



*Research article*

## Statistical modelling for Bladder cancer disease using the NLT-W distribution

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**Abstract:** In data science, it is frequent that new and sophisticated computational methods and tools are used to build predictive models to perform time to event data analysis. Such predictive models based on previously collected data from patients can support decision-making and prediction for the clinical data. Hence, this paper introduced a novel superior distribution, namely a new lifetime Weibull (NLT-W) distribution, using an efficient method to generate new distributions called the T-X method for generating new distributions. Parameter estimation has been done through maximum likelihood estimation (MLE) to show the significance of this proposed model over other competitive models. Comparison to two-parameter Weibull, Exponentiated Weibull (EW), and the and the Kumaraswamy Weibull (Ku-W) indicates that the proposed model could preform better to model various types of survival.

**Keywords:** parametric model; Weibull distribution; remission time; survival data analysis; information criteria

**Mathematics Subject Classification:** 62F09, 62G34

## 1. Introduction

Bladder cancer is ninth most diagnosed and widespread disease in medical science see Gurung [1]. Among various cancers around the globe 3% is the bladder cancer see Riester et al. [2]. Moreover, it is sixth and seventeenth most prevalent disease among men and women see Bray et al. [3]. There are lot of types and infection percentage as we can find that bladder-transitional cell carcinoma in the patients of bladder cancer are about 90%, bladder-squame cell carcinoma is greater than 5%, and bladder-squame cell carcinoma is less than 2% see Kim et al. [4], according to pathological histology. In the first diagnostic patient with bladder cancer, 70% to 85% has quasi bladder cancer and about 15% – 30% suffers from cancer of bladder muscle-invasive see Witjes et al. [5].

Exponential, Rayleigh, Weibull, log-normal, and gamma distributions were often utilised to model biomedical data for more details see Zhu et al. [6]. Medical science researchers have shown significant interest in the study of the survival of patients, particularly cancer patients see Aghamolaey et al. [7]. A fitting for parametric model often has importance to the survival study because it offers a succinct explanation of the behaviour of failure times and the danger feature which does not exist with the non-parametric models, see Wahed [8] for more details. Because the associated hazard rate does not behave constantly over time, the Weibull model is more robust than the Cox semi-parametric model, as mentioned in Zhu et al. [6].

Without a doubt, the parametric models mentioned above are extensively employed in survival research. Regrettably, these models still have certain shortcomings. The next part provides a succinct review of the drawbacks of earlier parametric models.

There are very common distributions that are used in modelling lifetime experiments. As an example of these distributions is the exponential which is very common used in life testing, also as we can say that there is another famous distribution which is the, Rayleigh, distributions and also the most efficient distribution in modelling lifetime data and engineering data which is called the Weibull distribution. These distributions are still the most usually applied parameter distributions, as we mentioned earlier. As it is known these distributions are not versatile enough to accommodate data types with high complexity. Here we speak about the issues of those well-known models. In nearly, all medical conditions, as an example each of the following the neck, bladder, breast cancer, and other types of cancer, their hazard rate is seen to have uni-modal or modified uni-modal form. The hazard rate of many cancer infections such as neck, cancer and also bladder cancer as well as breast cancer following to the surgery has been shown to be uni-modal. We refer to Efron [9] for neck cancer, Lee and Wang [10] for bladder cancer and Demicheli [11] for breast cancer, for the most accurate information. In the very early stages, The risk of cancer recurrence begins low and gradually increases after a final duration of time, before it hits a plateau until it decreases. Alot of examples for the unimodal form could be found by the hazard rates of certain new viruses infection, which rises from low levels in the early viruses until hitting a plateau and decreases, see Malki [12]. The exponential, Rayleigh and Weibull distributions may not be an acceptable choice for modelling such results.

We sometimes use the Kaplan-Meier product limit estimator, as it is considered as an efficient and versatile methods of modelling lifetime results. For more information and extensive reading about this method please see Miller [13], however this approach is also ineffective. Other methods with semi-parameters like proportional hazard modelling need to be taken into account as in Cox [14], which may not be possible. Meanwhile a host of parametric techniques to integrate a broad spectrum of

trends in survival data have been implemented. In the classical Weibull distribution, several of the parametric models suggested also provided a form parameter for additional potential danger forms. Among these, a tool used by Kalbfleisch [15] might be ineffective when dealing with incomplete or any type of censored data, because, it entails the calculating of heavy integrals such as gamma function integrals which is very hard to be evaluated even with advanced programs and statistical packages. Medical experts are continuing probing underneath the premises above for new distributions that model lifetime data with uni-modal hazard function. A concerted progress has been put and continues to expand rapidly in this regard; For more information and extra details we can refer to Ahmad et al. [16].

