The Weibull-Exponentiated exponential Cure Fraction Model for Right Censored Survival Data with applications to Cancer data

Abstract

The cure fraction model also known as the long-term survival model is used in fitting data from a population with two different types of individuals: individuals who experienced the event of interest (susceptible) and individuals that will never experience the event of interest (non-susceptible). The present paper introduced a cure fraction model considering the Weibull exponentiated exponential distribution that will be used in modelling such type of information. The parameters of the model were estimated via maximum likelihood procedure (MLE) under the assumption of right censoring. Furthermore, statistical properties of the model were studied comprehensively. Simulation study and medical data sets were used in demonstrating the applicability of the proposed methodology. Bias and standard error were used as discrimination criteria in the simulation study while Akaike Information criteria (AIC), Bayesian Information criteria (BIC) and Consistent Akaike Information criteria (CAIC) were used as discrimination criteria in the real life applications. Results from the applications showed that the Weibull exponentiated exponential non-mixture cure fraction model is a strong competitor.

Key words: Survival Analysis, Mixture Cure Fraction Model, Non-Mixture Cure Fraction model, Weibull Cure Fraction Model, Right censoring.

1 Introduction

Survival analyses are statistical methods for analyzing time-to-event data such as death, heart attack, device failure and so on. Different researchers have applied different techniques non-parametric methods (such as Kaplan-Meier estimator or log-rank test), semi-parametric methods (cox proportional hazard model) or parametric methods (using statistical distribution) to analyze this data (Martinez, Achcar, Jácome, & Santos, 2013). The Weibull distribution is one of the distributions that is widely used in this area because of the flexibility of its hazard function and the facility to estimates its parameters (Peto, Lee, & Paige, 1972). However, data sets in medical research requires more sophisticated parametric models (Martinez et al., 2013). To solve this problem, new extensions of the Weibull distribution have been proposed by different researchers. For instance, we have the exponentiated Weibull by (Mudholkar & Srivastava, 1993; Pal, Ali, & Woo, 2006), the generalized modified Weibull by (Carrasco, Ortega, & Cordeiro, 2008), log−beta Weibull by (Ortega, Cordeiro, & Kattan, 2013), Weibull exponentiated exponential by (Salem & Selim, 2014; Usman, Shamsuddeen, Arkilla, & Aliyu, 2020), Weibull−Burr III by (Yakubu & Doguwa, 2017), Weibull Kumaraswamy distribution by (Ishaq, Usman, Tasiâu, Aliyu, & Idris, 2017) among others. One important assumption in survival analysis is that each and every subject in the study population will eventually experience the event of interest if follow-up time is large. However, due to the recent advancements in the field of medicine

especially in the areas of new drugs and treatment regimens, many subjects have lived longer with diseases such as cancer and heart disease. For instance, it may be observed that cohorts of patients with certain types of cancer have been permanently cured, that is, they show no recurrence of the disease. Those patients who are cured and are not censored are referred to as long-term survivors or non-susceptible, while those that do not develop a recurrence of the disease are termed susceptible. Hence, the data is said to be a mixture of these two types of subjects: susceptible subjects who experienced the event of interest and non-susceptible subjects that will never experience the event of interest (Maller & Zhou, 1996). Cure fraction models are used in modelling such type of data. There are basically two types of cure fraction models: the mixture and the non-mixture cure fraction models.

The mixture cure rate model also referred to as the standard cure rate model is the most popular type of cure fraction model and was first developed by (Boag, 1949) and further developed by (Berkson & Gage, 1952). The model was later studied extensively by different researchers including (Achcar, Coelho-Barros, & Mazucheli, 2012; Farewell, 1986; Gamel, McLean, & Rosenberg, 1990; Kannan, Kundu, Nair, & Tripathi, 2010; Mazucheli, Coelho-Barros, & Achcar, 2013; Meeker, 1987; Ng & McLachlan, 1998; Peng, Dear, & Denham, 1998; Shao & Zhou, 2004; Sy & Taylor, 2000; Usman, Suleiman, Arkilla, & Aliyu, 2021; Usman, Shamsuddeen, Arkilla, & Yakubu, 2022) among many others. The study population in the mixture cure rate model assumed that a certain fraction of the population are long-term survivors or non-susceptible while the remaining fraction are susceptible to the event of interest. The non-mixture cure rate model also referred to as the bounded cumulative hazard model or the promotion time cure rate model was first introduced by (Yakovlev et al., 1993) and further discussed by (Andrei, Asselain, et al., 1996; Chen, Ibrahim, & Sinha, 1999; Tsodikov, Ibrahim, & Yakovlev, 2003). The model was motivated by the underlying biological mechanism and was developed under the assumption that the number of cancer cells that remain active after treatment follows poison distribution. Although the mixture cure rate model appears to be attractive and is widely used, Chen et al. (1999); Uddin, Islam, and Ibrahim (2006), have identified some drawback of the model: the model cannot have a proportional hazard structure in the presence of covariates, the model yields an improper posterior distribution for many type of non-informative priors when covariates are included through the cure fraction parameter and the model does not appear to describe the underlying biological process generating the failure time in the context of relapse where cure rate model are frequently used.

To model the proportion of immune, different parametric and non-parametric models have been used by different researchers. For example, the survival function of the failure time of uncured patients was modeled by a product of a log-normal survival function and the survival function of some background distribution for the normal population by (Boag, 1949). Jones, Powles, Machin, and Sylvester (1981) applied the exponential distribution for uncured patients in their mixture model while a simulation study for this model was carried out by (Goldman, 1984). This method was further studied by (Ghitany & Maller, 1992). The Weibull distribution was used in modelling the failure time of uncured patients by different researchers such as (Farewell, 1982, 1986; Ghitany & Maller, 1992). Peng et al. (1998) modeled the proportion of large-scale clinical trials with long follow-up of lymphoma patients using the generalized F distribution. Other distributions used to modeled the proportion of non-susceptible are exponentiated-weibull by (Cancho & Bolfarine, 2001), Burr XII distribution by Shao and Zhou (2004); Coelho-Barros, Achcar, and Mazucheli (2017), exponentiated exponential distribution by (Kannan et al., 2010; Mazucheli et al., 2013), negative binomial distribution by Cancho, Rodrigues, and Castro (2011), Weibull distribution by (Achcar et al., 2012), generalized modified Weibull distribution by (Martinez et al., 2013), Frechet distribution by (Ramos, Nascimento, & Louzada, 2017; Kutal & Qian, 2018), Nadarajah-Haghighi distribution by (Usman et al., 2021). The parameters of the non-mixture cure fraction model was estimated via maximum likelihood estimation procedure considering the data to be uncensored by (Uddin, Islam, & Ibrahim, 2006). While (Uddin, Sen, Noor, Islam, & Chowdhury, 2006) estimate the parameters of the non-mixture cure fraction model assuming uncensored data using non-parametric maximum likelihood method of estimation. A semi-parametric maximum likelihood estimation procedure for the non-mixture model for interval censored time-to-event data was developed by (Liu & Shen, 2009). Classical and non-classical methods of estimation were used to estimate the parameters of the non-mixture cure fraction model by (Lopes & Bolfarine, 2012). Herring and Ibrahim (2002) introduced a parametric method for estimating the parameters of the non-mixture model for a non-ignorable missing covariates.

In the present article, we introduced a non-mixture cure fraction model for survival data considering the Weibull exponentiated exponential distribution in the presence of cure fraction and censoring.

Properties of the model were studied and applications of the model to some real life data were provided. The rest of the paper is organized as follows: In section 2, we introduced the Weibull exponentiated exponential distribution to the non-mixture cure fraction model. Section 3 introduces the Maximum Likelihood Function method of estimation in estimating the parameters of the model assuming right censoring. While statistical properties of the model were provided in section 4. Simulations study and applications of the model were respectively provided in sections 5 and 6. We finally conclude in section 7.

