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A New Survival Regression Model with Application to HIV Data

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Abstract. Many studies are being conducted in the modern world to extend the life expectancy of people suffering from a range of illnesses, including fatal conditions like cancer and HIV/AIDS. Many patients are therefore anticipated to be permanently cured or cured for some time. A new survival regression model was proposed to study HIV data. An advantage of the new distribution is that it outperforms some of the existing distributions in the lifetime literature. We obtain the estimates of the parameters of the proposed model using the method of maximum likelihood. The survival regression model was fitted to a data set of 100 observations. Additionally, Cox-Snell residual analysis was considered. The proposed model proved its significance by fitting the HIV data well compared to other models. The proposed model can be recommended to fit data of this kind.

1. Introduction

Many studies are being conducted in the modern world to extend the life expectancy of people suffering from a range of illnesses, including fatal conditions like cancer and HIV/AIDS. Many patients are therefore anticipated to be permanently cured. They are not affected by "death" and are long-term survivors. We refer to these individuals as cured patients[1]. The human immunodeficiency virus (HIV) continues to be one of the biggest threats to public health since it has taken the lives of around 33 million people globally. HIV-positive individuals can live long, healthy lives if they take Antiretroviral medication (ART). However, in the absence of medical intervention, an individual living with HIV has an increased risk of developing Acquired Immunodeficiency Syndrome (AIDS), a serious illness. In addition to statistics and mathematics, probability distributions have been widely used in the applied sciences, engineering, and biological sciences. As a result, probability distributions are always developing significantly to accurately represent real-world situations and

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evaluate real-world data more effectively. In the process, other generalized distributions with more parameters and flexibility than the current one have been developed over the previous ten years, based on various modification techniques. However, according to [2], there are a lot of issues to resolve and examine when dealing with real data because any classical or conventional probability distributions do not take into account the various features of the data.

The Weibull distribution is one of the most popular distributions used to simulate lifespan data with consistent failure rates. Nevertheless, the Weibull distribution does not suit non-monotone failure rates very well. Beta Modified Weibull was investigated by [3]. Alpha power Topp-Leone Weibull distribution was considered by [4]. Weibull distribution has been applied to predict health events by [5]. Weibull regression and machine learning survival models were considered by [6].

In reliability and lifespan data analysis, several modified Weibull distributions with extra parameters have recently been proposed and investigated as lifetime distributions. This includes the log-exponentiated Weibull regression model by [7], the Beta exponentiated Weibull distribution by [8], the Odd Log-Logistic Exponentiated Weibull Distribution by [9], as well as the New Generalized Exponentiated Fréchet–Weibull Distribution by [10]. Moreover, a thorough review of the Weibull model with a focus on various parameterizations was presented by [11].

This paper presents a new extension of Weibull distribution using the Inverse Lomax Odd Exponentiated generator. The foundation of this extension lies in survival analysis. The extension proposed herein aims to provide an application to the Hiv dataset. The structure of the remaining sections of this paper is outlined as follows: Section 2 describes the methodology of the new extension of Weibull distribution, estimation of the parameters of the model, and residual analysis. The results and discussion are presented in Section 3. The paper is concluded in Section 4.

2. The Log-Inverse Lomax Odd Exponentiated Weibull Distribution (Log-ILOEWD)

The Inverse Lomax Odd Exponentiated family of distributions proposed by [12] has the cumulative distribution function (CDF) and probability density function (PDF) given as:

$$F(x;\lambda,\gamma,\theta,\Delta)=\left[1+\lambda\left\{\frac{(1-G(x;\Delta))}{G(x;\Delta)}\right\}^{\theta}\right]^{-\gamma};\qquad x>0,\lambda,\gamma,\theta,\Delta>0 \tag{1}$$

and

$$f(x;\lambda,\gamma,\theta,\Delta)=\frac{\theta\gamma\lambda g(x;\Delta)[1-G(x;\Delta)]^{\theta-1}}{[G(x;\Delta)]^{\theta+1}}\left[1+\lambda\left[\frac{(1-G(x;\Delta))}{G(x;\Delta)}\right]^{\theta}\right]^{-(1+\gamma)} \tag{2}$$