In this sense, researchers are still inspired to aim for new distribution families. As a result, we were interested in introducing a new novel and superior lifetime family that may be called (NLT-X). The suggested family of distributions is very versatile and ideally tailored to patients with bladder cancer.

The remain parts of this manuscript is ordered and outlined as we can find in: Section 2 introduces the steps and the suggested process to present the proposed model using the T-X family methodology. Section 3 defines a specific sub-model of the proposed family and provides the density, cumulative and hazard functions. Section 4 discusses the classical method of estimation of model parameters known as the MLE. Section 5 addresses the origins and essence of the bladder cancer results and the TTT plots for bladder cancer patients. Criteria for model selection and the values of information criteria that decide the superiority of the model against other competitive models are presented in Section 6. Section 7 demonstrates the significance of the new family in a real-life application of medical research compared to more generalized families of distributions namely EW distributions and Ku-W distribution that have the exponential, Weibull and Rayleigh distributions as special cases, using the Akaike information criteria (AIC) and Bayesian Information criteria (BIC). At last, Section 8 provides those final remarks and the concluded results from the paper associated with the major findings. For more elaboration on the deficiencies of these distributions, one can see that for :

The exponential distribution hazard function (hf) is given as follows

$$h(x; \gamma) = \gamma, \quad x > 0, \gamma > 0, \quad (1.1)$$

which is constant, it is obvious from Eq (1.1) that the exponential distribution can only model data for lifetimes utilizing constant hf. Also for Rayleigh distribution with

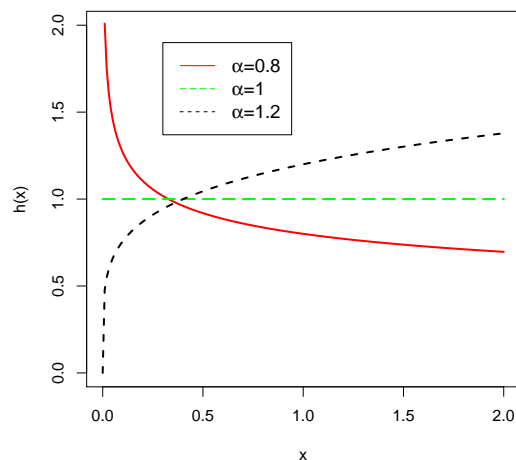
$$h(x; \gamma) = 2\gamma x, \quad x > 0, \gamma > 0. \quad (1.2)$$

We could see that Rayleigh distribution can only model real-life data with increasing hf.

Finally for the Weibull model which is one of the most common families that model lifetime data that give both exponential and Rayleigh distribution characteristics, with hf is defined by

$$h(x; \alpha, \gamma) = \alpha\gamma x^{\alpha-1}, \quad x > 0, \alpha > 0, \gamma > 0. \quad (1.3)$$

By referring to Eq (1.3), we can see immediately how useful the Weibull distribution is for modelling lifespan data, with hazard functions that are monotonically growing, constant, or decreasing, relying on the values assigned for shape parameter  $\alpha$ . This two-parameter model, however, is inapplicable when the hazard shape is unimodal or bathtub. By fixing the value of  $\gamma = 1$  and by using various values of  $\alpha$ , Figure 1 depicts the hazard function of the Weibull distribution.



**Figure 1.** The above plots describe the Weibull's distribution behaviour for the hazard rate function.

## 2. Development of the proposed model

Let us assume that we have a random variable noted as  $T$  and the corresponding probability density function (PDF) is  $v(t)$ , and the corresponding cumulative distribution function (CDF) is  $W[F(x)]$ , such that  $T \in [m, n]$  for  $-\infty \leq m < n < \infty$ . Then the CDF of the distribution must satisfy the following conditions:

- 1).  $W[F(x)] \in [m, n]$ ,
- 2).  $W[F(x)]$  must be able to be differentiated and is monotonous.
- 3).  $W[F(x)] \rightarrow m$  as  $x \rightarrow -\infty$  and  $W[F(x)] \rightarrow n$  as  $x \rightarrow \infty$ .

