EXTENDED EXPONENTIAL-WEIBULL REGRESSION MODEL FOR HANDLING SURVIVAL DATA IN THE PRESENCE OF COVARIATES

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DECLARATION

This thesis is my original work, except where due acknowledgment is made in the text, and to the best of my knowledge has not been previously submitted to the pan African university or any other institution for the award of a degree or a diploma.

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This thesis has been submitted to the pan African University Institute for Basic Sciences, Technology and Innovation with our approval as the Supervisors.

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DEDICATION

I dedicate this thesis to my father's soul. I also dedicate this thesis to my lovely mother, who was stronger and greater than every challenge we faced, and she deserves all of God's blessings. I wold like to Dedicate this thesis to my brothers and sisters for their ultimate support during the research journey.

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ABBREVIATIONS AND ACRONYMS

$ExEW$	Extended-exponential Weibull distribution
E	Exponential distribution
EE	Exponentiated exponential
EW	Exponentiated Weibull distribution
LL	Log-logistic distribution
GLL	Generalized log-logistic distribution
ExW	Exponential Weibull distribution
BEW	Beta extended-Weibull distribution
BW	Beta-Weibull distribution
MBW	Modified beta-Weibull distribution
$TanLL$	Tan-log-logistic distribution
MLE	Maximum likelihood estimation
EF	Exponentiated family
CDF	Cumulative density function
PDF	Probability density function
SF	Survival function
HRF	Hazarad rate function
$ChRf$	Cumulative HRF
$RCHRF$	reverse HRF
qf	quantile function
mgf	Moment generating function
AFT	Accelerated failure time
PH	Proportional hazards

AIC	Akaike information criterion
BIC	Bayesian information criterion
$CAIC$	Consistent AIC
$SPHBR$	Single-parameter hazard-based regression
AH	accelerated hazard
PO	proportional odds
AO	Accelerated odds
$IPASS$	Integrated Pain and Spinal Service

ABSTRACT

Incorporating covariates into the future lifetime distribution is crucial to the survival analysis. In this thesis a novel version of the exponential-Weibull distribution known as the extended exponential-Weibull (ExEW) distribution is developed and examined using the Lehmann alternative II (LAII) technique. The basic mathematical properties of the new ExEW distribution are derived. The maximum likelihood estimation (MLE) technique is used to estimate the unknown parameters of the ExEW distribution. The estimators' performance is further assessed using Monte Carlo simulations. Two real-world data sets are utilized to show the applicability of the new distribution. Moreover, a fully parametric accelerated failure time (AFT) model with a flexible, novel modified exponential Weibull baseline distribution called the extended exponential Weibull accelerated failure time (ExEW-AFT) model is developed. The model is presented using the multi-parameter survival regression model, where more than one distributional parameter is linked to the covariates. The model formulation, probabilistic functions, and some of its sub-models are derived. The parameters of the developed model are estimated using the maximum likelihood approach. An extensive simulation study is used to assess the estimates' performance using different scenarios based on the baseline hazard shape. The developed model is applied to a real-life right-censored COVID-19 data set from Sudan to illustrate the practical applicability of the developed ExEW-AFT model. A mixture cure model with ExEW distribution is presented to include the fraction of unsusceptible (cured) individuals in the study. The developed models are compared with existing models and are found to perform better.

CHAPTER 1

INTRODUCTION

1.1 Background

Analysis of lifetime data has seen applications in various fields including health, business, engineering, finance, etc (Ahmad et al., 2020; Nasiru et al., 2019b). The main objective of such analysis is usually to model the distribution time to an event and/or the determinants of time to event of interest.

For modeling lifetime data, a variety of probability models are available, including log-logistic, beta, gamma, Weibull, exponential, and others. Furthermore, in many cases, these traditional models are inappropriate for modeling lifetime data necessitating the use of updated versions of current distributions (Nasiru et al., 2019a). These models are inappropriate for survival data with a non-monotone failure rate function. New models bring up new possibilities for theoretical and practical researchers to solve real-world issues since they suit asymmetric and complicated random occurrences so well.

The Weibull distribution has been used to cope with several challenges in a wide range of survival data and to model lifespan data. The Weibull distribution, with its negatively and positively skewed density forms, is the primary option when modeling monotone hazard rates (He et al., 2020).

The parameters of this distribution's tremendous flexibility allow for a range of techniques, all of which have the same key property: the hazard rate is a monotone function that can be decreasing, constant, or increasing. The Weibull distribution is inappropriate for survival data with a non-monotone failure rate function. As a result, scientists explore extensions and modifications of the Weibull distribution. On other hand, over the past few decades, the semi-parametric Cox model has been extensively adopted in the analysis of survival data. Modifications to remove the assumption of "proportional hazards (PH)" are discussed in Cox's original paper (Cox, 1972). Many efforts have been made to increase the adaptability of hazard-based regression models using flexible functions for both the baseline hazard and the inclusion of time-dependent parameters, primarily using modified probability distributions (Ashraf-Ul-Alam and Khan, 2021; Khan and Khosa, 2016; Rubio et al., 2019).

The two most popular techniques for parametric hazard-based regression models of survival data are PH models and AFT models. Specifically, under the parametric PH assumption, only a few probability models are closed, and none of them are flexible enough to explain a large range of survival data (Lawless, 2011).

Other alternative PH models have been proposed, and they can directly account for the time-dependent effects of covariates. The AFT model is a notable example of these earliest alternatives to the PH (Aida et al., 2022). According to the AFT model, the covariates have a direct effect on the time to event, as opposed to the PH model, where the covariates affect the hazard rate function (HRF) only.

Some medical studies have shown that AFT models are frequently used to analyze survival data (Collett, 2015). In comparison to the interpretation of a hazard rate, which denotes a relative rise or decrease in the event rate, the interpretation of an acceleration factor can be thought of as being more obvious because it directly affects the survival time, either by increasing it or decreasing it. Additionally, parametric survival models are essential for assessing survival data (Sinha, 2019). These models can be applied to various applications. For instance, (i) when the baseline hazard is theoretically expected in a healthcare data set, a survival analysis can be applied to produce a relatively better estimation, (ii) the survival models are applicable to the spatial models that predict disease prevalence, (iii) the models can provide better estimates for mixed effects in the clustered survival data-sets, and (vi) the survival rates can be estimated using the random effects-frailty models, which are part of the parametric survival models.

Furthermore, to formulate the parametric AFT model framework, the Weibull, log-logistic, and log-normal distributions are commonly utilized as baseline HRFs (Lawless, 2011).

These distributions cannot accommodate both monotone and non-monotone HRFs. However, it is important to develop a baseline distribution that can handle different HRFs while remaining closed under the AFT model framework.

However, a common scenario in the study of survival data, particularly in cancer research, is when a portion of the population is not exposed to the problem event (Liu and Braun, 2009). Researchers often choose cure fraction models over parametric models in this scenario if the survival time distribution for vulnerable individuals is known (Omer et al., 2021). The study of survival data, including long-term survivors, makes use of cure fraction models, which are regarded as an enlarged form of conventional survival models. Since the 1940s, these models have been a subject of study (Omer et al., 2020). Moreover, a Kaplan-Meier (KM) curve, which exhibits a tall and constant level with dense censoring at the right extreme, frequently suggests the presence of cured subjects in a sample of data (Corbiere et al., 2009). The mixture and non-mixture cure are the two primary groups of cure fraction models. According to the underlying assumption of the mixed cure model, the population is divided into two groups: susceptible (cured) and unsusceptible (uncured). Boag (1949) first proposed the mixed cure model, then Berkson and Gage (1952) further improved it after three years. The mixed cure concept has been thoroughly investigated by numerous researchers succh as (Chen and Du, 2018; Tournoud and Ecochard, 2007,0; Tsodikov et al., 1996; Yin and Ibrahim, 2005).

This study developed a new version of the exponential-Weibull distribution known as the ExEW distribution by adding an additional shape parameter to increase the versatility and goodness-of-fit of modified distributions when analyzing lifetime data sets. Furthermore, with the covariate integrated into the ExEW distribution, a fully parametric accelerated failure time (AFT) model with a flexible, novel modified exponential Weibull baseline distribution known as the ExEW-AFT model is proposed.

1.2 Basic Concepts of Survival Analysis

Assume that T is a non-negative random variable that represents a individual's lifetime within a population. Assume that the distribution function of T is given by $F(t) = Pr\,(T \leq t)$, $t \in \mathbb{R}$. Assume that $F(.)$ is absolutely continuous with respect to the Lebesgue measure on the real line $\mathbb{R}$ and that $f(.)$ is the probability density function of T. We now discuss some fundamental quantities associated to the lifetime variate T distribution.

1.2.1 Survival Function

The survival function (SF), is the fundamental quantity used to analyze the lifetime data. It is defined by

$$S(t) = Pr\,(T > t) = \int_t^\infty f(u)du. \tag{1.2.1}$$

The probability that an individual will survive through time t is estimated using the function SF, where $S(t) = 1 - F(T)$. Therefore take note of that the SF is a monotone decreasing function with

1. $S(t) = 1$ for $t = 0$.

2. $S(t) = 0$ for $t = \infty$

The SF is known as the reliability function when used in reliability analysis.

1.2.2 Hazard Rate Function

The HRF is one of the fundamental ideas linked to the lifetime distribution and is defined by

$$h(t) = \lim_{\triangle t \to 0} \frac{Pr\left(t \leq T < t + \triangle t \mid T \geqslant t\right)}{\triangle t}. \tag{1.2.2}$$

Given that the individual survives for at least t units of time, the HRF describes the instantaneous rate of failure or death of an individual at time t. Therefore, given survival for at least t units of time, $h(t) \triangle t$ is the approximation of the probability of failure in $\big[t, t + \triangle t\big)$. Sometimes the HRF is referred to as the force of mortality. Furthermore, it can be increasing, decreasing, constant, or a combination of the two types of non-monotone function (bathtub or unimodal). Noting that the HRF is a non-negative function and connected to the SF and probability density function by identity.

$$h(t) = -\frac{d \log\left(S(t)\right)}{dt} = \frac{f(t)}{S(t)} \tag{1.2.3}$$

The cumulative hazard rate function (CHRF) is described as

$$H(t) = \int_0^t h(u)du. \tag{1.2.4}$$

It is well known that HRF, or alternatively CHRF, establishes the distribution in a unique manner based on the identification.

$$S(t) = \exp\Big(-H(t)\Big) = \exp\left(-\int_0^t h(u)du\right). \tag{1.2.5}$$

1.3 Features of Survival Data

We must first take into account the reasons why standard statistical techniques employed in data analysis are inapplicable to survival data. One explanation is that survival data are typically not distributed symmetrically (Collett, 2015; Klein and Moeschberger, 2003; Lemeshow et al., 2011; Leung et al., 1997; Lu, 2019). Time to-event-data typically consists of three primary features:

1.3.1 Skewness

First, time-to-event data are typically not symmetrically distributed, which is a feature of survival data. The survival times of a group of similar individuals will often generate a histogram that is favorably skewed, with a longer "tail" to the right of the interval that contains the most observations. As a result, it is unrealistic to assume that data of this type have a normal distribution. By first altering the data to get a more symmetric distribution, this problem could be solved. However, using a different distributional model for the initial data is a more effective strategy (Collett, 2015).

One crucial aspect of time-to-event data is its skewness. Due to the failure of the normal linear model theory, models like the Weibull, log-logistic, and log-normal as well as their extensions are widely utilized.

1.3.2 Censoring

The primary feature of survival data that makes conventional approaches inadequate is how frequently survival times are censored. When the end-point of interest has not been observed for a particular individual, the survival time of that individual is said to have been censored. This might be the case since the analysis of study data will take place while some study individuals are still alive. As an alternative, an individual's survival status at the time of the analysis might not be known since that individual was lost to follow-up.

There are numerous types of censorship that naturally take place in observational schemes. Right, left, interval, and other well-known censoring techniques are examples of censoring schemes. We will now provide a quick overview of different censorship schemes.

1.3.2.1 Right censoring

Times to event for right censored (C_R) observations are known to be greater than a specific time. This means that if T stands for the observed relative lifetimes rather than their lifetimes then $T = \min(T^*, C_R)$, where T^* is the time-to-event random variable. It is determined by an indicator variable whether a survival time is censored, that is

$$\delta = \begin{cases} 1, \text{if } T^* \leq C_R \\ 0, \text{otherwise.} \end{cases}$$

The expression of observations will be in terms of pairs (T, δ).
Depending on the features of the study, the C_R can be either fixed or random. The following right censoring types are produced by this situation:

(i) **Type I censoring**: Here, the experiment is stopped at a predetermined time, at which point any subjects remaining are considered right-censored.

(ii) **Type II censoring**: It is a special instance of Type I censoring in which the failure of a certain number of individuals determine the prefixed time for right censoring.

(iii) **Random right censoring**: This censoring issue arises when some research participants have a competing event that results in their exclusion from the study. Event and filtering times might not be independent in this case. The inference must be handled differently depending on whether the independence requirement is met. Accidental deaths and population movement are common instances of separate random censoring times of the primary event time of interest.

1.3.2.2 Left censoring

Time-to-event for left censored (CL) observations are known to be lower than a specific value. Observed and true survival times (T and T^*, respectively) are related as $T = \max(T^*, CL)$ with left censored denoting censoring time. The pairs of observations are (T, δ), and the current δ is a non-censoring indication with a value of 1 when the event is observed and 0 when it is not.

1.3.2.3 Interval censoring

The interval $[C_L; C_R]$ contains the time to event, which can be interpreted as a generalization of left and right censoring.

1.3.3 Truncation

Truncation happens when only individuals whose event time falls inside a specific observational window are observed $(T_L; T_R)$. The investigator is not aware of any information regarding an individual whose event time falls outside of this interval because they were not observed. In contrast, when someone is being suppressed, at least some information about that individual is available. The inference for truncated data is limited to conditional estimate because individual event times are a part of the observational window (Klein and Moeschberger, 2003). This is a challenge for frequentest inference, but Bayesian reasoning offers a clear and straightforward solution (Armero and Bayarri, 1994).
The truncation classes are listed below

(i) **Left truncation**: When people who have already reached the milestone at the time of research recruitment are excluded from the study, this is known as left truncation.

(ii) **Right truncation**: When data are only recorded for individuals whose survival time exceeds a random time, right truncation occurs.

(iii) **Double truncation**: Double truncation refers to the occurrence of both left and right truncation.

1.3.4 Non-parametric Models

Non-parametric methods of estimating survivor functions and/or cumulative hazard functions are often used in exploratory analysis of time-to-event data. Non-parametric approaches are effective for gaining insights into the main properties of the T distribution and are frequently used to evaluate the adequacy of a parametric model. The KM estimator of survivor functions (Kaplan and Meier, 1958) and the Nelson-Aalen estimator of cumulative hazard functions (Nelson, 1972)are the most extensively used non-parametric techniques in survival analysis.

1.3.4.1 Kaplan-Meier Estimator of the Survivor Function

Let $t_1 < \cdots < t_k$ be the ordered observed lifetimes from a sample of size n. In addition, Let r_j be the number of individuals who are at risk of failing at time $t = t_j$ (also known as the risk set), d_j be the number of individuals who encounter the event at time $t = t_j$, and c_j be the number of individuals who have censoring times in $[t_j; t_{j+1]})$, where $j = 0, 1, \ldots, k, t_0 = 0$ and $t_{k+1} = \infty$. In this case, $r_j = d_j + c_j + d_{j+1} + c_{j+1} + \cdots + d_k + c_k$. For more theoretical details see (Lawless, 2011). The KM estimator of the SF is provided by

$$\hat{S}(t) = \prod_{j|t_j<t} \left(1 - \frac{d_j}{r_j}\right), \tag{1.3.1}$$

which indicates that the conditional probability of an event occurring at each observed time t_j is equal to the observed conditional relative frequency of the event occurring at t_j (i.e., $\mid d_j/r_j$). It is worth noting that if a censoring time and a lifetime are both recorded as equal, the common rule is to consider the censoring time to be infinitesimally bigger in the definition of $\hat{S}(t)$. Lawless (2011) discusses the KM approach for calculating pointwise confidence intervals for $S(t)$.

1.3.4.2 Nelson-Aalen Estimator of the Cumulative Hazard Function

The CHRF Nelson-Aalen estimator is given by

$$\hat{H(t)} = \sum_{j|t_j<t} \frac{d_j}{r_j}. \tag{1.3.2}$$

A cumulative hazard plot is a plot of H vs t that is commonly used as a diagnostic tool to examine the assumptions of a parametric model. for more information on calculating H(t) and accumulated hazard plots, see (Nelson, 1972).

1.3.5 Parametric Failure Time model

Certain probability distributions are widely employed to model time-to-event data (Weibull, exponential, log-logistic, and exponentiated Weibull). These are popular in survival analysis due to (a) model parsimony, (b) simplicity of the method, (c) ability to adequately model data found in survival analysis, and (d) easily accessible statistical software programs.

In this section, some continuous probability distributions that can be used to study survival data are reviewed. log-logistic, exponential, and Weibull continuous probability distributions are the most common way to represent survival data. These are more likely in survival analysis because of (a) the model's simplicity, (b) the approach's flexibility, (c) the ability to satisfactorily represent data that already exist and are typically encountered in survival analysis, and (d) the availability of widely used statistical software tools (Mahmood et al., 2022). As a starting point for our extended distribution and a fundamental survival data generator for several simulation investigations in the thesis, respectively, the exponential Weibull distribution and the exponentiated Weibull distribution are examined, along with other Weibull extensions.

1.3.5.1 Exponential Distribution

A continuous probability distribution known as an exponential (E) has just one unknown parameter a. For models of lifetime distribution, it is the most straightforward distribution. In terms of hazard rate shapes for survival data, the distribution is not adaptable enough to describe typical situations. Let $X \sim$ exponential(a) with $a > 0$. Accordingly, the exponential random variable's PDF, CDF, SF, and HRF are:

(i) The PDF is

$$f(x) = a \exp\Big\{ -ax \Big\}, x > 0. \tag{1.3.3}$$

(ii) The CDF is

$$F(x) = 1 - \exp\Big\{ -ax \Big\}. \tag{1.3.4}$$

(iii) The SF is

$$S(x) = \exp\Big\{ -ax \Big\}. \tag{1.3.5}$$

(iv) The HRF is

$$h(x) = a. \tag{1.3.6}$$

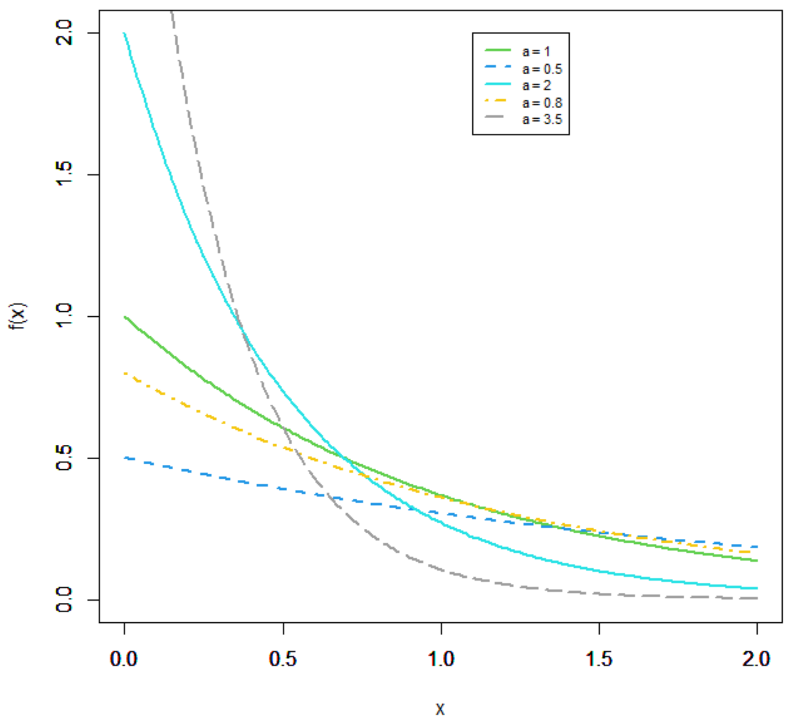

Figure 1.1: PDF of the E distribution with different values of the parameter.

1.3.5.2 Weibull Distribution

The Weibull distribution has been shown to be useful in describing a variety of systems with monotone failure rates (Weibull, 1951). This distribution is one of the most often used lifetime distributions in survival and reliability analysis. It is also utilized in many other applications, including the physical, social, economic, business, hydrological, and weather sciences.

A generalization of the exponential distribution is the Weibull distribution. It is an adaptable distribution that can adopt the behaviors of several kinds of continuous distributions. In contrast to the exponential, it has an extra parameter. Depending on the value of the form parameter, the extra parameter determines how the hazard functions are structured.

if $X \sim \mathrm{W}(a, b)$, then the PDF, CDF, SF, HRF, and CHRF are.

(i) The PDF of the Weibull distribution is:

$$f(x) = abx^{a-1} \exp\big\{ - bx^a \big\} x > 0. \tag{1.3.7}$$

(ii) The CDF of the Weibull distribution is

$$F(x) = 1 - \exp\big\{ - bx^a \big\}. \tag{1.3.8}$$

(iii) The SF of the Weibull distribution is

$$S(x) = \exp\big\{ - bx^a \big\}. \tag{1.3.9}$$

(iv) The HRF of the Weibull distribution is

$$h(x) = abx^{a-1}. \tag{1.3.10}$$

(v) The CHRF of the Weibull distribution is

$$H(x) = -\log S(X) = -\log\big(\exp\big\{ - bx^a \big\}\big) = bx^a \tag{1.3.11}$$

Where $b > 0$ is the scale parameter, and $a > 0$ is the shape parameter. The HRF decreases when $a < 0$, increases for $a > 0$, and constant $a = 1$. When$a = 1$, the Weibull distribution is reduced to the exponential distribution. It is important to note that the W distribution does not accommodate non-monotone HRFs.

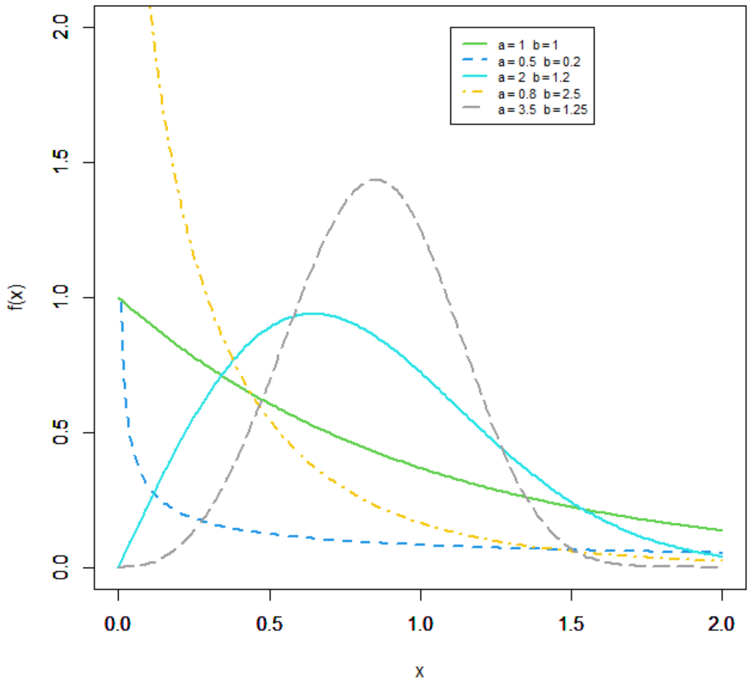

Figure 1.2: PDF of the Weibull distribution with different values of the parameters.

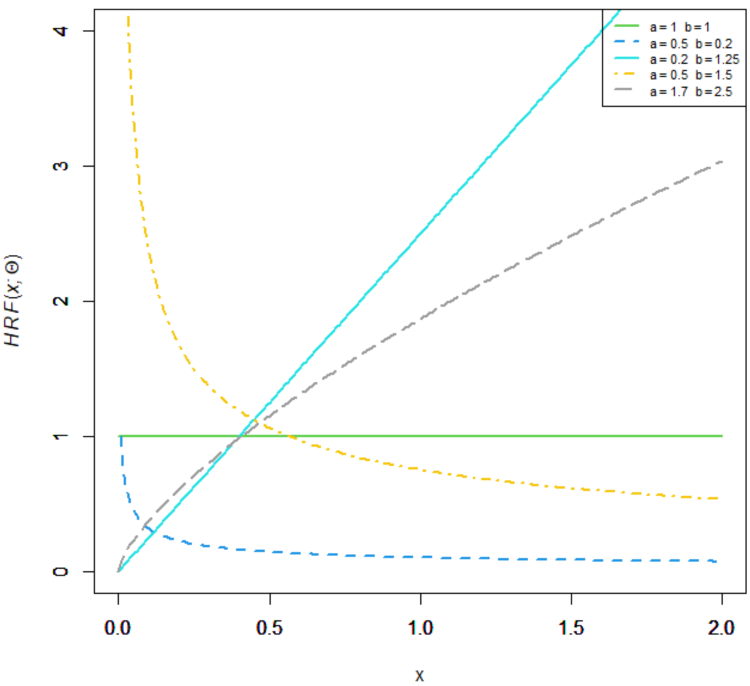

Figure 1.3: HRF of the Weibull distribution with different values of the parameters.

1.3.5.3 Log-logistic Distribution

The log-logistic (LL) distribution (also known as the Fisk distribution) is mainly valuable at modeling unimodal (non-monotone) hazard rate curves. Let $X \sim$ LL(a, b),the PDF, CDF, SF, and HRF of the LL distribution are as follows:

(i) The PDF is

$$f = \frac{ab(bx)^{a-1}}{[1+(bx)^a]^2}, x > 0. \tag{1.3.12}$$

(ii) The CDF is

$$F(x) = \frac{(bx)^a}{1+(bx)^a}. \tag{1.3.13}$$

(iii) The SF is

$$S(x) = \frac{1}{1+(bx)^a}. \tag{1.3.14}$$

(iv) The HRF is

$$h(x) = \frac{ab(bx)^{a-1}}{1+(bx)^a}. \tag{1.3.15}$$

Where $b > 0$ is The scale parameter, and (a $>$ 0) is the shape parameter.

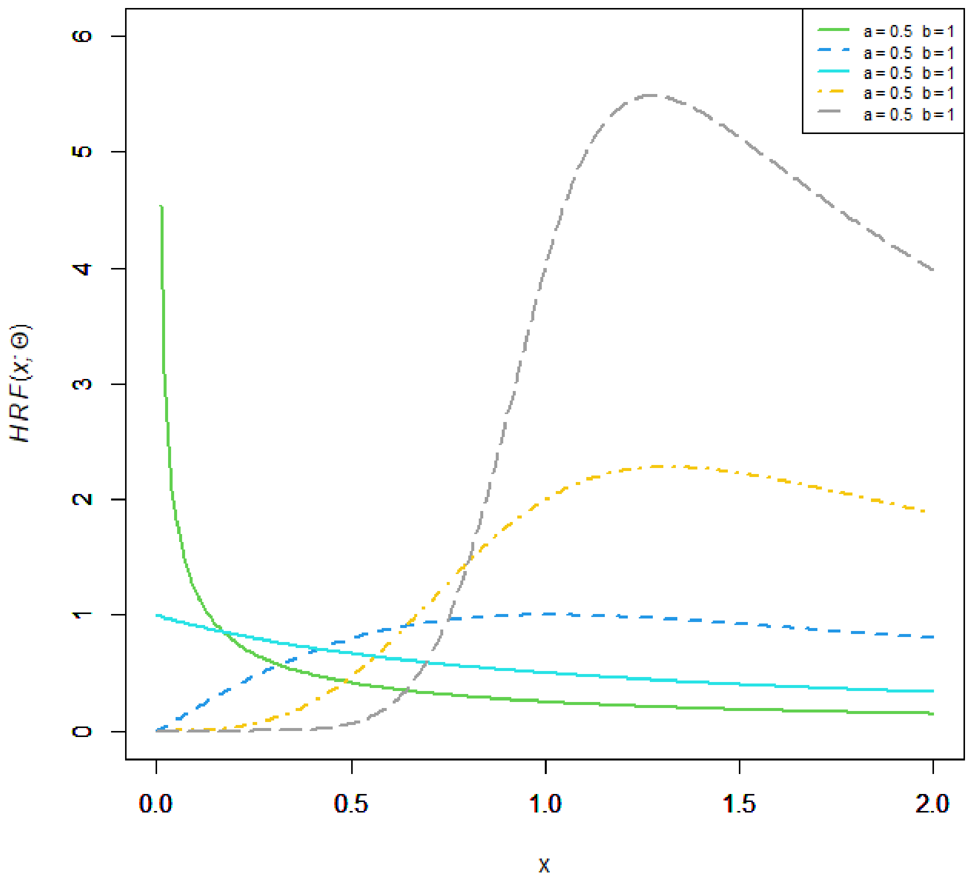

Figure 1.4: HRF of the LL distribution with different values of the parameters

1.3.5.4 Exponentiated Exponential Distribution

The exponentiated exponential (EE) distribution is a very appealing version of the exponential distribution presented by Kundu and Gupta (1999) has gotten a lot of attention. The density function and hazard function of the EE distribution are very similar to the PDF and HRF Weibull distribution.

Let $X \sim \mathrm{EE}(a, b)$, the PDF, CDF, SF, HRF, and of the EE distribution are given by:

(i) The PDF is

$$f(x) = ab \exp\big(-bx\big)\Big\{1 - \exp\big(-(bx)\big)\Big\}^{a-1}, x > 0. \tag{1.3.16}$$

(ii) The CDF is

$$F(x) = 1 - \left\{ \exp - \big(bx \big) \right\}^{a}, \tag{1.3.17}$$

where $b > 0$ is the scale parameter, and $a > 0$ is the shape parameter. When $a = 1$ the Equation 1.3.16 reduced to the exponential distribution.