2 The Non-Mixture Cure Rate Model

In this section, an alternative to the Weibull exponentiated exponential mixture cure rate model introduced by (Usman et al., 2022) called the Weibull exponentiated exponential non-mixture cure rate model was introduce considering the Weibull exponentiated exponential distribution in the presence of censoring.

Weibull exponentiated exponential distribution was introduced by (Salem & Selim, 2014) and later studied extensively by (Usman et al., 2020). The distribution is an extension of the well known Weibull distribution. The probability density function (*pdf*) of the distribution was shown to take several shapes. The graph of the hazard rate function of the distribution was shown to take various shapes which makes it to be more flexible in modelling real life data. The *pdf*, cumulative distribution function (*cdf*), survival function and hazard rate function of the Weibull exponentiated exponential distribution are respectively given as:

$$\begin{aligned} f(t) &= \frac{\alpha\beta\theta\phi\exp(-\beta t)}{1-(1-\exp(-\beta t))^{\alpha}}\left[-\ell n\left\{1-(1-\exp(-\beta t))^{\alpha}\right\}\right]^{\theta-1} \\ &\quad (1-\exp(-\beta t))^{\alpha-1}\exp\left[-\phi\left(-\ell n\left\{1-(1-\exp(-\beta t))^{\alpha}\right\}\right)^{\theta}\right] \quad (1) \\ F(t) &= 1-\exp\left[-\phi\left(-\ell n\left\{1-(1-\exp(-\beta t))^{\alpha}\right\}\right)^{\theta}\right] \quad (2) \\ S(t) &= \exp\left[-\phi\left(-\ell n\left\{1-(1-\exp(-\beta t))^{\alpha}\right\}\right)^{\theta}\right] \quad (3) \end{aligned}$$

and

$$h(t) = \frac{\alpha\beta\theta\phi\exp(-\beta t)(1-\exp(-\beta t))^{\alpha-1}\left[-\ell n\left\{1-(1-\exp(-\beta t))^{\alpha}\right\}\right]^{\theta-1}}{1-(1-\exp(-\beta t))^{\alpha}} \quad (4)$$

where α, β, ϕ and θ are positive parameters, α and ϕ are the shape parameters, θ and β are the scale parameters. As earlier mentioned, the non-mixture cure rate model was motivated by the underlying biological mechanism and the survival function following (Chen et al., 1999) is developed as follows:

Assume N be the number of cancer cells for a subject after treatment. Assume that the number of cancer cells is Poisson distributed with parameter μ since the number of cancer cells may grow rapidly and produce a detectable cancer disease. Also, let Z_k denote the random time for the kth cancer cell to produce a detectable cancer mass. Assuming Z_k are independently and identically distributed (iid) with a common distribution function and survival function ($F(T)$ and $S(T)$). Assume further, that Z_k are independent of N. Then, the time to relapse of cancer is defined by the random variable $T \in T = \min\{Z_k,\ 0 \leqslant k \leqslant N\}$, where $P(Z_0 = \infty) = 1$. Hence, the survival function of T is given by:

$$\begin{aligned} S(t) &= P(number\ of\ cancer\ by\ time\ t) \\ &= P(N=0) + P(Z_1 > t,\ Z_2 > t, \ldots, Z_N > t, N \geqslant 1) \\ &= \exp(-\mu) + \sum_{N=1}^{\infty} S^N(t)\frac{\mu^N}{N!}\exp(-\mu) \\ &= \exp(-\mu + \mu S_0(t)) \\ &= \exp(-\mu F_0(t)) \\ S(t) &= p^{F_0(t)} \quad (5) \end{aligned}$$

where $p = \exp(-\mu)$ is the proportion of non-susceptible that lies in the interval $[0, 1]$. The corresponding *cdf*, *pdf* and hazard rate function of the non-mixture cure rate model are respectively given

as:

$$F(t) = 1 - p^{F_0(t)} \tag{6}$$
$$f(t) = -\ell n(p) f_0(t) p^{F_0(t)} \tag{7}$$

and

$$h(t) = -\ell n(p) f_0(t) \tag{8}$$

where $S_0(t)$ is the survival function for the susceptible group. Considering the *WEE* distribution, the The survival function, *pdf* and hazard rate function for the Weibull exponentiated exponential non-mixture cure rate model (*WEENMCR*) are respectively:

$$S(t/\alpha,\beta,\theta,\phi) = p^{1-\exp\left[-\phi(-\ell n\{1-(1-\exp(-\beta x))^{\alpha}\})^{\theta}\right]} \tag{9}$$

$$\begin{aligned} f(t/\alpha,\beta,\theta,\phi) = {} & \frac{-\log(p)\,\alpha\beta\theta\phi\exp(-\beta x)}{1-(1-\exp(-\beta x))^{\alpha}}\left[-\ell n\left\{1-(1-\exp(-\beta x))^{\alpha}\right\}\right]^{\theta-1} \\ & \exp\left[-\phi\left(-\ell n\left\{1-(1-\exp(-\beta x))^{\alpha}\right\}\right)^{\theta}\right] \\ & (1-\exp(-\beta x))^{\alpha-1} p^{\exp\left[-\phi(-\ell n\{1-(1-\exp(-\beta x))^{\alpha}\})^{\theta}\right]} \end{aligned} \tag{10}$$

and

$$\begin{aligned} h(t/\alpha,\beta,\theta,\phi) = {} & \frac{-\log(p)\,\alpha\beta\theta\phi\exp(-\beta x)}{1-(1-\exp(-\beta x))^{\alpha}}(1-\exp(-\beta x))^{\alpha-1} \\ & \left[-\ell n\left\{1-(1-\exp(-\beta x))^{\alpha}\right\}\right]^{\theta-1} \\ & \exp\left[-\phi\left(-\ell n\left\{1-(1-\exp(-\beta x))^{\alpha}\right\}\right)^{\theta}\right] \end{aligned} \tag{11}$$

where $\alpha,\theta > 0$ are the shape parameters, $\beta,\phi > 0$ are scale parameters and p is the proportion of non-susceptible and it lies between zero and one. The *WEENMCR* model as its mixture counterpart also contains some well known non-mixture cure rate model in the literature as special case.

Sub-models of the *WEENMCR* Model

- when $\theta = \phi = 1$, the *WEENMCR* model reduces to the exponentiated exponential non-mixture model proposed by (Mazucheli et al., 2013).
- when $\alpha = \beta = 1$, it reduces to the Weibull non-mixture cure rate model investigated by (Achcar et al., 2012).
- when $\theta = \alpha = \beta = 1$, it reduces to the exponential non-mixture cure rate model.

3 Maximum Likelihood Estimation and Likelihood Ratio Test

Let t_i for $i = 1, 2, \cdots, n$ be right censored survival time for the ith subject in the study population. Assume δ_i be a censoring indicator such that $\delta_i = 1$ if the observed lifetime t_i is not censored and $\delta_i = 0$ if the observed lifetime t_i is censored. Then, $t_i = min(T_i, \delta_i)$. The likelihood function for the *WEENMCR* model is obtain as:

$$L(\Phi) = \prod_{i=1}^{n} h(t_i)^{\delta_i} S(t_i) \tag{12}$$

$$\begin{aligned} = \prod_{i=1}^{n} & \left[\frac{(-\log(p))\alpha\beta\theta\phi\exp(-\beta t)}{1-(1-\exp(-\beta t))^{\alpha}}(1-\exp(-\beta x))^{\alpha-1}\left[-\ell n\left\{1-(1-\exp(-\beta x))^{\alpha}\right\}\right]^{\theta-1}\right. \\ & \left.\exp\left[-\phi\left(-\ell n\left\{1-(1-\exp(-\beta x))^{\alpha}\right\}\right)^{\theta}\right]\right]^{\delta_i} p^{1-\exp\left[-\phi(-\ell n\{1-(1-\exp(-\beta x))^{\alpha}\})^{\theta}\right]} \end{aligned} \tag{13}$$

