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THE LOG-BURR XII REGRESSION MODEL FOR GROUPED SURVIVAL DATA

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The log-Burr XII regression model for grouped survival data is evaluated in the presence of many ties. The methodology for grouped survival data is based on life tables, where the times are grouped in k intervals, and we fit discrete lifetime regression models to the data. The model parameters are estimated by maximum likelihood and jackknife methods. To detect influential observations in the proposed model, diagnostic measures based on case deletion, so-called global influence, and influence measures based on small perturbations in the data or in the model, referred to as local influence, are used. In addition to these measures, the total local influence and influential estimates are also used. We conduct Monte Carlo simulation studies to assess the finite sample behavior of the maximum likelihood estimators of the proposed model for grouped survival. A real data set is analyzed using a regression model for grouped data.

Key Words: Burr XII distribution; Censored data; Grouped survival data; Regression model; Sensitivity analysis.

1. INTRODUCTION

Survival data are very common in clinical, chemical, and agronomic assays, among others. However, in practice, experiments are conducted so that all sample units are evaluated at the same time. These data are referred to as grouped survival data, which are a particular case of interval censoring and are characterized by an excessive number of ties. Grouped survival data have been studied by several authors and some more recent applications on grouped survival data can be found in the literature; for example, Thompson (1977) studied the treatment of grouped observation in life studies, Johnson and Koch (1978) proposed linear models analysis of competing risks for grouped survival times, Prentice and Gloeckler (1978) proposed a regression model for grouped survival data with application to

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breast cancer data, Allison (1982) discussed discrete-time methods for the analysis of event histories, Holford (1980) described analysis of rates and of survivorship using log-linear models, and Baker et al. (1993) presented regression analysis of grouped survival data considering informative censoring and double sampling. Further, Hertz-Piccioto and Rockhill (1997) studied the efficiency of approximation methods for tied survival times in Cox regression, Lam and Ip (2003) reported group-based modeling, Yu et al. (2004) proposed models with a cure fraction for grouped survival data under the parametric approach in the absence of explanatory variables, and Giolo et al. (2008) showed different basic methods to analyze grouped survival data.

In this article, we combine the works and propose a regression model for grouped data using the log-Burr XII distribution, "which is considered an extension of the work carried out by Silva et al. (2008)." In this work, the likelihood function has been modified to include failing individuals, at-risk individuals and censored individuals. We consider a classic analysis for regression models fitted to grouped survival data. The inferential part was carried out using the asymptotic distribution of the maximum likelihood estimators (MLEs), which may present difficult results to be justified when the sample size is small. As an alternative to the classic analysis, we explore the use of the jackknife estimator for the regression model. In such a case, it is not necessary to use the asymptotic distribution of the MLEs.

After modeling, it is important to check assumptions in the model and to conduct a thorough study in order to detect influential or extreme observations that can cause distortions in the results of the analysis. Numerous approaches have been proposed in the literature to detect influential or outlying observations. An efficient way to detect influential observations was proposed by Cook (1986). He suggested that more confidence can be put in a model that is relatively stable under small modifications. The best known perturbation schemes are based on case deletion introduced by Cook (1977), in which the effect of completely removing cases from the analysis is studied. This reasoning will form the basis of our global influence, introduced in section 3.1, and in doing so, it will be possible to determine which subjects might be influential for the analysis (see, e.g., Cook and Weisberg, 1982; Xie and Wei, 2007). Also, some authors have investigated the assessment of local influence in survival analysis models. For example, Carrasco et al. (2008) investigated local influence in log-modified Weibull regression models with censored data, Silva et al. (2008) adapted global and local influence methods in log-Burr XII regression models with censored data, and Ortega et al. (2009) investigated local influence in generalized log-gamma regression models with cure fraction. We develop a similar methodology to detect influential subjects in regression models for grouped survival data.

The article is organized as follows. In section 2, we suggest a log-Burr XII regression model for grouped survival data in addition to the maximum likelihood and jackknife estimators. We derive the score functions and the observed Fisher information matrix and propose an algorithm for estimating the regression coefficients and the remaining parameter. In section 3, we discuss the global and local influence methods. The likelihood displacement is used to assess the influence of the observations on the maximum likelihood estimator (MLE). Section 4 contains Monte Carlo simulations on the finite sample behavior of the MLEs and an analysis of a real data set. Some conclusions are given in section 5.