We can get the new CDF's form of the T-X family of distributions see Alzaatreh et al. [17], as follows

$$G(x) = \int_m^{W[F(x)]} v(t) dt, \quad x \in \mathbb{R}, \quad (2.1)$$

where,  $W[F(x)]$  encloses the above conditions. We will get the corresponding PDF to Eq (2.1)

$$g(x) = \left\{ \frac{\partial}{\partial x} W[F(x)] \right\} v\{W[F(x)]\}, \quad x \in \mathbb{R}.$$

Many authors prefer dealing with the T-X family methodology due to its effectiveness, as some new distribution groups have been presented in the literature see [16] for more reading about this method.

Now the proposed family is added. Let  $T \sim \text{exp}(1)$ , so the CDF have the form as below

$$V(t) = 1 - e^{-t}, \quad t \geq 0. \quad (2.2)$$

We can find the PDF for Eq (2.2) as below

$$v(t) = e^{-t}, \quad t > 0. \quad (2.3)$$

So if  $v(t)$  have the form as Eq (2.3) and assuming  $W[F(x)] = -\log\left(\frac{1-F(x)}{e^{F(x)}}\right)^\theta$  in Eq (2.1), we get the new CDF of the NLT-X family as follows:

$$G(x; \theta, \xi) = 1 - \left(\frac{1 - F(x)}{e^{F(x)}}\right)^\theta, \quad x \in \mathbb{R}. \quad (2.4)$$

We can find PDF for Eq (2.4) as below,

$$g(x; \theta, \xi) = \frac{\theta f(x) (1 - F(x; \xi))^{\theta-1}}{e^{\theta F(x)}} \{2 - F(x)\}, \quad x \in \mathbb{R}. \quad (2.5)$$

The following are the most important motives for the functional use of NLT-X distributions:

- A very easy way to improve current distributions.
- Improving the features and flexibility of current distributions.
- Introducing the expanded baseline distribution variant of closed distribution function form.
- In order to fit data in the healthcare along with other fields.
- One additional important reason for this technique is to add merely an additional parameter only and it can fits a lot of data that many other distribution even with more number of parameters can't fit.

### 3. Model description

The importance of this portion of the paper comes from that, we introduce a new lifetime Weibull distribution from the proposed family, which is considered as a special sub-model dubbed the (NLT-W). Let  $F(x; \xi)$  refers to Weibull distribution CDF that may have the form,  $F(x; \xi) = 1 - e^{-\gamma x^\alpha}$ ,  $x \geq 0$ ,  $\alpha, \gamma > 0$ , where  $\xi = (\alpha, \gamma)$ . The NLT-W model's CDF, PDF and hf, respectively are as below.

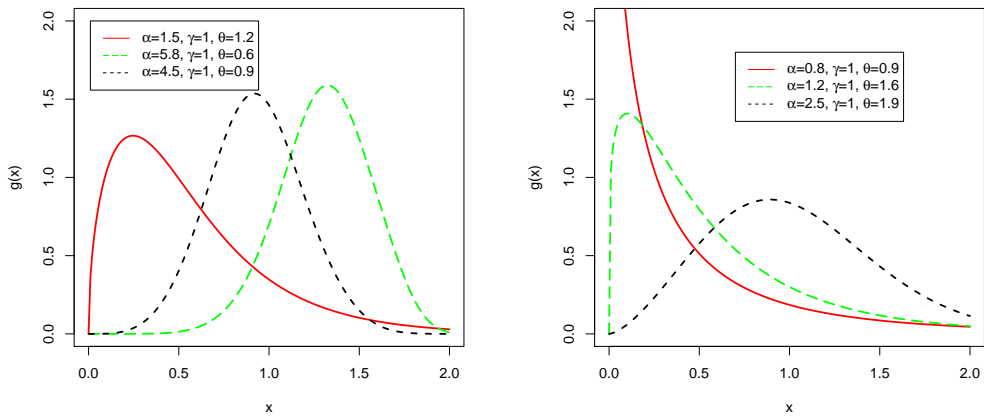
$$G(x; \alpha, \theta, \gamma) = 1 - \frac{e^{-\gamma \theta x^\alpha}}{e^{\theta(1-e^{-\gamma x^\alpha})}}, \quad x \geq 0, \alpha, \theta, \gamma > 0. \quad (3.1)$$

$$g(x; \alpha, \theta, \gamma) = \frac{\alpha \theta \gamma x^{\alpha-1} e^{-\gamma \theta x^\alpha} (1 + e^{-\gamma x^\alpha})}{e^{\theta(1-e^{-\gamma x^\alpha})}}, \quad x > 0, \quad (3.2)$$