The log-likelihood function is obtain by taking the natural logarithm of (13) which yields:

$$\begin{aligned} \ell(\Phi) = {} & qln(-ln(p)) + qln(\alpha) + qln(\beta) + qln(\theta) + qln(\phi) - b\sum \delta_i t_i + (\alpha-1)\sum \delta_i ln(1-e^{-\beta t_i}) - \\ & \sum \delta_i ln(1-(1-e^{-\beta t_i})^{\alpha}) + (\theta-1)\sum \delta_i ln\left(-ln(1-(1-e^{-\beta t_i})^{\alpha})\right) - \phi\sum \delta_i \left(-ln(1-(1-e^{-\beta t_i})^{\alpha})\right)^{\theta} + \\ & ln(p)\sum\left[1-exp\left(-\phi\left(-ln(1-(1-e^{-\beta t_i})^{\alpha})\right)^{\theta}\right)\right] \end{aligned} \tag{14}$$

differentiating (14) partially with respect to $\alpha,\ \beta,\ \theta,\ \phi$ and p and equating to zero gives the score function as:

$$\frac{\partial \ell}{\partial \alpha} = \frac{q}{\alpha} + \frac{1}{\alpha}\sum \frac{ln(b_i)}{1-b_i} + \frac{(\theta-1)}{\alpha}\sum \frac{b_i(1-b_i)ln(b_i)\delta_i}{c_i} + \frac{(\theta-1)}{\alpha}\sum b_i(1-b_i)ln(b_i)(-c_i)^{\theta-1}(\delta_i+d_i) \tag{15}$$

$$\frac{\partial \ell}{\partial \beta} = \frac{q}{\beta} - \sum \delta_i t_i + (\alpha-1)\sum \frac{\delta_i t_i a_i}{1-a_i} + \alpha\sum \frac{\delta_i t_i a_i(1-a_i)^{\alpha-1}}{1-b_i} + \alpha(\theta-1)\sum \frac{\delta_i t_i a_i(1-a_i)^{\alpha-1}(1-b_i)}{c_i}$$
$$+ \alpha\theta\phi\sum t_i a_i(1-a_i)^{\alpha-1}(1-b_i)(c_i)^{\theta-1}(\delta_i - d_i) \tag{16}$$

$$\frac{\partial \ell}{\partial \theta} = \frac{q}{\theta} + \sum \delta_i ln(-c_i) - \phi\sum(-c_i)^{\theta} ln(-c_i)(\delta_i - ln(p)d_i) \tag{17}$$

$$\frac{\partial \ell}{\partial \phi} = \frac{q}{\phi} + \sum(-c_i)^{\theta}(ln(p)d_i - \delta_i) \tag{18}$$

$$\frac{\partial \ell}{\partial p} = \frac{q}{p} + \frac{1}{p}\sum(1-d_i) \tag{19}$$

where $a_i = e^{\beta t_i},\ b_i = (1-a_i)^{\alpha},\ c_i = ln(1-b_i)$ and $d_i = e^{(-\phi(-c_i))^{\theta}}$. However, equating (19) to zero and solving for p yields

$$\hat{p}(\alpha,\beta,\theta,\phi) = exp\left(\frac{r}{\sum d_i - n}\right) \tag{20}$$

Thus, the *MLE* of p can be obtain algebraically using (20) while equations (15) to (18) can easily be solved using numerical methods. Interval estimation and hypothesis testing on the parameters of the *WEENMCR* model can be studied using the observed fisher information matrix $I(\Phi)$ given as:

$$I(\Theta) = -\begin{pmatrix} I_{\alpha\alpha} & I_{\alpha\beta} & I_{\alpha\theta} & I_{\alpha\phi} & I_{\alpha p} \\ & I_{\beta\beta} & I_{\beta\theta} & I_{\beta\phi} & I_{\beta p} \\ & & I_{\theta\theta} & I_{\theta\phi} & I_{\theta p} \\ & & & I_{\phi\phi} & I_{\phi p} \\ & & & & I_{pp} \end{pmatrix} \tag{21}$$

where $I_{\alpha\alpha} = \frac{\partial^2\ell}{\partial\alpha^2}$, $I_{\beta\beta} = \frac{\partial^2\ell}{\partial\beta^2}$, $I_{\theta\theta} = \frac{\partial^2\ell}{\partial\theta^2}$, $I_{\phi\phi} = \frac{\partial^2\ell}{\partial\phi^2}$, $I_{pp} = \frac{\partial^2\ell}{\partial p^2}$, $I_{\alpha\beta} = \frac{\partial^2\ell}{\partial\alpha\partial\beta}$, $I_{\alpha\theta} = \frac{\partial^2\ell}{\partial\alpha\partial\theta}$, $I_{\alpha\phi} = \frac{\partial^2\ell}{\partial\alpha\partial\phi}$, $I_{\alpha p} = \frac{\partial^2\ell}{\partial\alpha\partial p}$, $I_{\beta\theta} = \frac{\partial^2\ell}{\partial\beta\partial\theta}$, $I_{\beta\phi} = \frac{\partial^2\ell}{\partial\beta\partial\phi}$, $I_{\beta p} = \frac{\partial^2\ell}{\partial\beta\partial p}$, $I_{\theta\phi} = \frac{\partial^2\ell}{\partial\theta\partial\phi}$, $I_{\theta p} = \frac{\partial^2\ell}{\partial\theta\partial p}$ and $I_{\phi p} = \frac{\partial^2\ell}{\partial\phi\partial p}$. The asymptotic distribution of $\sqrt{n}\left(\hat{\Theta}-\Theta\right)$ is multivariate normal $N_5\left(0, I\left(\hat{\Theta}\right)^{-1}\right)$, where $I\left(\hat{\Theta}\right)^{-1}$ is the total observed information matrix computed at $\hat{\Theta}$. The diagonal elements of $I(\Theta)^{-1}$ are the variances of the corresponding parameters while the off-diagonal elements of $I(\Theta)^{-1}$ are covariances. Hence, the asymptotic $100(1-\varepsilon)\%$ confidence interval for any of the parameters of the $WEENMCR$ model are respectively $\alpha \pm z_{\frac{\varepsilon}{2}}\sqrt{var(\alpha)},\ \beta \pm z_{\frac{\varepsilon}{2}}\sqrt{var(\beta)},\ \theta \pm z_{\frac{\varepsilon}{2}}\sqrt{var(\theta)},\ \phi \pm z_{\frac{\varepsilon}{2}}\sqrt{var(\phi)}$ and $p \pm z_{\frac{\varepsilon}{2}}\sqrt{var(p)}$ where $z_{\frac{\varepsilon}{2}}$ is the $100(1-\varepsilon)\%$ quantile from the standard normal distribution.

4 Statistical properties of the *WEENMCR* Model

Statistical properties such as quantile function, median, simulation, moment generating function and moments of the *WEENMCR* model were discussed in this section.

4.1 Quantile Function and Simulation

The quantile function of the *WEENMCR* model is obtain as:

$$Q(u) = -\frac{1}{\beta}\ell n\left\{1 - \left[1 - \exp\left\{-\left(-\frac{1}{\phi}\ell n\left[\frac{\ell n(1-u)}{\ell n(p)}\right]\right)^{1/\theta}\right\}\right]^{1/\alpha}\right\} \tag{22}$$

by letting $u = 1 - p^{1-\exp\left[-\phi(-\ell n\{1-(1-\exp(-\beta t))^{\alpha}\})^{\theta}\right]}$, where u follows the uniform distribution with parameters zero and one. The first, second and third quantiles of the *WEENMCR* model are obtain

by substituting $u = 0.25, 0.50$ and 0.75 respectively in equation (22). Hence, the median of the *WEENMCR* model is given by:

$$\text{median} = -\frac{1}{\beta}\ell n\left\{1-\left[1-\exp\left\{-\left(-\frac{1}{\phi}\ell n\left[\frac{\ell n\left(0.5\right)}{\ell n\left(p\right)}\right]\right)^{1/\theta}\right\}\right]^{1/\alpha}\right\}$$

However, the median of the *WEENMCR* model is zero when p takes the value of 0.5. Galton coefficient of skewness and Moor coefficient of kurtosis can easily be obtain using the quantile function in (22) by making the appropriate substitutions.