(iii) The SF is given by

$$S(x) = \left\{ \exp - \big(bx \big) \right\}^{a}. \tag{1.3.18}$$

(iv) The HRF is

$$h(t) = \frac{ab \exp\big(-bx\big) \left\{ 1 - \exp\big(-(bx)\big) \right\}^{a-1}}{\left\{ \exp - \big(bx \big) \right\}^{a}}. \tag{1.3.19}$$

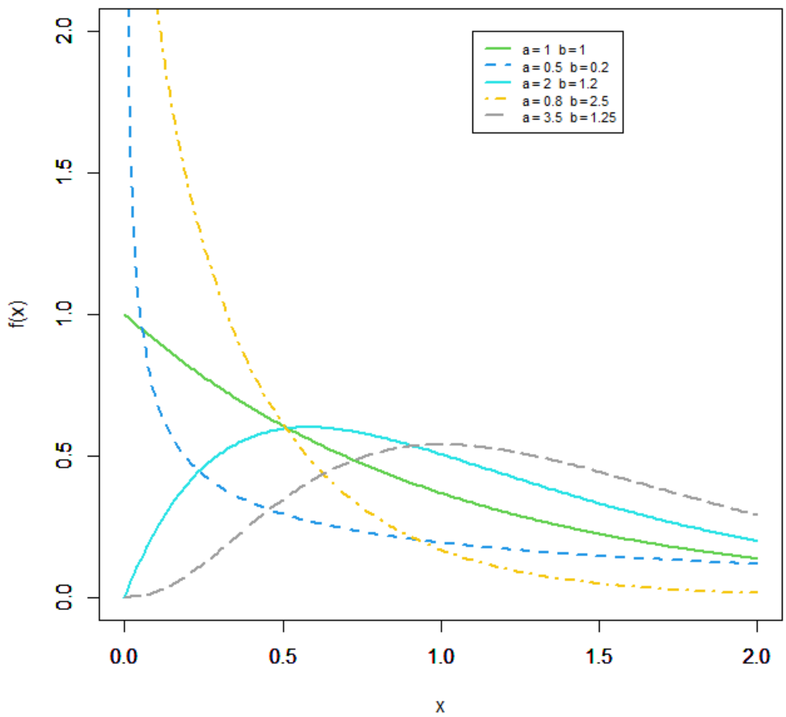

Figure 1.5: PDF of the EE distribution with different values of the parameters.

1.3.5.5 Exponentiated Weibull Distribution

Mudholkar and Srivastava (1993) developed an extension of the Weibull distribution known as the exponentiated Weibull (EW) distribution. The PDF, CDF, SF, HRF, and of the EE distribution are given by

(i) The PDF of the EW is

$$f(x) = cab^c x^{c-1} \exp\big[-(bx)^c\big]\Big\{1 - \exp\big[-(bx)^c\big]\Big\}^{a-1}, x > 0. \tag{1.3.20}$$

(ii) The CDF of the EW is

$$F(x) = \Big\{1 - \exp\big[-(bx)^c\big]\Big\}^{a}. \tag{1.3.21}$$

(iii) The SF of the EW is

$$S(X) = 1 - \Big\{1 - \exp\big[-(bx)^c\big]\Big\}^{a}. \tag{1.3.22}$$

(iv) The HRF is given by

$$h(x) = \frac{cab^c x^{c-1} \exp\big[-(bx)^c\big]\Big\{1 - \exp\big[-(bx)^c\big]\Big\}^{a-1}}{1 - \Big\{1 - \exp\big[-(bx)^c\big]\Big\}^{a}}, \tag{1.3.23}$$

where $a > 0$ and $c > 0$ are shape parameters, and $b > 0$ is scale parameter. It is worth noting that $a = 1$ reduces the EW distribution to the two-parameter Weibull distribution. According to Mudholkar and Srivastava (1993), the hazard function is (1) increasing for $ac \geq 1$and $c \geq 1$, (2) decreasing for $ac \leq 1$ and $c \leq 1$, (3) unimodal for $ac > 1$ and $c < 1$, and (4) bathtub-shaped for $ac \leq 1$ and $c > 1$.

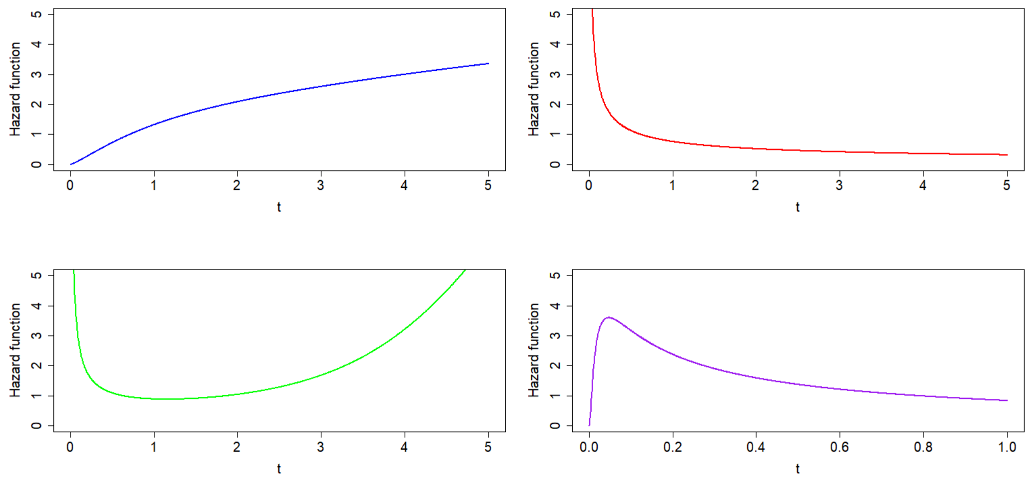

Figure 1.6: HR shapes for the EW distribution for all scenarios.

1.3.5.6 Exponential Weibull Distribution

The exponential-Weibull (ExW) distribution is proposed by Cordeiro et al. (2014) is an extension of exponential and Weibull distributions. Let $X \sim \text{ExW}(a, b, c)$, the CDF, PDF, SF, and HRF of the ExW distribution are as follows:

(i) The CDF of the ExW is given by

$$F(x) = 1 - \exp\Big\{-(ax + bx^c)\Big\}, x > 0. \tag{1.3.24}$$

Where b >0 is the scale parameter, $a > 0, c > 0$ are shape parameters.

(ii) The PDF of the ExW is

$$f(x) = (a + bcx^{c-1})\exp\Big\{-(ax + bx^c)\Big\}. \tag{1.3.25}$$

(iii) The SF of the ExW is

$$s(x) = \exp\Big\{-(ax + bx^c)\Big\}. \tag{1.3.26}$$

(iv) The HRF is given by

$$h(x) = a + bcx^{c-1}. \tag{1.3.27}$$

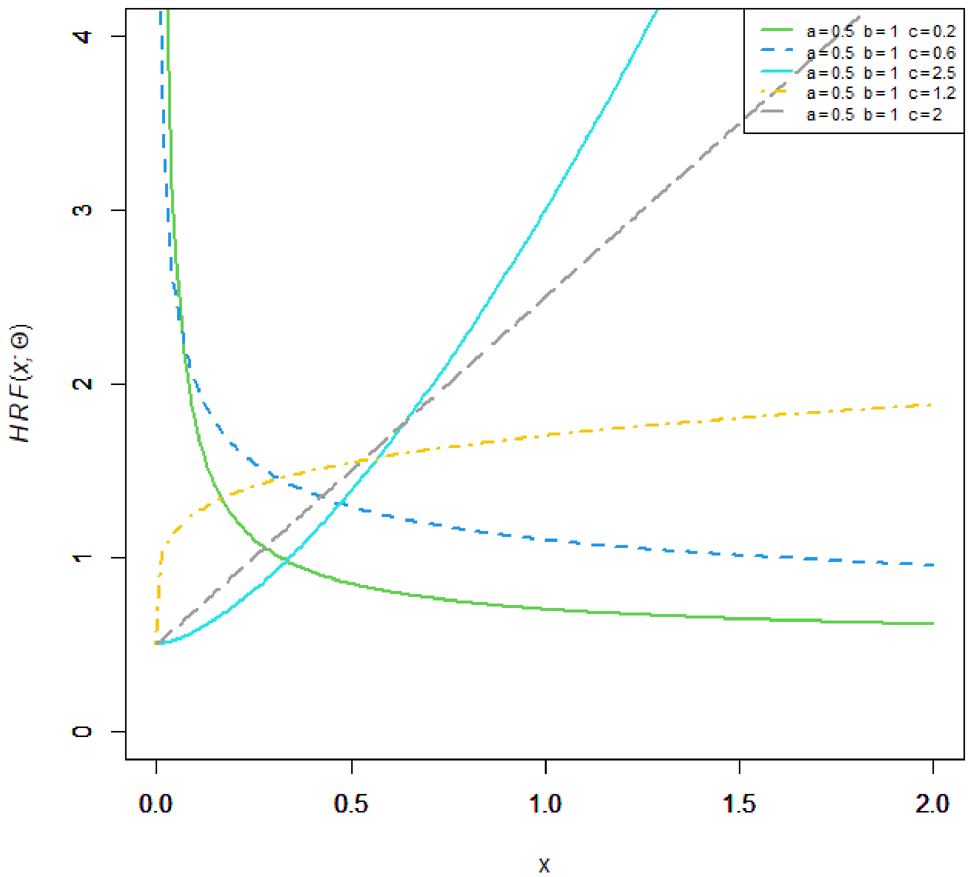

Figure 1.7: HRF of the ExW distribution with different values of the parameters

Other Generalization of the Weibull Distribution

Here are PDFs of some further generalizations of the Weibull distribution, which will be used as competing models with our proposed model, including beta-Weibull (BW) Lee et al. (2007), beta extended-Weibull (BEW) Cordeiro et al. (2012), and modified beta-Weibull (MBW) Nadarajah et al. (2014). Additionally, some generalizations of the log-logistic is presented including, tan-log-logistic (TanLL) distribution (Muse et al., 2021c) and and the generalized log-logistic (GLL) (Muse et al., 2021a) distribution.

(i) The PDF of BW distribution is

$$f(x) = \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \frac{c}{\alpha} \left(\frac{x}{\alpha}\right)^{c-1} \left[1 - e^{-(\frac{x}{\alpha})^c}\right]^{a-1} e^{-b(\frac{x}{\alpha})^c} x > 0. \tag{1.3.28}$$

(ii) The PDF of BEW distribution is

$$f(x) = \frac{\alpha}{\beta(c,d)} b a^b x^{b-1} e^{-ax^b} \left(1 - e^{-\alpha(1-e^{-ax^b})}\right)^{c-1} e^{-\alpha d\left(1-e^{-ax^b}\right)}. \tag{1.3.29}$$

(iii) The PDF of MBW is

$$f(x) = \frac{\alpha^c}{\beta(c,d)} \frac{b a^b x^{b-1} e^{1-ax^b} \left[1 - e^{-ax^b}\right]^{c-1} \left[e^{-ax^b}\right]^{d-1}}{\left(1 - (1-\alpha)(1 - e^{-ax^b})\right)^{c+d}}. \tag{1.3.30}$$

Other generalization of the Log-logistic distribution

(i) The PDF of TanLL distribution is

$$f(x) = \frac{\pi}{4} \{ \frac{(b/a)(x/a)^{b-1}}{(1+(x/a)^b)^2} \} \sec^2 [\frac{\pi}{4} \{ \frac{(x/a)^b}{(1+(x/a)^b)} \}]. \tag{1.3.31}$$

(ii) The PDF of the GLL distribution is given by

$$f(x) = \frac{ac(cx)^{a-1}}{[1+(bx)^a]^{\frac{c^a}{b^a}+1}}. \tag{1.3.32}$$

1.4 Statement of the Problem

The Weibull distribution has been widely used for modeling monotonic types of failure rate data (Prudente and Cordeiro, 2010). Furthermore, it has a severe flaw in that it is unable to accommodate non-monotone hazard rates. The problem at hand is that very few distributions can handle both monotone and non-monotone hazards rate functions (HRFs).

Most survival data usually include some explanatory variables/covariates and usually the interest is to check on the effect of these covariates on the survival rates. Therefore, new survival models being developed need to be extended to regression frameworks that help in assessing effect of covariates.

To solve this problem, we will propose extended-exponential Weibull regression model.

1.5 Objectives of the Thesis

1.5.1 General Objective

The main objective is to develop the extended exponential Weibull regression model for handling survival data in the presence of covariates.

1.5.2 Specific objectives

i. To develop the ExEW distribution using method of Lehmann alternative II.

ii. To derive the mathematical properties of the ExEW distribution.

iii. To develop the ExEW regression model.

iv. To estimate the parameters in the ExEW regression model using MLE method via BFGS algorithm.

v. To assess the performance of the estimators of the developed models via Monte Carlo simulation.

vi To apply the developed models to the real-life data.

1.6 Motivation Statement

Using the LAII parameter induction approach, a tractable extension of the Weibull distribution will be introduced, which provides increasing, decreasing, and constant hazard rate forms. To create a modified Weibull distribution with a more adaptable kurtosis compared to the standard Weibull model. Extending the parent Weibull distribution to one that is extended so that its density function can display symmetrical, asymmetrical, unimodal, J, and reversed-J shapes. furthermore, developed a more comprehensive model that can be used to represent different types of data in the fields of engineering, medicine, actuarial science, and other applied fields. This fact is demonstrated by modeling two real-life data sets from the engineering and medicine disciplines, demonstrating its superiority as compared to other competing distributions. Lastly, the motivation stems from the desire to demonstrate how the inclusion of a single parameter may increase the application and tractability of the parent distribution.
Additionally, proposed an ExEW-AFT model that is quite adaptable and can easily accommodate a variety of applications in reliability and survival analysis. The ExEW-AFT model could be viewed as a multiple-parameter survival regression, which is perhaps more adaptable than the common single-parameter survival regression model, including the Weibull and exponential AFT models.

1.7 Significance of the Thesis

1.7.1 Significance to Theory

The goal of this study, which focused on the frequentist approach for hazard-based regression models using a flexible baseline ExEW distribution. This research casts light on statistical model development and generalization methods, with a focus on parametric hazard-based regression models and the use of right-censored survival data sets. Furthermore, the study adds to and improves the utility of time-to-event data analysis. As a consequence, developing novel parametric hazard-based regression models for the use of modified baseline distributions that can incorporate various hazard rate shapes is important. As a result, a novel parametric hazard-based regression model was developed in this research using a flexible baseline distribution.

1.7.2 Significance to users and model consumers

This study contributes to the improvement of survival model teaching and learning in social science, engineering, medical research centers, and economics. The study's results are thus important to the academic and industrial fields.

1.8 Scope

This study's academic scope is restricted to parametric hazard-based regression models in right censoring time to event data with an extended exponential-Weibull accelerated failure time model.

1.9 Thesis Outline

This thesis includes Five chapter as follows. The introduction of the thesis is presented in Chapter (1). In the Chapter (2) the Literature review is discussed. Research methodology is presented in Chapter (3). Results and discussions are displayed in Chapter (4) In Chapter (5) conclusions and recommendations are presented.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

The art of parameter(s) induction to the baseline distributions, generalized and extended Weibull distributions, and survival regression modeling approaches are all briefly reviewed in this Chapter.

2.2 Art of parameter(s) induction to the saseline distributions

In recent years, the technique of parameter induction has attracted a lot of attention, for example, Tahir and Nadarajah (2015) reviewed the most common G families introduced for the last decade using the parameter induction technique. Tahir and Cordeiro (2016) presented a survey for probability families formulated by parameter induction techniques and they developed some new G-families. Ahmad et al. (2019) reviewed and presented a brief survey of recent advances in distribution theory with a focus on the parameter induction technique. Recently, Muse et al. (2021b) presented a survey of the LL distribution and its generalizations by focusing on the new LL distributions formulated from the parameter induction technique.

There exists many generalized (or generated) G family of distributions like Azzalini's skewed family (Azzalini, 1985), Marshall-Olkin extended (MOE) family Marshall and Olkin (1997), and our interested exponentiated family (EF) of distributions (Gupta et al., 1998).

2.2.1 Exponentiated-G family (EF) of distributions

The origins of this family may be traced back to the first half of the nineteenth century when Verhulst and Gompertz employed the cumulative distribution function (cdf) $G(t) = (1 - \rho e^{-\lambda t})^{\alpha}$ for $t > \lambda^{-1} \log \rho$, where ρ and λ are positive real numbers. To examine growth curve mortality,Ahuja and Nash (1967) developed the generalized Gompertz-Verhulst family of distributions. The EF of distributions was founded by Gompertz-Verhulst's cdf. The exponentiated exponential (EE) distribution is the special case for $\rho = 1$.

Many writers have investigated the properties and estimate methods for parameters of the EF of distributions such as: (Nadarajah, 2011) and (Jabeen and Jan, 2015). The EF of distributions is also known as Lehmann alternatives (LAs) or proportional reversed hazard rate model (PHRM) by (Gupta and Kundu, 2007). Some authors referred to the EF of distributions as max-stable family Ahuja and Nash (1967); Gupta and Kundu (1999) and F α - distributions Cordeiro et al. (2014); Gupta and Kundu (1999) and (Ahsanullah et al., 2012), and (Hamedani, 2013), and (Ghitany et al., 2013).

2.3 Generalization of Weibull distribution

The Swedish mathematician and physicist Weibull (1951), developed the Weibull (W) distribution. It is a continuous probability distribution that is closed in hazard-based regression models.

The Weibull family of distributions has been shown to be useful in describing a variety of systems with monotone failure rates (Nassar and Eissa, 2003). This statistical family includes distributions that can be used to describe data with increasing, decreasing, or exponential failure rates.

Moreover, the Weibull distribution has a wide range of applications. According to Lawless (2011), Weibull distribution is possibly the most extensively used lifetime model for instance, ball bearings, vehicle components, light bulbs, capacitors, disk drives, and electrical insulation are all examples of things where the distribution is widely utilized to estimate the lifetime or durability. It is also utilized in scientific and medical research, such as investigations of the time it takes for tumors, sickness, or death to occur in human populations or laboratory animals.

The hazard rate is a monotone function that can be decreasing, constant, or increasing (Santana et al., 2019). However, the Weibull distribution is inappropriate for survival data with a non-monotone failure rate function.

As a result, scientists explore for extensions and modifications of the Weibull distribution. Mudholkar and Srivastava (1993) presented the "exponentiated Weibull family" as an extension of the Weibull family, which includes distributions with bathtub shaped and unimodal failure rates, as well as a broader class of monotone failure rates. Lee et al. (2007) presented the BW distribution, which can be fitted to data sets with monotone and non-monotone HRF and includes the exponential, EE), and EW distributions as sub-models. Sarhan and Apaloo (2013) proposed a new life-time distribution model that primarily generalizes these two distributions, the exponentiated modified Weibull extension distribution was the name given to this new distribution. Cordeiro et al. (2014) presented a new three - parameter models named the ExW distribution. Salem and Selim (2014) proposed a new four-parameter model generalized Weibull - exponential distribution (GWED). Almheidat et al. (2016) suggested a generalization of the Weibull distribution, is described by four parameters that specify the shape and scale properties. Famoye et al. (2018) developed Weibull-Normal Distribution and found that the Weibull-normal distribution is to be unimodal or bimodal. Famoye et al. (2018) proposed the exponentiated Weibull Lomax, a novel five-parameter model derived from the exponentiated Weibull generated family. Aldahlan (2019) introduced a novel model called the inverse Weibull inverse exponential (IWIE) distribution. Hassan and Abd-Allah (2018) proposed the exponentiated Weibull Lomax, a novel five-parameter model derived from the exponentiated Weibull generated family. Furthermore, the are another several extensions of the Weibull developed by Afifya et al. (2016), ,Afify et al. (2018); Cordeiro et al. (2018), Mead et al. (2019), Nassar et al. (2020), Zhao et al. (2021), Aljohani et al. (2022), and Iqbal et al. (2023).

Additional important generalized forms of the Weibull model are introduced by Afify et al. (2017), Nassar et al. (2018), Alizadeh et al. (2018); Nasir et al. (2018), Abouelmagd et al. (2019a,0); Elbatal et al. (2019), Bhatti et al. (2019), Afify et al. (2020); Cordeiro et al. (2020); Mead et al. (2020), Afify et al. (2021), Afify et al. (2022), Hussein et al. (2022).

2.4 Survival regression models

Data sets on failure times often include information on covariates in addition to the survival time (T) and censoring status records. It is therefore particularly interesting to develop regression models to describe the connection between the response, T, and one or more covariates that are assumed to influence specific characteristics of the distribution of T (Khan, 2018).

In recent decades, many novel emerging methodologies for analyzing right-censored data have been developed, with the ultimate goal of estimating covariate effects on the HRF or the odds function (Muse et al., 2022b). Cox (1972) proposed PH model, Kalbfleisch and Prentice (1973) derived AFT model, Chen and Wang (2000) presented accelerated hazards (AH) model, Ciampi and Etezadi-Amoli (1985) proposed general hazard (GH) model Class, Yang and Prentice (2005) developed Yang and Prentice (YP) model class, Banerjee et al. (2007) introduced the generalized odds-rate class of regression models. Two further survival regression models are given, based on the mean residual life and vitality functions, respectively; Oakes and Dasu (1990) proposed proportional mean residual life model, and Shrahili et al. (2020) introduced proportional vitalities model.

2.4.1 The standard cox proportional hazards (PH) model

The Cox PH model Cox (1972) is the standard method for analyzing time-to-event data in medical research. This model enables us to measure and determine the impact of covariates without assuming any shape for the baseline HRF or the event time distribution. the Cox PH model is written as a baseline HRF, multiplied by the exponential function of the covariates, in the following form:

$$h(t; \boldsymbol{z}) = h_0(t) \exp(\boldsymbol{z}'\boldsymbol{\beta}), \tag{2.4.1}$$

where $h(t; \boldsymbol{z})$ is the HRF for a subject $\boldsymbol{z} = (z_1, z_2, \ldots z_n)'$ is the vector of covariates, $h_0(t)$ is the baseline HRF obtained with $\boldsymbol{x} = 0$, and $\boldsymbol{\beta} = (\beta_1, \beta_2, \ldots \beta_p)'$ represents the regression coefficients. As a result, the SF conditional on covariate X can be written as

$$S(t; \boldsymbol{z}) = \exp\left[-\int_0^t h_0(u) \exp(\boldsymbol{z}'\boldsymbol{\beta}) du\right] = S_0(t)^{\exp(\boldsymbol{z}'\boldsymbol{\beta})}, \tag{2.4.2}$$

whereas $S_0(t) = \exp\big[-\int_0^t h_0(u)du\big]$.

2.4.1.1 The Cox PH model's assumptions

Two assumptions are imposed by the standard Cox PH model. First, each continuous covariate's effect on the logarithm of the hazard is assumed to be linear (linearity assumption).

Cumulative martingale residuals and martingale residuals can be used to investigate the functional forms of the model's continuous covariates (Klein and Moeschberger, 2003; Therneau et al., 1990). Nevertheless, in many real-world applications, the linearity assumption is commonly taken for granted.

Second, the relationship between the covariates and the event's hazard is quantified using a hazard ratio (HR): $\exp(\boldsymbol{\beta}(\boldsymbol{Z_i} - \boldsymbol{Z_j}))$, which compares two vectors of covariate values, $\boldsymbol{Z}_i$ and $\boldsymbol{Z}_j$, the hazard ratio is not time dependent. This constraint is known as the Cox model's PH assumption, which states that the influence of each covariate on survival does not change over time. The log-log curve, the Schoenfeld residual plot, the Schoenfeld residual test, and tests based on interactions between time and the covariates can all be used to evaluate the PH assumption (Harrell and Harrell, 2015; Hess, 1995; Schoenfeld, 1982).

2.4.2 Accelerated failure time model

The AFT model has been proposed as a viable alternative to the Cox PH model (Fleming and Lin, 2000; Wei, 1992). The natural logarithm of the event time, log T, is typically described as a linear function of the covariate vector $\boldsymbol{Z}$ in an AFT model(Kalbfleisch and Prentice, 2011).

$$\log T = \boldsymbol{Z}'\boldsymbol{\beta} + \varepsilon. \tag{2.4.3}$$

Where ε is a random error term that is independent of the covariate.
In the medical literature, AFT models are frequently employed in a variety of contexts (Collett, 2015). As opposed to the interpretation of a hazard ratio, which denotes a relative change in the event rate, the interpretation of an acceleration factor can be seen of as more logical because it directly affects the survival time by either increasing it or reducing it (Swindell, 2009). When fitting an AFT model, a parametric approach is frequently utilized; nevertheless, parametric models are constrained by the flexibility of the selected distribution (Cox, 2008; Cox et al., 2007). In order to find the best-fitting model, it is important to fit a wide range of parametric models (either proportional hazards or accelerated failure time). Furthermore, to formulate the parametric AFT model framework, the Weibull, log-logistic, and log-normal distributions are commonly utilized as baseline HRFs (Lawless, 2011). The Weibull family can accommodate monotone HRFs (i.e., increasing and decreasing), while log-logistic and log-normal can accommodate non-monotone HRFs (Khan, 2018; Santana et al., 2019). These dis-

tributions cannot accommodate both monotone and non-monotone HRFs (Muse et al., 2022a). To address this problem some researchers proposed more flexible parametric regression survival models such as: Khan (2018) developed EW regression for time-to-event data which can can incorporate accommodate monotone non-monotone HRFs. Ashraf-Ul-Alam and Khan (2021) suggested generalized Topp-Leone-Weibull AFT model. Muse et al. (2022c) proposed Bayesian and frequentist approach for the generalized log-logistic AFT model with applications to larynx-cancer patients

2.5 Research gap

From the foregoing literature review, some gaps were identified and they form the main contributions of this thesis:

1. Develop a tractable, a novel version of the ExW distribution known as the ExEW distribution. The basic mathematical properties of ExEW distribution are derived.

2. The main contribution of this study is to offer a useful addition to the toolkit for analyzing survival data that can be used with different hazard regression models in a more general way. Therefore, the work described in this thesis is a unique contribution to the advancement of statistical methods in time-to-event investigations, with an emphasis on the AFT model. Although this method is less commonly used in survival analysis than the well-known Cox PH model, it merits further investigation due to its relevance for real-life investigations, particularly when the essential assumptions of the Cox model are violated.

CHAPTER 3

METHODOLOGY

3.1 Introduction

The principles pertaining to the techniques employed to accomplish the study's objectives are presented in this chapter. The Lehmann type-II method for generating new probability distributions, our estimation method and algorithm. Furthermore, regression analysis of time-to-event, the Schoenfeld residual, the mixture cure model, and statistical computing techniques. model comparisons, and the total time on test (TTT) technique for examining hazard rate shapes are covered.

3.2 The Method of Lehmann alternative II

To address the specific objective one, the exponentiated family of distributions is used, which includes two main methods to develop the exponentiated family (EF) of distributions in the literature. These techniques are: the Lehmann alternative I (LAI) technique which has gotten a lot of attention and the Lehmann alternative II (LAII) technique which has received less attention. The method of Lehmann alternative II (LAII) aids in the derivation and understanding of its many features. According to Tahir and Nadarajah (2015), Lehman II technique is defined as follows:

If $G(x)$ is the CDF and $\overline{G}(x) = 1 - G(x)$ is the SF of the existing distribution. Then, by taking one minus the α^{th} power of $\overline{G}(x)$, the CDF of the LAII family or the EF follows as

$$F(x) = 1 - [1 - G(x)]^{\alpha}. \tag{3.2.1}$$

According to Equation (3.2.1), the PDF is

$$f(x) = (\alpha)G(x)[1 - G(x)]^{\alpha-1}. \tag{3.2.2}$$

With every lifetime random variable (t),
The HRF, SF, RHRF, and CHRF are:
The SF defined as follows:

$$S(t) = [1 - G(t)]^{\alpha}. \tag{3.2.3}$$

The HRF is written by

$$h(t) = \frac{g(t)(\alpha)}{1 - G(t)}. \tag{3.2.4}$$

The RHRF is

$$r(t) = \frac{pdf}{cdf} = \frac{[1 - G(t)]^{\alpha-1} g(t)(\alpha)}{1 - [1 - G(t)]^{\alpha}}$$

by making more simple it becomes

$$r(t) = \frac{PDF}{CDF} = \frac{g(t)(\alpha)}{G(t)}. \tag{3.2.5}$$

The CHRF H(t) is:

$$H(t) = -\log[1 - G(t)](\alpha). \tag{3.2.6}$$

3.3 Maximum likelihood estimation

The most popular classical method for estimating the parameters of a probability distribution model is the maximum likelihood estimation (MLE) method, which is based on a likelihood function. The maximum value of the likelihood function is reached for a specific parameters value. Assume that the $X_1, X_2, \ldots, X_n$ are independent and identically distributed random variables of sample size n with PDF $f(x, \boldsymbol{\theta})$ where $\boldsymbol{\theta} = (\theta_1, \theta_2, \ldots, \theta_k)', k < n$ is the vector of parameters that controls the PDF. The joint PDF can be expressed as

$$f(x \mid \boldsymbol{\theta}) = \prod_{i=1}^{n} f(x_i, \boldsymbol{\theta}). \tag{3.3.1}$$

When the random sample is gathered, the joint PDF transforms into a function of $\boldsymbol{\theta}$, and this function is known as the likelihood function. Consequently, the likelihood function is defined as.

$$L(\boldsymbol{\theta} \mid x) = \prod_{i=1}^{n} f(x_i, \boldsymbol{\theta}). \tag{3.3.2}$$

Dealing with the likelihood logarithm function is more practical from a practical standpoint, ℓ represents the log-likelihood function, which is provided by

$$\ell\left(\boldsymbol{\theta} \mid x_1, x_2, \ldots, x_n\right) = \sum_{i=1}^{n} \log f(x_i, \boldsymbol{\theta}). \tag{3.3.3}$$

Since the logarithm is a monotone function, maximization of the likelihood function also results in maximization of the log-likelihood function, and vice versa. The values of $\boldsymbol{\theta}$ that maximize the likelihood function are the estimates $\hat{\boldsymbol{\theta}}$. Setting the first partial derivatives of ℓ with respect to theta to zero yields the likelihood equations, whereby

$$\frac{\partial \ell\left(\boldsymbol{\theta} \mid x_1, x_2, \ldots, xn\right)}{\partial \theta_i} = 0, i = 1, 2, \ldots, k. \tag{3.3.4}$$

The MLEs for the parameters are derived by resolving the set of likelihood equations in Equation (3.3.4) for $\theta_1, \theta_2, \ldots, \theta_k$.

3.3.1 Properties of MLEs

Under specific general situations, the MLEs possess some attractive properties. These properties are discussed in this subsection.