2. THE LOG-BURR XII MODEL FOR GROUPED SURVIVAL DATA

For modeling a lifetime T, Zimmer et al. (1998) considered the Burr XII distribution with parameters λ, γ, and φ, having a density function given by

$$f(t;\lambda,\varphi,\gamma)=\frac{\gamma\varphi}{\lambda^{\gamma}}t^{\gamma-1}\left[1+\left(\frac{t}{\lambda}\right)^{\gamma}\right]^{-(\varphi+1)},\quad t>0$$

Here, $\varphi>0$ and $\gamma>0$ are shape parameters and $\lambda>0$ is a scale parameter. The associated survival function is $S(t;\lambda,\varphi,\gamma)=\left[1+(t/\lambda)^{\gamma}\right]^{-\varphi}$ and then the failure rate function reduces to $h(t;\lambda,\varphi,\gamma)=\gamma\varphi(t/\lambda)^{\gamma-1}\{\lambda[1+(t/\lambda)^{\gamma}]\}^{-1}$. According to Zimmer et al. (1998), the failure rate function of this distribution can be decreased for $\gamma\leq 1$. If $\gamma>2$, the failure rate function reaches a maximum value and then decreases. The range of values for which it is increasing can be described by λ. If γ is between 1 and 2, the failure rate function can be essentially constant over much of the range of the distribution, which depends on λ values. The failure rate function has a unimodal shape property. Besides, $h(t)\to 0$ for $t\to 0$ or $t\to\infty$. When $1/\lambda=m$ and $\varphi=1$, the Burr XII distribution reduces to the log-logistic distribution.

In many practical applications, the lifetimes are affected by variables that are referred to as explanatory variables, such as cholesterol level, blood pressure, and many others. It is important to explore the relationship between lifetime and explanatory variables. An approach based on a regression model can be used. We consider a class of location-scale models, where the vector $\mathbf{x}=(x_1,x_2,\ldots,x_p)^T$ of explanatory variables is related to the response $Y=\log(T)$ through a regression structure. The density function of Y in terms of a re-parameterization $\gamma=1/\sigma$ and $\lambda=\exp(\mu)$ can be rewritten as

$$f(y;\varphi,\sigma,\mu)=\frac{\varphi}{\sigma}\exp\left(\frac{y-\mu}{\sigma}\right)\left[1+\exp\left(\frac{y-\mu}{\sigma}\right)\right]^{-(\varphi+1)},\quad -\infty<y<\infty \qquad (1)$$

where $\varphi>0$, $\sigma>0$ and $-\infty<\mu<\infty$. The distribution (1) is referred to as the log-Burr XII distribution. Its survival function is

$$S(y)=\left[1+\exp\left(\frac{y-\mu}{\sigma}\right)\right]^{-\varphi}$$

We can write the preceding distribution as a log-linear model,

$$Y=\mu+\sigma Z \qquad (2)$$

where the random variable Z has the density function (for $\varphi>0$)

$$f(z)=\varphi\exp(z)[1+\exp(z)]^{-(\varphi+1)},\quad -\infty<z<\infty \qquad (3)$$

The model (2) opens new possibilities for fitted many different types of data. For example, if Z has an extreme value (log-Weibull) distribution, then $f(z)$ (for $\sigma>0$) is given by

$$f(z)=\sigma^{-1}\exp[z-\exp(z)],\quad -\infty<z<\infty$$

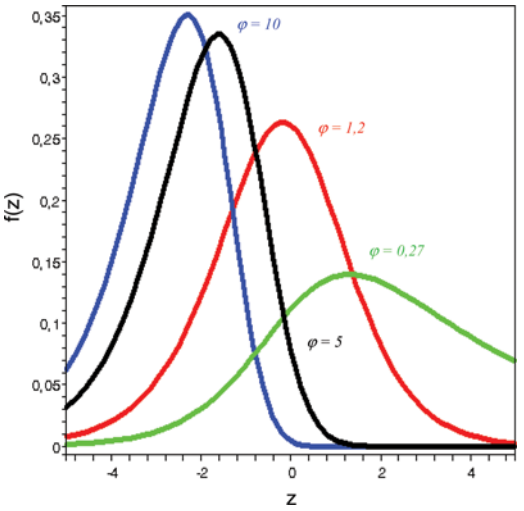


Figure 1 Plots of the density function (3) for selected parameters. (Color figure available online.)