Simulation

Simulation study could be used to examine the performance of the Maximum Likelihood Estimation method discussed in section 3. To generating right censored survival time data from the *WEENMCR* model inverse transform method could be employed since the quantile function of the *WEENMCR* model is in closed form. The following algorithm could be adopted in order to generate random sample of size n from the introduced methodology.

1. Generate a random sample of size n u_i for $i = 1, 2, \cdots n$ from the uniform distribution. That is, $u_i \sim U(0, 1)$.
2. Assume p is a cure fraction parameter, return the random survival time $t_i = -\frac{1}{\beta}\ell n\left\{1-\left[1-exp\left(-\left(-\frac{1}{\phi}\ell n(\frac{\ell n(1-u)}{\ell n(p)})\right)\right)^{\frac{1}{\theta}}\right]^{\frac{1}{\alpha}}\right\}$ when $u_i \leq 1-p$ else t_i is infinity.
3. Generate the censoring times c_i for $i = 1, \cdots, n$ from the *WEE* distribution.
4. $z_i = min\left(t_i, c_i\right)$ is the obtain right censored survival time.
5. The observed right censored survival data is $Z = (z_i, \delta_i)$ for $i = 1, 2, \cdots, n$, where δ_i is censoring indicator.

4.2 Characteristic Function

Assume T is a random variable that follows the *WEENMCR* model with survival and pdf given by equations (9) and (11) respectively. This pdf however, can be written in the form $f\left(t\right) = -\ell n\left(p\right) f_u\left(t\right) \exp\left(-\left(-\ell n\left(p\right)\right) F_u\left(t\right)\right)$ following Ibrahim et al (2001). Applying power series expansion gives:

$$f\left(t\right) = -\ell n\left(p\right) f_u\left(t\right) \sum_{j=1}^{\infty} \frac{\left(-1\right)^j}{j!} \left(-\ell n\left(p\right)\right)^j F_u\left(t\right)^j$$

substituting equations (1) and (2) yields:

$$\begin{aligned} f\left(t\right) = \frac{\alpha\beta\theta\phi\left(-\ell n\left(p\right)\right)\exp\left(-\beta t\right)}{1-\left(1-\exp\left(-\beta t\right)\right)^{\alpha}} \left(1-\exp\left(-\beta t\right)\right)^{\alpha-1} \left[-\ell n\left\{1-\left(1-\exp\left(-\beta t\right)\right)^{\alpha}\right\}\right]^{\theta-1} \\ \exp\left[-\phi\left(-\ell n\left\{1-\left(1-\exp\left(-\beta t\right)\right)^{\alpha}\right\}\right)^{\theta}\right] \\ \sum_{j=1}^{\infty} \frac{\left(-1\right)^j}{j!} \left\{1-\exp\left[-\phi\left(-\ell n\left\{1-\left(1-\exp\left(-\beta t\right)\right)^{\alpha}\right\}\right)^{\theta}\right]\right\}^j \end{aligned} \quad (23)$$

It is clear that as t approaches zero, $\left\{1-\exp\left[-\phi\left(-\ell n\left\{1-\left(1-\exp\left(-\beta t\right)\right)^{\alpha}\right\}\right)^{\theta}\right]\right\}^j$ tends to zero and as t approaches infinity, it tends to one. Hence, applying the binomial series expansion to this term, equation (23) becomes:

$$\begin{aligned} f\left(t\right) = \frac{\alpha\beta\theta\phi\exp\left(-\beta t\right)}{1-\left(1-\exp\left(-\beta t\right)\right)^{\alpha}} \left(1-\exp\left(-\beta t\right)\right)^{\alpha-1} \left[-\ell n\left\{1-\left(1-\exp\left(-\beta t\right)\right)^{\alpha}\right\}\right]^{\theta-1} \\ \sum_{j,k=1}^{\infty} \frac{\left(-1\right)^{j+k}\left(-\ell n\left(p\right)\right)^{j+1}}{\left(j-k\right)!k!} \exp\left[-\phi\left(1+k\right)\left(-\ell n\left\{1-\left(1-\exp\left(-\beta t\right)\right)^{\alpha}\right\}\right)^{\theta}\right] \end{aligned}$$

let $\gamma = \phi\,(j+1)$ and $\delta_{j,k} = \frac{(-1)^{j+k}(-\ell n(p))^{j+1}}{(j-k)!(j+1)!}$, then,

$$f\,(t) = \sum_{j,\,k=0}^{\infty} \delta_{jk} f\,(t/\alpha,\,\beta,\,\theta,\,\gamma)$$

where $f\,(t/\alpha,\,\beta,\,\theta,\,\gamma)$ is the pdf of WEE distribution with parameters $\alpha,\,\beta,\,\theta,\,\gamma$. The characteristic function of the *WEENMCR* model denoted by $\varphi_X\,(t)$ is evaluated as:

$$\begin{aligned}
\varphi_X\,(t) &= \int_{-\infty}^{\infty} e^{itx} f\,(x)\,dx \\
&= \int_{-\infty}^{\infty} e^{itx} \sum_{j,\,k=0}^{\infty} \delta_{jk} f\,(x/\alpha,\,\beta,\,\theta,\,\gamma)dx \\
&= \sum_{j,\,k=0}^{\infty} \delta_{jk} \int_{0}^{\infty} e^{itx} f\,(x/\alpha,\,\beta,\,\theta,\,\gamma)dx
\end{aligned} \tag{24}$$

let

$$\begin{aligned}
I = \int_0^{\infty} e^{itx} \frac{\alpha\beta\theta\gamma \exp\,(-\beta x)}{1-(1-\exp\,(-\beta x))^{\alpha}} \left[-\ell n\left\{1-(1-\exp\,(-\beta x))^{\alpha}\right\}\right]^{\theta-1} \\
(1-\exp\,(-\beta x))^{\alpha-1} \exp\left[-\gamma\left(-\ell n\left\{1-(1-\exp\,(-\beta x))^{\alpha}\right\}\right)^{\theta}\right] dx
\end{aligned} \tag{25}$$

let $u = \gamma\left(-\ell n\left\{1-(1-\exp\,(-\beta x))^{\alpha}\right\}\right)^{\theta}$ then

$$I = \int_0^{\infty} \left[1-\left(1-exp\left(-(\frac{u}{\gamma})^{\frac{1}{\theta}}\right)\right)^{\frac{1}{\alpha}}\right]^{-\frac{it}{\beta}} e^{-u} du \tag{26}$$

the series expansion of $(1-x)^{-q} = \sum_{l=0}^{\infty} \frac{(q+l-1)!}{(q-1)!l!} x^l$. Therefore, $\left[1-\left(1-exp\left(-(\frac{u}{\gamma})^{\frac{1}{\theta}}\right)\right)^{\frac{1}{\alpha}}\right]^{-\frac{it}{\beta}} = \sum_{l=0}^{\infty} \frac{(\frac{it}{\beta}+l-1)!}{(\frac{it}{\beta}-1)!l!} \left(1-exp\left(-(\frac{u}{\gamma})^{\frac{1}{\theta}}\right)\right)^{\frac{1}{\alpha}}$ as u tends to zero and as u tends to infinity, the limiting values of $\left(1-exp\left(-(\frac{u}{\gamma})^{\frac{1}{\theta}}\right)\right)^{\frac{1}{\alpha}}$ is between zero and one, hence applying binomial series expansion yields:

$$\left[1-\left(1-exp\left(-(\frac{u}{\gamma})^{\frac{1}{\theta}}\right)\right)^{\frac{1}{\alpha}}\right]^{-\frac{it}{\beta}} = \sum_{l,m}^{\infty} \frac{(-1)^m (\frac{l}{\alpha})!(\frac{it}{\beta}+l-1)!}{(\frac{it}{\beta}-1)!(\frac{l}{\alpha}-m)!l!m!} exp(-m(\frac{u}{\gamma})^{\frac{1}{\theta}}) \tag{27}$$

$$= \sum_{l,m,n}^{\infty} \frac{(-1)^{m+n} (\frac{l}{\alpha})!(\frac{it}{\beta}+l-1)!m^n \gamma^{\frac{n}{\theta}}}{(\frac{it}{\beta}-1)!(\frac{l}{\alpha}-m)!l!m!n!} u^{\frac{n}{\theta}} \tag{28}$$

substituting in (26), the integral becomes:

$$I = \sum_{l,m,n}^{\infty} \frac{(-1)^{m+n} (\frac{l}{\alpha})!(\frac{it}{\beta}+l-1)!m^n \gamma^{\frac{n}{\theta}}}{(\frac{it}{\beta}-1)!(\frac{l}{\alpha}-m)!l!m!n!} \int_0^{\infty} u^{\frac{n}{\theta}} e^{-u} du \tag{29}$$

and substituting (29) in (24), $\varphi_X\,(t)$ becomes:

$$\varphi_T\,(x) = \sum_{j,k,l,m,n=0}^{\infty} \delta_{jk} \frac{(-1)^{m+n} (\frac{l}{\alpha})! m^n \gamma^{\frac{n}{\theta}} \Gamma(\frac{n}{\theta}+1)}{(\frac{l}{\alpha}-m)!l!m!n!} \left(\frac{it}{\beta}\right)_l \tag{30}$$

where $\left(t/\beta\right)_l = t/\beta\left(t/\beta+1\right)\left(t/\beta+2\right)\cdots\left(t/\beta+k-1\right)$.

4.3 Moment Generating Function

The moment generating function *mgf* of the *WEENMCR* model denoted by $M_X(t)$ is defined by $M_X(t) = E(e^{tx})$. This is evaluated as:

$$\begin{aligned} M_X(t) &= \int_{-\infty}^{\infty} e^{tx} f(x)\, dx \\ &= \int_{-\infty}^{\infty} e^{tx} \sum_{i,\,j=0}^{\infty} \delta_{ij} f(x/\alpha,\, \beta,\, \theta,\, \gamma) dx \\ &= \sum_{i,\,j=0}^{\infty} \delta_{ij} \int_{0}^{\infty} e^{tx} f(x/\alpha,\, \beta,\, \theta,\, \gamma) dx \end{aligned} \tag{31}$$

following the same procedure as in section 4.2, the integral part is evaluated as:

$$\int_0^{\infty} e^{tx} f(x/\alpha,\, \beta,\, \theta,\, \gamma)\, dx = \sum_{k,\,l,\,m=0}^{\infty} \frac{(-1)^{l+m} \left(k/\alpha\right)! l^m \gamma^{m/\theta} \Gamma(m/\theta + 1)}{\left(k/\alpha - l\right)! k! l! m!} \left(t/\beta\right)_k \tag{32}$$

where $\left(t/\beta\right)_k = t/\beta \left(t/\beta + 1\right)\left(t/\beta + 2\right) \cdots \left(t/\beta + k - 1\right)$. Substituting (32) in (31), the moment generating function of the $WEENMCR$ model is derived as:

$$M_X(t) = \sum_{i,\,j,\,k,\,l,\,m=0}^{\infty} \frac{(-1)^{l+m} \delta_{ij} \left(k/\alpha\right)! l^m \gamma^{m/\theta} \Gamma(m/\theta + 1)}{\left(k/\alpha - l\right)! k! l! m!} \left(t/\beta\right)_k$$

4.4 Moments

The rth moment about the origin is easily obtain from the moment generating function using the relation $E(T^r) = \frac{d^r}{dt^r}\left(M_X(t)\right)|_{t=0}$. Hence,

$$E(T^r) = \sum_{i,\,j,\,k,\,l,\,m=0}^{\infty} \frac{(-1)^{l+m} \delta_{ij} \left(k/\alpha\right)! l^m \gamma^{m/\theta} \Gamma(m/\theta + 1)}{\left(k/\alpha - l\right)! k! l! m!} \frac{d^r}{dt^r} \left(\left(t/b\right)_k\right)|_{t=0}$$

For instance, the first and second moments about the origin are obtain as follows:

$$E(T) = \sum_{i,\,j,\,k,\,l,\,m=0}^{\infty} \frac{(-1)^{l+m} \delta_{ij} \left(\frac{k}{\alpha}\right)! l^m \gamma^{\frac{m}{\theta}} \Gamma\left(\frac{m}{\theta} + 1\right)}{\left(\frac{k}{\alpha} - l\right)! k! l! m!} \frac{d}{dt} \left(\left(t/b\right)_k\right)|_{t=0} \tag{33}$$

but $\frac{d}{dt}\left(\left(t/b\right)_k\right)|_{t=0} = \frac{(k-1)!}{b}$. Hence, substituting in (33), the first moment becomes:

$$= \sum_{i,\,j,\,k,\,l,\,m=0}^{\infty} \frac{(-1)^{l+m} \delta_{ij} \left(k/\alpha\right)! l^m \gamma^{m/\theta} \Gamma(m/\theta + 1)}{\left(k/\alpha - l\right)! l! m! k b} \tag{34}$$

on the other hand, the second moment is obtain as:

$$E\left(T^2\right) = \sum_{i,\,j,\,k,\,l,\,m=0}^{\infty} \frac{(-1)^{l+m} \delta_{ij} \left(k/\alpha\right)! l^m \gamma^{m/\theta} \Gamma(m/\theta + 1)}{\left(k/\alpha - l\right)! k! l! m!} \frac{d^2}{dx^2} \left(\left(x/b\right)_k\big|_{x=0}\right) \tag{35}$$

but the term $\frac{d^2}{dt^2}\left(\left(t/b\right)_k\Big|_{t=0}\right)$ in (35) can be evaluated as: $\frac{d^2}{dt^2}\left(\left(t/b\right)_k\Big|_{t=0}\right) = \frac{2(k-1)!}{b^2}\left(\psi(k) - \psi(1)\right)$. Hence, substituting in (35), the second moment becomes:

$$E\left(T^2\right) = \frac{2}{b^2} \sum_{i,\,j,\,k,\,l,\,m=0}^{\infty} \frac{(-1)^{l+m} \delta_{ij} \left(k/\alpha\right)! l^m \gamma^{m/\theta} \Gamma(m/\theta + 1)}{\left(k/\alpha - l\right)! l! m! k} \left(\psi(k) - \psi(1)\right) \tag{36}$$

Equations (34) and (36) can be used in order to find the variance of the $WEENMCR$ model using the relation $\mathrm{var}(\mathrm{X}) = E\left(X^2\right) - \left(E(X)\right)^2$.

5 Simulation Study

In this section, simulation studies was conducted so as to ascertain the performance of the maximum likelihood estimator of $\Theta = (\alpha, \beta, \theta\phi, p)'$ discussed in section 3. The algorithm discussed in section 4.1 was used in generating right censored survival times.