3.3.1.1 Consistency

Assume that $X_1, X_2, \ldots, X_n$ are independent uniformly distributed samples drawn at random from population X with density $f(x, \boldsymbol{\theta})$. It depends on the sample size n, if $\hat{\theta}$ is an estimator based on the sample size n. To demonstrate how depends of $\hat{\theta}$ on n, writing $\hat{\theta}$ as $\hat{\theta_n}$.
A series of $\boldsymbol{\theta}$ estimators $\left\{\hat{\theta_n}\right\}$ is consistent with $\boldsymbol{\theta}$ if and only if the series $\left\{\hat{\theta_n}\right\}$ converges in probability to the $\boldsymbol{\theta}$, which means for any $\varepsilon > 0$.

$$\lim_{n\to\infty} \Pr\left(\left|\hat{\boldsymbol{\theta}}_n - \boldsymbol{\theta}\right| \geq \varepsilon\right) = 0. \tag{3.3.5}$$

It is important to note that $\left\{\hat{\boldsymbol{\theta}}_n\right\}$ probabilistically converges to $\boldsymbol{\theta}$ if the mean squared error approaches zero as n approaches infinity. As a result, if the variance of $\hat{\boldsymbol{\theta}}_n$ is infinite and occurs for any n, then

$$\lim_{n\to\infty} E\left[\left(\hat{\boldsymbol{\theta}}_n - \boldsymbol{\theta}\right)^n\right] = 0, \tag{3.3.6}$$

furthermore, if $x > 0$, implies

$$\lim_{n\to\infty} \Pr\left(\left|\hat{\boldsymbol{\theta}}_n - \boldsymbol{\theta}\right| \geq \varepsilon\right) = 0.$$

As the sample size increases, the MLEs converge to the true parameter value.

3.3.1.2 Asymptotic normality

As the sample size increases, the MLEs distribution converges to a multivariate normal variate. Hence

$$\sqrt{n}\left(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}\right) \xrightarrow{Dis} N\left(\mathbf{0}, I^{-1}(\boldsymbol{\theta})\right),$$

where $\mathbf{0}$ is a mean zero vector with k dimensions, $\xrightarrow{Dis}$ indicates a distribution's convergence and $I(\boldsymbol{\theta})$ represents a Fisher information matrix with $k \times k$ dimensions. The Fisher Information matrix is described as the negative anticipated value of the second partial derivative matrix of the log-likelihood function evaluated at the true parameter $\boldsymbol{\theta}$. Hence,

$$I(\boldsymbol{\theta}) = -E\left[\frac{\partial^2 \dot{g}(x \mid \boldsymbol{\theta})}{\partial\boldsymbol{\theta}\partial\boldsymbol{\theta}'}\right] = -\int_{-\infty}^{\infty}\left[\frac{\partial^2 \dot{g}(x \mid \boldsymbol{\theta})}{\partial\boldsymbol{\theta}\partial\boldsymbol{\theta}'}\right]\dot{g}(x).dx. \tag{3.3.7}$$

By inverting the Fisher information matrix, the parameters' variance-covariance matrix is produced.

3.3.1.3 Asymptotic efficiency

In a class of unbiased estimators, more than one consistent estimator may be obtained in practice. So it is necessary to compare them and pick the estimator with the lowest variance. The most efficient estimator belongs to this class of unbiased estimators and has the lowest variance. Asymptotically, MLEs are the most effective. Mathematically, if an additional unbiased estimator $\bar{\boldsymbol{\theta}}$ exists, such that

$$\sqrt{n}\Big(\bar{\boldsymbol{\theta}} - \boldsymbol{\theta}\Big) \xrightarrow{Dis} N\Big(\mathbf{0}, I^{-1}(\boldsymbol{\Omega})\Big), \tag{3.3.8}$$

Consequently, $I^{-1}(\boldsymbol{\Omega})$ is always greater than or equal to $I^{-1}(\boldsymbol{\theta})$.

3.3.1.4 Invariance property

If $f(\boldsymbol{\theta})$ is a differentiable function, the maximum likelihood estimator for $f(\boldsymbol{\theta})$ is equal to the function evaluated at the maximum likelihood estimator for $\boldsymbol{\theta}$, In other words, if $\hat{\boldsymbol{\theta}}$ is the maximum likelihood estimator of $\boldsymbol{\theta}$, then $f(\hat{\boldsymbol{\theta}})$ is the maximum likelihood estimator of $f(\boldsymbol{\theta})$, and so on.

$$\sqrt{n}\Big(f(\hat{\boldsymbol{\theta}}) - f(\boldsymbol{\theta})\Big) \xrightarrow{Dis} N\left(\mathbf{0}, \Big[\frac{\partial f(\boldsymbol{\theta})}{\partial\boldsymbol{\theta}}\Big] I^{-1}(\boldsymbol{\theta}) \Big[\frac{\partial f(\boldsymbol{\theta})}{\partial\boldsymbol{\theta}}\Big]'\right). \tag{3.3.9}$$

3.3.2 Confidence intervals for parameters

Assume that the distribution's parameters $\gamma_1, \ldots, \gamma_k$ are also its corresponding variances $\sum_{11}, \ldots, \sum_{kk}$. Using the multivariate normal approximation, the parameters' $100(1-\eta)\%$ confidence intervals are estimated as follows:
$\gamma_1 \in \hat{\gamma_1} \mp z_{\frac{\eta}{2}}\sqrt{\sum_{11}}$, $\gamma_k \in \hat{\gamma_k} \mp z_{\frac{\eta}{2}}\sqrt{\sum_{kk}}$, where $z_{\frac{\eta}{2}}$ is the standard normal distribution's upper ηth percentile.

3.3.3 Broyden-Fletcher-Goldfarb-Shanno algorithm

When the parameter MLEs do not have a closed form, numerical methods are used to solve the system of equations. The BFGS method was used in this work to solve this particular system of equations. Independently developed by Broyden (1969)Broyden (1970), Fletcher (1970), Goldfarb (1970), and Shanno (1970), the BFGS algorithm is an iterative method for addressing unconstrained optimization problems. The process of optimizing a given function (ℓ) begins with a first guess, such as $\boldsymbol{\theta}_0$, and an approximate Hessian matrix $\boldsymbol{H}_0$. As $\boldsymbol{\theta}_i$ approaches the solution, the subsequent steps are then repeated.

1. First, obtain a direction by solving $\boldsymbol{a}_i$.

$$\boldsymbol{H}_i \boldsymbol{a}_i + \bigtriangledown \ell(\boldsymbol{\theta}_i) = 0.$$

2. The next step is to perform a one-dimensional optimization to find an appropriate step size γ_i in the direction determined in step 1.

3. Assign $\boldsymbol{b}_i = \gamma_i \boldsymbol{a}_i$, then update $\boldsymbol{\theta}_{i+1} = \boldsymbol{\theta}_i + \boldsymbol{b}_i$.

4. $y_i = \bigtriangledown \ell(\boldsymbol{\theta}_{i+1}) - \bigtriangledown \ell(\boldsymbol{\theta}_i)$.

5. $\boldsymbol{H}_{i+1} = \boldsymbol{H}_0 + \frac{y_i y_i'}{y_i' \boldsymbol{b}_i} - \frac{\boldsymbol{H}_i \boldsymbol{b}_i \boldsymbol{b}_i' \boldsymbol{H}_i}{\boldsymbol{b}_i' \boldsymbol{H}_i \boldsymbol{b}_i}$.

The gradient's norm, $|\bigtriangledown \ell(\boldsymbol{\theta}_i)|$ is used to observe the convergence of the procedure. The identity matrix, $\boldsymbol{H_0} = \mathbf{1}$, can be used to initialize $\boldsymbol{H}_0$ in practice to make the first step resemble a gradient descent, but additional steps are refined by the approximation of the Hessian, $\boldsymbol{H}_i$.

The Sherman-Morrison formula can be effectively used to the fifth step of the method to yield the inverse of $\boldsymbol{H}_i$, which is used in step one of the process. Hence,

$$\boldsymbol{H}_{i+1}^{-1} = \left(\boldsymbol{I} - \frac{\boldsymbol{b}_i\boldsymbol{y}_i'}{\boldsymbol{y}_i'\boldsymbol{b}_i}\right)\boldsymbol{H}_i^{-1}\left(\boldsymbol{I} - \frac{\boldsymbol{b}_i\boldsymbol{y}_i'}{\boldsymbol{y}_i'\boldsymbol{b}_i}\right) + \frac{\boldsymbol{b}_i\boldsymbol{b}_i'}{\boldsymbol{y}_i'\boldsymbol{b}_i}. \tag{3.3.10}$$

Since $\boldsymbol{y}_i'\boldsymbol{H}_i^{-1}\boldsymbol{y}_i$ and $\boldsymbol{b}_i'\boldsymbol{y}_i$ are scalar terms and $\boldsymbol{H}_{i+1}^{-1}$ is symmetric, Equation (3.3.10) can be calculated more efficiently by applying the expansion.

$$\boldsymbol{H}_{i+1}^{-1} = \boldsymbol{H}_i^{-1} + \frac{(\boldsymbol{b}_i'\boldsymbol{y}_i + \boldsymbol{y}_i'\boldsymbol{H}_i^{-1}\boldsymbol{y}_i)(\boldsymbol{b}_i\boldsymbol{b}_i')}{(\boldsymbol{b}_i'\boldsymbol{y}_i)^2} - \frac{\boldsymbol{H}_i^{-1}\boldsymbol{y}_i\boldsymbol{b}_i' + \boldsymbol{b}_i\boldsymbol{y}_i'\boldsymbol{H}_i^{-1}}{\boldsymbol{b}_i'\boldsymbol{y}_i} \tag{3.3.11}$$

Confidence intervals for the parameters in a classical estimation problem, such as the maximum likelihood, can be quickly obtained by inverting the final Hessian matrix.

3.4 Regression analysis of time-To-event

Statistical analysis is frequently required to prepare data summaries for prediction. One approach is to look for a theoretical model that adequately fits the observed data and discover the covariates that are strongly related to the response. For regression analysis of time-to-event data, there are two prevalent classes: odds-based and hazard-based regression models (Khan and Khosa, 2016). While the formulation in hazard-based models is dependent on the tractability of the baseline distribution's HRF and CHRF, the formulation in odds-based models is dependent on the tractability of the odds function and its derivative (Muse et al., 2022b).

The three common regression models in the context of hazard-based regression models are: PH (Khan and Khosa, 2016), AFT (Khan, 2018), and AH (Muse et al., 2022a) models. On the other hand, the three most popular regression models in the context of odds-based regression models are (Economou and Caroni, 2007), AO (Muse et al., 2022b), and AFT models. Hence, the AFT model is the only survival regression model that is closed under both odds-based and hazards-based regression models. These models are formulated on the link function $\psi(\boldsymbol{x'\beta})$, The link function has the following properties:

(i) $\psi(x) > 0$ for all $x \neq 0$.

(ii) $\psi(x)$ is one-to-one monotone function.

(iii) $\psi(0) = 1$.

The exponential function $\exp(\boldsymbol{z'\beta})$ is the most natural choice for $\psi(\boldsymbol{z'\beta})$. In this part, we will describe the AFT model with $\psi(\boldsymbol{z'\beta}) = \exp(\boldsymbol{z'\beta})$.

3.4.1 The accelerated failure time model

To address the specific objective 3 we will apply the AFT model. It is assumes that the effect of variables on survival time is multiplicative. The AFT model's assumption can be summarized as follows:

$$S(t \mid \boldsymbol{z}) = S_0[t\psi(\boldsymbol{z})], t \geq 0 \tag{3.4.1}$$

Where $S_0[t\psi(\boldsymbol{z})]$ is the baseline survival function (i.e, SF for an individual with $\boldsymbol{z} = \boldsymbol{0}$), $S(t \mid \boldsymbol{z})$ is the SF at the time t, and the $\psi(\boldsymbol{z})$ is the link function.
The covariates are linked to the lifetime by $\psi(\boldsymbol{z})$, satisfying

$$\psi(0) = 1, \psi(\boldsymbol{z}) > 0 \forall \boldsymbol{z} \neq 0.$$

With these characteristics of $\psi(\boldsymbol{z}), \boldsymbol{z} = 0$ implies $S(t \mid \boldsymbol{z}) = S_0(t \mid \boldsymbol{z})$

$$\psi(x) = \exp(\boldsymbol{z}'\boldsymbol{\beta}). \tag{3.4.2}$$

The vector $\boldsymbol{\beta}$ represents regression coefficients and $\boldsymbol{z}$ is a vector of non-random regressors. With Equation (3.4.2) the covariate accelerate ($\boldsymbol{z'\beta} > 0$) or decrease ($\boldsymbol{z}'\boldsymbol{\beta} < 0$) the rate at which a unit progresses in time in comparison to the baseline scenario.

Lifetime distribution functions for the AFT model

In this part, we construct the common probabilistics functions of the AFT model. Let $\boldsymbol{z}$ be a vector of explanatory variables, and $\psi(\boldsymbol{z'\beta})$ be the link function for the explanatory variables, where $\boldsymbol{\beta}$ is a vector of regression coefficients. The HRF function of the AFT model are expressed as follows:

$$h(t;\boldsymbol{z}) = h_0\left(t\psi(\boldsymbol{z}'\boldsymbol{\beta})\right)\psi(\boldsymbol{z}'\boldsymbol{\beta}), \quad t \geq 0 \tag{3.4.3}$$

In this study, we employed the link function as a standard exponential function. Hence, the HRF and SF of the AFT model can be re-written as follows:

$$h(t;\boldsymbol{z}) = h_0\left(te^{\boldsymbol{z}'\boldsymbol{\beta}}\right)e^{\boldsymbol{z}'\boldsymbol{\beta}}, \tag{3.4.4}$$

and using Equation (3.4.1)

$$S(t;\boldsymbol{z}) = S_0\left(te^{\boldsymbol{z}'\boldsymbol{\beta}}\right). \tag{3.4.5}$$

Using Equation (3.4.3), the AFT model's HRF is as follows:

$$h(t) = \frac{f(t)}{S(t)} = \psi(\boldsymbol{z})\frac{f_0[t\psi(\boldsymbol{z})]}{S_0[t\psi(\boldsymbol{z})]} = \psi(\boldsymbol{z})h_0[t\psi(\boldsymbol{z})] = e^{\boldsymbol{z}'\boldsymbol{\beta}}h_0\big[t\exp\left(\boldsymbol{z}'\boldsymbol{\beta}\right)\big] \tag{3.4.6}$$

For an AFT model using Equation (3.4.5), the other three frequent lifetime distribution representatives are as follows:
The AFT model's cumulative density function is:

$$F(t) = 1 - S(t) = 1 - S_0\big[t\psi(\boldsymbol{z})\big] = S_0\big[\exp(\boldsymbol{z}'\boldsymbol{\beta})t\big] \quad \text{for} \quad t \geq 0 \tag{3.4.7}$$

The AFT model's probability density function may be determined using the following equation:

$$f(t) = \psi(\boldsymbol{z})f_0[t\psi(\boldsymbol{z})] = \exp\left(\boldsymbol{z}'\boldsymbol{\beta}\right)f_0\big[te^{\boldsymbol{z}'\boldsymbol{\beta}}\big] \quad \text{for} \quad t \geq 0 \tag{3.4.8}$$

The AFT model's CHRF is as follows:

$$H(t) = -\log\big(S_0\big[t\psi(\boldsymbol{z})\big]\big) = H_0\big[t\psi(x)\big] = H_0[te^{-\boldsymbol{z}'\boldsymbol{\beta}}], \tag{3.4.9}$$

where $F_0(.), f_0(.), h_0(.)$, and $H_0(.)$, respectively, are the baseline CDF, PDF, HRF, and CHRF.

We can observe from the foregoing Equations (3.4.4 - 3.4.9) that the covariates work multiplicatively on time, causing the time to failure to accelerate or decelerate, thus the model's name. For an AFT model we are interested in measuring the direct effect of covariates on survival time.

3.4.2 Estimation of the AFT model parameter

To estimate the model parameter, MLE is used. Let $T_1, T_2, \ldots, T_n$ be the lifetimes of n individuals. If the data are subject to right censoring, then $t_i = \min(T_i, C_i)$, where $C_i > 0$ corresponding to a potential censoring time for individual i. Suppose that $\delta_i = I(T_i \leq C_i) = 1$ for $T_i \leq C_i$ and $\delta_i = 0$ otherwise. Hence, the observed data for an individual i consists of $\{t_i, \delta_i\}$, for $i = 1, 2, \ldots, n$, where t_i is a censoring time or lifetime according to whether $\delta_i = 0$ or 1, respectively and $\boldsymbol{z}_i = (z_{i1}, z_{i2}, \ldots, z_{in})$ is a column vector of n external covariates for the ith individual.

In this scenario, non-informative censoring is assumed to be in place, meaning that neither the distribution of survival times nor the distribution of censoring times can be inferred from one another.

It is important to note that the assumption of non-informative censoring is justifiable when censoring is random (it is assumed that the failure rates for observations that are censored, uncensored, and remain in the risk set are equal) and/or independent (in other words, censorship is supposed to be random within any interested subgroup); for additional information on the non-informative censoring (Kleinbaum and Klein, 2012).

In this setting, the censored likelihood function is therefore defined as follows:

$$L(\vartheta) = \prod_{i=1}^{n} \left[f\left(t; \boldsymbol{z}_i\right)\right]^{\delta_i} \left[S\left(t; \boldsymbol{z}_i\right)\right]^{1-\delta_i}, \tag{3.4.10}$$

where ϑ is the vector of the involved parameters.
Based on Equation (4.3.1), the log-likelihood function for a parametric AFT model is defined as follows:

$$\ell(\vartheta) = \sum_{i=1}^{n} \delta_i \log\left[f(t; \boldsymbol{z}_i)\right] + \sum_{i=1}^{n} (1-\delta_i) \log\left[S\left(t; \boldsymbol{z}_i\right)\right], \tag{3.4.11}$$

The Newton-Raphson optimization procedure can be used to directly optimize this, and interval estimates of the model parameters and hypothesis testing are both possible under the approximative normally distributed MLE estimates (Lawless, 2011).

3.4.3 The Schoenfeld residual

The Schoenfeld residuals test and Schoenfeld residuals plot test are tests based on correlations between time and covariates, and can all be used to assess the PH premise. This techniques based on Schoenfeld residuals were developed to examine the PH assumption in the Cox PH model (Grambsch and Therneau, 1994). The description of these residuals is based on Collett (2015) and Lawless (2011).
For the j^{th} covariate z, the i^{th} Schoenfeld residual is defined as

$$\hat{S}_{ij} = \delta_i\big(z_{ij} - a_{ij}\big), \tag{3.4.12}$$

$$a_{ij} = \frac{\sum_{\ell \in R(t_i)} Z_{ij} \exp(\boldsymbol{Z}_i' \hat{\boldsymbol{\beta}})}{\sum_{\ell \in R(t_i)} \exp(\boldsymbol{Z}_i' \hat{\boldsymbol{\beta}})} \tag{3.4.13}$$

where $\sum_{i=1}^{n} \hat{S}_{ij}$ is a first derivative estimate of the partial log-likelihood function in Equation (2.4.1) with regard to β_j,$j = 1, \ldots, p$ (the i^{th} component of the score vector examined at $\hat{\beta}_j$). Using the score function's features, we have, (i)

Schoenfeld residuals for a covariate must total zero, (ii) In big datasets, the expected value of $\hat{S}_{ij}$ is zero, and (iii).

3.5 The mixture cure model

It is commonly assumed in survival analysis that every individual in the research is susceptible to the event of interest. This assumption, however, may be unreasonable in some instances when a sub-population of individuals is immune to the occurrence of such an event. The conventional survival approach is ineffective. In order to measure the ability of a specific "treatment" to "cure," survival regression models must include a cure fraction. The present statistical methods for dealing with such data is extensive and is commonly referred to as cure rate models (Lambert, 2007).
In a cure model, the target population is a mix of susceptible and non-susceptible (cured) individuals. As a result, the primary goal of this model is to provide a simultaneous estimation of the proportion of "immune" individuals as well as the distribution of survival times for the " susceptible" ones.

Mixture cure rate model

The mixture cure model (MCM) is an approach that is widely used to model data containing long-term survivors. The MCM has the advantage of allowing covariates to effect individuals who are cured differently than how long vulnerable individuals survive.
In a mixture cure model, the population is divided into two groups: uncured (susceptible) subjects who will experience the event of interest and cured (non-susceptible) subjects who will not. "Cured subjects" or "long-term survivors" are those who do not develop the event of interest. Let T represent a subject's survival time and ε represent the cure indicator, with $\varepsilon = 0$ when the subject is cured and $\varepsilon = 1$ when the subject remains uncured. Let p represent the proportion of cured individuals and $1 - p$ represent the proportion of uncured subjects. That

is, $P(\varepsilon = 1) = 1 - p$, and $P(\varepsilon = 0 = p.)$ Then, $P(T \leq t \mid \varepsilon = 0) = 0$ and $P(T \leq t \mid \varepsilon = 1) = F(t)$, which is the CDF of uncured individuals. So, the CDF of the total population T is
$F_T(t) = P(T \leq t) = P(T \leq t \mid \varepsilon = 0)P(\varepsilon = 0) + P(T \leq t \mid \varepsilon = 1)P(\varepsilon = 1) = (1-p)F_T(t)$, and the SF of T is

$$S_T(t) = 1 - F_T(t) = 1 - (1-p)F_T(t) = p + (1-p)S_T(t), \tag{3.5.1}$$

where $S(t)$ specifies a correct SF for uncured subjects, it is important to note that $S_T(t)$ is incorrect.
The corresponding PDF of T is

$$f_T(t) = (1-p)f(t), \tag{3.5.2}$$

where $f(t)$ is the PDF of uncured subjects.

3.5.1 Likelihood function of the MCM

This sub-section presents the maximum likelihood to estimate model parameters in the mixture cure model.
Assume t_i is the right censored survival time for individual i, moreover $t_i = \min\big(T_i, C_i\big)$, where T_i is the failure time of the ith individual and C_i is the right censored variable of the ith individual, $i = 1, 2, \ldots, n$.
The observed survival time of ith individual is t_i, and the censoring indicator is δ_i, where $\delta_i = I\big(T_i, C_i\big)$, for $i = 1, 2, \ldots, n$. The MCM's likelihood function is therefore

$$L_{MCM}(\theta) = \prod_{i=1}^{m} f_T^{\delta_i}(t_i) S_T^{1-\delta_i}(t_i) = \prod_{i=1}^{m} \big[(1-\rho)f(t_i)\big]^{\delta_i} \big[\rho + (1-\rho)S(t_i)\big]^{1-\delta_i},$$

as well as the log-likelihood function

$$L_{MCM}(\theta) = \ln\big(L_{MCM}(\theta)\big) = \ln\big(1-p\big)\sum_{i=1}^{n}\delta_i + \sum_{i=1}^{n}\delta_i \ln\big(f(t_i)\big) + \sum_{i=1}^{n}\big(1-\delta_i\big)\ln\big(\rho + (1-\rho)S(t_i)\big). \quad (3.5.3)$$

Where θ is vector of parameter.

The maximum likelihood estimates of θ can be obtained by maximising Equation (3.5.3) directly, with respect to the parameter vector θ. By directly maximizing the total log-likelihood function with the help of the tools MATHEMATICA, R, and MATLAB, the parameter estimations can be derived.

3.6 Statistical computing techniques

Statistical computing is a branch of statistics that encompasses a wide range of methodologies for solving statistical issues. Among the techniques are computation or numerical techniques, graphical techniques, Monte Carlo technique, and significance sampling. Monte Carlo technique is simulation-based technique.In this part briefly we will present Monte Carlo simulation technique.

3.6.1 Monte Carlo simulation technique

Monte Carlo techniques are commonly utilized as a computational tool in modern applied statistics. It is a statistical method based on random sampling, that is, simulations are utilized to conduct analysis and produce inferences in this method. The mean squared error (MSE), average bias, and standard error, or other important variables can be used to estimate sampling distribution. They can be used to analyze the coverage probabilities for a confidence interval, as well as to compare the performance of various processes handling a problem. There is always some degree of uncertainty in the estimate; the Monte Carlo approach aids in the investigation of such issues.

Assuming $h(x)$ is a function, compute $\int_{-\infty}^{\infty} h(x)dx$ assuming the integral exists. If X is a random variable with a PDF $f(x)$, then

$$E\left[h(x)\right] = \int_{-\infty}^{\infty} f(x)h(x)dx$$

If a random sample from X|(X) is provided, the sample mean will represent an unbiased estimate of $E\left[h(x)\right]$.

3.6.2 The inverse transform technique

A popular probabilistic approach for creating datasets using regression survival models is the inverse transform technique (Austin, 2012; Bender et al., 2005; Leemis, 1987). This technique is based on the association between the CHRF of a lifetime random variable and a standard uniform random variable. Whenever the CHRF of the baseline distribution has an explicit form solution, it may be used, reversed, and easily used in R.
The CDF is derived from the SF as follows:

$$F(t; x) = 1 - S(t; z). \tag{3.6.1}$$

Given this, when generating data, if Y is a random variable that has this CDF, then $U = F(Y)$ follows a uniform distribution throughout the range $[0; 1]$ and $[1 - U]$ also follows a uniform distribution $U[0, 1]$. At the end, for a realization u of U, by using the baseline CHRF $H_0\left(t; x\right)$, we get

$$1 - u = \exp\left\{-H_0\left(t; z\right)\right\}. \tag{3.6.2}$$

The inverse of the CHRF must only be calculated if the baseline HRF is strictly positive for every t to simulate lifetime data. An expression of the random live corresponding to the AFT model is as follows:

$$T = \frac{H_0^{-1}\left(-\log(1 - U)\right)}{e^{\boldsymbol{z}'\boldsymbol{\beta}}}. \tag{3.6.3}$$

3.7 Model comparison

Two or more models may yield acceptable fits to real data in some cases. In such situations, comparing the fits is useful in order to give a choice to the alternatives. Although a graphical method, such as comparing residual plots, might give insight into what is going on, it may include subjective decision-making when choosing one model over the others. This is especially true when the fittings are close together. As a result, for model comparison, a more objective method (e.g., statistical tests, goodness of fit criteria) is preferable. Several model selection criteria have been developed based on various principles, including minimizing information loss (Akaike, 1974), maximizing posterior probability (Schwarz, 1978), deviance information criterion (David et al., 2002), and testing nested models. In this part, we present goodness-of-fit test and the analytical performance measures.

3.7.1 Goodness of fit test

If $X_1, \ldots, X_n$ are random sample from a given distribution, a goodness-of-fit test is an approach for determining whether the random samples originated from the specified distribution. In this study the likelihood ratio test (LRT) is used.

3.7.1.1 Likelihood ratio test

The LRT is used to determine how well a model fits a particular data set. The test compares two nested models. Assume that the random variable X has a PDF given by $\dot{g}(x;\theta)$ with an unknown parameter θ. The primary aim is to evaluate the null and alternative hypotheses, $\boldsymbol{H_0} : \theta \in \boldsymbol{\theta_0}$ and $\boldsymbol{H_1 : \theta \in \theta_1}$, where $\boldsymbol{\theta_0}$ and $\boldsymbol{\theta_1}$ are the parameter spaces of the simplified and full model, respectively. The test statistic is provided by

$$w = -2\log\left(\frac{L_0(\hat{\theta})}{L_1(\hat{\theta})}\right), \tag{3.7.1}$$

where L_0 and L_1 are the likelihood functions for the simplified and full model, respectively. Under $\boldsymbol{H-0}$, w is asymptotically distributed as a chi-square random variable with degrees of freedom equal to the difference in the number of parameters of the two models. When the null hypothesis is rejected, it indicates that the full model performs better than the reduced model on the data.

3.7.2 Analytical performance measures

Increasing the number of parameters generally enhances the fit of a particular model and, of course, the likelihood, regardless of whether the extra parameter is necessary or not. When the models are not nested, the analytical performance measures allow us to make this comparison. the Bayesian information criterion (BIC), the Akaike information criterion (AIC), consistent Akaike information criterion (CAIC) and Hannan- Quinn information criterion (HQIC) are the most commonly used analytical performance measures.

3.7.2.1 Akaike information criterion

Akaike et al. (1973) proposed the AIC, which was expanded upon in Akaike (1974). It is the most commonly used model selection tool among researchers. To implement AIC, one begins with some alternative models that are considered appropriate models for specific data. The test statistic is provided by

$$AIC = -2\log(\hat{\theta}) + 2k, \tag{3.7.2}$$

where ℓ refers to the log-likelihood function calculated at the MLEs, k is the parameter's number of models. The best model for the data collection is the one with the lowest AIC value when compared to other models. One of the AIC's advantages is its ability to penalize models with many parameters. The AIC presents good model selection for small sample. However, the AIC works reasonably well in small samples but is inconsistent and does not improve in large samples. As a result, the CAIC was developed to address this issue (Burnham et al., 1998). the CAIC is defined as follows

$$CAIC = \frac{2nk}{n-1-k} - 2(\ell), \tag{3.7.3}$$

where n is the sample size.

3.7.2.2 Bayesian information criterion

Schwarz (1978) developed the BIC, which is often referred to as the Schwarz information criterion (SIC) in literature. The fundamental principle of BIC is derived by approximating the Bayes factor under the presumption that the data are independent and identically distributed. The test statistics for the BIC are provided by

$$BIC = k(\log(n)) - 2(\ell), \tag{3.7.4}$$

Compared to the AIC and CAIC in both large and small samples, the BIC has the ability to penalize models with numerous parameters. In order to choose the best model out of a group of competing models, it is crucial to employ the BIC along with the AIC and CAIC. Similar to the AIC, the appropriate model is the one that has the lowest BIC value in comparison to other models.

3.8 Total time on test

TTT transform theory is well-known due to its applications in a variety of academic domains, including stochastic modeling, econometrics, survival and reliability research, and ordering of distributions (Nasiru, 2018). The form of the HRF for a particular data set is frequently of interest to researchers in survival and reliability studies. The TTT-transform gives the researchers with a graphical representation of the HRF shape.

The TTT-transform is used mostly in literature to solve problems related to survival and reliability, such as characterizing aging qualities, testing hypotheses, sorting life distributions, identifying models, and creating new classes of lifetime distributions. Barlow and Doksum (1972) developed the technique to solve statistical inference issues including order constraints.