In this article, we focus on the log-Burr XII model. Figure 1 shows that the log-Burr XII density function (3) is asymmetrical and that the parameter φ modifies the location and scale of the distribution.

The scale parameter μ_i depends on the explanatory vector $\mathbf{x}_i = (x_{i1}, \ldots, x_{ip})^T$ by $\mu_i = \mathbf{x}_i^T \boldsymbol{\beta}$. We consider a regression structure based on the log-Burr XII distribution (1) relating the response variable Y to the vector of explanatory variables $\mathbf{x}$, so that the model $Y \mid \mathbf{x}$ can be represented by

$$y_i = \mathbf{x}_i^T \boldsymbol{\beta} + \sigma z_i, \quad i = 1, \ldots, n \tag{4}$$

where $\boldsymbol{\beta} = (\beta_1, \ldots, \beta_p)^T$, $\sigma > 0$ and $\varphi > 0$ are unknown parameters and z_i follows the distribution (3). In this case, the survival function of $Y \mid \mathbf{x}$ is given by

$$S(y \mid \mathbf{x}) = \left[1 + \exp\left(\frac{y - \mathbf{x}^T \boldsymbol{\beta}}{\sigma}\right)\right]^{-\varphi}$$

For $\varphi = 1$, the log-logistic regression model is obtained as a special case. Applications of the log-Burr XII regression model in reliability and survival studies were investigated by Silva et al. (2008). On the other hand, if the observed data set, in addition to censoring, presents an excessive number of ties, the observed times are grouped in intervals.

The intervals are constructed such that the time axis is divided into k intervals defined by the cut points $a_1, \ldots, a_k$, so that the jth interval is denoted by $I_j = [a_{j-1}, a_j)$ for $j = 1, \ldots, k$, and the logarithms of the lifetimes y_i are grouped in k intervals. The survival functions of $\log(a_j) \mid \mathbf{x}$ and $\log(a_{j-1}) \mid \mathbf{x}$ are given by

$$S\big[\log(a_j) \mid \mathbf{x}\big] = \left\{1 + \exp\left[\frac{\log(a_j) - \mathbf{x}^T \boldsymbol{\beta}}{\sigma}\right]\right\}^{-\varphi} \quad \text{and}$$

$$S\big[\log(a_{j-1}) \mid \mathbf{x}\big] = \left\{1 + \exp\left[\frac{\log(a_{j-1}) - \mathbf{x}^T\boldsymbol{\beta}}{\sigma}\right]\right\}^{-\varphi} \tag{5}$$

respectively. This model will be referred to as the log-Burr XII regression model for grouped survival data. For $\varphi = 1$, the log-logistic regression model for grouped survival data is obtained as a special case. This model is an extension of the accelerated failure time model using the Burr XII distribution for grouped survival data.

2.1. Maximum Likelihood Estimation

Let $(y_1, \mathbf{x}_1), \ldots, (y_n, \mathbf{x}_n)$ be an observed sample of n independent observations, where y_i represents the failure-time logarithm or the censoring-time logarithm and $\mathbf{x}_i = (\mathbf{x}_{i1}, \ldots, \mathbf{x}_{ip})^T$ is the vector of explanatory variables associated with the ith individual. Consider that the times y_i are grouped in k intervals denoted by $I_j = \big[\log(a_{j-1}), \log(a_j)\big)$ for $j = 1, \ldots, k$. The likelihood function can be obtained by considering explanatory variables $\mathbf{x}_i$ such that the contribution from the ith individual in the jth interval is given by:

- If the ith individual failed in the jth interval, its contribution to the likelihood function is given by $1 - S\big[\log(a_j) \mid \mathbf{x}\big]/S\big[\log(a_{j-1}) \mid \mathbf{x}\big]$.
- If the ith individual survived (that is, it is at risk) in the jth interval, its contribution to the likelihood function is given by $S\big[\log(a_j) \mid \mathbf{x}\big]/S\big[\log(a_{j-1}) \mid \mathbf{x}\big]$.
- If the ith individual censored at time c_i in the jth interval, its contribution to the likelihood function is given by $S\big[\log(c_i) \mid \mathbf{x}\big]/S\big[\log(a_{j-1}) \mid \mathbf{x}\big]$, for which $\log(c_i) \in I_j$.