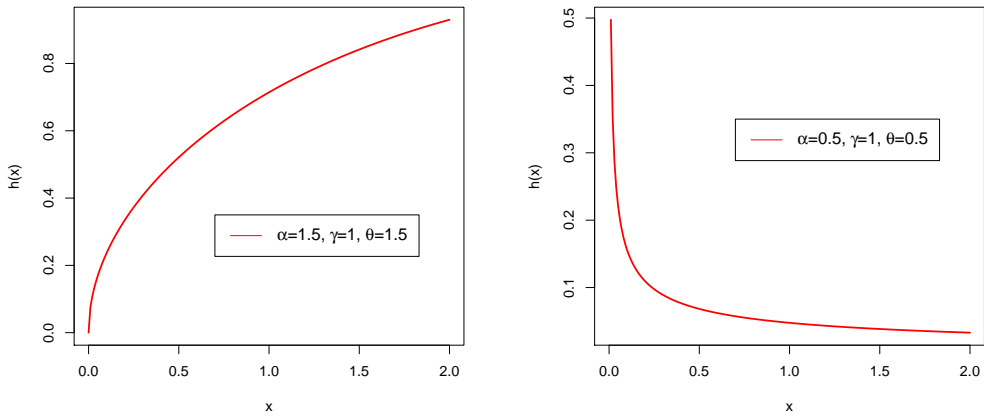
and

$$h(x; \alpha, \theta, \gamma) = \alpha \theta \gamma x^{\alpha-1} (1 + e^{-\gamma x^\alpha}), \quad x > 0. \quad (3.3)$$

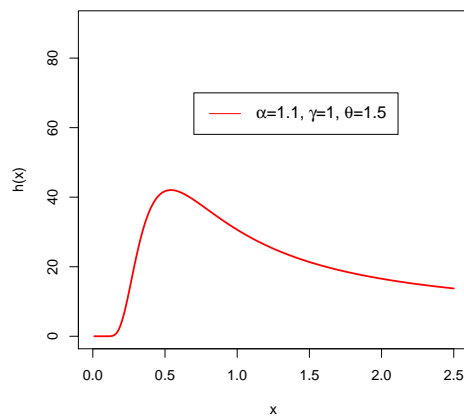
Graphs of the NLT-W distribution density function are seen in Figure 2 for various model parameter values. Beside this the graphs of the hf are displayed in Figures 3 and 4.



**Figure 2.** Different plots for NLT-W distribution density function.



**Figure 3.** The NLT-W distribution's increasing and decreasing hazard functions.



**Figure 4.** Uni-modal hazard function of the NLT-W distribution.

#### 4. Classical method of estimation (MLEs)

Here we analyse the NLT-W distribution's maximum likelihood estimators (MLEs). Now let us assume that  $x_1, x_2, \dots, x_n$ , represent a randomly generated sample. This one follows the distribution's PDF in Eq (3.2) with parameters  $\alpha, \theta$  and  $\gamma$ . By taking the log function for the likelihood function corresponding to Eq (3.2), we will consider the likelihood as  $L$ , so we will have the following form for it.

$$\begin{aligned} \log L(x_i, \alpha, \theta, \gamma) &= n \log \alpha + n \log \theta + n \log \gamma + (\alpha - 1) \sum_{i=1}^n \log x_i - \gamma \theta \sum_{i=1}^n x_i^\alpha \\ &\quad + \sum_{i=1}^n \log(1 + e^{-\gamma x_i^\alpha}) - \theta \sum_{i=1}^n (1 - e^{-\gamma x_i^\alpha}). \end{aligned} \quad (4.1)$$

