A New Long-Term Survival Distribution

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Abstract

In this paper a new long-term survival distribution named long term weighted Lindley distribution is proposed. This new model allows us to fit data where a part of the population is not susceptible to the event of interest. This model can be used in clinical studies where a portion of the population can be cured during a treatment. An account of mathematical properties of the new distribution is presented such as moments and survival properties. The maximum likelihood estimators (MLEs) for the parameters are presented. A numerical simulation is carried out in order to verify the performance of the MLEs. Finally, an important application related to the leukemia free-survival times for transplant patients are discussed to illustrates our proposed distribution.

Keywords: Long-term survival distribution; new distribution; Survival model Weighted Lindley distribution

Introduction

Advances in computational methods and numerical simulations has made possible to incorporate efficient models that are capable to be used for describing real problems. Although generalizations of the standard exponential distribution are more common, many new distributions have been proposed based on the Lindley distribution, e.g., the generalized Lindley [1], extended Lindley [2], exponential Poisson Lindley [3] and Power Lindley [4] distribution, to list a few. Another important generalized was presented by Ghitany et al. [5], such distribution is known as weighted Lindley (WL) and its probability density function (p.d.f) is given by

\[ f(t; \phi, \lambda) = \frac{\phi + 1}{(\phi + 1) \Gamma(\phi + 1)} t^{\phi + 1} e^{-\lambda t}. \]  

for all t>0, \( \phi > 0 \) and \( \lambda > 0 \) and \( \Gamma(\phi) = \int_0^\infty e^{-x} x^{\phi - 1} dx \) is the gamma function. Many properties of the WL were discussed earlier. Ghitany et al. [5] presented basic properties of the p.d.f., hazard function and the mean residual life function. Mazucheli et al. [6] compared different estimation procedures of the parameters of the WL distribution using numerical simulations. Wang &Wang [7] presented bias-corrected MLEs expression in which outperforms the other estimation procedures. Ali [8] considered a Bayesian approach and also presented the Bonferroni and the Lorenz curves, many entropies and order statistics for this distribution.

Recently, Ramos & Louzada [9] presented a three parameters generalized weighted Lindley distribution based on mixture of generalized gamma distribution. Although this distribution provided much flexibility in the hazard function, it does not allow us to fit data where a part of the population is not susceptible to the event of interest. For instance, in clinical studies a portion of the population can be cured during a treatment. Models that consider such characteristic are usually called long term survival models. In this study, a new long-term survival distribution is proposed, hereafter we shall call it the long term weighted Lindley distribution or simplistically the LWL distribution. Some mathematical properties for the LWL distribution is provided such as moments, survival properties and hazard function. The maximum likelihood estimators for the parameters and its asymptotic properties are discussed. We performed a numerical simulation to examine the performance of the MLEs. Finally, our proposed methodology is illustrated in a real data set related to the leukemia free-survival times (in months) for the 50 allogeneic transplant patients.

The paper is organized as follows. Section 2 reviews the weighted Lindley distribution. Section 3 presents the new long-term survival distribution. Section 4 discusses the inferential procedure based on MLEs. Section 5 displays the results of a simulation study in other to verify the
performance of the MLEs. Section 6 illustrates the relevance of our proposed methodology in a real lifetime data. Finally, Section 7 summarizes the study.

**Weighted Lindley Distribution**

Finite mixture models have been received special attention in order to describe heterogeneous survival data. The chosen model can be expressed as a mixture model given by

\[ f(t|\lambda,\phi) = p f_1(t|\lambda,\phi) + (1-p) f_2(t|\lambda,\phi), \]

where \( p = \frac{\lambda}{\lambda + \phi} \) and \( f_j(t|\lambda,\phi), j=1,2 \) has p.d.f Gamma \((\phi+j-1,\lambda)\) distribution. Many mathematical results can be derived using the proposed structure. For instance, the mean and variance of the WL distribution can be easily computed by

\[ \mu = \frac{\phi(\lambda+\phi+1)}{\lambda(\lambda+\phi)} \quad \text{and} \quad \sigma^2 = \frac{\phi^2(\lambda+\phi)^2 - \phi^2}{\lambda^2(\lambda+\phi)^2}. \]

Using this property Ghitany et al. [5] derived the survival function of \( T \) given by

\[ S(t|\lambda,\phi) = \frac{(\lambda+\phi)(\lambda+\phi+1)t^{-\phi}}{\lambda(\lambda+\phi)t^{-\phi}}. \]

where \( \phi \) is the upper incomplete gamma. The hazard function of the WL distribution is given by

\[ h(t|\lambda,\phi) = \frac{(\lambda+\phi)\lambda t^{-\phi-1}}{(\lambda)(\lambda+\phi)t^{-\phi}}. \]

The authors proved that the hazard rate function (2) is bathtub (increasing) shaped if \( 0 < \phi < 1 \) (\( \phi \geq 1 \)) for all \( \lambda > 0 \). Figure 1 shows some examples from its shapes under different values of \( \phi \) and \( \lambda \).