With a SF $S(x)$ and CDF (F(x)) for a random variable denoting a lifetime, the function defined on $[0, 1]$ by

$$H_F^{-1}(p) = \int_0^{F^{-1}(p)} S(u)du, p \in [0, 1]. \tag{3.8.1}$$

The TTT-transform of F is what it is termed. The SF is given by $S(u) = 1 - F(u)$. The scaled TTT transform is calculated by

$$\varphi G(p) = \frac{H^{-1(p)}}{H^{-1}(1)}. \tag{3.8.2}$$

Scaled TTT-transform is represented by curve G(p) versus $0 \leq p \leq 1$.

Using the scaled TTT-transform curve, Barlow and Doksum (1972) identified the HRF's shape as one of the following:

1. If the scaled TTT-transform curve is on the 45° line, the HRF is considered to be constant.

2. If the scaled TTT-transform curve is concave above the 45° line, the HRF is increasing.

3. If the scaled TTT-transform curve is convex below the 45° line, the HRF is decreasing.

4. If the scaled TTT-transform curve is initially convex below the 45° line, and subsequently concave above the line, the HRF displays a bathtub shape.

5. If the scaled TTT-transform is first concave above the 45° line and then convex below the 45° line, the HRF is uni-modal or has an inverse bathtub shape.

Ramos et al. (2014) produced Figure 3.1 to show how to test the hazard function's behavior.

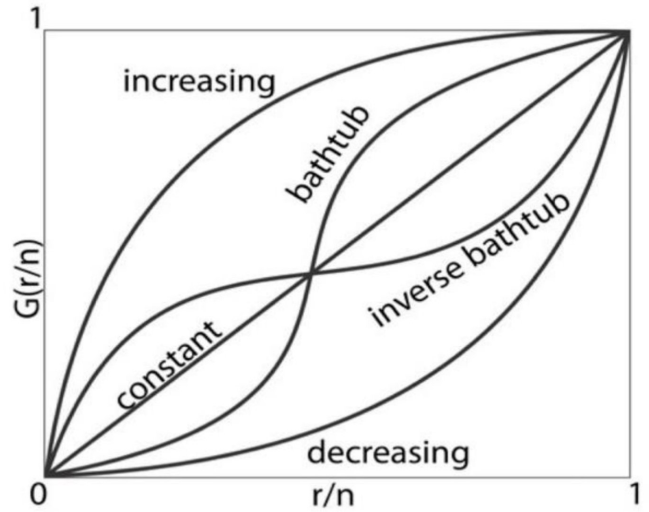

Figure 3.1: TTT plots for various distributions show the form of the hazard function

CHAPTER 4

RESULTS AND DISCUSSIONS

4.1 Introduction

This Chapter presents and discusses the results of the specific objectives of this study.

4.2 Development of the Extended Exponential-Weibull Distribution

The ExEW distribution generalizes the exponential-Weibull distribution. It is formulated by using LAII approach.
Let $X \sim$ ExEW(a, b, c, α) then the CDF of the ExEW distribution can define by applying Equation (3.2.1) as follows

$$F(x) = 1 - \left[e^{-\left(ax+bx^c\right)}\right]^{\alpha} = 1 - e^{-\alpha\left(ax+bx^c\right)}, x > 0. \quad (4.2.1)$$

Where $\alpha > 0$, $a > 0$, and $c > 0$ are shape parameters, $b > 0$, is scale parameter. Note that the additional shape parameter is α .

4.2.1 Sub-models

The proposed ExEW distribution has some sub-models that are often utilized in parametric survival modeling. Its sub-models include the E, Weibull, EE, and the ExW distributions . These sub-models are listed in Table 4.1.
The propositions below relate the proposed distribution to its sub-models.

The Exponential Distribution

Proposition 1. Let X $\sim$ ExEW(a,b,c,α) If $b = 0$ and $\alpha = 1$ in Equation (4.2.1) then the CDF of ExEW reduce to the CDF of the exponential distribution.
Proof. The ExEW distribution's CDF is written by

$$F(x) = 1 - [e^{-(ax+bx^c)}]^\alpha, x > 0.$$

If we change $b = 0$ and $\alpha = 1$, it given us

$$F(x) = 1 - [e^{-(ax+0x^c)}] = 1 - e^{-ax}, x > 0 \tag{4.2.2}$$

The Weibull distribution

Proposition 2. Let$X \sim$ NMEW(a,b,c,α) If $a = 0$ and $\alpha = 1$ in Equation (4.2.1) then the CDF of ExEW reduce to the CDF of the W distribution.
Proof. The ExEW distribution's CDF is written by

$$F(x) = 1 - [e^{-(ax+bx^c)}]^\alpha, x > 0.$$

If $a = 0$ and $\alpha = 1$, it given us

$$F(x) = 1 - [e^{-(a\times 0+bx^c)}] = 1 - e^{-bx^c}, x > 0. \tag{4.2.3}$$

The exponentiated exponential distribution

Proposition 3. Let X $\sim$ ExEW(a,b,c,α) If $b = 0$ in Equation (4.2.1) then the CDF of ExEW reduce to the CDF of the EE distribution.

Proof. The ExEW distribution's CDF is written by

$$F(x) = 1 - [e^{-(ax+bx^c)}]^\alpha, x > 0.$$

If we change $b = 0$, it given us

$$F(x) = 1 - [e^{-(a*x+0*x^c)}]^\alpha = 1 - [e^{-a*x}]^\alpha, x > 0. \tag{4.2.4}$$

The exponential Weibull distribution

Proposition 4. Let X $\sim$ ExEW(a,b,c,α) If $\alpha = 1$ in Equation (4.2.1) then the CDF of ExEW reduce to the CDF of the ExW distribution.

Proof. The ExEW distribution's CDF is defined by

$$F(x) = 1 - [e^{-(ax+bx^c)}]^\alpha, x > 0.$$

If we change $\alpha = 1$, it given

$$F(x) = 1 - [e^{-(a*x+b*x^c)}] = 1 - e^{-(a*x+b*x^c)}, x > 0. \tag{4.2.5}$$

Table 4.1: Sub-models of ExEW(a, b, c, α) distribution

Model	a	b	c	α
Exponential	a	0	0	1
Weibull	0	b	c	1
EE	a	0	0	α
EW	a	b	c	1

4.2.2 Probabilistic functions for the ExEW distribution

In this section, the PDF, HRF and SF of the ExEW are presented. In addition to the above probabilistic functions, CHRF and RHRF are also formulated.

1. The PDF corresponding to Equation (4.2.1) takes the form

$$f(x) = \alpha(a + b\,cx^{c-1})\exp\left[-\alpha(a\,x + b\,x^{c})\right], x > 0. \tag{4.2.6}$$

Figure 4.1 illustrates pdf shapes of the ExEW distribution for various choices of the parameters. The pdf of the ExEW distribution can be symmetrical, asymmetrical, unimodal, J, and reversed-J shapes.

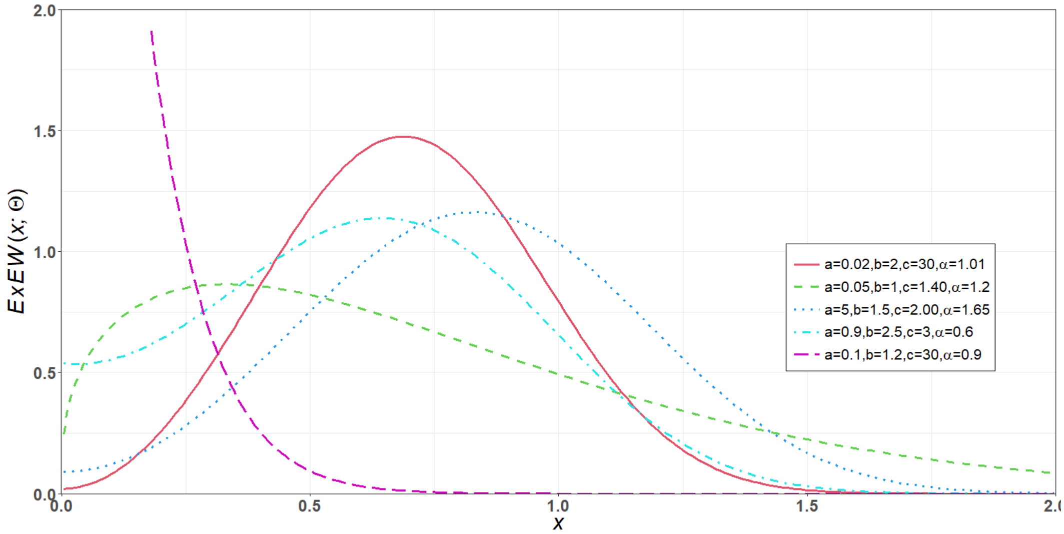

Figure 4.1: Shapes of the PDF of the ExEW distribution for various choices of the parameters

2. The SF corresponding to Equation (4.2.1) is as follows:

$$S(x) = \exp\left[-\alpha(a\,x + b\,x^{c})\right]. \tag{4.2.7}$$

3. The HRF of the ExEW distribution is expressed as:

$$h(x) = \alpha(a + b\,cx^{c-1}). \tag{4.2.8}$$

Figure 4.2 shows the HRF which is clearly decreasing, increasing, constant, J-shaped.

4. The RHRF is written as follows:

$$r(x) = \frac{\alpha(a + b\,cx^{c-1})\exp\left[-\alpha(a\,x + b\,x^c)\right]}{1 - \exp\left[-\alpha(a\,x + b\,x^c)\right]}. \tag{4.2.9}$$

5. The CHRF is obtained as:

$$H(x) = \alpha(a\,x + b\,x^c). \tag{4.2.10}$$

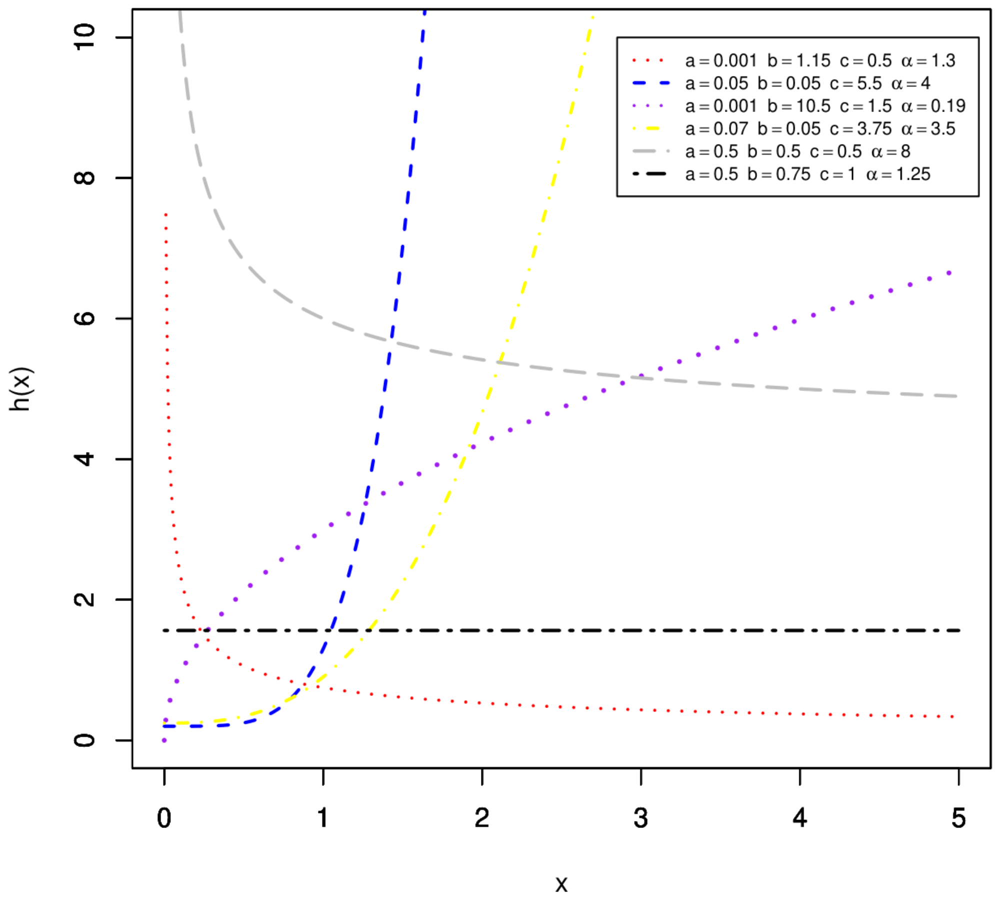

Figure 4.2: Shapes of the HRF of the ExEW distribution for different values of the parameters

4.3 Derivation of the mathematical properties of the ExEW distribution

The quantile function of the distribution, Moments, and related functions such as the mean, variance, central moments, residual life function, and its inverse, among others are discussed in this part. The mathematical properties can be used to describe and investigate lifetime distributions in addition to the functions presented in Subsection (4.2.2).

4.3.1 Quantile function

The quantile function (qf) is the reverse of the CDF and is significant in quantitative and statistical data analysis. A probability distribution can be described using either the qf or the CDF (Midhu et al., 2013).

Let $x = Q(u) = F^{-1}(u)$, for 0 < u < 1, then the qf of the ExEW distribution is given by reversing Equation (4.2.1), thus, $F(x) = 1 - e^{-\alpha(ax+bx^c)} = u$ for x, then the qf will be the solution of the equation,

$$ax + bx^c = -\ln\{1-u\}^{\frac{1}{\alpha}}. \tag{4.3.1}$$

4.3.2 Residual and reverse residual life functions

In reliability analysis and risk management, residual life has a wide range of applications. The residual life of the ExEW r.v. is:

$$R_{(t)}(x) = \frac{S(x+t)}{S(t)},$$

$$R_{(t)}(x) = \frac{\exp\Big\{-\alpha(a(x+t)+b(x+t)^c)\Big\}}{\exp\Big\{-\alpha(at+bt^c)\Big\}}. \tag{4.3.2}$$

Furthermore, the reverse Residual life of the ExEW distribution can be calculated as follows:

$$\hat{R}_{(t)}(x) = \frac{S(x-t)}{S(t)},$$

$$\hat{R}_{(t)}(x) = \frac{\exp\Big\{-\alpha(a(x-t)+b(x-t)^c)\Big\}}{\exp\Big\{-\alpha(at+bt^c)\Big\}}. \tag{4.3.3}$$

4.3.2.1 Moments

Moments can be used to analyze some of a distribution's most important characteristics and properties, such as dispersion, tendency, kurtosis, and skewness. The r^{th} moment of a r.v. $X \sim ExEW(a,b,c,\alpha)$ is

$$E(X^r) = \sum_{j,k,m=0}^{\infty} \frac{(-1)^{j+k+m}\mathit{\Gamma}(\alpha)}{j!k!m!\mathit{\Gamma}(\alpha-j)} a^m$$
$$\left\{ \frac{\alpha\, a\, \mathit{\Gamma}(\frac{r+k+m+-2c}{c})}{c\,[b(1+j)]^{\frac{r+k+m+1}{c}}} + \frac{b\, \mathit{\Gamma}(\frac{r+m-c}{c})}{[b(1+j)]^{\frac{r+c+m}{c}}} \right\}. \tag{4.3.4}$$

Proof: A r.v. X with pdf f(x), the r^{th} moment is written as follows

$$\mu_r' = \int_0^\infty x^r f(x) dx. \tag{4.3.5}$$

Equation (4.2.6) is substituted for Equation (4.3.5) and the result is

$$E(X^r) = \int_0^\infty x^r \alpha\alpha(a + b\, c x^{c-1}) e^{-\alpha(ax+bx^c)} dx \tag{4.3.6}$$

$$= \int_0^\infty x^r \alpha a e^{-\alpha(ax+bx^c)} dx + \int_0^\infty x^r bcx^{c-1} e^{-\alpha(ax+bx^c)} dx \tag{4.3.7}$$

$$E(X^r) = \alpha a \int_0^\infty x^r e^{-\alpha(ax+bx^c)} dx + bc \int_0^\infty x^r x^{c-1} e^{-\alpha(ax+bx^c)} dx. \tag{4.3.8}$$

Applying binomial expansion and further simplification, Equation (4.3.8) becomes

$$E(X^r) = \alpha a \int_0^\infty x^r e^{-(ax+bx^c)} \sum_{j=0}^\infty \frac{(-1)^j \Gamma(\alpha)}{j!\Gamma(\alpha - j)}$$
$$\sum_{k=0}^\infty \frac{(-1)^k (aj)^k x^k}{k!} e^{-jbx^c} dx + bc \int_0^\infty x^{r+c-1} e^{-(ax+bx^c)}$$
$$\sum_{j=0}^\infty \frac{(-1)^j \Gamma(\alpha)}{j!\Gamma(\alpha - j)} \sum_{k=0}^\infty \frac{(-1)^k (aj)^k x^k}{k!} e^{-jbx^c} dx. \quad (4.3.9)$$

$$E(X^r) = \sum_{j,k=0}^\infty \frac{(-1)^{j+k} \Gamma(\alpha)(aj)}{j!k!\Gamma(\alpha - j)} \alpha a \int_0^\infty x^{r+k} e^{-(ax+bx^c)}$$
$$e^{-jbx^c} dx + \sum_{j,k=0}^\infty \frac{(-1)^{j+k} \Gamma(\alpha)(aj)}{j!k!\Gamma(\alpha - j)}$$
$$bc \int_0^\infty x^{r+c-1} e^{-(ax+bx^c)} - jbx^c dx. \quad (4.3.10)$$

But

$$e^{-(ax+bx^c)} = e^{-ax} \times e^{-bx^c}. \quad (4.3.11)$$

By using McLaurin's series expansion

$$e^{-ax} = \sum_{m=0}^\infty (-1)^m \times \frac{a^m x^m}{m!}. \quad (4.3.12)$$

Substituting (21) in (19), we have

$$E(X^r) = \sum_{j,k,m=0}^\infty \frac{(-1)^{j+k+m} \Gamma(\alpha)}{j!k!m!\Gamma(\alpha - j)} \left\{ \alpha a^{m+1} \int_0^\infty x^{r+k+m} e^{-bx^c(1+j)} dx \right\} +$$
$$\left\{ bca^m \int_0^\infty x^{r+c+m-1} e^{-bx^c(1+j)} dx \right\}. \quad (4.3.13)$$

Let

$$w = bx^c(1+j).$$

We get,

$$x^c = \frac{w}{b(1+j)} \Rightarrow \frac{w^{1/c}}{[b(1+j)]^{1/c}}.$$

Hence,

$$x = \frac{w^{1/c}}{[b(1+j)]^{1/c}}.$$

Then,

$$\frac{dx}{dw} = \frac{1/cw^{\frac{1-c}{c}}}{[b(1+j)]^{1/c}},$$

which is follows that

$$dx = \frac{w^{\frac{1-c}{c}}}{c[b(1+j)]^{1/c}} dw. \tag{4.3.14}$$

Substituting Equation (4.3.14) in Equation(4.3.13), we obtain

$$E(X^r) = \sum_{j,k,m=0}^{\infty} \frac{(-1)^{j+k+m} \Gamma(\alpha)}{j!k!m!\Gamma(\alpha-j)} \left\{ \alpha a^{m+1} \int_0^{\infty} \frac{w^{\frac{r+k+m}{c}}}{[b(1+j)]^{\frac{r+k+m}{c}}} e^{-w} \right\} \times$$
$$\left\{ \frac{w^{\frac{1-c}{c}}}{c[b(1+j)]^{1/c}} dw + bca^m \int_0^{\infty} \frac{w+c+m-\frac{1}{c}}{[b(1+j)]^{r+c+m-\frac{1}{c}}} e^{-w} \times \frac{w^{\frac{1-c}{c}}}{c[b(1+j)]^{1/c}} dw \right\}. \tag{4.3.15}$$

After simplification, Equation (4.3.15) becomes

$$E(X^r) = \sum_{j,k,m=0}^{\infty} \frac{(-1)^{j+k+m} \Gamma(\alpha)}{j!k!m!\Gamma(\alpha-j)} a^m$$
$$\left\{ \frac{\alpha\, a\, \Gamma(\frac{r+k+m+-2c}{c})}{c\,[b(1+j)]^{\frac{r+k+m+1}{c}}} + \frac{b\, \Gamma(\frac{r+m-c}{c})}{[b(1+j)]^{\frac{r+c+m}{c}}} \right\}.$$

Table 4.2 reports the values of the first five moments, standard deviation (SD), coefficient of variation (CV), skewness (CS), and kurtosis (CK) of the ExEW model for various parameter values.

Table 4.2: Numerical values of the first five moments, SD, CV, CS, and CK for various parametric values

	a,b,c, α	a,b,c, α	a,b,c, α	a,b,c, α	a,b,c, α
Moments	(1,10,1.9,0.05)	(0.1,1,1.1,1.05)	(0.5,7,0.5,1.1)	(0.1,1,1.05,1.1)	(1,7,1.1,2.1)
μ_1'	1.197	0.584	0.208	0.557	0.035
μ_2'	3.0132	0.433	0.119	0.414	0.012
μ_3'	1.007	0.344	0.079	0.329	0.009
μ_4'	4.173	0.286	0.058	0.273	0.003
μ_5'	2.047	0.244	0.045	0.233	0.002
SD	5.357	0.305	0.275	0.322	0.106
CV	4.474	0.522	1.323	0.577	3.068
CS	5.869	-0.594	1.109	-0.508	3.843
CK	4.513	2.239	3.036	2.008	19.828

From Table 4.2, the ExEW distribution is quantitatively versatile in terms of mean and variance. As evidenced by its values, CS can be right-skewed, almost symmetrical, or somewhat left-skewed. The CK values indicate whether the ExEW distribution is leptokurtic, platykurtic, or mesokurtic. All of these features point to the ExEW distribution's versatility, which makes it an ideal choice for modeling.

4.3.3 Moment generating function (mgf)

The mgf of the ExEW distribution is written as follows:

$$M_t(t) = E(e^{tx}) = \int_{-\infty}^{\infty} e^{tx} f_{ExEW}(x)dx. \tag{4.3.16}$$

Using the results from Subsection 4.3.2.1, we can get closed-form for the mgf. Then, the mgf of ExEW distribution reduces to

$$E(e^{tx}) = \sum_{j,k,m=0}^{\infty} \frac{(-1)^{j+k+m}\Gamma(\alpha)}{k!m!j!\Gamma(-j+\alpha)} \frac{(t)^r}{r!} a^m \left\{ \alpha a \frac{\Gamma(\frac{r+k+m+-2c}{c})}{c[b(1+j)]^{\frac{r+k+m+1}{c}}} + b \frac{\Gamma(\frac{r+m-c}{c})}{[b(1+j)]^{\frac{r+c+m}{c}}} \right\}. \tag{4.3.17}$$

4.4 Estimation of the parameter of the ExEW distribution

Maximum likelihood (ML) is used to estimate the unknown parameters of the ExEW distribution using a full sample.
If $X_1, X_2, \ldots, X_n$ denote a random sample from the ExEW distribution with an unknown parameter vector $\boldsymbol{\theta} = (a, b, c, \alpha)$.
Then, the ML function follows as

$$L(\boldsymbol{\theta}) = \prod_{i=1}^{n} \alpha(a + bcx_i^{c-1})e^{-\alpha(ax_i + bx_i^c)}. \tag{4.4.1}$$

Then, the log-likelihood function reduces to

$$\ell(\boldsymbol{\theta}) = n\log a + n\log b + n\log c + n\log\alpha + n\log(c-1)\sum_{i=1}^{n}\log x_i - \sum_{i=1}^{n}(\alpha(ax_i + bx_i^c)) \tag{4.4.2}$$

The parameter estimates are produced by performing a partial derivative of $\ell(\boldsymbol{\theta})$ with respect to each parameter, as shown below.

$$\frac{\partial \ell}{\partial a} = \frac{n}{a} - \alpha\sum_{i=1}^{n} x_i. \tag{4.4.3}$$

$$\frac{\partial \ell}{\partial b} = \frac{n}{b} - \alpha\sum_{i=1}^{n} x_i^c. \tag{4.4.4}$$

$$\frac{\partial \ell}{\partial c} = \frac{n}{c} + \frac{n}{(c-1)}\sum_{i=1}^{n}\log x_i - b\alpha\sum_{i=1}^{n} x_i^c \log x_i \tag{4.4.5}$$

and

$$\frac{\partial \ell}{\partial \alpha} = \frac{n}{\alpha} - \sum_{i=1}^{n} x_i(ax_i + bx_i^c). \tag{4.4.6}$$

The unknown parameters can be calculated via resetting the aforementioned equations to zero and calculating them all at once. These equations can alos be numerically solved using statistical software (for example, the adequacymodel package in R software) or an iterative technique such as the Newton-Raphson algorithm.

Because of predicted information matrix is too complicated to set confidence intervals for the parameters, the observed information matrix $I_{(\boldsymbol{\theta})}$ is used.
The following is how the information matrix is obtained:

$$I_{(\boldsymbol{\theta})} = -\begin{bmatrix} \frac{\partial \ell^2}{\partial a^2} & \frac{\partial \ell^2}{\partial a \partial b} & \frac{\partial \ell^2}{\partial a \partial c} & \frac{\partial \ell^2}{\partial a \partial \alpha} \\ & \frac{\partial \ell^2}{\partial b^2} & \frac{\partial \ell^2}{\partial b \partial c} & \frac{\partial \ell^2}{\partial b \partial \alpha} \\ & & \frac{\partial \ell^2}{\partial c^2} & \frac{\partial \ell^2}{\partial \alpha \partial c} \\ & & & \frac{\partial \ell^2}{\partial \alpha^2} \end{bmatrix}.$$

Whereas the regularity criteria are satisfied and the parameters are within the interior of the parameter space but not on the boundary, $\sqrt{n}(\cong \hat{\boldsymbol{\theta}} - \boldsymbol{\theta})$ converges in distribution to $N_4(0, I^{-1}(\boldsymbol{\theta}))$, where $I_{(\boldsymbol{\theta})}$ is the predicted. When $I_{(\boldsymbol{\theta})}$ is substituted by the observed information matrix assessed at $J_{(\hat{\boldsymbol{\theta}})}$, the asymptotic behavior remains true. To construct $100(1-\tau)\%$ two-sided 95% confidence interval for model parameters, use the asymptotic multivariate normal distribution $N_4(0, I^{-1}(\hat{\boldsymbol{\theta}})$, where τ is the significance level.

4.5 Development of the Extended Exponential-Weibull Regression Model

4.5.1 The extended exponential-Weibull accelerated failure time model

The proposed AFT model is developed by extending the ExEW(a, b, c, α) distribution to incorporate covariates. The corresponding SF with covariate vector $\boldsymbol{z}$

is given by

$$S(t;\boldsymbol{z}) = \exp\left\{-\alpha\left[a\left(te^{\boldsymbol{z}'\boldsymbol{\beta}}\right) + b\left(te^{\boldsymbol{z}'\boldsymbol{\beta}}\right)^{c}\right]\right\}, \quad t > 0, \tag{4.5.1}$$

which corresponds to the SF of the ExEW distribution under the following configuration: $a^* = ae^{\boldsymbol{z}'\boldsymbol{\beta}}$ and $b^* = b\left(e^{\boldsymbol{z}'\boldsymbol{\beta}}\right)^c$, that is

$$S(t;\boldsymbol{z}) = \exp\left[-\alpha\left(a^*t + b^*t^c\right)\right], \quad t > 0.$$

This demonstrates that, under the AFT model framework, the ExEW distribution is closed in the distributional sense.
Furthermore, the HRF with covariates $\boldsymbol{z}$ is written as follows:

$$h(t;\boldsymbol{z}) = \alpha\left[a + b\,c\left(te^{\boldsymbol{z}'\boldsymbol{\beta}}\right)^{c-1}\right]e^{\boldsymbol{z}'\boldsymbol{\beta}}, \quad t > 0. \tag{4.5.2}$$

The PDF with covariates vector $\boldsymbol{z}$ is given by

$$f(t;\boldsymbol{z}) = \alpha\left[a + b\,c\left(te^{\boldsymbol{z}'\boldsymbol{\beta}}\right)^{c-1}\right]\exp\left\{-\alpha\left[a\,\left(te^{\boldsymbol{z}'\boldsymbol{\beta}}\right) + b\,\left(te^{\boldsymbol{z}'\boldsymbol{\beta}}\right)^{c}\right]\right\}, \quad t > 0. \tag{4.5.3}$$

Single-parameter hazard-based regression (SPHBR) models are commonly used to relate covariates to one parameter of specific interest. In these SPHBR models, the role of the other (explanatory independent variables) parameters are often little more than to give the model sufficient generality to adapt to the data. A more tractable method is to relate these other parameters to covariates; this method is known as multi-parameter hazard-based regression (MPHBR) models (Burke et al., 2020a,0; Jaouimaa et al., 2021; Peng et al., 2020). The primary focus of this study is the development of MPHBR models in the context of time-to-event analysis.
In our case, this is a multi-parameter AFT model, which is different from a single-parameter AFT model, like the Weibull AFT model or the log-logistic AFT model, among others, where only the scale parameter is changed. As a result, except for the α parameter, the covariates influence the majority of the baseline

distribution parameters. This is what makes our work unique and different from the common classical AFT models.