Thus, the likelihood function for the parameter vector $\boldsymbol{\theta} = (\varphi, \sigma, \boldsymbol{\beta}^T)^T$ reduces to

$$L(\boldsymbol{\theta}) = \prod_{j=1}^{k} \left\{ \prod_{i \in F_j} \Big[1 - S\big[\log(a_j) \mid \mathbf{x}\big]/S\big[\log(a_{j-1}) \mid \mathbf{x}\big]\Big] \times \prod_{i \in R_j} \Big[S\big[\log(a_j) \mid \mathbf{x}\big]/S\big[\log(a_{j-1}) \mid \mathbf{x}\big]\Big] \prod_{i \in C_j} \Big[S_i\big[\log(c_i)\big]/S_i\big[\log(a_{j-1})\big]\Big] \right\} \tag{6}$$

Here, F_j denotes the set of failing individuals in the jth interval, R_j denotes the number of individuals at risk in the jth interval, and C_j denotes the censored individuals in the jth interval. In practice, Eq. (6) is too complicated to be used, since the times $\log(c_i)$ are unknown if the data are grouped in intervals. In this case, an alternative is to associate a uniform distribution in the interval $\big[\log(a_{j-1}), \log(a_j)\big)$ to log-censoring time $\log(c_i)$ and consider the failing rate as a constant in the jth interval (see, e.g., Thompson, 1977). The contribution of the censored individuals in the jth interval can be expressed as

$$\frac{S\big[\log(c_i)\big]}{S\big[\log(a_{j-1})\big]} = \left\{\frac{S\big[\log(a_j)\big]}{S\big[\log(a_{j-1})\big]}\right\}^{1/2} \tag{7}$$

According to Colosimo and Giolo (2006), the interpretation of the quantity 1/2 is that observations for which censoring occurred in the interval I_j are treated as if they were at risk during half of the interval under consideration. Inserting Eq. (7) in Eq. (6) and considering the survival function (5), the log-likelihood function for the parameter vector $\boldsymbol{\theta} = (\varphi, \sigma, \boldsymbol{\beta}^T)^T$ becomes

$$l(\boldsymbol{\theta}) = \sum_{j=1}^{k} \left\{ \sum_{i \in F_j} \log\left\{1 - \left[\frac{1+\exp(z_{ij})}{1+\exp(z_{ij-1})}\right]^{-\varphi}\right\} - \varphi \sum_{i \in R_j} \log\left[\frac{1+\exp(z_{ij})}{1+\exp(z_{ij-1})}\right] - \frac{\varphi}{2} \sum_{i \in C_j} \log\left[\frac{1+\exp(z_{ij})}{1+\exp(z_{ij-1})}\right]\right\} \tag{8}$$

where $z_{ij} = [\log(a_j) - \mathbf{x}_i^T\boldsymbol{\beta}]/\sigma$ and $z_{ij-1} = [\log(a_{j-1}) - \mathbf{x}_i^T\boldsymbol{\beta}]/\sigma$.

The MLE $\hat{\boldsymbol{\theta}}$ of the model parameters in $\boldsymbol{\theta} = (\varphi, \sigma, \boldsymbol{\beta}^T)^T$ can be obtained by maximizing the log-likelihood function (8). We use the matrix programming language Ox (MaxBFGS function) (see Doornik, 2006) to compute the estimate $\hat{\boldsymbol{\theta}}$. Under conditions that are fulfilled for the parameter vector $\boldsymbol{\theta}$ in the interior of the parameter space but not on the boundary, the asymptotic distribution of $\sqrt{n}(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta})$ is multivariate normal $N_{p+2}(0, K(\boldsymbol{\theta})^{-1})$, where $K(\boldsymbol{\theta})$ is the information matrix. The asymptotic covariance matrix $K(\boldsymbol{\theta})^{-1}$ of $\hat{\boldsymbol{\theta}}$ can be approximated by the $(p+2) \times (p+2)$ inverse of the observed information matrix $-\ddot{\mathbf{L}}_{\theta\theta}$. Thus, the asymptotic inference for the parameter vector $\boldsymbol{\theta}$ can be based on the normal approximation $N_{p+2}(0, -\ddot{\mathbf{L}}_{\theta\theta}^{-1})$ for $\hat{\boldsymbol{\theta}}$. The elements of the observed information matrix are