**Cure Rate Model**

An important aspect to be considered is the presence of long-term survivors where a portion of the population may be not susceptible to the event of interest (Maller and Zhou, [10]; or Perdona & Louzada [11]). In this case, we assume that the population is divided in two groups: a not susceptible to the event with probability \( \pi \) and the other susceptible (in risk) to the event with probability \( 1-\pi \). The long-term survivor is expressed as

\[ S(t) = \pi + (1-\pi) S_0(t), \]

where \( \pi \in (0,1) \) and \( S_0(t) \) is the survival function related to the susceptible group. The obtained survival function (not conditional) is improper and its limit corresponds to the individual proportion cure. From the survival function one can easily derive the p.d.f. given by

\[ f(t) = \frac{\pi}{S_0(t)} f_0(t) - \frac{(1-\pi)}{S_0(t)} f_0(t), \]

where \( f_0(t) \) is the p.d.f. related to the susceptible group. Thus, from (3) and (4) the hazard function is given by

\[ h(t) = \frac{(1-\pi)f_0(t)}{x} + \frac{\pi}{S(t)} f_0(t). \]

Considering that \( f_0(t) \) follows a WL distribution, then the p.d.f. of the LWL distribution is given by

\[ f(t|\theta) = \frac{(1-\pi)f_0(t)\Gamma(\phi+1)}{\lambda^\phi \Gamma(\phi+\theta)} (\lambda+\phi)^{\phi+\theta} t^{-\phi-\theta}. \]

The survival function and the hazard function of the LWL distribution is given by

\[ S(t|\theta) = \prod_{i=1}^n\frac{(\lambda+\phi)(\lambda+\phi+1)t^{-\phi}}{\lambda(\lambda+\phi)t^{-\phi}} \]

\[ h(t|\theta) = \frac{(\phi+\theta)(\phi+\theta+1)t^{-\phi-\theta}}{(\lambda+\phi)(\phi+\theta+1)t^{-\phi-\theta}}. \]

The survival function and the hazard function of the LWL distribution is given by

\[ L_0(t;\theta) = \prod_{i=1}^n f(t_i|\theta), S(t_i;\theta)^{-\pi}. \]

Figure 2 displays some examples from the shapes of the p.d.f. and the survival function of the LWL distribution.

**Inference**

Let us consider the case where the failure time of the \( i^{th} \) individual may not be observed and is subject to right censoring. Additionally, the random censoring times \( C_{in} \) are independent of \( T_{in} \) (non censored time) and their distribution does not depend on the parameters. In a sample of size \( n \), the
data set is \( D = \{ t_i \delta_i \} \), where \( t_i = \min (T_i, C_i) \) and \( \delta_i = I (T_i \leq C_i) \). This random censoring scheme has as special case type I and II censoring mechanism. The likelihood function is given by

\[
L(\theta; D) = \prod_{i=1}^{n} f ( t_i ; \phi ) S ( t_i ; \theta )^{-\delta_i}.
\]

Let \( T_1, \ldots, T_n \) be a random sample of LWL distribution, the likelihood function considering data with random censoring is given by

\[
L ( \theta ; D ) = \frac { \prod_{i=1}^{n} \Gamma ( \phi ( t_i ) + 1 ) \Gamma ( \phi ( t_i ) + 1 - \delta_i ) } { \prod_{i=1}^{n} \Gamma ( \phi ( t_i ) + 1 ) \Gamma ( \phi ( t_i ) + 1 - \delta_i ) } = \left( \prod_{i=1}^{n} \Gamma ( \phi ( t_i ) + 1 ) \Gamma ( \phi ( t_i ) + 1 - \delta_i ) \right) \left( \prod_{i=1}^{n} \Gamma ( \phi ( t_i ) + 1 ) \Gamma ( \phi ( t_i ) + 1 - \delta_i ) \right)^{-1}.
\]