4.6 Estimation of the ExEW-AFT parameters

The likelihood function in the ExEW-AFT model is given by

$$L(\theta, D) = \prod_{i=1}^{n} [f(t_i; a, b, c, \alpha, \boldsymbol{\beta}, \boldsymbol{z}_i)]^{\delta_i} [S(t_i; a, b, c, \alpha, \boldsymbol{\beta}, \boldsymbol{z}_i)]^{1-\delta_i}, \tag{4.6.1}$$

where $S(t; a, b, c, \alpha, \boldsymbol{\beta}, \boldsymbol{z})$ and $f(t; a, b, c, \alpha, \boldsymbol{\beta}, \boldsymbol{z})$ of the ExEW-AFT model are derived from Equations (4.5.1) and (4.5.3), $\theta = (a, b, c, \alpha, \boldsymbol{\beta})$, $D = ((t_1, \delta_1, \boldsymbol{z}_1), (t_2, \delta_2, \boldsymbol{z}_2), \ldots, (t_n, \delta_n, \boldsymbol{z}_n))$. We recall that the censoring indicator satisfies $\delta = 0$ if the observation is censored and $\delta = 1$ if the observation is failed, and $\boldsymbol{z}_i$ is the matrix of covariates, which is known as the design matrix or model matrix. After expressing the PDF in terms of HRF and SF and taking the logarithm of both sides of the likelihood function, the log-likelihood can be written as follows:

$$\ell(\theta; D) = \sum_{i=1}^{n} \left[\delta_i \log h(t_i; a, b, c, \alpha, \boldsymbol{\beta}, \boldsymbol{z}_i) + \log S(t_i; a, b, c, \alpha, \boldsymbol{\beta}, \boldsymbol{z}_i)\right]. \tag{4.6.2}$$

As a result, the full log-likelihood function for the ExEW-AFT model can be written as follows:

$$\begin{aligned} \ell(\theta; D) = \sum_{i=1}^{n} \delta_i \log &\left[\alpha \left(a + b\, c \left(t e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\right)^{c-1} \right) e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\right] \\ &+ \sum_{i=1}^{n} \log \left[-\alpha \left(a \left(t e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\right) + b \left(t e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\right)^{c} \right)\right]. \end{aligned} \tag{4.6.3}$$

The MLEs of $\theta' = (a, b, c, \alpha)$ and $\boldsymbol{\beta}$ can be obtained by maximising Equation (4.6.3) directly with respect to θ. The log-likelihood function's first derivative can be solved (non-linear equations below).

$$\frac{\partial \ell}{\partial a} = \frac{e^{\boldsymbol{z_i}'\boldsymbol{\beta}} \sum_{i=1}^{n} t_i}{a\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + b\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c} + \frac{e^{\boldsymbol{z_i}'\boldsymbol{\beta}} \sum_{i=1}^{n} t_i \delta_i}{a\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + bc\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c}, \tag{4.6.4}$$

$$\frac{\partial \ell}{\partial b} = \frac{\sum_{i=1}^{n} \big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c}{a\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + b\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c} + \frac{c \sum_{i=1}^{n} \delta_i \big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c}{a\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + bc\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c}, \tag{4.6.5}$$

$$\frac{\partial \ell}{\partial c} = \frac{b \sum_{i=1}^{n} \big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c \log \big[t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big]}{a\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + b\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c} + \frac{\sum_{i=1}^{n} \delta_i \Big(b\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c + bc\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c + \log \big[t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big] \Big)}{a\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + bc\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c}, \tag{4.6.6}$$

$$\frac{\partial \ell}{\partial \alpha} = \frac{\sum_{i=1}^{n} \delta_i}{\alpha} - \frac{\sum_{i=1}^{n} \Big(- a\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) - b\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c \Big)}{\Big(a\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + b\big(t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big)^c \Big)\alpha}, \tag{4.6.7}$$

$$\frac{\partial \ell}{\partial \boldsymbol{\beta}} = \frac{\sum_{i=1}^{n} \Big(a\big(\boldsymbol{z_i} t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + bc\big(\boldsymbol{z_i} t_i e^{(\boldsymbol{z_i}'\boldsymbol{\beta})^{c-1}}\big) \Big)}{a\big(t_i e^{\boldsymbol{z_i'\beta}}\big) + b\big(t_i e^{\boldsymbol{z_i'\beta}}\big)^c} + \frac{\sum_{i=1}^{n} \delta_i \Big(a\big(\boldsymbol{z_i} t_i e^{\boldsymbol{z_i}'\boldsymbol{\beta}}\big) + bc^2\big(\boldsymbol{z_i} t_i e^{(\boldsymbol{z_i}'\boldsymbol{\beta})^{c-1}}\big) \Big)}{a\big(t_i e^{\boldsymbol{z_i'\beta}}\big) + bc\big(t_i e^{\boldsymbol{z_i'\beta}}\big)^c}. \tag{4.6.8}$$

It is crucial to remember that $\theta' = (a, b, c, \alpha)$ and $\boldsymbol{\beta}$ cannot be analytically solved. Numerical iteration techniques like the Newton-Raphson algorithm are employed to solve these equations.

Tests and interval estimates for the model parameters are made based on the maximum likelihood estimators' approaching normality. With a mean θ and covariance matrix $\sum = I(\hat{\theta})^{-1}$, the asymptotic distribution of $\hat{\theta}$ is approximately a $(p{+}4)$ variate normal distribution. For the extended exponential-Weibull model, the observed information matrix is represented as

$$I(\hat{\theta}) = - \begin{bmatrix} \frac{\partial^2 \ell(\theta)}{\partial a^2} & \frac{\partial^2 \ell(\theta)}{\partial a \partial b} & \frac{\partial^2 \ell(\theta)}{\partial a \partial c} & \frac{\partial^2 \ell(\theta)}{\partial a \partial \alpha} & \frac{\partial^2 \ell(\theta)}{\partial a \partial \boldsymbol{\beta}} \\ & \frac{\partial^2 \ell(\theta)}{\partial b^2} & \frac{\partial^2 \ell \theta}{\partial b \partial c} & \frac{\partial^2 \ell}{\partial b \partial \alpha} & \frac{\partial^2 \ell(\theta)}{\partial b \partial \boldsymbol{\beta}} \\ & & \frac{\partial^2 \ell}{\partial c^2} & \frac{\partial^2 \ell}{\partial \alpha \partial c} & \frac{\partial^2 \ell(\theta)}{\partial c \partial \boldsymbol{\beta}} \\ & & & \frac{\partial^2 \ell(\theta)}{\partial \alpha^2} & \frac{\partial^2 \ell(\theta)}{\partial \alpha \partial \boldsymbol{\beta}} \\ & & & & \frac{\partial^2 \ell(\theta)}{\partial \boldsymbol{\beta}_p^2} \end{bmatrix}$$

a $(p{+}4) \times$ a $(p{+}4)$ observed information matrix (second derivatives of $\ell(\theta)$. By the multivariate delta method, the asymptotic distribution of $\hat{\theta}$ is also approximately normal with mean θ and covariance matrix $D\sum D^{`}$, where D is the $(p+4)\times$ a $(p+4)$ diagonal matrix.

4.6.1 Extended exponetial-Weibull mixture cure model

The ExEW mixture cure model (ExEW-MCM) in this Subsection is proposed with the aim of accounting for the fraction of susceptible (cured) subjects in the study. According to the Equations (4.2.6) and (4.2.7) for the ExEW distribution and Equations (3.5.1) and (3.5.2) for MCM, we can formulate the ExEW-MCM as follows

- The $S_{(MCM)}(t)$ for ExEW model is given by

$$S_{(MCM)}(t) = \rho + (1-\rho).\exp\Big\{-\alpha(a\,t_i + b\,t_i^c)\Big\}, \tag{4.6.9}$$

- the $f_{(MCM)}(t)$ or ExEW model can be written as follows

$$f_{(MCM)}(t) = (1-\rho)\alpha(a + b\,cx^{c-1})\exp\Big\{-\alpha(a\,x + b\,x^c)\Big\}, x > 0. \tag{4.6.10}$$

4.7 Estimation of the ExEW-MCM parameters

In this Section we employ the maximum likelihood to estimate the ExEW-MCM parameters. Let $\theta = \big(a, b, c, \alpha, \rho\big)'$. substituting Equations (4.2.6) and (4.2.7) into equation (3.5.3) of the MCM with ExEW susceptible distribution, we obtain the log-likelihood:

$$\begin{aligned}\ell(\theta) = \log\big(L_{MCM}(\theta)\big) = \log\big(1-p\big)\sum_{i=1}^{n}\delta_i + \sum_{i=1}^{n}\delta_i\log\Bigg(\alpha(a+b\,ct_i^{c-1})\exp\Big\{-\alpha(a\,t_i+b\,t_i^c)\Big\})\Bigg)\\ +\sum_{i=1}^{n}\big(1-\delta_i\big)\log\Bigg(\rho + (1-\rho)\exp\big\{-\alpha(a\,t_i + b\,t_i^c)\big\}\Bigg).\end{aligned} \tag{4.7.1}$$

The MLE of $\theta = \big(a, b, c, \alpha, \rho\big)'$ is one that maximizes $\ell(\theta)$, As indicated by the $\hat{\theta}$. The following scoring functions are derived from partial derivatives of the log-likelihood function in Equation (4.7.1) with respect to θ:

$$\frac{\partial \ell}{\partial a} = \frac{n}{a} + \sum_{i=1}^{n} \frac{\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\big(1-\rho\big)\alpha t_i\big(1-\delta_i\big)}{\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\big(1-\rho\big) + \rho}, \tag{4.7.2}$$

$$\frac{\partial \ell}{\partial b} = \log(c-1)\sum_{i=1}^{n}\big(t_i^c + 1\big) + \sum_{i=1}^{n} \frac{\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\big(1-\rho\big)\alpha t_i^c\big(1-\delta_i\big)}{\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\big(1-\rho\big) + \rho}, \tag{4.7.3}$$

$$\begin{aligned}\frac{\partial \ell}{\partial c} = \frac{n}{c} + \log(c-1)\sum_{i=1}^{n} -\big(t_i^c \log(t_i) + \alpha b\big) + \frac{\sum_{i=1}^{n} t_i\big(-\alpha\big(at_i + bt_i^c\big)\big)}{(c-1)} + \\ \sum_{i=1}^{n} \frac{b\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\big(1-\rho\big)\alpha\log(t_i)t_i^c\big(1-\delta_i\big)}{\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\big(1-\rho\big) + \rho},\end{aligned} \tag{4.7.4}$$

$$\begin{aligned}\frac{\partial \ell}{\partial \alpha} = \frac{n}{\alpha} + (c-1)\sum_{i=1}^{n} t_i\big(-\big(at_i + bt_i^c\big)\big) + \\ \sum_{i=1}^{n} \frac{(1-\rho)\Big(at_i\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\} + bt_i^c\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\Big)(1-\delta_i)}{\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}(1-\rho) + \rho},\end{aligned} \tag{4.7.5}$$

$$\frac{\partial \ell}{\partial \rho} = \sum_{i=1}^{n} \frac{\Big(1 - \exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\Big)\big(1-\delta_i\big)}{\exp\Big\{\alpha\big(at_i + bt_i^c\big)\Big\}\big(1-\rho\big) + \rho} - \frac{\sum_{i=1}^{n}\delta_i}{1-\rho}. \tag{4.7.6}$$

The MLE is the solution to the scoring equations if the log-likelihood function has a global maximizer. The Newton-Raphson method is used to compute the numerical solution since it is a nonlinear system.

4.8 Simulation Study

4.8.1 Introduction

This Section presents extensive simulation studies to evaluate the developed models, including the ExEW model and the ExEW-AFT model.

4.8.2 Simulation study of the ExEW distribution

In this part, a comprehensive numerical inspection using Monte Carlo simulations is achieved to evaluate the capability of the ML estimates (MLEs) for the ExEW model. The absolute biases (AB), root mean square errors (RMSEs), and coverage probability (CP) are calculated for different small and large samples and parameter settings, to evaluate the performance of MLEs. To produce random samples from the ExEW distribution, the qf (4.3.1) is employed. With $n = 25, 50, 75, 100, 150$, and 200, the simulation experiments are repeated $N = 1000$ times. For set I: $a = 1, b = 1, c = 1.5$, $\alpha = 0.12$, set II: $a = 1, b = 1, c = 1.5$, $\alpha = 0.14$, set III: $a = 1, b = 1, c = 1.5$, $\alpha = 0.25$, and set IV: $a = 1, b = 1, c = 1.5$, $\alpha = 0.50$.

The AB and RMSE values of the parameters a, b, c, and α for various sample sizes are shown in Tables 4.3 and 4.4. The visual comparisons of these results are shown in Figures 4.3–4.10. The findings show that the RMSE decreases as the sample size grows until it hits zero. Furthermore, the AB decreases as the sample size grows. As a result, the MLEs and their asymptotic features can be used to build confidence ranges even for tiny sample numbers. Additionally, the confidence intervals' CPs are quite close to the nominal 95 percent level.

Table 4.3: The results of AB_s, RMSEs, and CP for the MLEs of ExEW distribution for I & II.

		I			II		
Parameters	n	AB_s	RMSEs	CP	AB_s	RMSEs	CP
	25	2.327	3.646	0.995	2.390	3.643	1.000
a	50	1.784	2.897	0.998	1.804	2.927	0.999
	75	1.603	2.675	1.0	1.571	2.698	1.000
	100	1.247	2.223	0.999	1.122	2.121	1.000
	150	0.818	1.555	1.000	0.793	1.583	1.000
	200	0.631	1.273	1.00	0.539	1.113	1.000
	25	0.695	0.818	0.872	0.710	0.829	0.859
b	50	0.570	0.736	0.926	0.578	0.749	0.914
	75	0.518	0.708	0.93	0.514	0.709	0.927
	100	0.451	0.651	0.952	0.403	0.642	0.959
	150	0.334	0.571	0.982	0.324	0.576	0.975
	200	0.281	0.535	0.99	0.259	0.528	0.993
	25	1.332	1.910	0.97	1.509	2.139	0.957
c	50	0.884	1.362	0.969	1.035	1.562	0.957
	75	0.785	1.263	0.97	0.857	1.376	0.964
	100	0.609	1.047	0.971	0.595	1.046	0.976
	150	0.387	0.705	0.971	0.404	0.764	0.971
	200	0.292	0.518	0.98	0.285	0.546	0.975
	25	0.033	0.057	0.999	0.041	0.067	0.999
α	50	0.028	0.044	1.000	0.036	0.051	1.000
	75	0.027	0.040	1.000	0.032	0.045	1.000
	100	0.021	0.034	1.000	0.023	0.038	1.000
	150	0.015	0.027	1.000	0.017	0.031	1.000
	200	0.012	0.023	1.000	0.013	0.025	1.000

Table 4.4: The results of AB_s, RMSEs, and CP for the MLEs of ExEW distribution for III & IV.

		III			IV		
Parameters	n	AB_s	RMSEs	CP	AB_s	RMSEs	CP
	25	1.750	2.816	0.996	1.304	2.243	0.999
a	50	1.362	2.330	1.000	1.111	2.070	0.997
	75	1.029	1.965	0.999	0.798	1.543	1.000
	100	0.871	1.617	0.999	0.742	1.372	0.999
	150	0.578	1.222	1.000	0.463	1.045	1.000
	200	0.455	01.036	1.00	0.361	0.998	1.000
	25	0.592	0.725	0.87	0.518	0.685	0.914
b	50	0.494	0.658	0.912	0.449	0.647	0.925
	75	0.386	0.617	0.944	0.370	0.593	0.943
	100	0.367	0.595	0.954	0.361	0.577	0.964
	150	0.285	0.536	0.976	0.250	0.508	0.988
	200	0.240	0.489	0.99	0.187	0.476	0.986
	25	1.764	2.671	0.946	2.417	3.911	0.938
c	50	1.179	1.892	0.969	1.705	2.917	0.955
	75	0.844	1.480	0.977	1.174	2.153	0.965
	100	0.745	1.314	0.976	0.984	1.726	0.966
	150	0.487	0.933	0.981	0.569	1.12	0.974
	200	0.352	0.711	0.973	0.466	1.054	0.983
	25	0.063	0.111	1.000	0.092	0.197	1.000
α	50	0.054	0.085	1.000	0.082	0.160	1.000
	75	0.040	0.071	1.000	0.062	0.136	1.000
	100	0.035	0.065	1.000	0.061	0.121	1.000
	150	0.025	0.049	1.000	0.035	0.093	1.000
	200	0.017	0.041	1.000	0.028	0.083	1.000

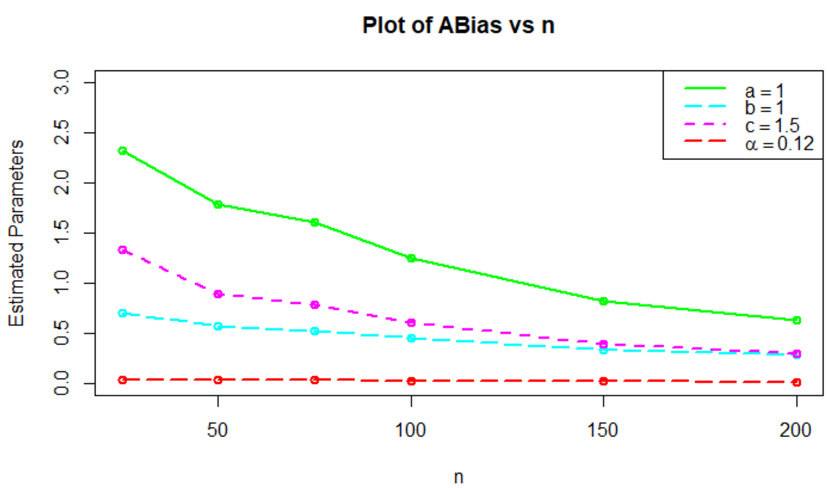

Figure 4.3: The plots of ABs for the ExEW parameters in set I

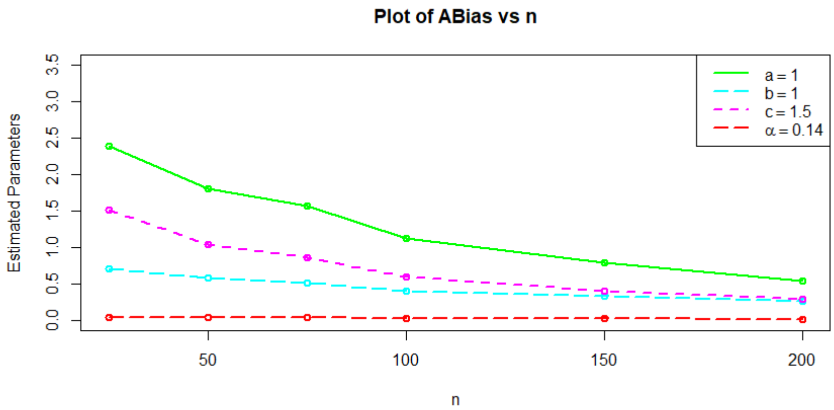

Figure 4.4: The plots of ABs for the ExEW parameters in set II

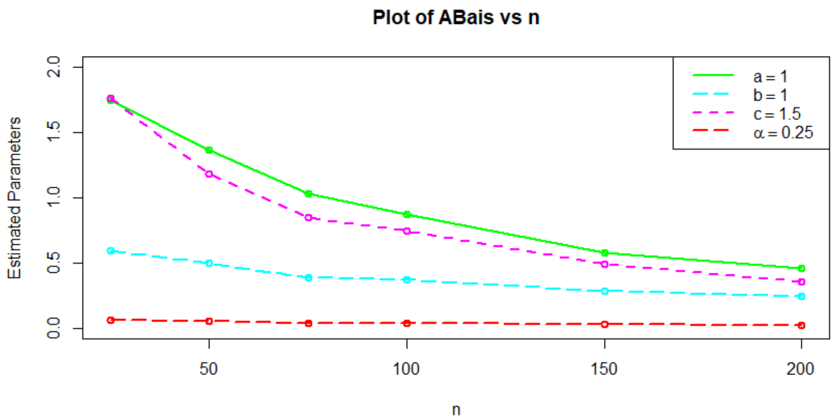

Figure 4.5: The plots of ABs for the ExEW parameters in set III

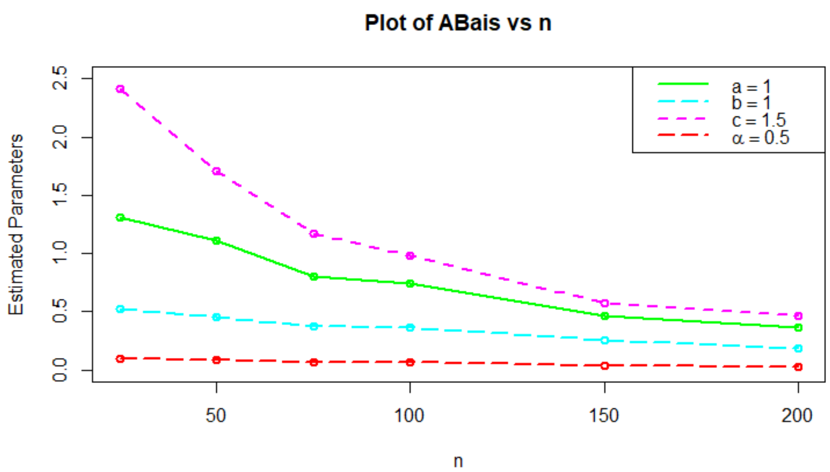

Figure 4.6: The plots of ABs for the ExEW parameters in set IV

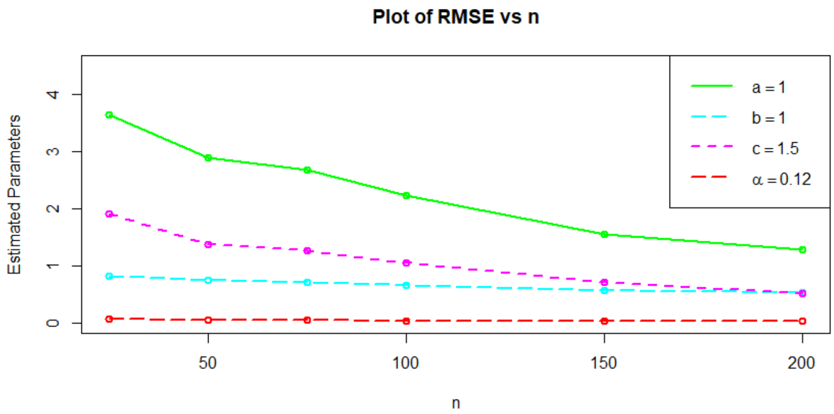

Figure 4.7: The plots of RMSEs for the ExEW parameters in set I

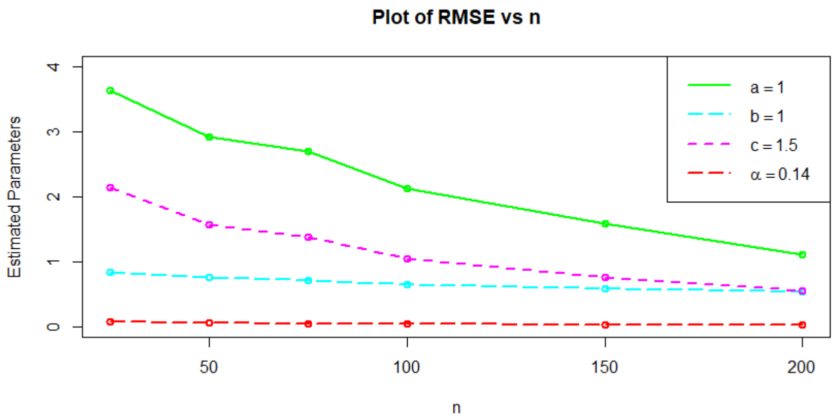

Figure 4.8: The plots of RMSEs for the ExEW parameters in set II

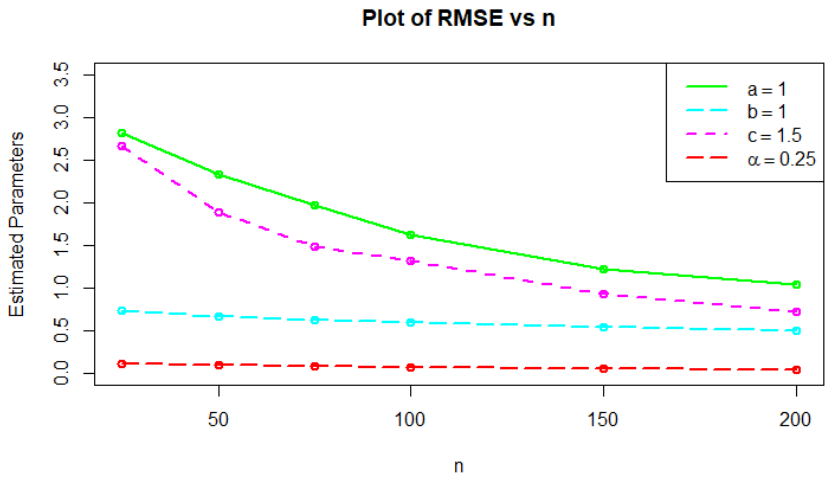

Figure 4.9: The plots of RMSEs for the ExEW parameters parameters in set III

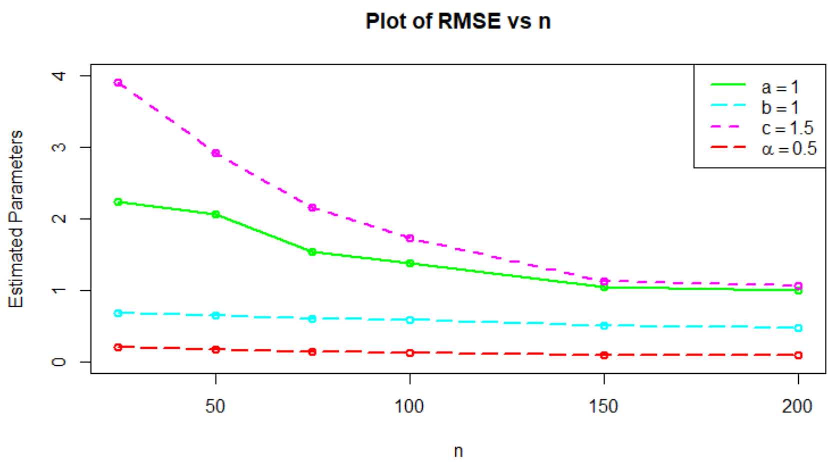

Figure 4.10: The plots of RMSEs for the ExEW parameters in set IV

4.8.3 Simulation study of the ExEW-AFT model

In this Subsection, we demonstrate the inferential capabilities of the proposed model using simulation results. Here, we demonstrate parameter estimation, the inclination to recover baseline HRF shapes using standard error (SE), average bias (AB), mean square error (MSE), and relative bias (RB) to pick models that accurately reflect the underlying HRF shape, and the effect of censoring proportions on the model's inferential features.

4.8.3.1 Simulation designs and data generation

Assuming the AFT regression model framework presented in Equation (4.5.2), we specifically simulated $n = 1000$ and 5000 data sets. Four variables were taken into account in the simulation study when we considered covariates. Two binary covariates, x_1 and x_2, are produced using the Bernoulli (0.5) distribution, while two continuous covariates, x_3 and x_4, were produced using the standard normal distribution. The covariate vector $\boldsymbol{x} = (x_1, x_2, x_3, x_4)'$ corresponds to the values for the AFT regression coefficients, which are selected to be $(-2, 0.75, -0.75, 0.5, -0.5)$. Using the inverse transform technique, the exponentiated Weibull (EW) distribution is used to simulate lifetime data from the AFT model framework (Leemis et al., 1990).
In the regression equation, the effects of the covariates and the intercept are presumptive.

4.8.3.2 Simulation algorithm

The following are the steps for executing the proposed AFT model:

(i) Set the parameters of the model's initial values,

(ii) Utilize the inverse transform technique, create the lifetime data by inverting the CHRF of the proposed model,

(iii) Utilize the various estimates to evaluate the estimations' values,

(iv) Analyze the inferential properties of the estimates, taking into account the SE, AB, MSE, and RB.

(v) The superior model should be chosen based on the AIC.

In this study, we used the EW baseline distribution to generate survival times that can accommodate all of the basic HRF shapes, including decreasing, constant, increasing, unimodal, and bathtub shapes. The EW distribution is likewise closed in the context of AFT regression model (Khan, 2018).

As a last comment, we recall that the CHRF of the EW model is

$$H_0(t;a,b,c) = -\log\left[1 - \left(1 - e^{-(bt)^a}\right)^c\right]. \tag{4.8.1}$$

and thus the inverse of the CHRF is written as follows:

$$H_0^{-1}(t;a,b,c) = \frac{\left(-\log\left[(e^{-t}-1)^{1/c}-1\right]\right)^{\frac{1}{a}}}{b}. \tag{4.8.2}$$

4.8.3.3 Simulated scenarios

Based on the Figure 1.7 we provide the results of four simulation scenarios based on non-monotone HRF (bathtub or unimodal), and monotone HRF (decreasing or increasing) to evaluate the performance of the ExEW-AFT model in comparison with the Weibull AFT (W-AFT), log-logistic AFT (LL-AFT), and EW-AFT models and to investigate the impact of the baseline HRF shape specification on the AFT model's inferential qualities.

Scenario 1: monotone (increasing) HRF :
The lifetime data for this scenario are created using the EW model, and the parameter for ($a = 1.0, b = 1.5$, and $c = 1.5$), and censoring times generated from the exponential distribution with rate parameter (λ):
For $n = 1000, \lambda = 0.33$ and 0.2.
For $n = 5000, \lambda = 0.4$ and 0.22

Scenario 2: monotone (decreasing) HRF:
The EW model was used to create the lifetime data for this scenario, and the parameter values for ($a = 0.80, b = 0.80$, and $c = 1.9$), The censoring times generated from the exponential distribution with rate parameter (λ):
For $n = 1000, \lambda = 0.38$ and 0.25
For $n = 5000, \lambda = 0.47$ and 0.25

Scenario 3: non-monotone (bathtub) HRF:
The EW model was used to create the lifetime data for this scenario, and the

parameter values for ($a = 0.75, b = 1.50$, and $c = 2.0$), and the censoring times generated from the exponential distribution with rate parameter (λ):

For $n = 1000, \lambda = 0.33$ and 0.2

For $n = 5000, \lambda = 0.65$ and 0.22

Scenario 4: non-monotone (unimodal) HRF:

The EW model was used to create the lifetime data for this scenario, and the parameter values for ($a = 1.65, b = 1.50$, and $c = 0.95$), and the censoring times generated from the exponential distribution with rate parameter (λ):

For $n = 1000, \lambda = 0.29$ and 0.18

For $n = 5000, \lambda = 0.47$ and 0.21

Figure 1.7 shows the four scenarios 1–4 (increasing (blue line), decreasing (red line), bathtub (green line), and unimodal (purple line) respectively), depending on the parameter values we chose, there were, on average, 20 and 30 percent censored observations.

4.8.3.4 Analyses of simulated data

To evaluate the inferential properties of the proposed models in all simulated scenarios, the ExEW-AFT model is fitted to the appropriate true generating model from the EW-AFT model. We also fitted the sub-models into each scenario. Furthermore, the estimates of the regression coefficients for each model are evaluated for stability based on the SE, RB, MSE, and the AB.