Where $G(x;\Delta)$ is a baseline CDF. For survival regression, we consider the Weibull distribution of this form $G(x;\eta,\kappa)=1-e^{-(\eta x)^{\kappa}}$ and $g(x;\eta,\kappa)=\eta^{\kappa}\kappa x^{\kappa-1}e^{-(\eta x)^{\kappa}}$ as the baseline distribution. Then, the CDF and PDF of the ILOEWD are given by:

$$F(x;\eta,\kappa,\gamma,\theta,\lambda)=\left[1+\lambda\left(\frac{e^{-(\eta x)^{\kappa}}}{[1-e^{-(\eta x)^{\kappa}}]}\right)^{\theta}\right]^{-\gamma}\quad \eta,\kappa,\gamma,\theta,\lambda>0 \tag{3}$$

and

$$f(x;\eta,\kappa,\gamma,\theta,\lambda)=\frac{\theta\eta^{\kappa}\kappa\lambda\gamma x^{\kappa-1}[e^{-(\eta x)^{\kappa}}]^{\theta-1}e^{-(\eta x)^{\kappa}}}{[1-e^{-(\eta x)^{\kappa}}]^{\theta+1}}\left[1+\lambda\left(\frac{e^{-(\eta x)^{\kappa}}}{[1-e^{-(\eta x)^{\kappa}}]}\right)^{\theta}\right]^{-(1+\gamma)} \quad \eta,\kappa,\gamma,\theta,\lambda \tag{4}$$

where η, and λ are the scale parameters, and κ, γ, and θ, are the shape parameters. Let $Y=log(X)$, $\eta=e^{-\mu}$, and $\kappa=\frac{1}{\delta}$. Moreover, Let Y follows log-ILOEWD with parameters (θ, λ,γ,μ,δ). Since $Y=log(X)$, $\frac{dy}{dx}=\frac{1}{x} \implies \frac{dx}{dy}=x=e^{y}$. To find the density function of Y, we begin with the random variable transformation of the form

$$f(y;\delta,\mu,\gamma,\theta,\lambda)=f(x;\delta,\mu,\gamma,\theta,\lambda)|\frac{dx}{dy}|$$

$$=\frac{\lambda\gamma\theta e^{\frac{-\mu}{\delta}}e^{\frac{y}{\delta}}e^{-y}e^{y}e^{-(e^{-\mu}e^{y})^{\frac{1}{\delta}}}[e^{-(e^{-\mu}e^{y})^{\frac{1}{\delta}}}]^{\theta-1}}{\delta[1-e^{-(e^{-\mu}e^{y})^{\frac{1}{\delta}}}]^{\theta+1}}\left[1+\lambda\left(\frac{e^{-(e^{-\mu}e^{y})^{\frac{1}{\delta}}}}{[1-e^{-(e^{-\mu}e^{y})^{\frac{1}{\delta}}}]}\right)^{\theta}\right]^{-(1+\gamma)}$$

$$=\frac{\lambda\gamma\theta e^{\left(\frac{y-\mu}{\delta}\right)}e^{-\left(e^{\frac{y-\mu}{\delta}}\right)}[e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}]^{\theta-1}}{\delta[1-e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}]^{\theta+1}}\left[1+\lambda\left(\frac{e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}}{\left[1-e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}\right]}\right)^{\theta}\right]^{-(1+\gamma)}$$

Then, finally, the transformed PDF and survival function of the ILOEWD can be given as:

$$f(y;\delta,\mu,\gamma,\theta,\lambda)=\frac{\lambda\gamma\theta e^{\left(\frac{y-\mu}{\delta}\right)}e^{-\left(e^{\frac{y-\mu}{\delta}}\right)}[e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}]^{\theta-1}}{\delta[1-e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}]^{\theta+1}}\left[1+\lambda\left(\frac{e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}}{\left[1-e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}\right]}\right)^{\theta}\right]^{-(1+\gamma)};$$

$$\delta,\mu,\gamma,\theta,\lambda>0 \tag{5}$$

and

$$S(y;\delta,\mu,\gamma,\theta,\lambda)=1-\left[1+\lambda\left(\frac{e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}}{\left[1-e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}\right]}\right)^{\theta}\right]^{-(\gamma)} \quad \delta,\mu,\gamma,\theta,\lambda>0 \tag{6}$$