We can find a solution for Eq (4.1) by maximizing it either explicitly or by finding a solution for nonlinear equations of the distribution model that we can get it from the differentiation of Eq (4.1). Here we obtained the MLEs by combining the fitness function in R with the "BFGS" technique. After that we differentiate Eq (4.1) to get the first derivative of parameters. Partial derivatives of Eq (4.1) are denoted by the three equations below:

$$\begin{aligned} \frac{\partial}{\partial \alpha} \log L(x_i, \alpha, \theta, \gamma) &= \frac{n}{\alpha} + \sum_{i=1}^n \log x_i - \gamma \theta \sum_{i=1}^n (\log x_i) x_i^\alpha - \gamma \theta \sum_{i=1}^n (\log x_i) x_i^\alpha e^{-\gamma x_i^\alpha} \\ &\quad - \gamma \sum_{i=1}^n \frac{((\log x_i) x_i^\alpha e^{-\gamma x_i^\alpha})}{1 + e^{-\gamma x_i^\alpha}}, \end{aligned} \quad (4.2)$$

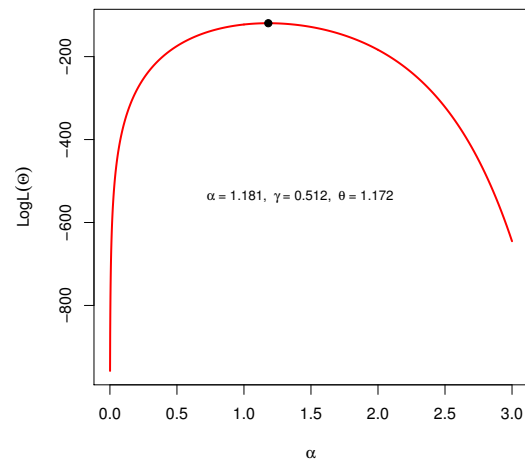
$$\frac{\partial}{\partial \theta} \log L(x_i, \alpha, \theta, \gamma) = \frac{n}{\theta} - \gamma \sum_{i=1}^n x_i^\alpha - \sum_{i=1}^n (1 - e^{-\gamma x_i^\alpha}), \quad (4.3)$$

and

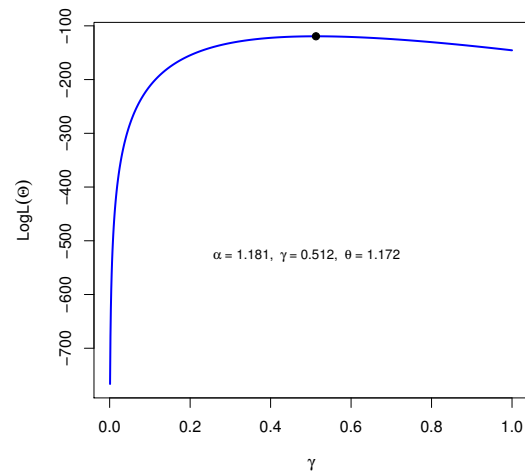
$$\frac{\partial}{\partial \gamma} \log L(x_i, \alpha, \theta, \gamma) = \frac{n}{\gamma} - \theta \sum_{i=1}^n x_i^\alpha - \theta \sum_{i=1}^n x_i^\alpha e^{-\gamma x_i^\alpha} - \sum_{i=0}^n \frac{x_i^\alpha}{(1 + e^{-\gamma x_i^\alpha})}. \quad (4.4)$$

Setting Eqs (4.2)–(4.4), equal to zero and numerically resolving, simultaneously generates MLEs of  $(\alpha, \theta, \gamma)$ . From Eqs (4.2)–(4.4), as we see the above equations can't solved mathematically but can be solved numerically. Therefore, computer software algorithm methods as an example the Newton-Raphson algorithms may be utilised to get a solution to the MLEs that is unique.