Table 1: Maximum Likelihood, bias and standard error (SE)

n	para - meters	a=1.5; b=2.0; θ=3.0; ϕ=2.0; p=0.05			a=1.5; b=2.0; θ=3.0; ϕ=2.0; p=0.10			a=1.5; b=2.0; θ=3.0; ϕ=2.0; p=0.15		
		estim-ates	bias	SE	estim-ates	bias	SE	estim-ates	bias	SE
30	a	2.9505	1.0905	2.1459	2.6343	1.1343	2.896	2.9113	1.4113	3.1985
	b	2.3951	-1.6049	0.9266	2.2513	-1.2487	1.306	2.3826	-1.6174	1.4735
	θ	2.8962	1.3862	1.4916	3.153	1.4153	1.8446	3.7062	1.2762	1.9604
	ϕ	2.9372	1.4372	3.9728	2.9822	1.4822	5.1827	3.0518	1.6518	5.2474
	p	0.0529	0.0029	0.0408	0.1048	0.0048	0.0545	0.1511	0.0011	0.0633
50	a	2.2343	-1.0167	1.8075	2.2982	-1.1218	2.0291	2.5763	1.2763	2.2437
	b	2.1406	-1.2994	0.932	2.1844	-1.2156	1.0383	2.3092	-1.3908	1.3546
	θ	2.9838	1.2993	1.3216	3.1486	1.386	1.6923	3.4071	1.2717	1.5334
	ϕ	2.6591	1.1591	3.1641	2.9014	1.4014	3.4856	2.9007	1.6007	4.2769
	p	0.0529	0.0029	0.0316	0.1044	0.0044	0.0423	0.1515	0.0015	0.0497
75	a	1.8289	-0.9871	1.2122	1.9383	-0.9617	1.3791	2.1755	-1.0245	1.6114
	b	1.8375	-1.2625	0.6114	1.9096	1.2024	0.7957	2.0974	-1.1026	0.8775
	θ	3.1929	1.2929	1.2006	3.1171	1.3701	1.2759	3.3697	1.2697	1.2796
	ϕ	2.5902	1.0902	2.8256	2.8621	1.3621	2.8527	1.7876	1.5876	3.7113
	p	0.0515	0.0025	0.0255	0.1026	0.0026	0.0345	0.1516	0.0016	0.0409
100	a	1.6895	-0.9705	1.0079	1.7765	-0.9235	1.1558	1.9822	-1.0078	1.3903
	b	1.8968	-1.2132	0.6108	1.9174	1.1986	0.7347	2.0233	-1.0267	0.8132
	θ	3.1595	1.2595	1.1692	3.1377	1.3337	1.2704	3.1716	1.2476	1.2705
	ϕ	2.4117	0.9117	2.644	2.6052	1.1052	2.7345	2.5063	1.5263	3.6644
	p	0.0512	0.0021	0.0222	0.1026	0.0026	0.0301	0.1515	0.0015	0.0355
150	a	1.5699	-0.9301	0.7909	1.6296	-0.8704	0.9649	1.806	-0.9694	1.0846
	b	1.753	-1.2047	0.476	1.9382	-1.1618	0.6365	1.8813	-1.1874	0.7064
	θ	3.1298	1.2681	0.9147	3.1505	1.3205	1.0583	3.1265	1.2265	1.1225
	ϕ	2.2931	0.7931	2.0383	2.2626	0.7626	2.0341	2.3861	1.5261	3.1747
	p	0.0519	0.0019	0.0182	0.102	0.0024	0.0246	0.1508	0.0008	0.0291
200	a	1.3985	-0.9015	0.7008	1.5157	-0.7843	0.7218	1.6883	-0.8117	0.834
	b	1.8494	-1.1506	0.4566	1.9585	-1.1415	0.5415	1.8942	-1.1258	0.5395
	θ	3.1295	1.1395	0.8424	3.1352	1.3052	0.9344	3.1147	1.1814	0.8834
	ϕ	2.2045	0.5045	1.665	2.1628	0.6628	1.8247	1.8466	1.3466	2.2782
	p	0.0508	0.002	0.0159	0.1021	0.0021	0.0213	0.1508	0.0008	0.0251
250	a	1.4124	-0.8876	0.6706	1.4933	-0.7067	0.6705	1.6126	-0.8074	0.7504
	b	1.8768	-1.1232	0.4192	1.9601	-1.1399	0.4585	1.9333	-1.1067	0.4662
	θ	3.0846	1.0846	0.8056	3.1295	1.295	0.864	3.1095	1.1795	0.8456
	ϕ	1.9864	0.4864	1.4778	2.0845	0.5845	1.461	2.2909	1.1609	1.7938
	p	0.0509	0.0019	0.0141	0.1017	0.0017	0.019	0.1507	0.0007	0.0225
300	a	1.5636	-0.364	0.6441	1.4963	-0.6037	0.6234	1.5538	-0.7462	0.6454
	b	1.9398	-1.0602	0.4166	1.9647	-1.1053	0.4297	1.9494	-1.0506	0.4484
	θ	3.0514	1.0514	0.7157	3.1074	1.2774	0.7874	3.1076	1.1676	0.7623
	ϕ	1.9857	0.357	1.2282	2.0275	0.4275	1.0718	2.2717	1.0717	1.0573
	p	0.0506	0.0012	0.013	0.1015	0.0015	0.0174	0.1501	0.0001	0.0206

Samples of size $n = 30, 50, 75, 100, 150, 200, 250$ and 300 with different proportions of cure fraction values were generated for the parameter values $\alpha = 2.5, \beta = 3.0, \theta = 2.0$ and $\phi = 1.5$ as the first setting and $\alpha = 1.75, \beta = 2.0, \theta = 1.5$ and $\phi = 2.5$ as the second setting. In each of these setting, the cure fraction parameter takes the value $p = 0.05, 0.10$ and 0.15.

Table 2: Maximum Likelihood, bias and standard error (SE)

n	para-meters	a=1.25; b=1.5; θ=2.5; ϕ=2.5; p=0.05			a=1.25; b=1.5; θ=2.5; ϕ=2.5; p=0.1			a=1.25; b=1.5; θ=2.5; ϕ=2.5; p=0.15		
		estim-ates	bias	SE	estim-ates	bias	SE	estim-ates	bias	SE
30	a	1.9989	0.9489	1.7998	2.0342	0.8242	1.9156	2.3819	0.6319	1.9308
	b	1.8751	0.9849	1.1941	2.1065	0.9565	1.3272	2.4368	0.4368	1.438
	θ	2.3465	-1.2865	1.5477	2.4601	1.3601	1.6506	2.3806	1.6806	1.6032
	ϕ	2.7076	0.2576	4.061	2.6126	0.1626	3.8456	2.3579	-0.1681	3.5531
	p	0.0514	0.0014	0.046	0.1032	0.0032	0.06	0.1495	-0.0008	0.0694
50	a	1.6639	-0.8861	1.2628	1.6491	-0.8109	1.432	1.9073	0.5173	1.4856
	b	1.6234	-0.9766	0.8516	1.9498	-0.9503	1.1499	2.1436	0.3956	1.222
	θ	2.3969	1.1969	1.2088	2.5913	-1.0513	1.3782	2.4407	1.4097	1.3261
	ϕ	2.6907	0.1907	3.3803	2.448	-0.152	2.9477	2.3855	-0.1645	2.918
	p	0.051	0.001	0.0349	0.1033	0.0031	0.0459	0.1506	0.0006	0.0533
75	a	1.3818	-0.8682	1.0119	1.4314	-0.6816	1.1016	1.586	-0.4614	1.2573
	b	1.4461	-0.9039	0.6709	1.7073	-0.8927	0.9369	1.976	-0.3624	1.1228
	θ	2.5113	1.0113	1.0708	2.5559	1.0559	1.3548	2.475	1.0975	1.1507
	ϕ	2.6843	0.1843	3.3502	2.6037	0.1237	2.5144	2.49	-0.1407	2.6273
	p	0.0508	0.0008	0.0285	0.1018	0.0018	0.0375	0.1501	0.0004	0.0436
100	a	1.3401	-0.7099	0.8425	1.2876	-0.6424	0.8453	1.403	-0.4347	0.9767
	b	1.4734	-0.8666	0.6539	1.6564	-0.7436	0.7428	1.8749	-0.3251	0.9068
	θ	2.5043	1.0043	1.0395	2.5391	1.0191	1.063	2.5931	1.0231	1.1294
	ϕ	2.4244	-0.0756	2.51	2.4832	-0.1168	2.444	2.4637	-0.1363	2.3595
	p	0.0498	-0.0008	0.0247	0.1012	0.0012	0.0324	0.1504	0.0004	0.0377
150	a	1.2741	-0.6759	0.6884	1.1896	-0.5604	0.7082	1.2462	-0.3938	0.8546
	b	1.5347	-0.7753	0.5352	1.5859	-0.6141	0.7142	1.7741	-0.2959	0.9036
	θ	2.492	0.992	0.8984	2.5203	-0.9703	0.9616	2.5566	1.0066	1.1113
	ϕ	2.544	0.044	2.5083	2.4194	-0.1086	1.968	2.5182	-0.1348	2.2903
	p	0.0504	0.0004	0.0202	0.1014	0.001	0.0265	0.1501	0.0003	0.0309
200	a	1.2491	-0.5009	0.5038	1.1375	-0.5125	0.6152	1.1746	-0.3754	0.6459
	b	1.4945	-0.7055	0.4199	1.6431	-0.5569	0.6275	1.7168	-0.2832	0.7885
	θ	2.4587	0.9517	0.7242	2.5187	0.9187	0.8502	2.5706	0.9706	0.8527
	ϕ	2.5019	0.0402	1.7973	2.5965	-0.0635	1.3769	2.5094	-0.1106	1.7401
	p	0.0502	0.0003	0.0174	0.1013	0.001	0.0229	0.1502	0.0002	0.0268
250	a	1.2674	-0.4826	0.5138	1.2725	-0.4775	0.5548	1.1213	-0.3287	0.6269
	b	1.5047	-0.6953	0.4185	1.6034	-0.3966	0.6323	1.733	-0.267	0.6848
	θ	2.5121	0.9121	0.7175	2.5482	0.9182	0.8201	2.5817	0.9581	0.8094
	ϕ	2.4578	-0.022	1.849	2.4371	-0.0529	1.2676	2.4976	-0.1052	1.539
	p	0.05	0.0003	0.0155	0.1009	0.0009	0.0206	0.1499	-0.0001	0.0239
300	a	1.2477	-0.4023	0.4787	1.2595	-0.3905	0.4383	1.0801	-0.3099	0.4969
	b	1.3935	-0.6665	0.3775	1.5204	-0.4796	0.4733	1.6988	-0.2012	0.6065
	θ	2.4981	0.8981	0.6618	2.5365	0.9135	0.7538	2.5159	0.9405	0.7462
	ϕ	2.5344	-0.0656	1.6005	2.5573	-0.0427	1.1764	2.4946	-0.0854	1.4
	p	0.0508	0.0001	0.0143	0.1007	0.0007	0.0187	0.1507	0.0001	0.0219