$$\ddot{\mathbf{L}}_{\theta\theta} = \begin{pmatrix} \ddot{\mathbf{L}}_{\varphi\varphi} & \ddot{\mathbf{L}}_{\varphi\sigma} & \ddot{\mathbf{L}}_{\varphi\beta_m} \\ . & \ddot{\mathbf{L}}_{\sigma\sigma} & \ddot{\mathbf{L}}_{\sigma\beta_m} \\ . & . & \ddot{\mathbf{L}}_{\beta_m\beta_s} \end{pmatrix}$$

where $m, s = 1, \ldots, p$, and the submatrices are given in the appendix.

The approximate multivariate normal $N_{p+2}(0, -\ddot{\mathbf{L}}_{\theta\theta}^{-1})$ distribution can be used to construct confidence regions for some parameters in $\boldsymbol{\theta}$ and for the hazard and survival functions. In fact, a $100(1-\alpha)\%$ asymptotic confidence interval for each parameter θ_v is given by

$$ACI_v = \left(\hat{\theta}_v - z_{\alpha/2}\sqrt{-\widehat{\ddot{L}}^{v,v}}, \hat{\theta}_v + z_{\alpha/2}\sqrt{-\widehat{\ddot{L}}^{v,v}}\right)$$

where $-\widehat{\ddot{L}}^{v,v}$ denotes the vth diagonal element of the inverse of the estimated observed information matrix $-\widehat{\ddot{\mathbf{L}}}_{\theta\theta}^{-1}$ and $z_{\alpha/2}$ is the $(1-\alpha/2)$th quantile of the standard normal distribution, for $v = 1, \ldots, p+2$. We now investigate the use of the log-logistic regression model for grouped survival data, which is a simpler model than the proposed one. Since the log-Burr XII and log-logistic regression models for grouped survival data are embedded, the likelihood ratio (LR) test can be used to discriminate between such models. In this case, the hypotheses are H_0: $\varphi = 1$ versus H_1: $\varphi \neq 1$. The LR statistic is given by $w = 2\{l(\hat{\boldsymbol{\theta}}) - l(\hat{\boldsymbol{\theta}}_0)\}$, where $\hat{\boldsymbol{\theta}}_0$ is the MLE

of $\boldsymbol{\theta}$ under H_0. The null hypothesis is rejected if $w > \chi^2_{1-\alpha}(1)$, where $\chi^2_{1-\alpha}(1)$ is the quantile of the chi-squared distribution with one degree of freedom.

2.2. Jackknife Estimator

The idea of jackknifing can be thought of as a method for converting the problem of estimating any population parameter into the problem of estimating a population mean. An important work for implementing the jackknife method is given by Lipstiz et al. (1990), who suggested an alternative robust estimator of the covariance matrix based on the jackknife for analyzing data from repeated measurement studies. Here, we use this method as an alternative to estimate $\boldsymbol{\theta}$.

Suppose that $Y_1, \ldots, Y_n$ is a random sample of n values. Let $\hat{\boldsymbol{\theta}}$ be the parameter vector estimator of $\boldsymbol{\theta}$ based on all n observations and $\hat{\boldsymbol{\theta}}_{-l}$, for $l = 1, \ldots, n$, be the estimator of $\boldsymbol{\theta}$ obtained by eliminating the lth observation. Thus, the pseudo-values are calculated by

$$\hat{\boldsymbol{\theta}}^*_l = n\hat{\boldsymbol{\theta}} - (n-1)\hat{\boldsymbol{\theta}}_{-l}, \quad l = 1, \ldots, n$$

Therefore, the jackknife estimator of $\boldsymbol{\theta}$ is given by

$$\hat{\boldsymbol{\theta}}^* = \frac{\sum_{l=1}^{n} \hat{\boldsymbol{\theta}}^*_l}{n}$$

Manly (1997) studied the pseudo-values as a random sample of independent estimates and then suggested that a $100(1-\alpha)\%$ confidence interval for $\boldsymbol{\theta}$ is given by $\hat{\boldsymbol{\theta}}^* \pm t_{\alpha/2,n-1} s/\sqrt{n}$, where $t_{\alpha/2,n-1}$ is the upper $(1-\alpha/2)$ point of the t distribution with $(n-1)$ degrees of freedom, which has the effect of removing the bias term of order $1/n$. The jackknife estimate calculations for the log-Burr XII regression model for survival grouped data are performed for $\boldsymbol{\theta} = (\varphi, \sigma, \boldsymbol{\beta}^T)^T$ and confidence intervals are calculated separately for each parameter.