Also let us define the standardized random variable Z as $Z=(y-\mu)/\delta$. Then, equation (5) can be re-written as

$$f(z;\gamma,\theta,\lambda)=\frac{\lambda\gamma\theta e^{z}e^{-(e^{z})}[e^{-e^{(z)}}]^{\theta-1}}{\delta[1-e^{-e^{(z)}}]^{\theta+1}}\left[1+\lambda\left(\frac{e^{-e^{(z)}}}{[1-e^{-e^{(z)}}]}\right)^{\theta}\right]^{-(1+\gamma)} \tag{7}$$

The linear regression model that is connecting the dependent variable y_i and the covariates or independent variables $m_{i1},m_{i2},m_{i3},.....m_{ip}$ is given by

$$y_i=\sum_{j=1}^{p}m_{i,j}\tau_j+\delta z_i,\quad i=1,2,3,....,n. \tag{8}$$

where z_i is the random error with density presented in equation (7) with μ=0 and δ=1, $\mu_i = \sum_{j=1}^{p} m_{i,j}\tau_j$, $\boldsymbol{\phi} = (\tau_1, \tau_2, \tau_3, ...\tau_p)'$ is a p× 1 vector associated with the independent variables. Equation (8) can be used to fit different kinds of data in which the covariates have significant effects on the response variable.

2.1. **Inference for the Log-ILOEWD.** Think of a size-n random sample poised by (y_1, δ_1, x_1), (y_2, δ_2, x_2), (y_3, δ_3, x_3), ..., (y_n, δ_n, x_n), where $yi = min\{log(T_i), log(C_i)\}$, δ_i is the censoring indicator in which 0 is censored and 1 is failure, and $\mathbf{x}_i$ is connected to the covariate vector as the i^{th} individual. Lets assume that the observed lifespan and censoring time are independent and that there is no informative censoring. Equation (8) provides the model's log-likelihood function for the vector of parameter $\Phi = (\theta, \lambda, \gamma, \delta, \tau')'$ takes the form:

$$l(\Phi; y) = \sum_{i \in F} log[f(y; \Phi)] + \sum_{i \in C} log[S(y; \Phi)] \tag{9}$$

where the set of censored observations is indicated by C, and the set of uncensored observations is denoted by F, $f(y; \Phi)$ is the density given by equation (5) and $S(y; \Phi)$ is the survival function in equation (6). More details can be found in [13] and [14].

2.2. **Residual Analysis for the Log-ILOEWD Model.** Following the Log-ILOEWD's formulation, the examination of the residuals is a crucial step. It is employed to confirm whether the model's underlying assumptions have changed significantly. Here, Cox and Snell's residual is taken into account. One kind of residual used in survival analysis to evaluate a survival model's goodness-of-fit is the Cox-Snell residual. They offer a means of assessing the degree to which the model matches the observed survival data. They are able to be stated as:

$$e_i = -log\left\{S(y_i; \mathbf{x}_i)\right\}; \quad i = 1, 2, 3, 4, \ldots, n. \tag{10}$$

The following provides the Cox-Snell residuals corresponding to the Log-ILOEWD regression model:

$$e_i = -log\left\{1 - \left[1 + \lambda\left(\frac{e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}}{\left[1 - e^{-e^{\left(\frac{y-\mu}{\delta}\right)}}\right]}\right)^{\theta}\right]^{-(\gamma)}\right\}; \quad i = 1, 2, 3, 4, \ldots, n. \tag{11}$$

If the fitted model is sufficient, the residuals have an exponential distribution as expected [13].

3. Results and Discussions of the Data

3.1. **Data Description.** This HIV data is from the Health Maintenance Organization-Human Immunodeficiency Virus(HMO-HIV+) study as reported by [15]. The data consists of a data frame with 100 observations on 7 variables. The variables are the patients (id) from 1-100, the date the participants entered the study, the date of the end of the study, survival time (between entry and end of the study), age, drug(No=0, Yes=1), as well as censoring(I=Death, 0=Alive). For this study, the survival time (in month) is considered as the dependent variable (y_i), while the covariates are drug(x_1), placebo (x_2), age less or equal 25 (x_3), age between 26 and 30 (x_4), age between 31 to 35 (x_5), age between 36 to 40 (x_6), and age between 41 to 51 (x_7). The Log-ILOEWD model was fitted alongside the Log-Topp Leone Odd Log-Logistic Weibull Distribution (Log-TLOLLWD) by [?], as well as Log-Weibull Distribution (Log-WD). This data is also available in R as AidsSurvival.df under the Bolstad2 package by [16].