As mentioned in the algorithm, the censoring variable were assumed to follow the *WEE* susceptible distribution. The performance of the estimates were assess using bias and standard error (*SE*) of the estimates. Additionally, in this simulation settings, all results were replicated 1000 times for each parameter setting considered.

Table 1 gives the maximum likelihood estimates together with bias and SE for the parameter settings: $a = 1.5, b = 2.0, \theta = 3.0$ and $\phi = 2.0$. The maximum likelihood estimates for the parameter setting: $a = 1.25, b = 1.5, \theta = 2.5$ and $\phi = 2.5$ were given in table 2. Bias and standard error of the estimates were also given in this table. The bias and standard error of the estimates were found to be small and decreases as sample size increases for all the different parameter settings. Hence, the estimates get closer to the true parameter value as sample size increases. This indicates that the proposed method of estimation has a good performance overall.

6 Real Data Applications

In this section, two data sets were used in illustrating the methodology of the *WEENMCR* model. The first data is the melanoma data from the Eastern Cooperative Oncology Group (ECOG) phase III clinical trial e1684 available in the smcure package in R software. The data consists of 287 patients with high-risk melanomas who were accrued to E1684 between 1984 and 1990. The patients were randomized to observation group or adjuvant high dose IFN (20 MU/m IV 5 days per week for 4 weeks, followed by 10 MU/m 3 days per week SC for 48 weeks) and were treated either with wide local excision or with complete regional lymph node dissection. Two observations were deleted because they obtained missing information. Hence, the analysis of treatment effects against observation group was based on 285 patients who were randomized to IFN or observation group. Furthermore, one hundred and forty (140) patients were in the observation group and one hundred and forty five (145) patients were in the IFN treatment group.

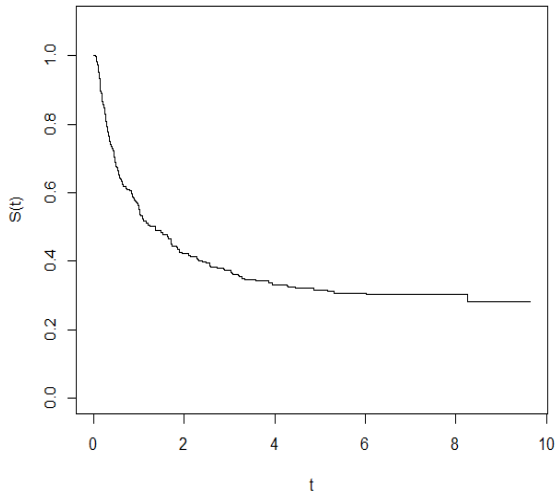

Figure 1: Kaplan-Meier relapse-free survival curve

The Kaplan-Meier survival curve of this data is given in figure 1. According to (Corbière, Commenges, Taylor, & Joly, 2009), the presence of long-term survivors is usually suggested by the Kaplan-Meier survival curve when the curve level-off. Hence, we observe from the Kaplan-Meier survival curve in figure 1 that after about 8-years follow-up, some patients have not experienced any recurrence after treatments. That is, the curve level off at a value between 0.15 and 0.2. Hence, we conclude that, there is presence of long-term survivors in the data. The data was fitted to the *WEENMCR* model and compared its performance with the fits of Weibull non-mixture cure rate *WNMCR*, exponentiated exponential non-mixture cure rate *EENMCR* and exponential non-mixture cure rate *ENMCR* models. The maximum likelihood estimates of the parameters, their SE, 95% confidence interval (*CI*) and the statistics: *AIC*, *BIC* and *CAIC* of the fitted models were given in Table 3. From the statistics in this table, we conclude that the *WEENMCR* model is more efficient compared to the *WNMCR*,

EENMCR and *ENMRC* models, since it has the lowest *AIC*, *BIC* and *CAIC* values. This can also be observed from the fits of the Kaplan-Meier survival curve overlaid with that of WEENMCR, WNMCR, EENMCR and ENMCR survival curves shown in figure **??**.

Table 3: Maximum Likelihood Estimates, SE, 95% *CI*, *AIC*, *BIC* and *CAIC* for e1684 data Non-Mixture Models

Model	parameters	estimate	SE	95% CI	AIC	BIC	CAIC
WEENMCR	α	3.8913	0.0021	(3.8873,3.8954)	756.8194	775.0818	747.0345
	β	3.8521	0.001	(3.8501,3.854)			
	θ	0.5403	0.0396	(0.4626,0.6179)			
	ϕ	0.3689	0.0534	(0.2642,0.4735)			
	p	0.2672	0.0385	(0.1917,0.3426)			
WNMCR	θ	0.9904	0.0577	(0.8773,1.1036)	772.4918	783.4493	766.5772
	ϕ	0.6182	0.0613	(0.498,0.7383)			
	p	0.2929	0.0282	(0.2376,0.3483)			
EENMCR	α	1.0741	0.094	(0.8898,1.2583)	771.766	782.7235	765.8514
	β	0.6700	0.0868	(0.4998,0.8402)			
	p	0.2911	0.0277	(0.2368,0.3454)			
ENMCR	β	0.621	0.0612	(0.5011,0.7408)	770.4236	777.7286	766.4662
	p	0.2912	0.028	(0.2363,0.3461)			