3. SENSITIVITY ANALYSIS

3.1. Global Influence

The first tool to perform sensitivity analysis, as previously stated, is by means of global influence by starting from the case deletion (see Cook, 1977). Case deletion is a common approach to study the effect of dropping the ith case from the data set. Case deletion for model (4) is given by

$$Y_l = \mathbf{x}_l^T \boldsymbol{\beta} + \sigma z_l, \quad l = 1, \ldots, n, \;\; l \neq i \tag{9}$$

Accordingly, a quantity with subscript "(i)" means the original quantity with the ith observation deleted. For model (9), the log-likelihood function is denoted by $l_{(i)}(\boldsymbol{\theta})$.

Let $\hat{\boldsymbol{\theta}}_{(i)} = (\hat{\varphi}_{(i)}, \hat{\sigma}_{(i)}, \hat{\boldsymbol{\beta}}^T_{(i)})^T$ be the MLE of $\boldsymbol{\theta}$ obtained by maximizing $l_{(i)}(\boldsymbol{\theta})$. To assess the influence of the ith observation on the MLE $\hat{\boldsymbol{\theta}} = (\hat{\varphi}, \hat{\sigma}, \hat{\boldsymbol{\beta}}^T)^T$, the basic idea is to compare the difference between $\hat{\boldsymbol{\theta}}_{(i)}$ and $\hat{\boldsymbol{\theta}}$. If deletion of an observation seriously influences the estimates, more attention should be paid to that observation.

Hence, if $\hat{\boldsymbol{\theta}}_{(i)}$ is far away from $\hat{\boldsymbol{\theta}}$, then the case is regarded as an influential observation. A first measure of global influence is defined as the standardized norm of $\hat{\boldsymbol{\theta}}_{(i)} - \hat{\boldsymbol{\theta}}$ (generalized Cook distance)

$$GD_i(\boldsymbol{\theta}) = (\hat{\boldsymbol{\theta}}_{(i)} - \hat{\boldsymbol{\theta}})^T \{ -\ddot{\mathbf{L}}_{\theta\theta} \} (\hat{\boldsymbol{\theta}}_{(i)} - \hat{\boldsymbol{\theta}})$$

Another alternative is to assess values $GD_i(\varphi)$, $GD_i(\sigma)$, and $GD_i(\boldsymbol{\beta})$, which reveal the impact of the ith observation on the estimates of φ, σ, and $\boldsymbol{\beta}$, respectively. Another popular measure of the difference between $\hat{\boldsymbol{\theta}}_{(i)}$ and $\hat{\boldsymbol{\theta}}$ is the likelihood displacement,

$$LD_i(\boldsymbol{\theta}) = 2\{ l(\hat{\boldsymbol{\theta}}) - l(\hat{\boldsymbol{\theta}}_{(i)}) \}$$