Table (1) reports the estimated parameter values, the -2ll, and the Akaike Information Criteria (AIC) for the regression model fitted by maximum likelihood estimation (MLE). Given that the Log-ILOEWD regression model has the lowest AIC and -2ll values among the other regression models (Log-TLOLLWD, Log-WD), we may infer that the Log-ILOEWD regression model yields a superior fit. At the 5% level, the regression parameters τ_0, τ_1, τ_3, τ_4, τ_5, and τ_7 are determined to be statistically significant for the Log-ILOEWD model. Moreover, the parameters θ, λ, as well as γ were also significance. The computed regression parameters indicate that drug-using people have shorter lifespans than non-drug-using people. Furthermore, people's lifetimes get shorter as they get older. The fitted regression equation is given in equation (12).

$$y_i = \tau_0 + \sum_{j=1}^{7} \tau_j x_{ij} + \delta z_i; \quad i = 1, 2, 3, \ldots, 100. \tag{12}$$

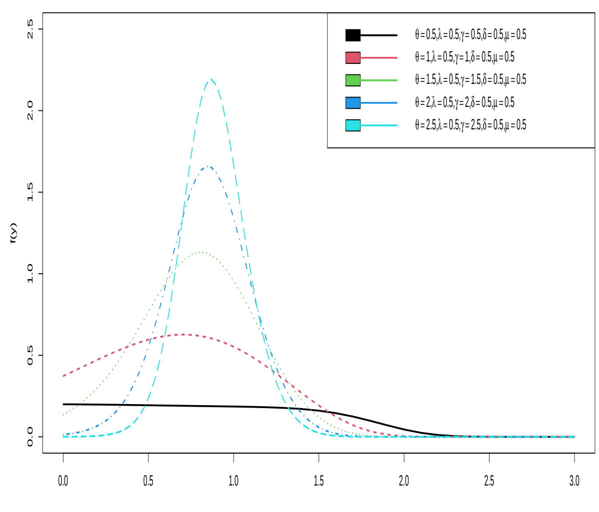

Figure 1. PDF of the Log-ILOEWD at various parameter values

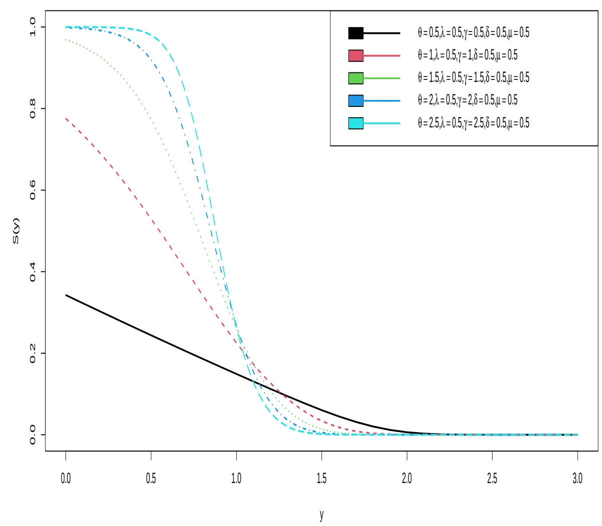

Figure 2. Survival function of the Log-ILOEWD at various parameter values

Figures (1) and (2) show the PDF and Survival function of the Log-ILOEWD. The PDF can take various shapes based on the choice of the parameter values.

Table 1. MLEs for four fitted models to Hiv Data and values of the -2ll and AIC statistic.