Instead of examining the properties of the optimization process, our purpose was to examine the qualities of the estimates.

In all circumstances, we used the parameter values from the generating model as our optimization step starting points. The R programming language is used to do the analysis. The optimization stage was completed using the R software "nlminb()".

4.8.3.5 Performance measures

The flexibility of the models for the covariates is evaluated in this study using measures such as the mean (estimated), AB, MSE, RB, and SE. Furthermore, the AIC is employed to compare the studied models.

4.8.3.6 Simulation results

According to the findings of scenario 1 in Tables 4.5–4.8, the AIC indicates that the proposed model performed better than others. AIC values in Tables 4.6 differ only slightly. Moreover, the SE, AB, MSE, and RB indicate that the proposed model performed better than others. Furthermore, it appears that sample size and censoring percentage have an effect on how well models match data. When censoring and sample size are increased, our proposed ExEW-AFT model often outperforms the W-AFT and LL-AFT models. As anticipated, all models equally integrated the increasing HRF. However, our proposed model performs better in the case of heavy censoring.

Theoretically, the findings of scenario 2 in Tables 4.9–4.12 show that all of the competing models can take into account the decreasing HRF shape. The AIC indicates that the proposed model performed better than others. Our proposed ExEW-AFT model outperformed the W-AFT and LL-AFT models, and even the genuine produced model in terms of SE, AB, MSE, and RB. Moreover, when the censoring and sample size increase, our proposed model is once again the best-suited one and makes a wise choice of heavy censoring.

The results of scenario 3 in Tables 4.13–4.16, reveal that the only model that has the lowest value in terms of SE, AB, MSE, and RB is our proposed ExEW-AFT model. Generally, the W-AFT and LL-AFT models generated the least accurate estimates for AB, MSE, and RB according to Scenario 3, as expected (i.e., bathtub hazard).

The findings of scenario 4 in Tables 4.17–4.20 show that the proposed ExEW-AFT model produced estimates that had the lowest bias, MSE, and RB values for all the regression coefficients while producing estimates that are equivalent to the genuine model in terms of the AIC value. Finally, the proposed AFT model outperforms the other competing models in all circumstances, including heavy censoring.

Table 4.5: Simulation study for scenario 1 ($n = 1000$) with about 20% censored observations.

Model	Parameter	(True value)	Mean 20% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-1.118	10.444	0.882	-2.749	-0.441
(AIC = 1342.993)	β_1	0.75	1.144	0.057	0.394	0.746	0.525
	β_2	-0.75	-1.233	0.062	-0.483	0.958	0.644
	β_3	0.50	0.924	0.116	0.424	0.604	0.848
	β_4	-0.50	-0.789	0.116	-0.288	0.371	0.576
	a	1.0	-8.288				
	b	1.50	8.463				
	c	1.50	1.010				
	α	0.033	0.165				
EW	β_o	-2.0	-3.381	85.370	-0.880	4.293	0.440
(AIC = 1342.156)	β_1	0.75	1.179	0.066	0.429	0.828	0.572
	β_2	-0.75	-1.265	0.069	-0.515	1.037	0.687
	β_3	0.50	0.952	0.127	0.452	0.657	0.904
	β_4	-0.50	-0.813	0.122	-0.313	0.411	0.626
	a	1.0	1.027				
	b	1.50	0.827				
	c	1.50	1.784				
W-AFT	β_o	-2.0	-2.288	44.235	-0.288	1.236	0.144
(AIC = 1342.835)	β_1	0.75	1.206	0.060	0.456	0.891	0.608
	β_2	-0.75	-1.268	0.066	-0.518	1.046	0.691
	β_3	0.50	0.974	0.122	0.474	0.698	0.948
	β_4	-0.50	-0.815	0.119	-0.315	0.414	0.630
	a	1.0	1.288				
	b	1.50	0.685				
LL-AFT	β_o	-2.0	-2.288	2.785	-0.288	1.236	0.144
(AIC = 1341.037)	β_1	0.75	1.206	0.066	0.456	0.891	0.608
	β_2	-0.75	-1.268	0.068	-0.518	1.046	0.691
	β_3	0.50	0.974	0.013	0.474	0.698	0.948
	β_4	-0.50	0.012	0.815	-0.315	0.414	0.630
	a	1.0	1.288				
	b	1.50	0.685				

Table 4.6: Simulation study for scenario 1 ($n = 5000$) with about 20% censored observations.

Model	Parameter	(True value)	Mean 20% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-1.356	1.507	0.644	-2.161	-0.322
(6107.316)	β_1	0.75	1.255	0.028	0.505	1.013	0.673
	β_2	-0.75	-1.297	0.029	-0.547	1.120	0.729
	β_3	0.50	0.948	0.054	0.448	0.649	0.896
	β_4	-0.50	-0.830	0.053	-0.330	0.439	0.660
	a	1.0	-6.156				
	b	1.50	6.649				
	c	1.50	1.026				
	α	0.033	0.083				
EW-AFT	β_o	-2.0	-3.288	11.628	-0.811	3.900	0.406
(AIC = 6100.729)	β_1	0.75	1.283	0.031	0.533	1.083	0.711
	β_2	-0.75	-1.321	0.032	-0.571	1.181	0.761
	β_3	0.50	0.973	0.057	0.473	0.697	0.946
	β_4	-0.50	-0.852	0.056	-0.352	0.476	0.704
	a	1.0	1.034				
	b	1.50	0.744				
	c	1.50	2.078				
W-AFT	β_o	-2.0	-1.931	12.884	-1.224	6.394	0.612
(AIC = 6116.419)	β_1	0.75	1.253	0.029	0.503	1.008	0.671
	β_2	-0.75	-1.299	0.030	-0.549	1.126	0.732
	β_3	0.50	0.937	0.055	0.437	0.628	0.874
	β_4	- 0.50	-0.823	0.054	-0.323	0.428	0.646
	a	1.0	1.961				
	b	1.50	1.241				
LL-AFT	β_o	-2.0	-2.310	4.515	0.141	-0.543	-0.070
(AIC = 6104.668)	β_1	0.75	1.292	0.029	0.503	1.009	0.671
	β_2	-0.75	-1.322	0.032	-0.557	1.146	0.743
	β_3	0.50	0.985	0.057	0.479	0.709	0.958
	β_4	-0.50	-0.866	0.057	-0.359	0.487	0.718
	a	1.0	1.310				
	b	1.50	0.688				

Table 4.7: Simulation study for Scenario 1 ($n = 1000$) with about 30% censored observations.

Model	Parameter	(True value)	Mean 30% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-0.694	6.442	1.306	-3.518	-0.653
(AIC = 1925.137)	β_1	0.75	1.053	0.043	0.303	0.546	0.404
	β_2	-0.75	-1.087	0.045	-0.337	0.619	0.449
	β_3	0.50	0.756	0.087	0.256	0.322	0.512
	β_4	-0.50	-0.821	0.089	-0.321	0.424	0.642
	a	1.0	-8.194				
	b	1.50	8.315				
	c	1.50	1.013				
	α	0.033	0.195				
EW-AFT	β_o	-2.0	-2.329	13.650	-0.296	1.271	0.148
(AIC = 1927.636)	β_1	0.75	1.067	0.047	0.317	0.576	0.423
	β_2	-0.75	-1.099	0.048	-0.349	0.645	0.465
	β_3	0.50	0.746	0.090	0.246	0.306	0.492
	β_4	-0.50	-0.837	0.092	-0.337	0.451	0.644
	a	0.50	1.572				
	b	1.50	0.920				
	c	1.50	1.821				
W-AFT	β_o	-2.0	-1.121	11.686	0.879	-2.743	-0.440
(AIC = 1929.452)	β_1	0.75	1.043	0.044	0.293	0.526	0.391
	β_2	-0.75	-1.087	0.045	-0.337	0.619	0.449
	β_3	0.50	0.730	0.088	0.230	0.283	0.460
	β_4	- 0.50	-0.822	0.089	-0.322	0.426	0.644
	a	1.0	7.959				
	b	1.50	1.385				
LL-AFT	β_o	-2.0	-1.963	8.908	0.037	-0.148	-0.018
(AIC = 1928.382)	β_1	0.75	1.083	0.047	0.333	0.610	0.444
	β_2	-0.75	-1.104	0.048	-0.354	0.656	0.472
	β_3	0.50	0.745	0.071	0.245	0.304	0.490
	β_4	-0.50	-0.841	0.070	-0.341	0.458	0.682
	a	1.0	0.963				
	b	1.50	0.601				

Table 4.8: Simulation study for scenario 1 ($n = 5000$) with about 30% censored observations.

Model	Parameter	(True value)	Mean 30% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-1.839	2.163	0.161	-0.618	-0.080
(AIC = 9321.257)	β_1	0.75	1.130	0.020	.380	0.714	0.507
	β_2	-0.75	-1.149	0.021	-0.399	0.758	0.532
	β_3	0.50	0.828	0.039	0.328	0.436	0.656
	β_4	-0.50	-0.766	0.039	-0.266	0.337	0.532
	a	1.0	-4.313				
	b	1.50	5.871				
	c	1.50	1.105				
	α	0.033	0.093				
EW-AFT	β_o	-2.0	-2.495	6.116	-0.495	2.227	0.248
(AIC = 9317.443)	β_1	0.75	1.142	0.022	0.392	0.742	0.523
	β_2	-0.75	-1.157	0.022	-0.407	0.776	0.543
	β_3	0.50	0.828	0.040	0.328	0.435	0.656
	β_4	-0.50	-0.771	0.039	-0.271	0.344	0.542
	a	1.0	1.277				
	b	1.50	0.862				
	c	1.50	2.032				
W-AFT	β_o	-2.0	-1.194	102.989	0.806	-2.575	-0.403
(AIC = 93341.946)	β_1	0.75	1.119	0.012	0.369	0.690	0.492
	β_2	-0.75	-1.143	0.020	-0.393	0.745	0.524
	β_3	0.50	0.804	0.039	0.304	0.396	0.608
	β_4	- 0.50	-0.749	0.038	-0.249	0.311	0.498
	a	1.0	7.893				
	b	1.50	1.377				
LL-AFT	β_o	-2.0	-2.698	2.097	-0.698	3.281	0.349
(AIC = 9333.703)	β_1	0.75	1.144	0.022	0.394	0.746	0.525
	β_2	-0.75	-1.170	0.021	-0.420	0.807	0.560
	β_3	0.50	0.850	0.039	0.350	0.473	0.700
	β_4	-0.50	-0.750	0.039	-0.250	0.312	0.500
	a	1.0	0.297				
	b	1.50	0.574				

Table 4.9: Simulation study for scenario 2 ($n = 1000$) with about 20% censored observations.

Model	Parameter	(True value)	Mean 20% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-2.190	0.287	-0.190	0.798	0.095
(AIC = 1155.018)	β_1	0.75	1.431	0.312	0.681	1.486	0.908
	β_2	-0.75	-1.447	0.311	-0.697	1.531	0.929
	β_3	0.50	1.104	0.219	0.605	0.970	1.210
	β_4	-0.50	-1.103	0.182	-0.603	0.968	1.206
	a	0.80	-0.977				
	b	0.80	1.427				
	c	1.90	0.701				
	α	0.09	0.114				
EW-AFT	β_o	-2.0	-2.529	0.275	-0.529	2.394	0.264
(AIC = 1212.930)	β_1	0.75	1.433	0.285	0.683	1.491	0.911
	β_2	-0.75	-1.445	0.286	-0.695	1.526	0.927
	β_3	0.50	1.126	0.207	0.626	1.018	1.252
	β_4	-0.50	-1.114	0.180	-0.614	0.990	1.228
	a	0.80	0.816				
	b	0.80	0.263				
	c	1.90	3.846				
W-AFT	β_o	-2.0	-2.864	0.288	-0.864	4.202	0.432
(AIC = 1162.468)	β_1	0.75	1.450	0.323	0.700	1.540	0.933
	β_2	-0.75	-1.454	0.319	-0.704	1.552	0.939
	β_3	0.50	1.135	0.222	0.635	1.039	1.270
	β_4	- 0.50	-1.110	0.181	-0.610	0.982	1.220
	a	0.80	1.664				
	b	0.80	1.368				
LL-AFT	β_o	-2.0	-2.864	0.278	-0.864	4.201	0.432
(AIC = 1173.484)	β_1	0.75	1.450	0.288	0.700	1.539	0.933
	β_2	-0.75	-1.454	0.290	-0.704	1.551	0.939
	β_3	0.50	1.135	0.210	0.635	1.038	1.270
	β_4	-0.50	-1.110	0.180	-0.610	0.982	1.220
	a	0.80	1.663				
	b	0.80	1.368				

Table 4.10: Simulation study for scenario 2 ($n = 5000$) with about 20% censored observations.

Model	Parameter	(True value)	Mean 20% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-2.190	0.287	-0.190	0.798	0.095
(AIC = 7012.171)	β_1	0.75	1.431	0.312	0.681	1.486	0.908
	β_2	-0.75	-1.447	0.311	-0.697	1.531	0.929
	β_3	0.50	1.105	0.219	0.605	0.970	1.210
	β_4	-0.50	-1.103	0.182	-0.603	0.968	1.206
	a	0.80	-0.087				
	b	0.80	0.719				
	c	1.90	0.743				
	α	0.09	0.074				
EW-AFT	β_o	-2.0	-2.529	4.844	-0.529	2.394	0.264
(AIC = 7366.012)	β_1	0.75	1.433	0.123	0.683	1.491	0.911
	β_2	-0.75	-1.445	0.125	-0.695	1.526	0.927
	β_3	0.50	1.126	0.235	0.626	1.018	1.252
	β_4	-0.50-	-1.114	0.235	-0.614	0.990	1.228
	a	0.80	0.816				
	b	0.80	0.263				
	c	1.90	3.846				
W-AFT	β_o	-2.0	-5.213	49.582	-3.213	23.173	1.606
(AIC = 7127.747)	β_1	0.75	1.417	0.114	0.667	1.446	0.889
	β_2	-0.75	-1.449	0.117	-0.699	1.537	0.932
	β_3	0.50	1.077	0.227	0.577	0.911	1.154
	β_4	- 0.50	-1.101	0.228	-0.601	0.963	1.202
	a	0.80	0.823				
	b	0.80	0.640				
LL-AFT	β_o	-2.0	-2.864	0.124	-0.864	4.201	0.432
(AIC = 7189.352)	β_1	0.75	1.450	0.129	0.700	1.539	0.933
	β_2	-0.75	-1.454	0.130	-0.704	1.551	0.939
	β_3	0.50	1.135	0.094	0.635	1.038	1.270
	β_4	-0.50	-1.110	0.081	-0.610	0.982	1.220
	a	0.80	1.664				
	b	0.80	1.368				

Table 4.11: Simulation study for scenario 2 ($n = 1000$) with about 30% censored observations.

Model	Parameter	(True value)	Mean 30% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-2.029	0.522	-0.029	0.118	0.015
(AIC = 1193.398)	β_1	0.75	1.212	0.076	0.462	0.907	0.616
	β_2	-0.75	-1.187	0.076	-0.437	0.848	0.583
	β_3	0.50	0.822	0.156	0.322	0.426	0.644
	β_4	-0.50	-0.930	0.158	-0.430	0.614	0.860
	a	0.80	0.869				
	b	0.80	-0.556				
	c	1.90	1.082				
	α	0.09	0.583				
EW-AFT	β_o	-2.0	-0.422	17.156	1.577	-3.821	-0.788
(AIC = 1282.736)	β_1	0.75	1.254	0.098	0.504	1.011	0.672
	β_2	-0.75	-1.375	0.101	-0.625	1.328	0.833
	β_3	0.50	1.056	0.189	0.556	0.866	1.112
	β_4	-0.50	-1.185	0.192	-0.685	1.154	1.370
	a	0.80	1.301				
	b	0.80	0.244				
	c	1.90	5.801				
W-AFT	β_o	-2.0	-4.290	75.287	-2.290	14.406	1.145
(AIC =1215.912)	β_1	0.75	1.247	0.089	0.497	0.992	0.663
	β_2	-0.75	-1.389	0.094	-0.639	1.366	0.852
	β_3	0.50	1.038	0.183	0.538	0.828	1.076
	β_4	-0.50	-1.176	0.186	-0.676	1.132	1.352
	a	0.80	1.099				
	b	0.80	0.699				
LL-AFT	β_o	-2.0	-2.524	59.316	-0.524	2.371	0.262
(AIC = 1239.634)	β_1	0.75	1.278	0.095	0.528	1.071	0.704
	β_2	-0.75	-1.386	0.053	-0.636	1.359	0.848
	β_3	0.50	1.056	0.019	0.556	0.866	1.112
	β_4	-0.50	-1.184	0.019	-0.684	1.152	1.368
	a	0.80	1.324				
	b	0.80	1.210				

Table 4.12: Simulation study for scenario 2 ($n = 5000$) with about 30% censored observations.

Model	Parameter	(True value)	Mean 30% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-3.402	0.169	-1.402	7.573	0.701
(AIC = 7142.843)	β_1	0.75	1.106	0.011	0.356	0.661	0.475
	β_2	-0.75	-1.159	0.021	-0.409	0.781	0.545
	β_3	0.50	0.888	0.040	0.388	0.539	0.776
	β_4	-0.50	-0.768	0.039	-0.268	0.340	0.536
	a	0.80	-0.391				
	b	0.80	1.464				
	c	1.90	1.234				
	α	0.09	1.067				
EW-AFT	β_o	-2.0	-1.541	7.520	0.459	-1.624	-0.2304
(AIC = 7581.023.736)	β_1	0.75	1.142	0.022	0.392	0.742	0.523
	β_2	-0.75	-1.157	0.022	-0.407	0.776	0.543
	β_3	0.50	0.828	0.040	0.328	0.435	0.656
	β_4	-0.50	-0.771	0.040	-0.271	0.344	0.542
	a	0.80	3.314				
	b	0.80	0.862				
	c	1.90	2.032				
W-AFT	β_o	-2.0	-1.795	117.420	0.205	-0.776	-0.102
(AIC =7320.311)	β_1	0.75	1.119	0.020	0.369	0.690	0.492
	β_2	-0.75	-1.143	0.020	-0.393	0.745	0.524
	β_3	0.50	0.804	0.038	0.304	0.396	0.608
	β_4	-0.50	-0.749	0.038	-0.249	0.311	0.498
	a	0.80	4.324				
	b	0.80	1.377				
LL-AFT	β_o	-2.0	2.086	21.810	-0.086	0.353	0.043
(AIC = 7422.633)	β_1	0.75	1.153	0.022	0.403	0.767	0.537
	β_2	-0.75	-1.158	0.021	-0.408	0.777	0.544
	β_3	0.50	0.836	0.040	0.336	0.449	0.672
	β_4	-0.50	-0.783	0.000	-0.283	0.363	0.566
	a	0.80	0.886				
	b	0.80	0.594				

Table 4.13: Simulation study for scenario 3 ($n = 1000$) with about 20% censored observations.

Model	Parameter	(True value)	Mean 20% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-2.204	0.762	-0.204	0.857	0.102
(AIC = 1295.954)	β_1	0.75	1.114	0.046	0.364	0.678	0.485
	β_2	-0.75	-1.170	0.045	-0.420	0.807	0.560
	β_3	0.50	0.786	0.094	0.286	0.368	0.572
	β_4	-0.50	-0.707	0.093	-0.207	0.249	0.414
	a	0.50	-0.925				
	b	1.50	1.351				
	c	2.0	1.171				
	α	1.0	0.449				
EW-AFT	β_o	-2.0	-1.580	8.413	0.420	-1.503	-0.210
(AIC = 1298.139)	β_1	0.75	1.116	0.051	0.366	0.683	0.488
	β_2	-0.75	-1.150	0.052	-0.400	0.760	0.533
	β_3	0.50	0.821	0.095	0.321	0.423	0.642
	β_4	-0.50	-0.770	0.093	-0.270	0.343	0.540
	a	0.50	2.788				
	b	1.50	0.849				
	c	2.00	2.572				
W-AFT	β_o	-2.0	-1.769	38.554	0.231	-0.871	-0.116
(AIC = 1303.820)	β_1	0.75	1.071	0.046	0.321	0.584	0.428
	β_2	-0.75	-1.134	0.049	-0.384	0.723	0.512
	β_3	0.50	0.777	0.092	0.277	0.353	0.554
	β_4	- 0.50	-0.750	0.091	-0.250	0.313	0.500
	a	0.50	4.3492				
	b	1.50	1.588				
LL-AFT	β_o	-2.0	-2.263	69.060	-0.263	1.123	0.132
(AIC = 1294.980)	β_1	0.75	1.133	0.000	0.383	0.722	0.511
	β_2	-0.75	-1.151	0.048	-0.401	0.763	0.535
	β_3	0.50	0.830	0.093	0.330	0.440	0.660
	β_4	-0.50	-0.777	0.092	-0.277	0.354	0.554
	a	0.50	0.763				
	b	1.50	0.524				

Table 4.14: Simulation study for scenario 3 ($n = 5000$) with about 20% censored observations.

Model	Parameter	(True value)	Mean 20% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-2.510	0.172	-0.510	2.300	0.255
(AIC = 5190.614)	β_1	0.75	1.137	0.023	0.387	0.731	0.516
	β_2	-0.75	-1.231	0.025	-0.481	0.953	0.641
	β_3	0.50	0.863	0.044	0.363	0.495	0.726
	β_4	-0.50	-0.733	0.043	-0.233	0.288	0.466
	a	0.50	-0.485				
	b	1.50	2.241				
	c	2.00	1.414				
	α	1.00	0.249				
EW-AFT	β_o	-2.0	-1.550	9.767	0.450	-1.597	-0.225
(AIC = 1185.402)	β_1	0.75	1.205	0.026	0.455	0.888	0.607
	β_2	-0.75	-1.229	0.026	-0.479	0.949	0.639
	β_3	0.50	0.906	0.046	0.406	0.571	0.812
	β_4	-0.50	-0.793	0.045	-0.293	0.378	0.586
	a	0.50	2.105				
	b	1.50	0.788				
	c	2.00	2.763				
W-AFT	β_o	-2.0	-0.755	9.161	1.245	-3.429	-0.623
(AIC = 5191.767)	β_1	0.75	1.172	0.023	0.422	0.810	0.563
	β_2	-0.75	-1.207	0.024	-0.457	0.894	0.609
	β_3	0.50	0.868	0.044	0.368	0.503	0.736
	β_4	- 0.50	-0.765	0.043	-0.265	0.336	0.530
	a	0.50	9.709				
	b	1.50	1.541				
LL-AFT	β_o	-2.0	-2.145	29.658	-0.145	0.601	0.072
(AIC = 5192.280)	β_1	0.75	1.210	0.026	0.460	0.901	0.613
	β_2	-0.75	-1.229	0.029	-0.479	0.947	0.639
	β_3	0.50	0.909	0.047	0.409	0.577	0.818
	β_4	-0.50	-0.800	0.045	-0.300	0.390	0.600
	a	0.50	0.645				
	b	1.50	0.542				

Table 4.15: Simulation study for scenario 3 ($n = 1000$) with about 30% censored observations.

Model	Parameter	(True value)	Mean 30% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-2.273	0.381	-0.273	1.165	0.136
(AIC = 1467.579)	β_1	0.75	0.906	0.019	0.156	0.258	0.208
	β_2	-0.75	-0.970	0.023	-0.220	0.378	0.293
	β_3	0.50	0.645	0.035	0.145	0.167	0.290
	β_4	-0.50	-0.621	0.038	-0.121	0.135	0.242
	a	0.50	-0.165				
	b	1.50	0.953				
	c	2.00	2.311				
	α	1.00	0.851				
EW-AFT	β_o	-2.0	-2.074	4.228	-0.074	0.303	0.037
(AIC = 1478.715)	β_1	0.75	0.902	0.020	0.152	0.252	0.203
	β_2	-0.75	-0.917	0.0207	-0.167	0.279	0.223
	β_3	0.50	0.607	0.038	0.107	0.119	0.214
	β_4	-0.50	-0.636	0.038	-0.136	0.154	0.272
	a	0.50	0.993				
	b	1.50	1.886				
	c	2.00	2.253				
W-AFT	β_o	-2.0	-1.182	7.313	0.818	-2.603	-0.409
(AIC = 1486.010)	β_1	0.75	0.884	0.018	0.134	0.220	0.179
	β_2	-0.75	-0.906	0.019	-0.156	0.258	0.208
	β_3	0.50	0.590	0.037	0.090	0.099	0.180
	β_4	- 0.50	-0.629	0.037	-0.129	0.146	0.258
	a	0.50	3.165				
	b	1.50	3.148				
LL-AFT	β_o	-2.0	-1.857	14.83	0.1437	-0.551	-0.072
(AIC = 1480.315)	β_1	0.75	0.911	0.020	0.161	0.268	0.215
	β_2	-0.75	-0.923	0.021	-0.173	0.289	0.231
	β_3	0.50	0.611	0.038	0.111	0.124	0.222
	β_4	-0.50	-0.634	0.039	-0.134	0.152	0.268
	a	0.50	0.357				
	b	1.50	0.252				

Table 4.16: Simulation study for scenario 3 ($n = 5000$) with about 30% censored observations.

Model	Parameter	(True value)	Mean 30% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-2.233	0.628	-0.233	0.987	0.116
(AIC = 7839.672)	β_1	0.75	0.999	0.013	0.249	0.436	0.332
	β_2	-0.75	-0.987	0.012	-0.237	0.412	0.316
	β_3	0.50	0.729	0.024	0.228	0.280	0.456
	β_4	-0.50	-0.548	0.023	-0.048	0.051	0.096
	a	0.50	-0.051				
	b	1.50	0.919				
	c	2.00	2.192				
	α	1.00	0.302				
EW-AFT	β_o	-2.0	-1.285	7.195	0.715	-2.350	-0.358
(AIC = 7846.99)	β_1	0.75	0.994	0.013	0.244	0.426	0.325
	β_2	-0.75	-1.006	0.013	-0.256	0.450	0.341
	β_3	0.50	0.690	0.024	0.190	0.226	0.380
	β_4	-0.50	-0.664	0.024	-0.164	0.191	0.328
	a	0.50	3.459				
	b	1.50	1.625				
	c	2.00	1.703				
W-AFT	β_o	-2.0	-1.191	26.590	0.809	-2.581	-0.404
(AIC = 7842.666)	β_1	0.75	0.980	0.012	0.230	0.397	0.307
	β_2	-0.75	-0.997	0.012	-0.247	0.431	0.329
	β_3	0.50	0.676	0.023	0.176	0.207	0.352
	β_4	- 0.50	-0.652	0.023	-0.152	0.175	0.304
	a	0.50	4.701				
	b	1.50	2.325				
LL-AFT	β_o	-2.0	-2.038	13.067	-0.038	0.153	0.019
(AIC = 7855.242)	β_1	0.75	1.007	13.202	0.257	0.452	0.343
	β_2	-0.75	-1.012	0.000	-0.262	0.461	0.349
	β_3	0.50	0.704	0.024	0.204	0.246	0.408
	β_4	-0.50	-0.678	0.024	-0.177	0.208	0.354
	a	0.50	0.539				
	b	1.50	0.350				

Table 4.17: Simulation study for scenario 4 ($n = 1000$) with about 20% censored observations.

Model	Parameter	(True value)	Mean 20% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-1.704	2.801	0.296	-1.097	-0.148
(AIC = 1751.955)	β_1	0.75	1.310	0.093	0.560	1.154	0.747
	β_2	-0.75	-1.410	0.092	-0.660	1.425	0.880
	β_3	0.50	1.115	0.179	0.615	0.993	1.230
	β_4	-0.50	-1.019	0.176	-0.519	0.789	1.038
	a	1.650	3.176				
	b	1.500	-2.714				
	c	0.95	1.021				
	α	0.90	0.178				
EW-AFT	β_o	-2.0	-3.877	33.412	-1.877	11.033	0.939
(AIC = 1808.559)	β_1	0.75	1.303	0.093	0.553	1.136	0.737
	β_2	-0.75	-1.413	0.096	-0.663	1.433	0.884
	β_3	0.50	1.114	0.181	0.614	0.992	1.228
	β_4	-0.50	-1.013	0.178	-0.513	0.776	1.026
	a	1.65	1.851				
	b	1.50	0.730				
	c	0.95	1.205				
W-AFT	β_o	-2.0	-5.793	14.192	-3.793	29.562	1.897
(AIC = 1756.782)	β_1	0.75	1.289	0.087	0.539	1.100	0.719
	β_2	-0.75	-1.405	0.094	-0.655	1.412	0.873
	β_3	0.50	1.101	0.178	0.601	0.962	1.202
	β_4	- 0.50	-1.004	0.176	-0.504	0.758	1.008
	a	1.65	0.318				
	b	1.50	0.844				
LL-AFT	β_o	-2.0	-2.328	38.052	-0.328	1.419	0.164
(AIC = 1768.577)	β_1	0.75	1.343	0.096	0.593	1.242	0.791
	β_2	-0.75	-1.419	0.098	-0.669	1.452	0.892
	β_3	0.50	1.144	0.000	0.644	1.059	1.288
	β_4	-0.50	-1.022	0.018	-0.522	0.794	1.044
	a	1.65	1.978				
	b	1.50	1.046				

Table 4.18: Simulation study for scenario 4 ($n = 5000$) with about 20% censored.