The log-likelihood function is given as

\[
\ell ( \theta ; D ) = \sum_{i=1}^{n} \sum_{j=1}^{2} \left[ \ln \Gamma ( \phi ( t_i ) + 1 ) - \Gamma ( \phi ( t_i ) + 1 - \delta_i ) \right].
\]

The maximum likelihood estimation method is widely used in statistical inference. It has many desirable properties, including consistency, asymptotic efficiency and in-variance. The maximum likelihood estimators are obtained from the maximization of the log-likelihood function (10). Here, we performed directly the maximization of log-likelihood function using existing statistical packages. Further information about the numerical procedures will be discussed in the next section.

Under mild conditions the obtained estimators are consistent and efficient with an asymptotically normal joint distribution given by

\[
\hat{\theta} - N_3 ( \theta, I^{-1} ( \theta ) ) \text{ as } n \to \infty,
\]

where \( I ( \theta ) \) is the Fisher information matrix, \( 3 \times 3 \) and \( l ( \theta ) \), is the Fisher information of \( \theta \) in \( i \) and \( j \) given by

\[
l_{ij} ( \theta ) = \sum_{i=1}^{n} \sum_{j=1}^{2} \left[ \frac { \partial^2 } { \partial \theta_i \partial \theta_j } \ln \Gamma ( \phi ( t_i ) + 1 ) \right].
\]

Since it is not possible to compute the Fisher information matrix, an alternative is to consider the observed information matrix, where the terms is given by

\[
H ( \theta ) = - \frac { \partial^2 } { \partial \theta_i \partial \theta_j } \ln \Gamma ( \phi ( t_i ) + 1 ) , i, j = 1, 2, 3.
\]

For large samples, approximated confidence intervals can be constructed for the individual parameters \( \theta_i \) \( i = 1, \ldots, 3 \), assuming a confidence coefficient \( 100 ( 1 - \gamma ) \)%s, the marginal distributions is given by

\[
\hat{\theta}_i - N ( \theta_i, H ( \theta ) ) \text{ form } \Gamma
\]

Simulation Study

In this section a simulation study is presented to compare the efficiency of the maximum likelihood method. This procedure is conducted by computing the mean relative errors (MRE) and the mean square errors (MSE) by

\[
\text{MRE}_i = \frac { 1 } { n } \sum_{j=1}^{n} \hat{\theta}_i - \theta_i, \quad \text{MSE}_i = \frac { 1 } { n } \sum_{j=1}^{n} ( \hat{\theta}_i - \theta_i )^2.
\]

where \( N \) is the number of estimates obtained through the MLE approach. The 95% coverage probabilities of the asymptotic confidence intervals are also evaluated. From our approach, it is expected that the MLEs returns the MREs closer to one with smaller RMSEs. Additionally, considering a 95% confidence level, the frequencies of intervals that covered the true values of \( \theta \) should be closer to 95%.

The simulation study is performed considering the values: \( \theta = (0.5, 2, 0.3), (0.5, 2, 0.6), (3, 2, 0.3), (3, 2, 0.6) \), \( n = 10,000 \) and \( n = (10, 25, 50, 100, 200) \). We have considered two scenarios where we obtained approximately 0.3 and 0.6 proportions of censored data, i.e., 30% and 60% of censorship. Since the censoring is random, we may observe different proportions of censoring for each data set. However, considering this approach we expected that the mean of the proportions of censored observations \( M_p \) return the nominal level assumed. It is worth mentioning that, the results of this simulation study were similar for different choices of \( \theta \). The maxLik package available [12] in R was considered to find the maximization of the log-likelihood function (10). This estimation procedure is well-behaved as we have not faced numerical problems, such as evidence of failure of convergence or end on multiple maxima. The programs can be obtained, upon request. Tables 1-4 display the MREs, MSEs, and the coverage probability with a 95% confidence level (C95%) of the estimates obtained through the MLE. From Tables 1-4, we observed that the estimates of \( \lambda, \varphi \) and \( \pi \) are asymptotically unbiased, i.e., the MREs tend to one when \( n \) increases and the MSEs decrease to zero for \( n \) large. Additionally, the coverage probabilities tend to 0.95, i.e., the MLEs has good coverage properties for the parameter estimators. Therefore, this estimation procedure can be used in practical applications as will be shown in the next section.