	Log-ILOEWD		Log-TLOLLWD		Log-WD	
Parameter	Estimate	P-value	Estimate	P-value	Estimate	P-value
θ	0.8758	0.02016	5.5592	0.2901	—	—
λ	0.1697	0.4341	2.7216	0.0075	—	—
γ	6.7628	0.41645	—	—	—	—
δ	1.1778	0.2109	7.5595	0.3812	0.8851	2.2E-16
τ_0	0.7264	0.6002	5.7699	0.0025	-1.5156	0.0184
τ_1	-0.1804	0.0001	-1.9071	0.0569	1.9303	2.88E-08
τ_2	0.6669	0.3367	-1.1476	0.2112	3.0433	2.2E-16
τ_3	3.1159	0.0129	2.6186	0.0108	3.2857	0.0026
τ_4	1.3354	0.2695	0.8447	0.3896	1.724	0.0869
τ_5	1.1139	0.3464	0.5316	0.5759	1.5908	0.10497
τ_6	0.8294	0.4916	0.1465	0.8796	1.3928	0.1588
τ_7	0.3319	0.7811	-0.3477	0.7163	0.6944	0.481
-2ll	251.948		254.457		258.426	
AIC	275.948		276.457		276.426	
Rank	1		3		2	

Table 2. MLEs for four fitted Models to Cox-Snell Residuals and values of the -2ll and AIC Statistic.

	Log-ILOEWD		Log-TLOLLWD		Log-WD	
Parameter	Estimate	P-value	Estimate	P-value	Estimate	P-value
θ	34.0409	0.0714	0.0226	<2.2E-16	—	—
λ	0.7453	0.9628	6.7060	2.661E-14	—	—
γ	0.2645	0.0114	—	—	—	—
δ	11.6796	0.7127	0.7031	9.172E-16	0.8517	<2.2E-16
τ_0	2.5799	0.7396	5.001	<2.2E-16	5.2131	<2.2E-16
τ_1	0.7457	0.8513	3.9091	<2.2E-16	4.8601	<2.2E-08
τ_2	1.4342	0.7184	4.2724	<2.2E-16	3.8268	<2.2E-16
τ_3	2.2410	0.0013	20.0261	0.0013	3.3830	0.0006
τ_4	1.2257	0.0460	1.3964	0.0005	1.8194	0.0432
τ_5	1.0552	0.0636	1.0631	0.0009	1.6046	0.1049
τ_6	0.9184	0.1209	0.8440	0.0069	0.8615	0.3268
τ_7	0.4586	0.4392	1.0510	0.0041	0.8615	0.3268
-2ll	241.1869		271.2702		257.5180	
AIC	273.1869		293.2702		275.5180	
Rank	1		3		2	

Table (1) shows that Log-ILOEWD is the best model with minimum values of the -2ll and AIC. At 5% level, the regression parameters τ_1 and τ_3 are determined to be significant for the Log-ILOEWD. Moreover, the parameter θ is also significant. The computed regression parameters indicated that drug-using people have shorter lifespans than non-drug-using people. Table (2) indicated that the Log-ILOEWD is the best fitted model. Also, the Cox-Snell residual plots for the HIV survival models (Log-ILOEWD, Log-TLOLLWD, and Log-WD) are shown in figures (3), (4), and (5) respectively. On the plots, the Y-axis shows the transformed residuals and the X-axis shows the residuals (differences between predicted and actual survival probabilities). Plots show that compared to the expected exponential curves for the log-TLOLLWD and log-WD, the expected exponential curve for the Log-ILOEWD model is more similar to the actual curve. Log-ILOEWD is therefore the optimal model.