Model	Parameter	(True value)	Mean 20% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-3.163	3.356	-1.163	6.002	0.582
(AIC = 1751.955)	β_1	0.75	1.576	0.054	0.826	1.920	1.101
	β_2	-0.75	-1.633	0.055	-0.883	2.103	1.177
	β_3	0.50	1.208	0.102	0.708	1.210	1.416
	β_4	-0.50	-1.095	0.101	-0.595	0.950	1.190
	a	1.650	-0.715				
	b	1.500	3.136				
	c	0.95	0.744				
	α	0.90	0.107				
EW-AFT	β_o	-2.0	-0.047	6.920	1.953	-3.998	-0.977
(AIC = 1808.559)	β_1	0.75	1.591	0.057	0.841	1.968	1.121
	β_2	-0.75	-1.644	0.058	-0.894	2.142	1.192
	β_3	0.50	1.270	0.105	0.770	1.363	1.540
	β_4	-0.50	-1.139	0.105	-0.639	1.047	1.278
	a	1.65	7.015				
	b	1.50	0.245				
	c	0.95	4.711				
W-AFT	β_o	-2.0	-3.650	16.810	-1.650	9.324	0.825
(AIC = 1756.782)	β_1	0.75	1.572	0.053	0.822	1.909	1.096
	β_2	-0.75	-1.639	0.055	-0.889	2.124	1.185
	β_3	0.50	1.191	0.102	0.691	1.169	1.382
	β_4	- 0.50	-1.084	0.101	-0.584	0.925	1.168
	a	1.65	5.055				
	b	1.50	0.655				
LL-AFT	β_o	-2.0	-2.540	96.820	-0.540	2.451	0.270
(AIC = 1768.577)	β_1	0.75	1.600	0.056	0.850	1.998	1.133
	β_2	-0.75	-1.646	0.057	-0.896	2.147	1.195
	β_3	0.50	1.257	0.104	0.757	1.329	1.514
	β_4	-0.50	-1.133	0.103	-0.633	1.034	1.266
	a	1.65	2.190				
	b	1.50	1.316				

Table 4.19: Simulation study for scenario 4 ($n = 1000$) with about 30% censored observations.

Model	Parameter	(True value)	Mean 30% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-2.197	3.087	-0.197	0.828	0.098
(AIC = 1829.568)	β_1	0.75	1.144	0.066	0.394	0.747	0.525
	β_2	-0.75	-1.235	0.069	-0.485	0.963	0.647
	β_3	0.50	0.887	0.132	0.387	0.538	0.774
	β_4	-0.50	-0.931	0.133	-0.431	0.618	0.862
	a	1.650	-5.965				
	b	1.500	6.806				
	c	0.95	0.989				
	α	0.9	0.260				
EW-AFT	β_o	-2.0	-3.049	25.049	-1.049	5.294	0.524
(AIC = 1902.871)	β_1	0.75	1.151	0.067	0.401	0.763	0.535
	β_2	-0.75	-1.237	0.069	-0.487	0.967	0.649
	β_3	0.50	0.894	0.133	0.394	0.549	0.788
	β_4	-0.50	-0.940	0.134	-0.440	0.634	0.880
	a	1.65	1.648				
	b	1.50	0.724				
	c	0.95	1.397				
W-AFT	β_o	-2.0	-1.975	33.399	0.025	-0.101	-0.013
(AIC = 1844.159)	β_1	0.75	1.137	0.064	0.387	0.731	0.516
	β_2	-0.75	-1.229	0.067	-0.479	0.947	0.639
	β_3	0.50	0.880	0.129	0.380	0.524	0.760
	β_4	- 0.50	-0.924	0.130	-0.424	0.603	0.848
	a	1.65	6.545				
	b	1.50	0.922				
LL-AFT	β_o	-2.0	-1.909	18.106	0.091	-0.356	-0.046
(AIC = 1865.730)	β_1	0.75	1.169	0.071	0.419	0.803	0.559
	β_2	-0.75	-1.234	0.072	-0.484	0.959	0.645
	β_3	0.50	0.900	0.097	0.400	0.561	0.800
	β_4	-0.50	-0.961	0.097	-0.461	0.674	0.922
	a	1.65	1.559				
	b	1.50	0.928				

Table 4.20: Simulation study for scenario 4 ($n = 5000$) with about 30% censored observations.

Model	Parameter	(True value)	Mean 30% Censoring	SE	AB	MSE	RB
ExEW-AFT	β_o	-2.0	-3.159	0.409	-1.159	5.982	0.580
(AIC = 10501.254)	β_1	0.75	1.279	0.029	0.529	1.073	0.705
	β_2	-0.75	-1.279	0.030	-0.529	1.074	0.705
	β_3	0.50	0.925	0.056	0.425	0.605	0.850
	β_4	-0.50	-0.873	0.056	-0.373	0.513	0.746
	a	1.650	2.843				
	b	1.500	1.372				
	c	0.95	0.835				
	α	0.9	0.114				
EW-AFT	β_o	-2.0	-3.107	10.417	-1.107	5.654	0.553
(AIC = 10857.357)	β_1	0.75	1.297	0.032	0.547	1.119	0.729
	β_2	-0.75	-1.313	0.032	-0.563	1.161	0.751
	β_3	0.50	0.950	0.060	0.450	0.652	0.900
	β_4	-0.50	-0.870	0.059	-0.370	0.506	0.740
	a	1.65	1.716				
	b	1.50	0.715				
	c	0.95	1.432				
W-AFT	β_o	-2.0	-2.209	0.059	-0.209	0.878	0.104
(AIC = 10600.042)	β_1	0.75	1.280	0.030	0.530	1.076	0.707
	β_2	-0.75	-1.303	0.031	-0.553	1.134	0.737
	β_3	0.50	0.931	0.058	0.431	0.618	0.862
	β_4	- 0.50	-0.855	0.057	-0.355	0.481	0.710
	a	1.65	5.863				
	b	1.50	0.924				
LL-AFT	β_o	-2.0	-1.970	26.224	0.030	-0.119	-0.015
(AIC = 10692.546)	β_1	0.75	1.313	0.000	0.563	1.162	0.751
	β_2	-0.75	-1.316	0.033	-0.566	1.170	0.755
	β_3	0.50	0.971	0.061	0.471	0.693	0.942
	β_4	-0.50	-0.888	0.061	-0.388	0.539	0.776
	a	1.65	1.620				
	b	1.50	0.915				

4.9 Applications to real-life data for the ExEW distribution

4.9.1 Introduction

This Section introduces the applications of developed models to different real-world data-sets.

4.9.2 Applications to real-life data for the ExEW distribution

To illustrate the applicability of the ExEW distribution, we analyze and compare the fitting of the ExEW distribution with other competing models by using two real-life data sets. The ExEW distribution is compared to sub-models such as: the Weibull, EE, and ExW distributions, and other common lifetime distributions LL, BW, BEW, MBW, and TanLL distributions.

To specify which statistical distribution best fits the two data, a variety of analytical measures are applied, such as the Bayesian information criterion (BIC), the Akaike information criterion (AIC), consistent AIC (CAIC) and Hannan–Quinn information criterion (HQIC). Moreover, goodness-of-fit measures like the log-likelihood is also adopted.

4.9.2.1 Likelihood ratio tests

The ExEW distribution has some sub-models including the Weibul , EE, ExW distributions. As a result, the LRT is used to evaluate the following hypotheses:

1. $H_0 : a = 0$, and $\alpha = 1$, this means that the sample comes from the Weibull distribution.

   $H_1 : a \neq 0$, and $\alpha \neq 1$, this means that the sample comes from the ExEW distribution.

2. $H_0 : b = 0$, this indicates that the sample size is comes from the EE distribution.

   $H_1 : b \neq 0$, this indicates that the sample size comes from the ExEW distribution.

3. $H_0 : \alpha = 1$ this means that the sample comes from the ExW distribution.

   $H_1 : \alpha \neq 0$, this means that the sample comes from the ExEW distribution.

4.9.2.2 Application to airplane windshield data

The airplane windshield data consists of 84 observations. This data set on failure time for a particular model windshield, this data is studied lately by Ramos et al. Ramos et al. (2013). The data set is reported in Table 4.21, and its descriptive statistical analysis are shown in Table 4.22 which indicates that the skewness coefficient has a positive value, the data is right skewed. Due to the kurtosis has negative value, the data is platykurtic.

Figure 4.11 illustrates the TTT transform plot with a concavity pattern, indicating that the data has an increasing hazard rate shape. This confirms that the hrf in Figure 4.2 is appropriate for analyzing this data.

Table 4.21: The airplane windshield failure times data (in thousand hours)

0.040, 1.866, 2.385, 3.443, 0.301, 1.876, 2.481, 3.467, 0.309, 1.899, 2.610,
3.478, 0.557, 1.911, 2.625, 3.578, 0.943, 1.912, 2.632, 3.595, 1.070, 1.914,
2.646, 3.699, 1.124, 1.981, 2.661, 3.779, 1.248, 2.010, 2.688, 3.924, 1.281,
2.038, 2.823, 4.035, 1.281, 2.085, 2.890, 4.121, 1.303, 2.089, 2.902, 4.167,
1.432, 2.097, 2.934, 4.240, 1.480, 2.135, 2.962, 4.255, 1.505, 2.154, 2.964,
4.278, 1.506, 2.190, 3.000, 4.305, 1.568, 2.194, 3.103, 4.376, 1.615, 2.223,
3.114, 4.449, 1.619, 2.224, 3.117, 4.485, 1.652, 2.229, 3.166, 4.570, 1.652,
2.300, 3.344, 4.602, 1.757, 2.324, 3.376, 4.663

Table 4.22: Descriptive analysis of airplane windshield data

μ	Mid	Mode	Var	CS	CK	Min	Max
2.55745	2.3545	2.25	1.25177	0.09949	-0.65232	0.04	4.663

The MLEs of the parameters of the fitted models, as well as the corresponding standard errors are shown in Table 4.24. At the 5% significance level, all of the ExEW parameters are significant. The ExEW model fits the airplane windshield data better than its sub-models and other rival distributions. Table 4.25 shows that the ExEW has the highest log-likelihood and the lowest CAIC, HQIC, BIC, and AIC values as compared to the other models. Although the ExEW model provides the greatest fit to the data, the W distribution is a suitable option since its fit values are more similar to the ExEW model.

Figure 4.12 illustrates the fitted density shapes for competitive models, demonstrating that the ExEW distribution fits aircraft windshield better.

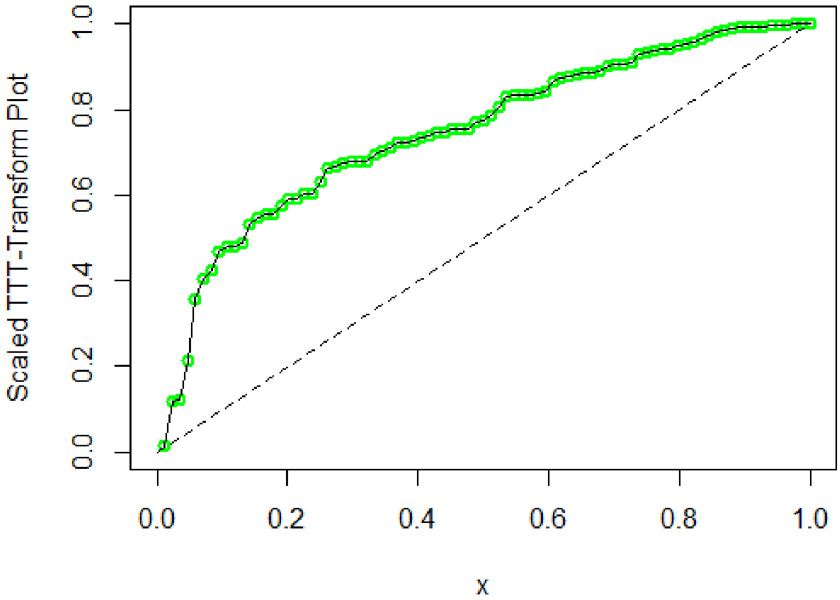

Figure 4.11: The TTT Plot of the airplane windshield data.

Table 4.23: The LRT statistic for the windshield data.

Dis	Hypothesis	LRT	p-value
Weibull	$H_0 : a = 0$, and $\alpha = 1$ vs $H_1 : H_0$ is false	260	< 0.001
EE	$H_0 : b = 0$ vs $H_1 : H_0$ is false	253	< 0.001
ExW	$H_0 : \alpha = 1$ vs $H_1 : H_0$ is false	280	< 0.001

Table 4.24: The MLEs of the competing models with standard errors for windshield data

model	$\hat{a}$	$\hat{b}$	$\hat{c}$	$\hat{\alpha}$	d
ExEW	0.712	0.504	2.931	0.0715	-
	(6.338)	(5.510)	(0.354)	(0.637)	-
Weibull	2.375	2.863	-	-	-
	(0.210)	(0.138)	-	-	-
EE	3.560	0.758	-	-	-
	(0.611)	(0.077)	-	-	-
EW	-0.017	0.159	1.701	-	-
	(0.023)	(0.041)	(0.183)	-	-
LL	2.391	.224	-	-	-
	(0.137)	(0.297)	-	-	-
BW	0.271	0.783	5.911	3.770	-
	(0.258)	(0.784)	(4.604)	(1.117)	-
	(0.754)	(401)	(1.013)	(0.419)	-
BEW	0.262	5.182	5.208	6.212	7.063
	(0.032)	(1.203)	(0.053)	(0.054)	(0.053)
MBW	0.348	11.855	0.129	4.630	4.663
	(0.414)	(23.226)	(0.266)	(4.660)	(0.888)
TanLL	2.139	3.340	-	-	-
	(0.126)	(0.304)	-	-	-

Table 4.25: The analytical performance measures for comparing distributions for windshield data

Model	AIC	BIC	CAIC	HQIC	(ℓ)
ExEW	261.310	271.033	261.816	265.218	-126.655
Weibull	264.107	268.968	264.255	266.061	-130.0533
EE	283.681	288.543	283.829	285.635	-139.841
EW	280.794	288.087	281.094	283.726	-137.397
LL	283.163	288.024	283.311	285.117	-139.581
BW	263.167	272.890	263.673	267.075	-127.583
BEW	265.641	277.795	266.410	270.526	-127.820
MBW	264.563	276.717	265.332	269.449	-127.281
TanLL	283.89	288.752	284.038	285.844	-139.945

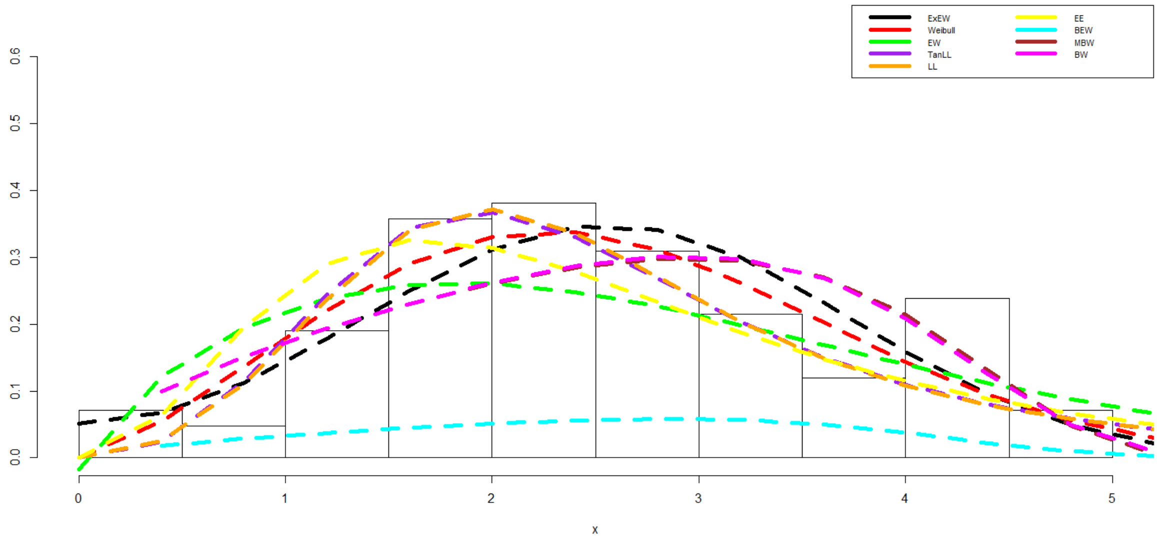

Figure 4.12: The fitted density shapes of the ExEW distribution and other distributions for windshield data.

4.9.2.3 Application to COVID-19 fatality rate data

The second set of data about COVID-19 fatality rate from Mexico contains 108-day, and it collected between March 4 and July 20, 2020. It is available at `https://covid19.who.int`. The data is recently studied by Almongy et al. (2021). Table 4.26 lists the data observations and Table 4.27 shows the descriptive statistical analysis of the data. Because the skewness coefficient has a positive value, the data is right-skewed. The data is platykurtic since the kurtosis is smaller than three. Figure 4.13 displays the TTT plot with a concavity shape, indicating that the data has an increasing failure rate. This demonstrates that the ExEW distribution is appropriate for analyzing this type of data.

Table 4.29 shows the MLEs of the parameters of the fitted models, together with the standard errors in brackets. At the 5% significance level, all of the ExEW parameters are significant. Table 4.30 provides the analytical measures of competing distributions and shows that the ExEW provides the best fit to the data. The fitted densities for competing models is depicted in Figure 4.14, demonstrating that the ExEW distribution fits the COVID-19 mortality rate data better.

Table 4.26: COVID-19 fatality rate data set

8.826, 6.105, 10.383, 7.267, 13.220, 6.015,10.855, 6.122, 10.685, 10.035, 5.242,
7.630, 14.604, 7.903, 6.327, 9.391, 14.962, 4.730, 3.215, 16.498, 11.665, 9.284,
12.878, 6.656, 3.440, 5.854, 8.813, 10.043, 7.260, 5.985, 4.424, 4.344, 5.143,
9.935,7.840,9.550,6.968,6.370,3.537,3.286,10.158,8.108,6.697,7.151,
6.560, 2.988, 3.336, 6.814, 8.325, 7.854, 8.551, 3.228, 3.499, 3.751, 7.486,
6.625, 6.140, 4.909, 4.661, 1.871, 2.838, 5.392, 12.042, 8.696, 6.412, 3.395,
1.815, 3.327, 5.406, 6.182, 4.949, 4.089, 3.359, 2.070, 3.298, 5.317, 5.442,
4.557, 4.292, 2.500, 6.535, 4.648, 4.697, 5.459, 4.120, 3.922, 3.219, 1.402,
2.438, 3.257, 3.632, 3.233, 3.027, 2.352, 1.205, 2.077, 3.778, 3.218, 2.926,
2.601, 2.065 ,1.041, 1.800, 3.029, 2.058, 2.326, 2.506, 1.923

Table 4.27: Descriptive statistics of COVID-19 fatality rate data.

μ	Mid	Mode	Var	CS	CK	Min	Max
5.758	5.193	3	10.5893	0.98668	0.68134	1.041	16.498

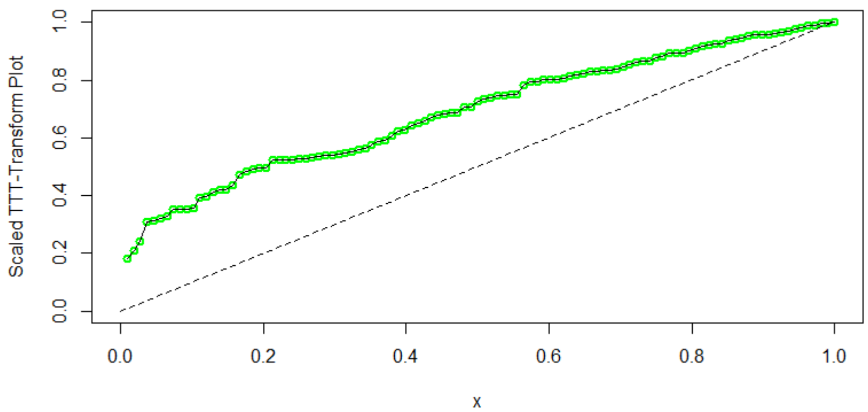

Figure 4.13: The TTT Plot of the COVID-19 fatality rate data

Table 4.28: The LRT statistic for COVID-19 fatality rate data.

Dis	Hypothesis	LRT	p-value
W	$H_0 : a = 0$, and $\alpha = 1$ vs $H_1 : H_0$ is false	0.920	0.631
EE	$H_0 : b = 0$ vs $H_1 : H_0$ is false	40.055	< 0.001
ExW	$H_0 : \alpha = 1$ vs $H_1 : H_0$ is false	6.479	< 0.039

Table 4.29: MLEs of the competing models with standard errors for COVID-19 fatality rate data

Model	$\hat{a}$	$\hat{b}$	$\hat{c}$	$\hat{\alpha}$	d
ExEW	-2.422	2.285	1.059	1.227	-
	(0.005)	(0.015)	(0.001)	(0.020)	-
W	1.897	6.521	-	-	-
	(0.138)	(0.350)	-	-	-
EE	3.998	0.362	-	-	-
	(0.674)	(0.035)	-	-	-
EW	-0.410	0.395	1.272	-	-
	(0.232)	(0.206)	(0.092)	-	-
LL	4.973	2.935	-	-	-
	(0.288)	(0.231)	-	-	-
BW	2.531	0.158	1.544	1.698	-
	(0.567)	(0.017)	(0.009)	(0.012)	-
	(0.162)	(2.297)	(0.126)	(0.122)	-
BEW	4.345	8.915	2.495	0.949	33.450
	(6.153)	(14.228)	(3.654)	(0.686)	(47.771)
MBW	3.323	0.451	9.698	2.038	5.103
	(5.260)	(0.255)	(10.930)	(0.950)	(3.619)
TanLL	4.418	3.054	-	-	-
	(0.258)	(0.237)	-	-	-

Table 4.30: The analytical performance measures for comparing distributions for COVID-19 fatality rate data.

Model	**AIC**	**BIC**	**CAIC**	**HQIC**	**(ℓ)**
ExEW	506.444	517.172	506.832	510.794	-249.222
W	541.911	547.275	542.025	544.086	-268.955
EE	536.352	541.716	536.466	538.527	-266.176
EW	516.850	524.897	517.081	520.113	-255.425
LL	542.164	547.527	542.279	544.339	-269.082
BW	563.167	549.962	539.622	5543.584	-265.617
BEW	542.686	556.096	543.274	548.123	-266.343
MBW	539.714	553.124	540.302	545.151	-264.857
TanLL	541.295	546.659	541.409	543.470	-268.647

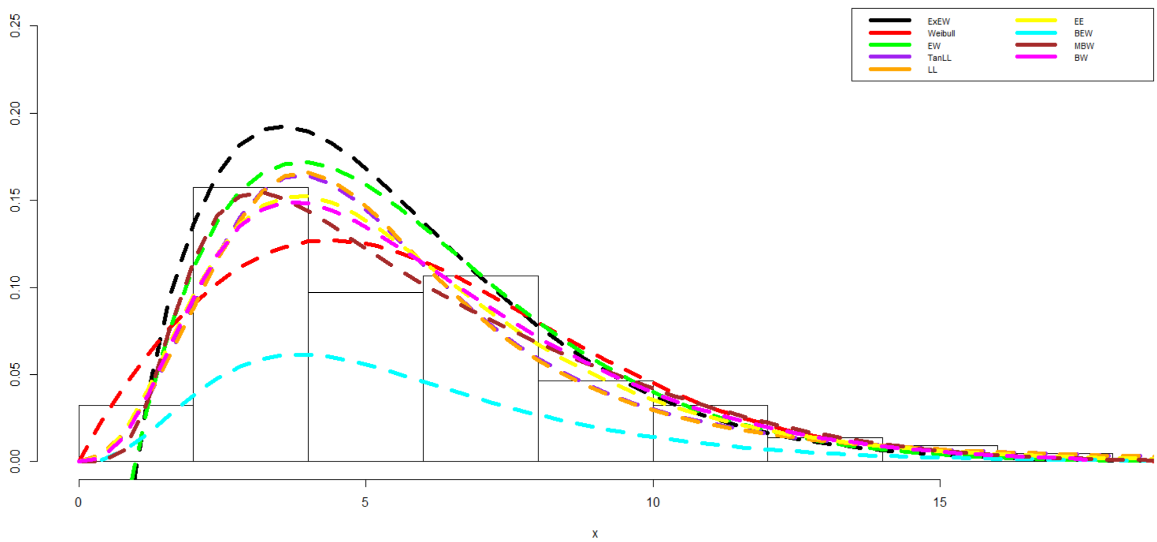

Figure 4.14: The fitted density shapes of the ExEW distribution and other distributions for COVID-19 fatality rate data.

4.9.3 Application of Sudan COVID-19 data to the ExEW-AFT model

In this Section, we demonstrate the adaptability and utility of the ExEW-AFT model, considering real-world right-censored COVID-19 data from Sudan.

4.9.3.1 Sudan COVID-19 data

COVID-19 is an infectious illness. Many studies have been conducted since it was declared a global health emergency to better understand the disease's clinical, epidemiological, and prognostic aspects Cabore et al. (2022); Cordeiro et al. (2021); Kiarie et al. (2022); Liu and Tian (2020); Marinho et al. (2021).
In Sudan, the epidemiological data are disclosed by the epidemiology department of the federal ministry of health (FMH) `www.fmoh.gov.sd`. Therefore, according to the investigation of FMH, there are 35,321 patients who are infected with the virus. Moreover, every positive case between 13 March 2020 and 31 December 2021 is included in the study sample. The period from the date of admission until the date of the sample result is considered the length of the hospital stay.COVID-

19 is an infectious illness. Many studies have been conducted since it was declared a global health emergency to better understand the disease's clinical, epidemiological, and prognostic aspects (Cabore et al., 2022; Cordeiro et al., 2021; Kiarie et al., 2022; Liu and Tian, 2020; Marinho et al., 2021). In Sudan, the epidemiological data are disclosed by the epidemiology department of the federal ministry of health (FMH) `www.fmoh.gov.sd`. Therefore, according to the investigation of FMH, there are 35,321 patients who are infected with the virus. Moreover, every positive case between 13 March 2020 and 31 December 2021 is included in the study sample. The period from the date of admission until the date of the sample result is considered the length of the hospital stay.

Overview of covariates of OVID-19 data

For each patient ($i = 1, \ldots, 35, 321$), the following covariates are taken into account.

- y : The length of stay in the hospital (by days).
- Status: For censoring.
- x_1 : Age.
- x_2 : Sex group.
- x_3 : The comorbidity group.

Table 4.31 shows some descriptive statistics of these covariates. The average hospital stays last three days. The scaled total time on test (TTT) plot for the COVID-19 hazard rate shape is displayed in Figure 4.15, which shows that the hazard rate shape of COVID-19 is unimodal. The initial density shape of the length of stay in the hospital is reported using the non-parametric kernel density estimation (KDE) approach in Figure 4.16, beside the histogram. It is noted that the density is asymmetrical and positively skewed, which is a common feature for survival data and makes the normal distribution inappropriate to analyze (Alvares et al., 2021). This is one of the points that motivated us to use the ExEW distribution as a baseline hazard in the AFT model to fit this data. The box plot and violin plot in Figure 4.16 are used to identify the extremes, and they reveal that some of these extreme observations are recorded.

Table 4.31: Statistical summary of the covariates for COVID-19 data

Covariate		Number of observations (%)	Mean (standard deviation (SD))
Length of stay in the hospital (in days)		-	3 (6.227)
Age (in years)		-	45 (18.750)
Status	1	32731(92.7%)	-
	0	2590(7.3%)	-
Comorbidity	yes	845(2.4%)	-
	no	34476(97.6%)	-
Sex	male	20654(58.5%)	-
	female	14667(41.5%)	-

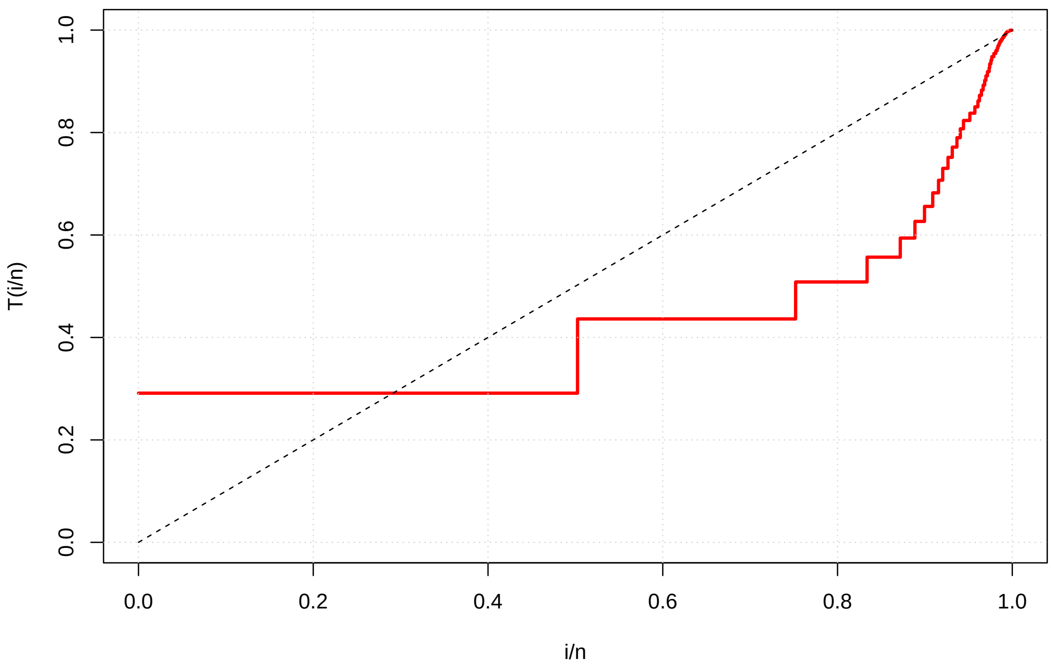

Figure 4.15: TTT plot for Sudan COVID-19 data.

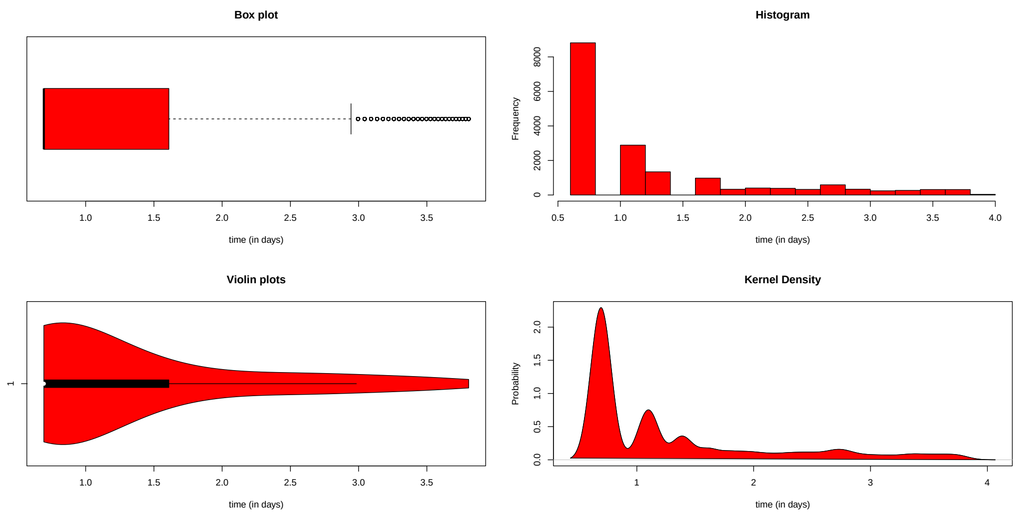

Figure 4.16: Plots for the Sudan COVID-19 data.