The asymptotic variance covariance matrix for the proposed *WEENMCR* model fitted to the e1684 data is

$$\begin{pmatrix} & \alpha & \beta & \theta & \phi & p \\ \alpha & 4.29\times10^{-6} & -8.55\times10^{-7} & -4.21\times10^{-7} & 1.86\times10^{-7} & -9.49\times10^{-8} \\ \beta & -8.55\times10^{-7} & 9.47\times10^{-7} & 1.17\times10^{-7} & -1.14\times10^{-7} & 1.59\times10^{-8} \\ \theta & -4.21\times10^{-7} & 1.17\times10^{-7} & 1.57\times10^{-3} & 4.82\times10^{-4} & 6.29\times10^{-4} \\ \phi & 1.86\times10^{-7} & -1.14\times10^{-7} & 4.82\times10^{-4} & 2.8\times10^{-3} & 1.43\times10^{-3} \\ p & -9.49\times10^{-8} & 1.59\times10^{-8} & 6.29\times10^{-4} & 1.43\times10^{-3} & 1.48\times10^{-3} \end{pmatrix}$$

6.0.1 Likelihood Ratio Test

Likelihood ratio test was conducted to test for the superiority of the *WEENMCR* model over its sub-models at 5% significance level. The computed test statistic for the comparison between *WEENMCR* model with *ENMCR* model, *WEENMCR* model with *WNMCR* model and *WEENMCR* model with *EENMCR* model are respectively evaluated as:

$$\tau_E = 2(--373.4097-(-383.2118)) = 19.6042$$
$$\tau_W = 2(-373.4097-(-383.2459)) = 19.6724$$

and

$$\tau_{EE} = 2(-373.4097-(-382.883)) = 18.9466$$

The summary statistics for the likelihood ratio test between the *WEENMCR* model and its sub-models are shown in table 4. The p-values of *ENMCR*, *WNMCR* and *EENMCR* models are all significant. This show that, the *WEENMCR* model is more efficient than its sub-models.

Table 4: Likelihood ratio test statistics for the test between *WEENMCR* and *ENMCR*, *WNMCR* and *EENMCR*

Model compared with	Hypothesis	τ	p-value
EMCR Model	$H_0: \alpha=\theta=\phi=1$ Vs $H_1: H_0$ is not true	19.6042	0.0002
WMCR Model	$H_0: \alpha=\beta=1$ Vs $H_1: H_0$ is not true	19.6724	0.0001
EEMCR Model	$H_0: \theta=\phi=1$ Vs $H_1: H_0$ is not true	18.9466	0.0001

6.0.2 Malaysian Colorectal Cancer Data

Colorectal cancer has been ranked the third most commonly diagnosed malignancy (Naishadham, Lansdorp-Vogelaar, Siegel, Cokkinides, & Jemal, 2011), the second most frequent cancer in women and the third most frequent cancer in men (Naishadham et al., 2011; Magaji, Moy, Roslani, & Law, 2014). It is also ranked the fourth leading cause of cancer related death in the world (Magaji et al., 2014; Magaji, Moy, Roslani, & Law, 2017). Medical records of 80 patients diagnosed of colorectal cancer and treated by surgery and chemotherapy/radiotherapy between January 2001 and December 2010 in the University of Malaya medical center (UMMC) were obtained. The survival time was defined to be the time from the date of commencement of treatment to death, loss to follow-up or end of the study.

Different statistical methods have been used to analyzed medical information of patients suffering from colorectal cancer. These include: (Magaji et al., 2014) provides analysis on colorectal cancer patients who underwent treatment in the University of Malaya Medical Centre from 2001 to 2010, the rates of survival and its predictors among colorectal cancer patients in Malaysia was studied by (Magaji et al., 2017), also in Malaysia, survival analysis and prognostic factors for colorectal cancer patients was studied by (Hassan et al., 2016) while (Ghazali, 2018) modelled the survival time and incidence for colorectal cancer patients. In Thai, (Kittrongsiri et al., 2020) assess the overall and stage-specific colorectal cancer survival and identify the prognostic factors among the patients.

However, none of these work model colorectal cancer data using the cure fraction model. Hence, we model this data using the *WEENMCR* model and compared its performance with the fits of generalized gompertz non-mixture cure rate (GGNMCR), modified Weibull non-mixture cure rate (MWNMCR) and generalized modified Weibull non-mixture cure rate (GMWNMCR) models.

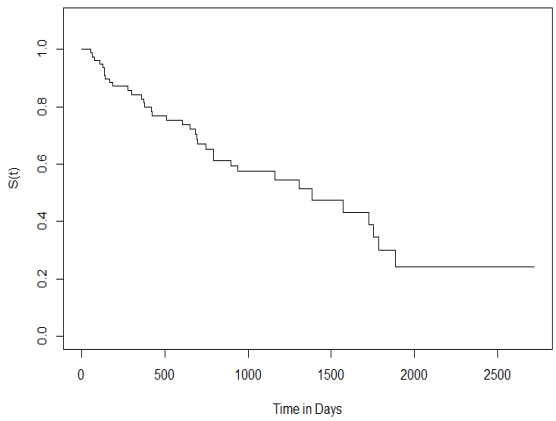

Figure 2: Kaplan-Meier survival curve for Colorectal Cancer patients

The Kaplan-Meier curve for the patients is given in figure 2. From these graphs, we observed that after about 1800 days, the curve level off at a value close to 0.25. This suggest the presence of long-term survivors in the data set as mentioned earlier according to (Corbière et al., 2009). The statistical summaries of the fits of this data to the *WEENMCR*, *GGNMCR*, *MWNMCR* and *GMWNMCR* models are given in table 5. The information criteria: *AIC*, *BIC* and *CAIC* values were also given in this table. The information criteria values from this table showed that the *WEENMCR* model fits the data better than the *GGNMCR*, *MWNMCR* and *GMWNMCR* models.

Table 5: Maximum likelihood estimates for the fits on colorectal cancer data

model	parameter	estimate	SE	95% CI	AIC	BIC	CAIC
WEENMCR	α	1.801	1.0136	(-0.1856, 3.7875)	622.743	634.6531	613.5538
	β	0.0039	0.0005	(0.0029, 0.0050)			
	θ	0.8452	0.244	(0.3669, 1.3236)			
	ϕ	0.0674	0.0155	(0.0370, 0.0978)			
	p	0.0206	0.0241	(-0.0266, 0.0678)			
GGNMCR	β	0.0007	0.0005	(-0.0011,0.0017)	632.2858	641.8139	624.5525
	λ	1.9293	0.9631	(0.0417,3.817)			
	ψ	0.0003	0.0007	(-0.0002,0.0018)			
	p	0.3011	0.1507	(0.0058,0.5965)			
MWNM	β	0.5249	0.0601	(0.4071,0.6428)	623.9012	633.4293	616.1679
	λ	0.1285	0.0969	(0.0615,0.3184)			
	α	0.0005	0.0002	(0.0002,0.0009)			
	p	0.3368	0.1205	(0.1006,0.573)			
GMWNMCR	β	0.0014	0.0005	(0.0004,0.0023)	624.4096	636.3197	614.815
	λ	0.4685	0.116	(0.2413,0.6958)			
	α	0.0095	0.0036	(0.0023,0.0166)			
	γ	0.2976	0.1353	(0.0325,0.5627)			
	p	0.5351	0.0793	(0.3797,0.6905)			

7 Conclusion

In medical applications, the presence of cure fraction usually occur in the data. To model such type of data, the cure rate models are used. In this article, a non-mixture cure rate model was introduced using the *WEE* distribution. The model contain the Weibull non-mixture cure rate, exponentiated exponential non-mixture cure rate and exponential non-mixture cure rate models as special case. Maximum likelihood estimation method was used to estimate the parameters of the model assuming right censoring. Simulation was conducted so as to evaluate the performance of the *MLE*s and it was found that on average, the method performs well. Furthermore, the applicability of the model was demonstrated using two real data sets. Results from the fits showed that the proposed *WEENMCR* model is better than the *WNMCR*, *EENMCR*, *ENMCR*, *GGNMCR*, *MWNMCR* and *GMWNMCR* models.

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