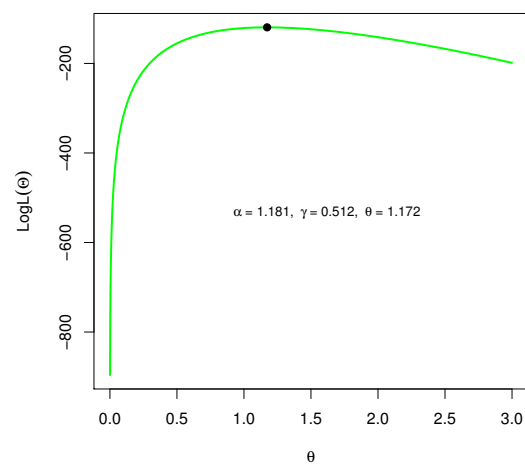
Among the most key aspects of the likelihood function for any distribution function is that the estimates of the parameters conducted from the MLEs is to be maximum in order to make sure of that concern. We make the plots for the log-likelihood function as we can see in Figures 5–7 and by studying the plots of the log-likelihood function and the data, we can see that Figures 5–7 confirm that the estimates conducted from the MLEs for the proposed model parameters are global maximum, not local maximum for all model's parameters.



**Figure 5.** The graph above is for log-likelihood as a function of  $\alpha$ .



**Figure 6.** The graph above is for log-likelihood as a function of  $\gamma$ .



**Figure 7.** The The graph above is log-likelihood as a function of  $\theta$ .



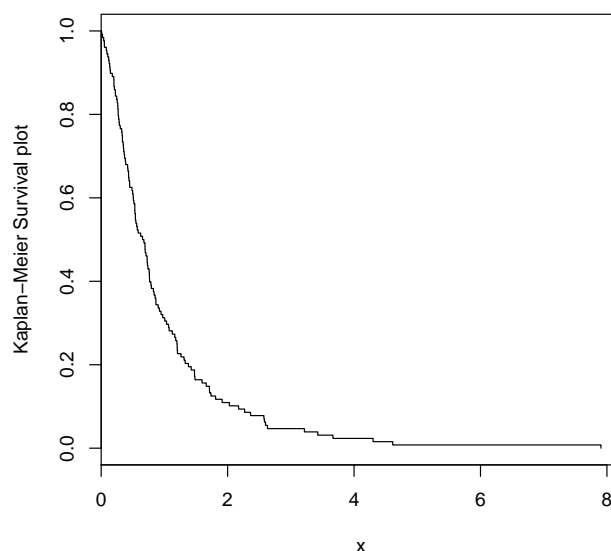
## 5. The real data analysis

In this part of the paper we apply a real data set. These data are used in this analysis. The data indicates recovery periods for 128 cancer patients (in months). These relapse periods are a subset of results from a bladder cancer analysis which are just meant to explain it. Table 1 describes the descriptive measures of the results:

**Table 1.** Descriptive statistics for the lifetime experiment used in the application.

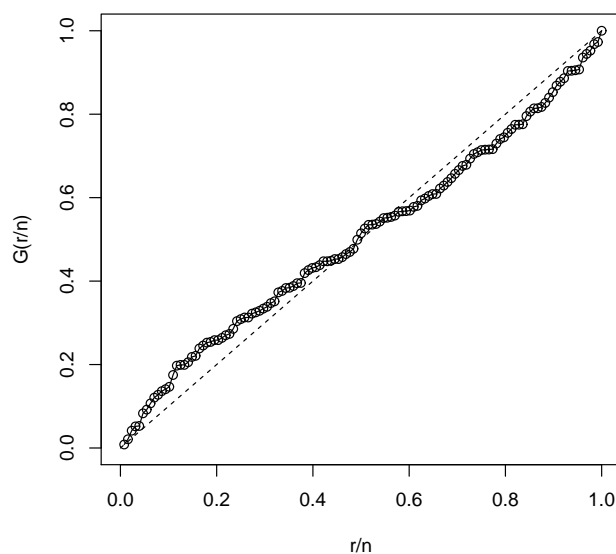
Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
0.0080	0.3348	0.6650	0.9535	1.1990	7.9050

As seen in Figure 8, the probability of survival falls as time goes. The total time test (TTT) graph is a critical graphical technique for determining whether or not the data may be fitted to a certain distribution. The TTT plot is used to examine the data's behaviour and determine if the hazard function is monotonic or non-monotonic. The hf can be constant or increasing, decreasing or even a u-shaped. The hf is constant when the TTT graph is straight diagonal, decrease when the TTT graph is convex and increase when it is concave, also can have u-shaped if the TTT graph is convex and then changed concave. And at last if the TTT graph is first concave and then changed to convex then the hf will have a uni-modal plot.