| \( \phi = 0.5 \) | \( \lambda = 2 \) | \( \pi = 0.3 \) |
|---|---|---|
| \( n \) | MRE | MSE | C95% | MRE | MSE | C95% | MRE | MSE | C95% | MRE | MSE | C95% |
| 10 | 1.518 | 0.34 | 0.981 | 1.698 | 7.777 | 0.988 | 1.011 | 0.018 | 0.87 | 0.306 |
| 25 | 1.158 | 0.049 | 0.962 | 1.228 | 1.306 | 0.963 | 1.001 | 0.008 | 0.943 | 0.303 |
| 50 | 1.07 | 0.015 | 0.958 | 1.093 | 0.372 | 0.955 | 1.002 | 0.004 | 0.938 | 0.303 |
| 100 | 1.032 | 0.006 | 0.955 | 1.041 | 0.144 | 0.956 | 1.0 | 0.002 | 0.943 | 0.302 |
| 200 | 1.014 | 0.003 | 0.953 | 1.02 | 0.063 | 0.955 | 1.001 | 0.001 | 0.945 | 0.303 |

Table 1: MREs, MSEs, C95% estimates for 10000 considering \( n = (10, 25, 50, 100, 200) \) and 30% of censorship.
Table 2: MREs, MSEs, C95% estimates for 10000 considering n = (10,25,50,100,200) and 60% of censorship.

| n   | φ = 0.5 MRE | MSE | C95% | λ = 2 MRE | MSE | C95% | π = 0.6 MRE | MSE | C95% | Mp |
|-----|-------------|-----|------|-----------|-----|------|-------------|-----|------|-----|
| 10  | 1.922       | 1.002 | 0.986 | 2.063     | 14.19 | 0.994 | 0.935       | 0.021 | 0.931 | 0.563 |
| 25  | 1.342       | 0.168 | 0.974 | 1.454     | 3.913 | 0.978 | 0.997       | 0.009 | 0.942 | 0.599 |
| 50  | 1.134       | 0.038 | 0.959 | 1.19      | 0.997 | 0.964 | 1.000       | 0.005 | 0.938 | 0.602 |
| 100 | 1.059       | 0.013 | 0.96  | 1.079     | 0.307 | 0.956 | 1.000       | 0.002 | 0.947 | 0.602 |
| 200 | 1.03        | 0.005 | 0.952 | 1.04      | 0.127 | 0.953 | 1.000       | 0.001 | 0.95  | 0.601 |

Table 3: MREs, MSEs, C95% estimates for 10000 considering n = (10,25,50,100,200) and 30% of censorship.

| n   | φ = 0.5 MRE | MSE | C95% | λ = 2 MRE | MSE | C95% | π = 0.3 MRE | MSE | C95% | Mp |
|-----|-------------|-----|------|-----------|-----|------|-------------|-----|------|-----|
| 10  | 1.49        | 6.235 | 0.987 | 1.571     | 2.86 | 0.987 | 0.977       | 0.017 | 0.872 | 0.299 |
| 25  | 1.295       | 2.53  | 0.985 | 1.319     | 1.008 | 0.987 | 0.998       | 0.008 | 0.947 | 0.305 |
| 50  | 1.165       | 1.033 | 0.974 | 1.178     | 0.386 | 0.978 | 1.000       | 0.004 | 0.933 | 0.306 |
| 100 | 1.079       | 0.369 | 0.97  | 1.086     | 0.132 | 0.981 | 1.000       | 0.002 | 0.946 | 0.306 |
| 200 | 1.037       | 0.158 | 0.964 | 1.04      | 0.055 | 0.974 | 0.999       | 0.001 | 0.95  | 0.306 |

Table 4: MREs, MSEs, C95% estimates for 10000 considering n = (10,25,50,100,200) and 60% of censorship.

| n   | φ = 0.5 MRE | MSE | C95% | λ = 2 MRE | MSE | C95% | π = 0.6 MRE | MSE | C95% | Mp |
|-----|-------------|-----|------|-----------|-----|------|-------------|-----|------|-----|
| 10  | 1.509       | 7.187 | 0.983 | 1.675     | 4.046 | 0.984 | 0.906       | 0.022 | 0.916 | 0.547 |
| 25  | 1.373       | 3.815 | 0.984 | 1.439     | 1.727 | 0.985 | 0.98        | 0.009 | 0.947 | 0.591 |
| 50  | 1.258       | 1.962 | 0.982 | 1.286     | 0.79  | 0.984 | 0.995       | 0.005 | 0.946 | 0.6   |
| 100 | 1.143       | 0.786 | 0.977 | 1.159     | 0.301 | 0.981 | 0.999       | 0.002 | 0.949 | 0.603 |
| 200 | 1.076       | 0.319 | 0.968 | 1.085     | 0.117 | 0.976 | 0.997       | 0.001 | 0.948 | 0.602 |

Cancer Data Application

In this section, we considered the data set presented by Ghitany & Al-Awadhi [13]. The data describes the leukemia free-survival times (in months) for the 50 allogeneic transplant patients. Table 5 shows the full data set (+ indicates censored observations).