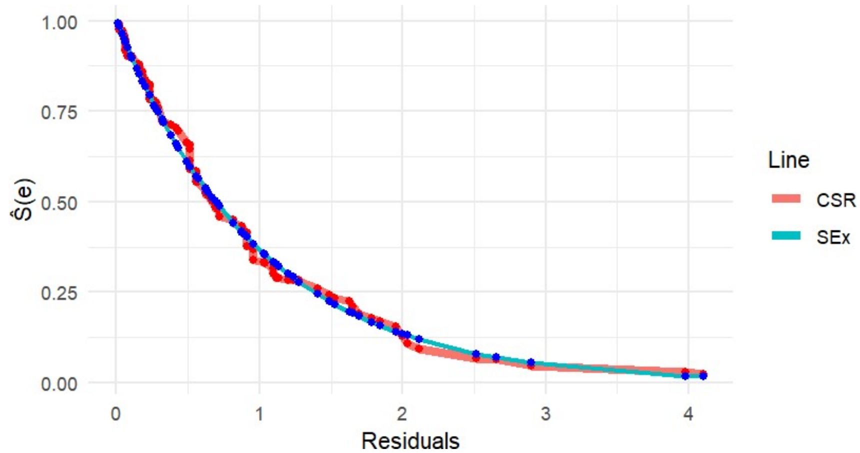

FIGURE 3. The Cox-Snell residual plot of the Log-ILOEWD for the fitted Hiv data

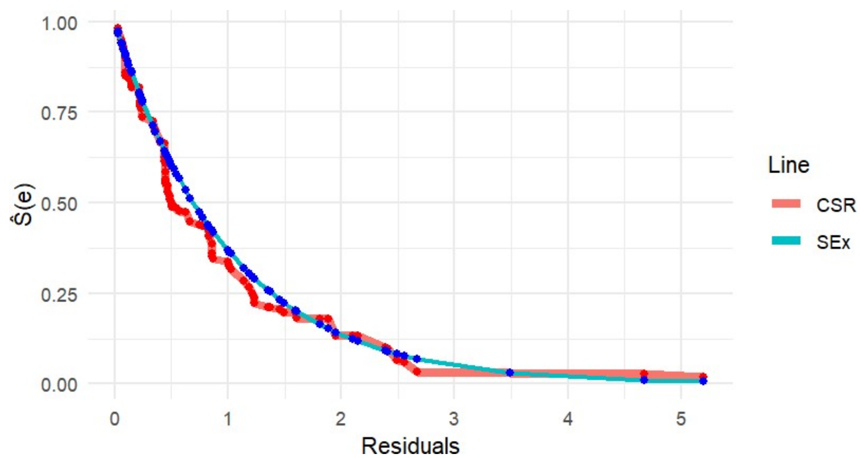

FIGURE 4. The Cox-Snell residual plot of the Log-WD for the fitted Hiv data

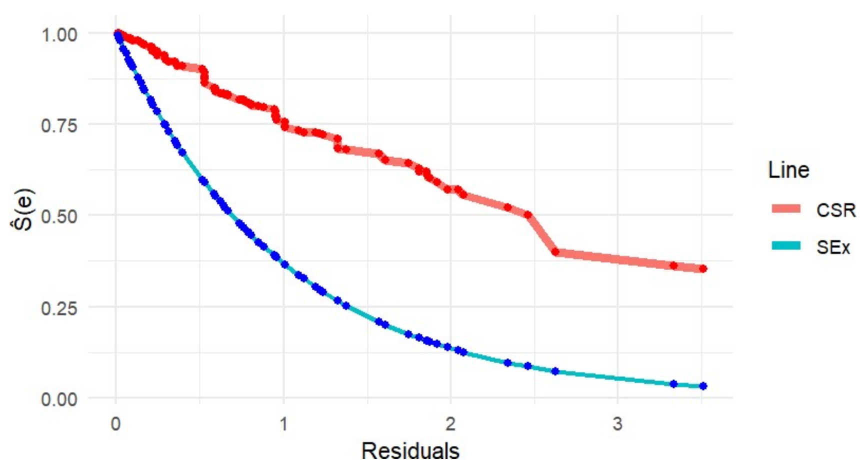

FIGURE 5. The Cox-Snell residual plot of the Log-TLOLLWD for the fitted Hiv data

3.2. **Applications of Kaplan-Meier Survival Probability.** A non-parametric statistic called the Kaplan-Meier estimator sometimes referred to as the product-limit estimator, is used in survival analysis to calculate the survival function given lifetime data. This technique, which was proposed by [17], is frequently used in medical research to calculate the percentage of patients that survive for a specific time following therapy. The survival function, which indicates the likelihood that a patient will survive past a specific time, can be estimated in an intuitive manner using the Kaplan-Meier estimator. This is essential to comprehending how well medicines work over time. Here, the Kaplan-Meier survival probability for the two datasets was presented.

