followed by LEDNMCM are better than LED due to the presence of cure parameter in the models based on treatment group II data.

The results in Tables 1 and 2 also revealed that the estimates of the cured proportion or cured fraction parameter are higher for treatment group I than group II which implies a higher probability survival for patients receiving treatment I than those receiving treatment II, and this result is in line with the Kaplan-Meier estimate of survival plots in Figure 1. It is also revealed that the estimates of the cured proportion are higher for the LEDMCM than the LEDNMCM meaning that the LEDMCM is more appropriate for modelling cure. The result above is in line previous studies (Kutal and Qinan, 2018; Lázaro et al., 2020; Omer et al., 2021).

Table 3: MLEs of the Parameter with Standard errors, Z-value, P-value, AIC and BIC for the entire ALL Dataset

Parameter	Estimates	Standard Error	Z-value	*P*-value	AIC	BIC
LED	$\hat{\alpha}=2.0568834$	0.7559961	2.7208	0.006513 **	1273.809	1281.308
	$\hat{\beta}=2.8233459$	0.0054181	521.0964	< 2.2e-16 ***		
	$\hat{\lambda}=0.0052816$	0.0027525	1.9189	0.055002		
LEDMCM	$\hat{\alpha}=6.4304915$	6.4489316	0.9971	0.3187	961.9114	971.9107
	$\hat{\beta}=9.0680156$	0.1516066	59.8128	< 2.2e-16 ***		
	$\hat{\lambda}=0.0084536$	0.0091540	0.9235	0.3558		
	$\hat{p}=0.2238806$	0.0457764	4.8907	1.005e-06 ***		
LEDNMCM	$\hat{\alpha}=6.9080e+00$	5.0393e-05	1.3708e+05	< 2.2e-16 ***	963.3571	973.3564

$\hat{\beta} = 1.0637e+01$	6.6155e-06	1.6079e+06	< 2.2e-16 ***
$\hat{\lambda} = 5.1824e-03$	1.0147e-03	5.1076e+00	3.263e-07 ***
$\hat{p} = 2.1710e-01$	4.7671e-02	4.5542e+00	5.258e-06 ***

* means significant at 5% level of significance

The result in Table 3 presents the MLEs, standard errors, Z-values, P-values, AIC and BIC of the LED), LEDMCM and LEDNMCM fitted to the entire ALL data. Based on Table 3, all the parameters are significant in the LEDNMCM, two of the parameters (β and p) are significant in LEDMCM, and all the parameters are significant in LED except one parameter (λ), at the 5% level of significance. It also shows that the LEDMCM has lower values of AIC and BIC than the LEDNMCM and LED, so the LEDMCM followed by LEDNMCM are better than LED due to the inclusion of cure parameter in the models from the entire ALL data. The results in Tables 3 also revealed that the estimates of the cured proportion are higher for the LEDMCM than the LEDNMCM meaning that the LEDMCM is more appropriate for modelling cure.

4 Conclusion

This paper derived and studied mixture and non-mixture cure fraction models based on the Lomax-exponential distribution (LED) with the maximum likelihood estimation of parameters and applications to acute lymphoblastic leukemia (ALL) data. The results revealed that the estimates of the cured proportion based on LED are higher for treatment group I than group II which implies a higher probability survival for patients receiving treatment I than those receiving treatment II. It is also revealed that the estimates of the cured proportion are higher for the LEDMCM than the LEDNMCM meaning that the LEDMCM is more appropriate for modelling cure. It also shows that the LEDMCM has lower values of AIC and BIC than the LEDNMCM and LED, meaning that

the LEDMCM followed by LEDNMCM are better than LED due to the inclusion of cure parameter in the models.

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