We analyze and compare the fitting of the ExEW-AFT model with that of sub-models such as the W-AFT, the exponentiated exponential (EE) AFT (EE-AFT), and the exponential Weibull AFT (ExW-AFT) models.
The AFT models for the competing models are as follows:

1. The W-AFT model:

$$f_{W-AFT}(t;\boldsymbol{\beta},\boldsymbol{x}) = ac\left(te^{\boldsymbol{x}'\boldsymbol{\beta}}\right)^{a-1}\exp\left\{-c\left(te^{\boldsymbol{x}'\boldsymbol{\beta}}\right)^{a}\right\}e^{\boldsymbol{x}'\boldsymbol{\beta}}, t>0. \tag{4.9.1}$$

2. The EE-AFT model:

$$f_{EE-AFT}(t;\boldsymbol{\beta},\boldsymbol{x}) = ac\left[\exp\left\{-c\left(te^{\boldsymbol{x}'\boldsymbol{\beta}}\right)\right\}\right]\left[1-\exp\left\{-c\left(te^{\boldsymbol{x}'\boldsymbol{\beta}}\right)\right\}\right]^{a-1}e^{\boldsymbol{x}'\boldsymbol{\beta}}, t>0. \tag{4.9.2}$$

3. The ExW-AFT model:

$$f_{ExW-AFT}(t;\boldsymbol{\beta},\boldsymbol{x}) = \left[a+bc\left(te^{\boldsymbol{x}'\boldsymbol{\beta}}\right)^{c-1}\right]\exp\left\{-a\left(te^{\boldsymbol{x}'\boldsymbol{\beta}}\right)+b\left(te^{\boldsymbol{x}'\boldsymbol{\beta}}\right)^{c}\right\}e^{\boldsymbol{x}'\beta}, t>0. \tag{4.9.3}$$

The aforementioned Equations (4.9.1)–(4.9.3) demonstrate how the covariates act multiplicatively on time, causing an acceleration or a deceleration of time. The analytical measurements, such as the BIC, and the CAIC are used to decide which

AFT model matches the COVID-19 data the best. Additionally, goodness-of-fit metrics like the LRT are used. The BIC is given by

$$BIC = k\log(n) - 2\ell \tag{4.9.4}$$

and the CAIC is provided by

$$CAIC = \frac{2nk}{n-k-1} - 2\ell, \tag{4.9.5}$$

where ℓ refers to the log-likelihood function calculated at the MLEs, k for the number of model parameters, and n for the sample size.

4.9.3.2 Cox PH model

To ascertain the relationship between survival time and the covariates thought to affect survival time, the Cox PH model is conducted. The Cox PH model parameters are estimated.

Table 4.32 shows the regression analysis of the Cox-PH model, including regression coefficients, SE, p-value, LRT, and BIC values. Furthermore, all of the covariates (age, sex, and comorbidity) significantly affect the length of stay in the hospital at a 5% level of significance.

Table 4.32: Results of Cox-PH model including the coefficients, SE, p-value, LRT, BIC, and CAIC

Covariates	coefficients	SE	p-value
Age	-0.005	0.000	< 0.022
Sex	-0.103	0.011	< 0.022
Comorbidity	0.792	0.044	< 0.022
LRT	909.600		< 0.000
BIC	621599		
CAIC	621587		

Testing PH assumption

The Schoenfeld residual is used in this study to test the PH assumption as follows: Based on the test, the Schoenfeld residuals are obtained for age and sex as covariates. The results in Table 4.33 provide evidence of the rejection of the assumption of PH for all covariates considered in the COVID-19 data. Additionally, Figure 4.17, shows that all covariates reject the null hypothesis of the test of the proportional hazards. In other words, the PH models present an inadequate fit for this COVID-19 data.

Table 4.33: Chi-square (χ^2) test and p-value for Schoenfeld residual test at level of significance 1%

Covariate	χ^2	$p-value$
Age	65.75	$<$-0.000
Sex	84.88	$<$-0.000
Comorbidity	2.07	$<$-0.15
Global	171.46	$<$ 0.000

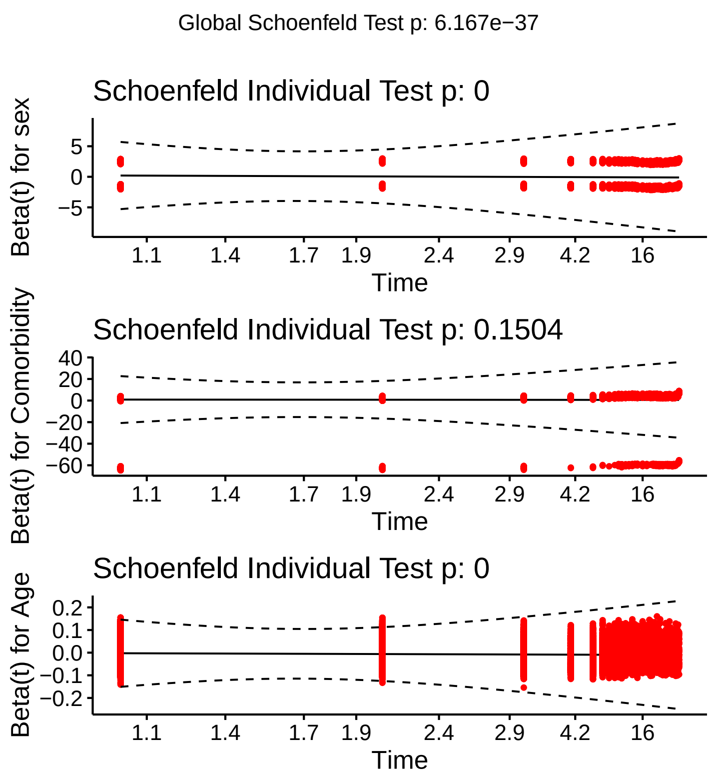

Figure 4.17: The conventional Schoenfeld residuals from the application of the COVID-19 data-sett.

4.9.4 AFT model analysis

In this subsection, we present the analysis of the ExEW-AFT, W-AFT, EE-AFT, and ExW-AFT models using the Sudan COVID-19 data.

We calculated the LRT statistics for the three sub-models. According to the LRT statistics in Table 4.34, the ExEW-AFT model fits the COVID-19 data the best. Table 4.35 showed that the SE of $\hat{\beta}s$ for the ExEW-AFT, W-AFT, EE-AFT, and ExW-AFT models is small enough. Moreover, at 5% significance level, the parameters of all AFT models are significant, as shown in Table 4.36. Furthermore, the analytical measures of competing AFT models are shown in Table 4.37 which reveals that the ExEW-AFT model has the lowest BIC, and CAIC. In conclusion, the ExEW-AFT model is the best fit for the data among the W-AFT, EE-AFT, and ExW-AFT models under consideration. Moreover, at 5% level of significance, all the covariates (age, sex, and comorbidity) significantly influence the length of stay at the hospital.

Figure 4.18 shows the KM survival curve, Yes the curve is KM plot. However, the test done to compare survival functions between the two groups is the Log-Rank test. Furthermore, the comparison is for comorbidity and non-comorbidity group. Figure 4.19 depicts estimated HRFs for the competitive baseline hazards, and Figure 4.20 represents the average KM estimator and population SF. All of these figures show that our proposed ExEW-AFT model fits the data better than its competitors, including the Cox-PH and its sub-models.

Table 4.34: The LRT statistics for COVID-19 data at significance level 1%

Model	Hypothesis	LRT	p-value
W-AFT	$H_0 : a = 0$, and $\alpha = 1$ vs $H_1 : H_0$ is false	1987.469	< 0.000
EE-AFT	$H_0 : b = 0$ vs $H_1 : H_0$ is false	2197.355	< 0.000
ExW-AFT	$H_0 : \alpha = 1$ vs $H_1 : H_0$ is false	1544.978	< 0.000

Table 4.35: MLE fits of the ExEW, W, EW, ExW AFT models with SE (in parentheses) for COVID-19 data

model	$\hat{a}$	$\hat{b}$	$\hat{c}$	$\hat{\alpha}$	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$
ExEW-AFT	0.469	0.568	0.977	1.516	-0.201	0.017	0.506
	(0.029)	(0.029)	(0.001)	(0.037)	(0.007)	(0.014)	(0.021)
W-AFT	3.772	0.869	-	-	-0.147	-0.001	0.050
	(0.615)	(0.003)	-	-	(0.005)	(0.009)	(0.075)
EE-AFT	1.107	0.027	-	-	-0.105	0.050	1.175
	(0.009)	(0.002)	-	-	(0.005)	(0.011)	(0.032)
ExW-AFT	0.007	0.141	0.867	-	-0.108	0.027	0.466
	(0.016)	(0.002)	(0.008)	-	(0.006)	(0.011)	(0.038)

Table 4.36: z-value, p-value and confidence interval (CI) for the AFT estimates for each model at level of significance 5%

Model	Mean	z-value	$p-value$	CI 95%
ExEW-AFT	$(\hat{a}=0.469)$	16.378	<0.000	$(0.4120.525)$
	$(\hat{b}=0.568)$	19.461	<0.000	$(0.510, 0.625)$
	$(\hat{c}=0.977)$	805.912	<0.000	$(0.975, 0.979)$
	$(\hat{\alpha}=1.516)$	40.551	<0.000	$(1.443, 1.589)$
	$(\hat{\beta}_1=-0.201)$	27.457	<0.000	$(-0.215, -0.187)$
	$(\hat{\beta}_2=0.017)$	7.482	<0.000	$(0.010, 0.045)$
	$(\hat{\beta}_3=0.506)$	23.692	<0.000	$(0.464, 0.548)$
W-AFT	$(\hat{a}=3.772)$	6.136	<0.000	$(2.567, 4.977)$
	$(\hat{b}=0.869)$	340.541	<0.000	$(0.864, 0.874)$
	$(\hat{\beta}_1=-0.147)$	-27.114	<0.000	$(-0.158, -0.137)$
	$(\hat{\beta}_2=-0.001)$	-0.098	<0.018	$(-0.100, -0.080)$
	$(\hat{\beta}_3=0.050)$	12.734	<0.000	$(0.035, 0.065)$
EE-AFT	$(\hat{a}=1.107)$	126.464	<0.000	$(1.090, 1.124)$
	$(\hat{b}=0.027)$	15.592	<0.000	$(0.024, 0.030)$
	$(\hat{\beta}_1=-0.105)$	-19.384	<0.018	$(-0.116, -0.094)$
	$(\hat{\beta}_2=0.050)$	4.724	<0.922	$(0.029, 0.071)$
	$(\hat{\beta}_3=1.0175)$	36.634	<0.000	$(1.112, 1.238)$
ExW-AFT	$(\hat{a}=0.007)$	0.425	0.671	$(-0.024, 0.037)$
	$(\hat{b}=0.141)$	56.618	<0.000	$(0.136, 0.146)$
	$(\hat{c}=0.867)$	108.2542	<0.000	$(0.851, 0.882)$
	$(\hat{\beta}_1=-0.108)$	-17.067	<0.000	$(-0.121, -0.096)$
	$(\hat{\beta}_2=0.027)$	2.493	<0.013	$(0.006, 0.049)$
	$(\hat{\beta}_3=0.466)$	39.738	<12.266	$(0.392, 0.541)$

Table 4.37: The analytical performance measures for comparing AFT models for COVID-19 data

Model	**BIC**	**CAIC**
ExEW-AFT	147089	147096
W-AFT	149056	149061
EE-AFT	149266	149271
ExW-AFT	148624	148630

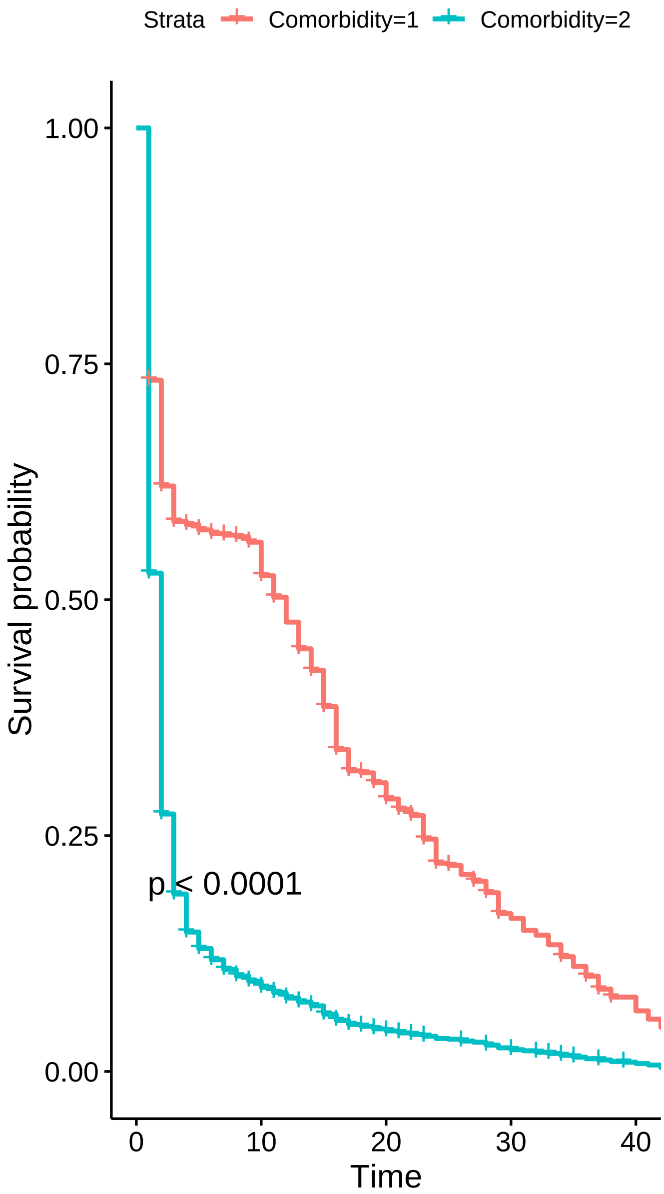

Figure 4.18: Plot of the KM curves for time.

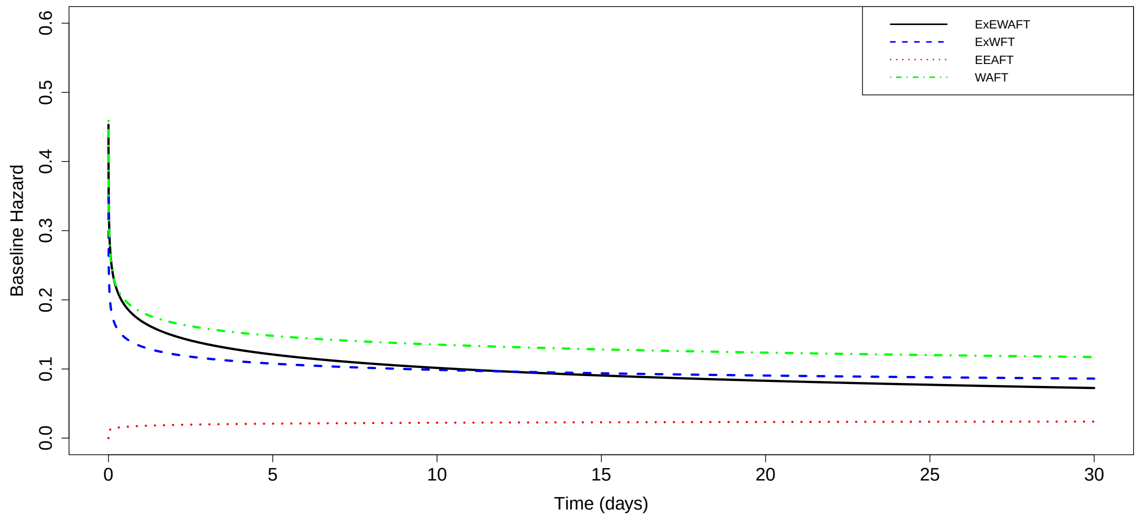

Figure 4.19: Estimated HRFs for the competing baseline hazards.

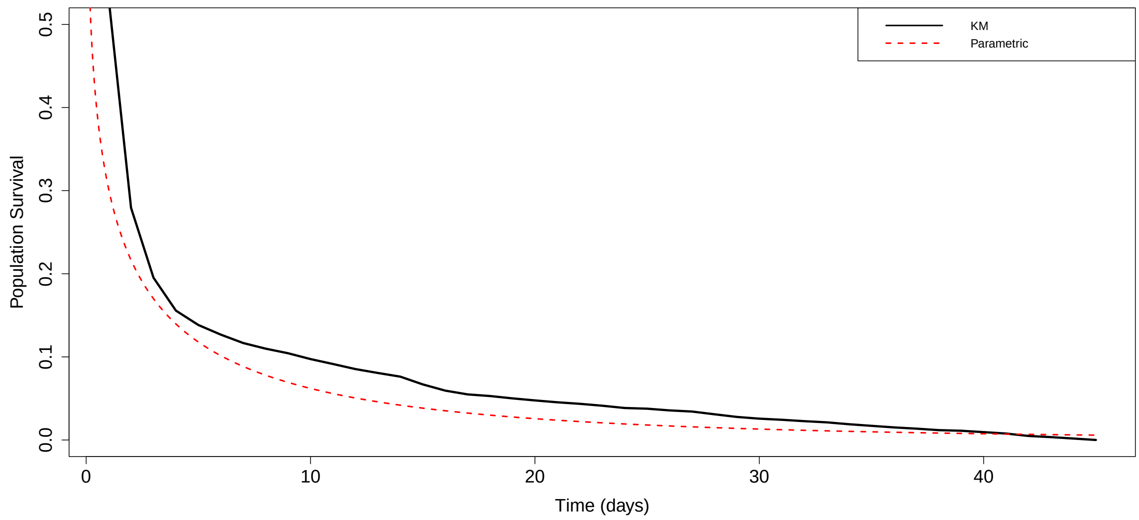

Figure 4.20: Average KM estimator and population SF.

4.9.5 Extended exponential-Weibull mixture cure model with application to cancer clinical trails data

To illustrate the applicability of the proposed mixture cure model, we analyze the rebuilt IPASS clinical trial data that was published by Argyropoulos and Unruh (2015). The data set is available in the R package *AHSurv* see `https://cran.r-project.org/web/packages/AHSurv/index.html`]. The data base covers the time frame from March 2006 to April 2008, which is consisting 1217 observations.

The TTT transform plot in Figure 4.21 shows a concavity pattern, illustrating the data's increasing hazard rate shape. This demonstrates that the hrf in Figure 4.2 is suitable for analyzing this data.

The proposed model is compared to the another-models such as: Weibull, LL, ExW, and the GLL models.

The AIC and BIC are used to determine which mixture cure mode (MCM) matches the data the best.

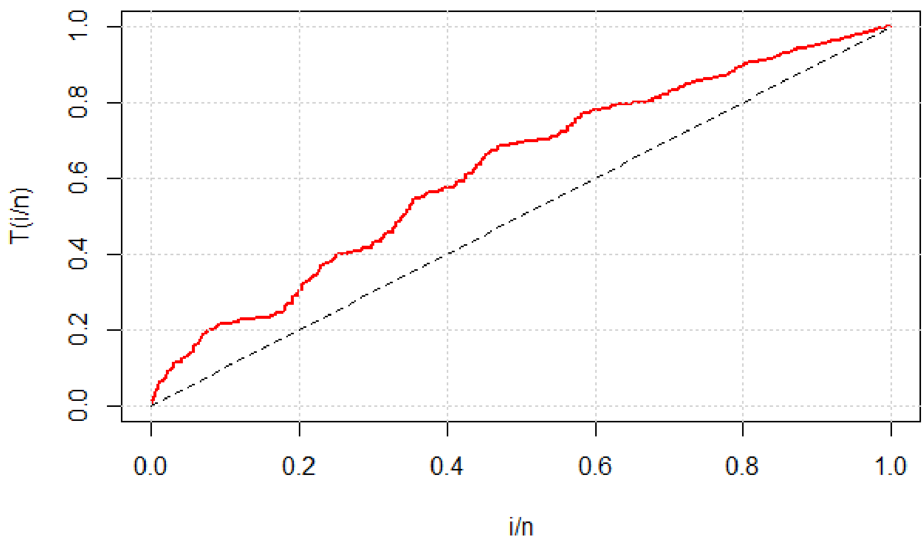

Figure 4.21: The TTT Plot of the rebuilt IPASS clinical trial data.

Table 4.38 displays the ML estimates of the fitted models' parameters with standard error. The ExEW MCM model more closely matches the data from the rebuilt IPASS clinical trial than any other comparable MCM model. Moreover, at 5% significance level, the parameters of the ExEW-MCM is significant, as shown in Table 4.39.

Table 4.40 shows that the ExEW MCM model has the lowest AIC and BIC values when compared to the other MCM models. means that the ExEW MCM model provides the greatest fit to the data-st.

Table 4.38: Parameters of competing models estimated with SE (in parentheses)

model	$\hat{a}$	$\hat{b}$	$\hat{c}$	$\hat{\alpha}$	ρ
ExEW	1.099	0.707	1.597	0.041	0.021
	(0.259)	(0.150)	(0.059)	(0.005)	(0.011)
W	7.432	1.371	-	-	0.013
	(0.241)	(0.041)	-	-	(0.013)
LL	1.566	6.591	-	-	0.145
	(0.075)	(0.324)	-	-	(0.025)
ExW	0.018	0.056	1.393	-	0.016
	(0.014)	(0.014)	(0.058)	-	(0.012)
GLL	0.140	1.422	0.044	-	-0.013
	(0.007)	(0.072)	(0.035)	-	(0.030)

Table 4.39: z-value, p-value and CI for the AFT estimates for each model at level of significance 5%

Model	Mean	z-value	$p - value$	CI 95%
ExEW	$(\hat{a} = 1.099)$	4.236	< 0.000	$(0.590, 1.607)$
	$(\hat{b} = 0.707)$	4.710	< 0.000	$(0.413, 1.001)$
	$(\hat{c} = 1.597)$	26.843	< 0.000	$(1.480, 1.713)$
	$(\hat{\alpha} = 0.041)$	8.825	< 0.000	$(0.032, 0.050)$
	$(\hat{\rho} = 0.021)$	1.809	< 0.070	$(0.002, 0.043)$
W	$(\hat{a} = 7.425)$	30.856	< 0.000	$(6.953, 7.897)$
	$(\hat{b} = 1.353)$	33.084	< 0.000	$(1.272, 1.434)$
	$(\hat{\rho} = 0.011)$	0.988	< 0.323	$(-0.015, 0.036)$
LL	$(\hat{a} = 1.566)$	27.213	< 0.000	$(1.453, 1.679)$
	$(\hat{b} = 6.591)$	20.334	< 0.000	$(5.956, 7.227)$
	$(\hat{\rho} = 0.145)$	5.909	< 0.000	$(0.097, 0.194)$
ExW	$(\hat{a} = 0.018)$	1.223	< 0.222	$(-0.011, 0.046)$
	$(\hat{b} = 0.056)$	3.964	< 0.000	$(0.029, 0.084)$
	$(\hat{c} = 1.393)$	24.048	$< .000$	$(1.280, 1.507)$
	$(\hat{\rho} = 0.016)$	1.299	< 0.194	$(-0.008, 0.040)$
GLL	$(\hat{a} = 0.140)$	19.198	< 0.000	$(0.126, 0.155)$
	$(\hat{b} = 1.422)$	19.820	< 0.000	$(1.282, 1.563)$
	$(\hat{c} = 0.044)$	1.255	< 0.209	$(-0.025, 0.113)$
	$(\hat{\rho} = 0.013)$	0.438	< 0.661	$(-0.072, 0.046)$

Table 4.40: The analytical performance measures for comparing models

Model	AIC	BIC
ExEW	5704.828	5721.365
W	5708.104	5723.447
LL	5712.876	5728.255
ExW	5714.956	5741.853
GLL	5708.614	5729.031

CHAPTER 5

CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

The study was designed to develop a more versatile lifetime model is called the extended exponential-Weibull (ExEW). The mathematical and statistical properties of the ExEW are proposed and described. The ExEW model includes several known sub-models as special cases. Some mathematical features of the new model are derived. The ExEW parameters are estimated via the maximum likelihood method and the estimators' behaviour is evaluated via Monte Carlo simulations. Based on goodness-of-fit statistics and analytical performance measurements, the ExEW model fits the two real-world data sets better than its sub-models and other typical parametric survival models. As a consequence, we conclude that the ExEW distribution is the most fitting model among the models studied and is a good contender for modeling lifetime events.

Furthermore the study also intended to produce a more flexible and general survival regression model named extended exponential-Weibull accelerated failure time (ExEW-AFT) model. We assessed the performance of the proposed model's estimators through a comprehensive Monte Carlo simulation study. The proposed model was also applied to Sudan COVID-19 Data. The choice of the AFT model is, therefore, sound as covariates directly relate to the time to event, which eases interpretability.

Considering the four different hazard rate (HR) shapes, including (increasing, decreasing, unimodal, and bathtub HR shapes), the simulation results showed that the ExEW model is capable of representing monotone decreasing, monotone increasing, unimodal, and bathtub HR functions more accurately than the existing AFT models such as: exponentiated-Weibull, Weibull, and log-logistic AFT models. Additionally, the SE, AB, RB, and MSE values showed that the proposed ExEW-AFT model performed well.

A real right-censored COVID-19 data set from Sudan reveals that it is misleading to trust the analysis based on the usual PH model, especially when the data exhibits characteristics such as the proportionality assumption Patel et al. (2006). This choice induces wrong conclusions, which, in turn, may lead to inappropriate clinical practices in terms of the best model that fits the data Aida et al. (2022); Yang et al. (2020). As demonstrated in our analysis, using different information criteria and some goodness-of-fit tests, including the likelihood ratio test, our proposed AFT model fits the data very well as compared to the common Cox-PH model and some other AFT single-parameter regression models (EW-AFT, W-AFT, and LL-AFT models). The three covariates (age, sex, and comorbidity) are significantly associated with the length of stay in the hospital.

The developed model provided an important contribution to the tool-set for assessing survival data and can be used with overall hazard regression models.

No research is without limits, our model has some limitations. The model is unable to handle survival data with crossing survival curves.

Another limitation arrases from the application perspective of the study with respect to covariates used. In the analysis of the ExEW-AFT, only age, sex, and comorbidity covariates were used. Vaccination and place of residence (urban and rural) as variables to analyze the length of stay in the hospital could be very useful, but no information from those variables was collected. Additionally, mixture cure models can be used to estimate the cured individuals' likelihood function. However, when there are no cure individuals in the population under study, these models can be reduced to the classical survival models. Furthermore, in this study, the maximum likelihood estimates analysis for the four-parameter ExEW distribution in the existence of cured individuals, censored observations is presented. The limitation of this model that it is cannot verify the property of proportional hazard functions.

5.2 Recommendation for further research

The future will see the development of residual analysis techniques and diagnostic measures for assessing the goodness of fit of the ExEW-AFT model. Additionally, this work can be extended by proposing an AFT multi-parameter regression model for other types of censored survival data sets, including left censoring, interval censoring, middle censoring, and double censoring mechanisms. Furthermore,it can be extended to more complex survival models, including competing risk models, frailty models, and mixed effects AFT models, to apply to spatial and clustered survival data sets. Finally, in the future study the ExEW distribution can be extended to the non-mixture cure model.

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APPENDIX ONE FIRST PAPER

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Research Article

The Extended Exponential Weibull Distribution: Properties, Inference, and Applications to Real-Life Data

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A novel version of the exponential Weibull distribution known as the extended exponential Weibull (ExEW) distribution is developed and examined using the Lehmann alternative II (LAII) generating technique. The new distributions basic mathematical properties are derived. The maximum likelihood estimation (MLE) technique is used to estimate the unknown parameters of the proposed distribution. The estimators' performance is further assessed using the Monte Carlo simulation technique. Eventually, two real-world data sets are utilized to show the applicability of the new distribution.

APPENDIX TWO SECOND PAPER

mathematics

MDPI

Article

The Extended Exponential-Weibull Accelerated Failure Time Model with Application to Sudan COVID-19 Data

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Abstract: A fully parametric accelerated failure time (AFT) model with a flexible, novel modified exponential Weibull baseline distribution called the extended exponential Weibull accelerated failure time (ExEW-AFT) model is proposed. The model is presented using the multi-parameter survival regression model, where more than one distributional parameter is linked to the covariates. The model formulation, probabilistic functions, and some of its sub-models were derived. The parameters of the introduced model are estimated using the maximum likelihood approach. An extensive simulation study is used to assess the estimates' performance using different scenarios based on the baseline hazard shape. The proposed model is applied to a real-life right-censored COVID-19 data set from Sudan to illustrate the practical applicability of the proposed AFT model.

Keywords: baseline hazard; survival regression model; maximum likelihood; Monte Carlo simulation; COVID-19 data

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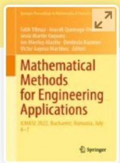

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Extended Exponential-Weibull Mixture Cure Model for the Analysis of Cancer Clinical Trials

Adam Braima Mastor, Oscar Ngesa, Joseph Mung'atu, Ahmed Z. Afify & Abdisalam Hassan Muse

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Abstract

In the examination of survival statistics, it is frequently assumed that all the study subjects would ultimately experience the concerning event. However, it is unquestionably predicted that some of these subjects will never be exposed to the interesting event. This kind of data is typically modelled using the cure rate models. In this study, it is proposed a maximum likelihood estimates method for analyzing the four-parameter extended exponential-Weibull (ExEw) distribution where cured subjects, censored data, and predictors are present. The extended exponential-Weibull mixture cure model in this paper is proposed with the aim of accounting for the fraction of susceptible (cured) subjects in the study.The proposed mixture cure model is the superior model that fits the real data from Cancer clinical trials.

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