Table 5: Leukemia free-survival times (in months) for the 50 allogeneic transplant patients (+ indicates censored observations).

|          | 0.03 | 0.493 | 0.855 | 1.184 | 1.1283 | 1.48 | 1.776 | 2.138 |
|----------|------|-------|-------|-------|--------|------|-------|-------|
| 2.5      | 2.763 | 2.993 | 3.324 |       | 3.421  | 4.178 | 4.441+ | 5.691 |
| 5.855+   | 6.941+ | 6.941+ | 7.993+ |       | 8.882  | 8.882 | 9.145+ | 11.48 |
| 11.513   | 12.105+ | 12.796 | 12.933+ |       | 13.849+ | 16.612+ | 17.138+ | 20.066 |
| 20.329+  | 22.368+ | 26.766+ | 28.717+ |       | 28.717+ | 32.928+ | 33.783+ | 34.221+ |
| 34.770+  | 39.539+ | 41.118+ | 45.033+ |       | 46.033+ | 46.941+ | 48.289+ | 57.041+ |
| 58.322+  | 60.625+ |       |       |       |       |       |       |       |

The main authors considered the Burr XII distribution to fit the data under random censoring scheme. Although the maximum likelihood estimators were presented successfully, the data clearly indicates the presence of a not susceptible group to the event of interest. Therefore, long-term survival distributions are more suitable to describe the proposed data set. Having discovered that, we considered the proposed LWL distribution to fit the data. However, firstly we would like to verify the behavior of the empirical hazard function. This can be achieved considering the TTT-plot (total time on test) proposed by Barlow and Campo [3]. The TTT-plot is obtained through the consecutive plot of the values \(r/n, G(r/n)\) where

\[G(r/n) = \frac{\sum_{i=1}^{r} \prod_{j=1}^{n-r} (1 - F(t_j))}{\sum_{i=1}^{r} \prod_{j=1}^{n-r} (1 - F(t_j))}\]

and \(t_i\) is the order statistics. In case of the curve is concave (convex), the hazard function is increasing (decreasing), on the other hand if it’s starts convex and then concave (concave and then convex) the hazard function has bathtub (inverse bathtub) shape.

Figure 3 presents the TTT-plot [14], the empirical survival function adjusted by the Kaplan-Meier estimator and the LWL survival distribution. Based on the TTT-plot there is an

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indication that the hazard function has bathtub failure rate. Comparing the empirical survival function with the adjusted by the LWL distribution we observed a goodness of the fit for our proposed model. The MLEs were obtained using the same procedure described in Section 5. Table 6 displays the MLEs, the standard error (SE) and the confidence intervals under 95% confidence level for $\varphi$, $\lambda$. Therefore, through our proposed methodology the data related to the leukemia free-survival times (in months) for the 50 allogeneic transplant patients can be described by the LWL distribution.

**Table 6:** MLE, SE, and confidence intervals under 95% confidence level for $\varphi$, $\lambda$ and $\pi$.

| $\theta$ | MLE   | SE     | CI95%($\theta$) |
|----------|-------|--------|-----------------|
| $\varphi$ | 0.6066 | 0.2142 | (0.1868;1.0263) |
| $\lambda$ | 0.2317 | 0.065  | (0.1041;0.3593) |
| $\pi$     | 0.5305 | 0.0749 | (0.3837;0.6773) |

**Discussion**

In this paper, we have proposed a new long-term survival distribution, the so called long term weighted Lindley distribution and its mathematical properties were studied. The maximum likelihood estimators of the parameters and their asymptotic properties were discussed. The simulation study showed that the MLEs present efficient estimators for three unknown parameters even for small sample sizes. The practical importance of the LWL distribution was reported using an important data set related to the leukemia free-survival times (in months) for the 50 allogeneic transplant patients.

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