**Figure 8.** The above figure sketches the Kaplan Meier survival plot of the bladder cancer patients data.

For more elaborations and reading one can refer to Aarset et al. [18]. The graph of TTT plot is located in Figure 9, and by referring to the graph of it we can see that the data under consideration provides uni-modal shaped hf.



**Figure 9.** The TTT plot of the bladder cancer patients data.

## 6. Model selection criteria

The selection of models for specific data is one of the basic tasks of scientific study in choosing the best model that outperforms other candidates. Several statistical methods are used to determine the fitness of the distributions to any kind of data. These methods determine which distribution is the most fit candidate to the data under consideration. The most often utilised criteria are as follows: The AIC and BIC, the model with the fewest values may be considered as the most suitable fit for the real data set. These methods are determined with the following formulas:

- In order to compute the AIC we can use the following equation,

$$AIC = 2k - 2\ell.$$

and

- In order to compute the BIC we can use the following equation,

$$BIC = k \log(n) - 2\ell,$$

$\ell$  is defined as the log-likelihood function's value under the MLE,  $k$  refers to the suggested model's parameter count and  $n$  is the sample size. We take the AIC and BIC tests to demonstrate that the distribution presented is the most right fit for the data. For more reading about the AIC and BIC see [19–25].

## 7. Results and discussion

This section is devoted for finding the results of the data analysis for remission times of bladder cancer patients see [26, 27]. In order to find whether or not the used data fits the proposed model we

made a fitting test to the data and we deduced that the data fits this the proposed model, and also we made a comparison between the new distribution and the Weibull, EW and Kumaraswamy Weibull Ku-W models. Competitor distributions' CDFs are:

- Weibull distribution

$$G(x; \alpha, \gamma) = 1 - e^{-\gamma x^\alpha}, \quad x \geq 0, \quad a, \alpha, \gamma > 0.$$

- EW distribution

$$G(x; a, \alpha, \gamma) = \left(1 - e^{-\gamma x^\alpha}\right)^a, \quad x \geq 0, \quad a, \alpha, \gamma > 0.$$

- Ku-W distribution

$$G(x; \alpha, \gamma, a, b) = 1 - \left[1 - \left(1 - e^{-\gamma x^\alpha}\right)^a\right]^b, \quad x \geq 0, \quad \alpha, \gamma, a, b > 0.$$

Table 2 provides MLEs with standard errors of competing models for the bladder cancer results. Whereas AIC and BIC values are tabulated in Table 3. Regarding to 3, it is obvious that our proposed model the NLT-W model outperforms all its competitors, as we can see its AIC and BIC values are the smallest. we used `optim()` R-function with `method = "BFGS"`.

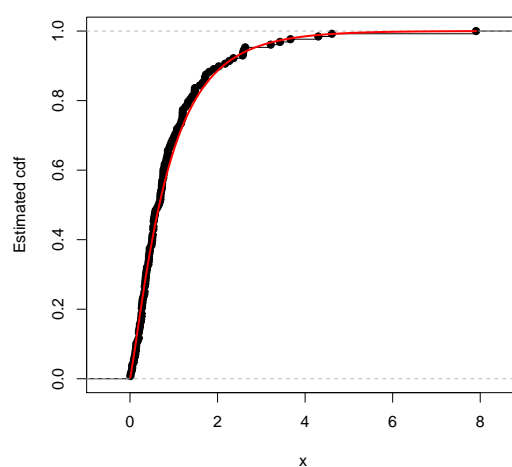
**Table 2.** This table contains the values of the estimates of the parameters using the MLEs and its standard error (in parentheses) of the competing models for the bladder cancer patients data.

Dist.	$\hat{\alpha}$	$\hat{\gamma}$	$\hat{\theta}$	$\hat{a}$	$\hat{b}$
NLT-W	1.181 (0.0863)	0.512 (0.3630)	1.172 (0.7412)		
Weibull	1.046 (0.0677)	1.029 (0.0955)			
EW	1.172 (0.7412)	0.512 (0.3630)		1.181 (0.0863)	
Ku-W	0.471 (0.5788)	1.368 (0.9657)		3.875 (5.8529)	2.894 (3.1197)