Table 3. Kaplan-Meier Survival Probability for the Hiv Dataset

Times (in Month)	Number of Risk	Number of event	Survival probability	Standard Error	Lower 95% C.I	Upper 95% C.I
1	100	12	0.88	0.0325	0.819	0.946
2	83	5	0.827	0.0382	0.755	0.905
3	73	9	0.725	0.0462	0.64	0.822
4	61	2	0.701	0.0477	0.614	0.801
5	56	4	0.651	0.0504	0.56	0.758
6	49	2	0.625	0.0517	0.531	0.735
7	46	6	0.543	0.0546	0.446	0.662
8	39	2	0.515	0.0553	0.418	0.636
9	35	1	0.501	0.0556	0.403	0.622
10	32	1	0.485	0.056	0.387	0.608
11	28	1	0.468	0.0566	0.369	0.593
12	25	2	0.43	0.058	0.33	0.56
15	19	1	0.408	0.0592	0.307	0.542
56	5	1	0.326	0.0869	0.193	0.55

Table (3) presents the Kaplan-Meier survival probability for the Hiv Dataset, while Figures (6), (7), (8), and (9) shows the Hiv data Kaplan-Meier survival curve, fitted Log-ILOEWD, Log-TLOLLWD, and Log-WD to Hiv survival probability and Kaplan-Meier, respectively. From the table, a steeper decline in survival probability between months 3 and 7 can be noticed, followed by a more gradual decrease. This might suggest a higher risk of death during this earlier period.

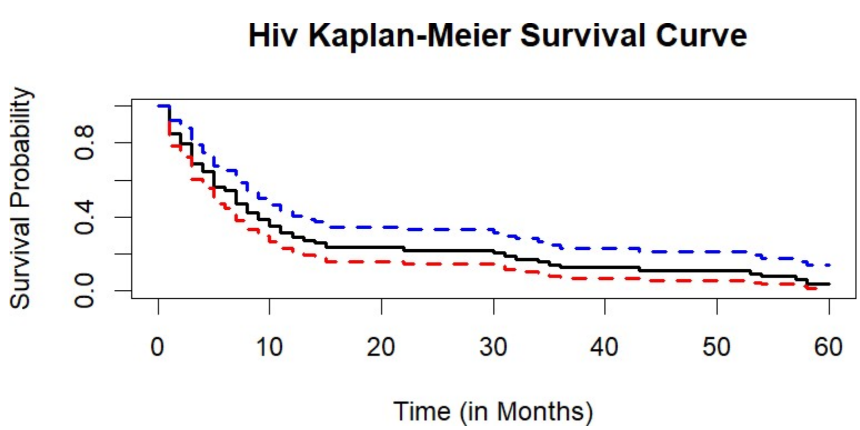

Figure 6. Hiv data Kaplan-Meier Survival Curve

Figure (6) is the graphical representation of Table (3). From the graph, one can notice that the survival probability generally decreases over time, as expected. This indicates that the probability of surviving without the event (death) decreases as the follow-up time increases.

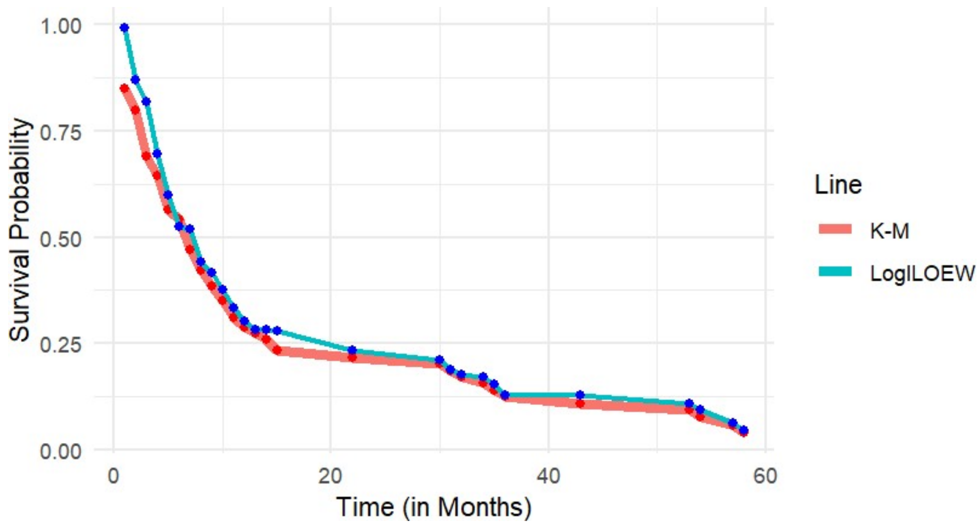

Figure 7. Hiv data Kaplan-Meier and Log-ILOEWD Survival Curve

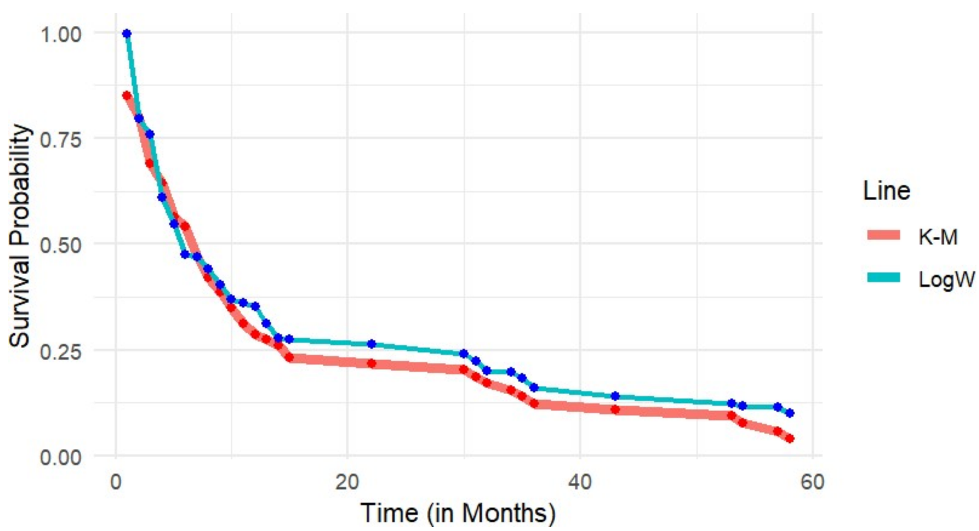

Figure 8. Hiv Kaplan-Meier and Log-WD Survival Curve

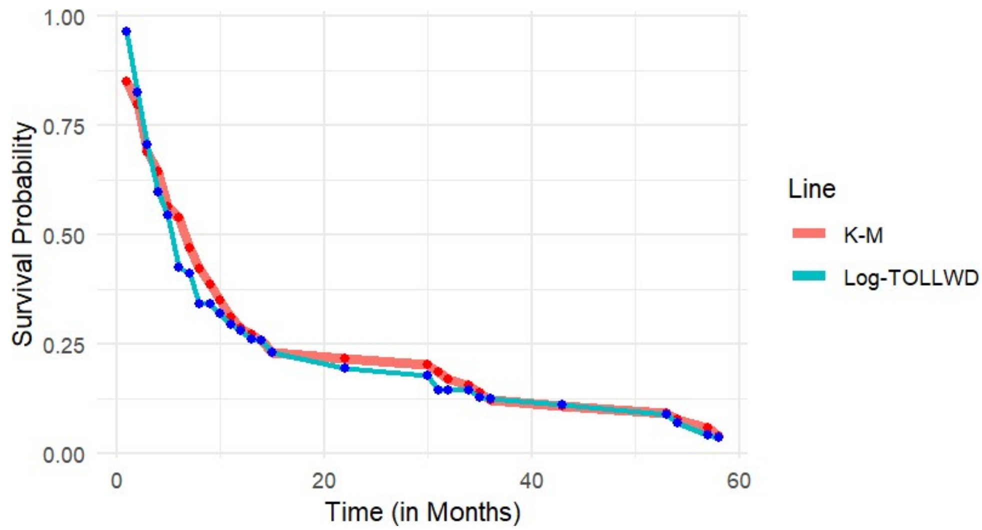

Figure 9. Hiv Kaplan-Meier and Log-TLOLLWD Survival Curve

Figures (7), (8), and (9) show the fitted Log- ILOEWD, Log-TLOLLWD, and Log-WD to HIV survival probability and Kaplan-Meier, respectively. Figure (7) indicated that Log-ILOEWD is the best-fitted model.

4. Conclusion

In this paper, a survival regression model called Log-ILOEWD were introduced and fitted to HIV data. The parameters of the Log-ILOEWD was estimated using the method of maximum likelihood. Cox-Snell residuals were presented as exploratory data analysis. Moreover, the Kaplan-Meier survival probability for the data was also considered. The proposed model appears to be the best when comparing with two other models, based on the HIV data. However, other datasets can be employed to fit Log-ILOEWD perhaps with other models.

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