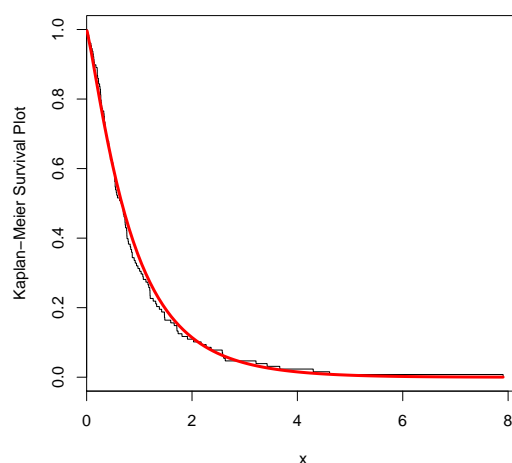
**Table 3.** The discrimination measures of the competing models for the bladder cancer patients data.

Dist.	AIC	BIC
NLT-W	244.919	253.475
Weibull	247.330	255.035
EW	246.159	254.715
Ku-W	245.146	254.550

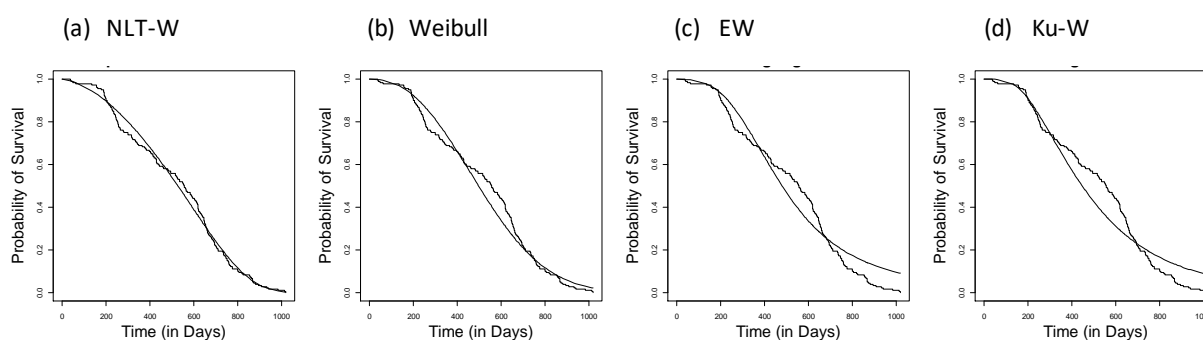
Figures 10 and 11 illustrate the empirical CDF and Kaplan Meier survival graphs for the NLT-W distribution, respectively. These plots demonstrate that the NLT-W model was very efficient and adequate in fitting the application data quite well. Similarly, non-parametric estimates are often used for assessing the quality of a particular parametric model. To check the adequacy of our proposed NLT-W model, we plot the survivor functions based on the competitive and our proposed parametric model and the Kaplan-Meier method, superimposed on the same graph. The Kaplan-Meier estimates as a function of time should be close to the survivor function if the parametric model performs better. Also the graph in Figure 12 assures our numerical results as we can see that the proposed outperforms all competitive distributions.



**Figure 10.** This figure discusses the fitting of the CDF to the real data set for the bladder cancer.



**Figure 11.** The Kaplan-Meier survival plot of the NLT-W distribution for the bladder cancer data.



**Figure 12.** Diagnostic plot based on data set for the bladder cancer, as we can see NLT-W outperforms all of its competitive models.

## 8. Concluding Remarks

In this paper we have presented new novel distribution namely the new NLT-W to avoid the deficiencies of the other competitive models. Such as two-parameter Weibull model only accommodate simple monotonous hazard shapes and unable to accommodate the unimodal type of hazard function, that is essential for bio-medical research. On the other hand, the latest Weibull concept extension have a uni-modal hazard rate plot. In order to present the proposed model superiority in fitting bio-medical lifetimes we made a comparison between the proposed model and the most famous competitors such as the extension of the Weibull and Kumaraswamy distributions which are known with their efficiencies in modelling lifetime data. We used them as competitive models for the remission periods of patient data on bladder cancer. We made a comparison between the above models and our new proposed model and it was the shown that the later model best fits the data. Based on the AIC and BIC, indicating that the NLT-W distribution is a very a excellent and viable choice for bladder cancer data modelling and other health science data.

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## Conflict of interest

The authors declare no conflict of interest.

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