3.2. Local Influence

Another approach is suggested by Cook (1986), giving weights to the observations instead of removing them. Local influence calculation can be carried out for model (4). If likelihood displacement $LD(\boldsymbol{\omega}) = 2\{l(\hat{\boldsymbol{\theta}}) - l(\hat{\boldsymbol{\theta}}_{\boldsymbol{\omega}})\}$ is used, where $\hat{\boldsymbol{\theta}}_{\boldsymbol{\omega}}$ denotes the MLE under the perturbed model, the normal curvature for $\boldsymbol{\theta}$ at direction $\mathbf{d}$ ($\|\mathbf{d}\| = 1$) is given by $C_{\mathbf{d}}(\boldsymbol{\theta}) = 2|\mathbf{d}^T \boldsymbol{\Delta}^T \ddot{\mathbf{L}}_{\theta\theta}^{-1} \boldsymbol{\Delta} \mathbf{d}|$, where $\boldsymbol{\Delta}$ is a $(p+2) \times n$ matrix that depends on the perturbation scheme, whose elements are given by $\Delta_{vi} = \partial^2 l(\boldsymbol{\theta} \mid \boldsymbol{\omega}) / \partial\theta_v \partial\omega_i$, for $i = 1, \ldots, n$ and $v = 1, \ldots, p+2$, evaluated at $\hat{\boldsymbol{\theta}}$ and $\boldsymbol{\omega}_0$, where $\boldsymbol{\omega}_0$ is the no perturbation vector. For the log-Burr XII regression model, the elements of $\ddot{\mathbf{L}}(\boldsymbol{\theta})$ are given in the appendix. We can also calculate normal curvatures $C_{\mathbf{d}}(\boldsymbol{\theta})$ to perform various index plots, for instance, the index plot of $\mathbf{d}_{max}$, the eigenvector corresponding to $C_{\mathbf{d}_{max}}$, the largest eigenvalue of the matrix $\mathbf{B} = -\boldsymbol{\Delta}^T \ddot{\mathbf{L}}_{\theta\theta}^{-1} \boldsymbol{\Delta}$, and the index plots of $C_{\mathbf{d}_i}(\boldsymbol{\theta})$, so-called the total local influence (see, e.g., Lesaffre and Verbeke, 1998), where $\mathbf{d}_i$ represents an $n \times 1$ vector of zeros with one in the ith position. Thus, the curvature at direction $\mathbf{d}_i$ takes the form $C_i = 2|\boldsymbol{\Delta}_i^T \ddot{\mathbf{L}}_{\theta\theta}^{-1} \boldsymbol{\Delta}_i|$, where $\boldsymbol{\Delta}_i^T$ denotes the ith row of $\boldsymbol{\Delta}$. It is usual to point out those cases such that $C_i \geq 2\overline{C}$, where $\overline{C} = \frac{1}{n} \sum_{i=1}^{n} C_i$.

Next, we calculate, under model (4), the log-likelihood function (8) for two perturbation schemes and the matrix

$$\boldsymbol{\Delta} = (\boldsymbol{\Delta}_{vi})_{(p+2)\times n} = \left(\frac{\partial^2 l(\boldsymbol{\theta} \mid \boldsymbol{\omega})}{\partial\theta_i \partial\boldsymbol{\omega}_v} \right)_{(p+2)\times n}, \quad v = 1, \ldots, p+2 \text{ and } i = 1, \ldots, n.$$

We define the vector of weights $\boldsymbol{\omega} = (\omega_1, \ldots, \omega_n)^T$.

Case-Weight Perturbation. In this case, the log-likelihood function becomes

$$l(\boldsymbol{\theta} \mid \boldsymbol{\omega}) = \sum_{j=1}^{k} \left\{ \sum_{i \in F_j} \omega_i \log(1 - b_{ij}^{-\varphi}) - \varphi \sum_{i \in R_j} \omega_i \log(b_{ij}) - \frac{\varphi}{2} \sum_{i \in C_j} \omega_i \log(b_{ij}) \right\}$$

where $b_{ij} = [1 + \exp(z_{ij})]/[1 + \exp(z_{ij-1})]$, $0 \leq \omega_i \leq 1$, and $\boldsymbol{\omega}_0 = (1, \ldots, 1)^T$. We omit the matrix $\boldsymbol{\Delta} = (\boldsymbol{\Delta}_{\varphi}^T, \boldsymbol{\Delta}_{\sigma}^T, \boldsymbol{\Delta}_{\boldsymbol{\beta}}^T)^T$ in this work.

Explanatory Variable Perturbation. Here we consider an additive perturbation on a particular continuous explanatory variable, say x_t, by making $x_{it\omega} = x_{it} + \omega_i S_x$, where S_x is a scaled factor and $\omega_i \in \mathbf{R}$. This perturbation scheme leads to the log-likelihood function

$$l(\boldsymbol{\theta}) = \sum_{j=1}^{k} \left\{ \sum_{i \in F_j} \log(1 - b_{ij}^{*-\varphi}) - \varphi \sum_{i \in R_j} \log(b_{ij}^{*}) - \frac{\varphi}{2} \sum_{i \in C_j} \log(b_{ij}^{*}) \right\}$$

where $b_{ij}^{*} = \left[1 + \exp(z_{ij}^{*})\right] / \left[1 + \exp(z_{ij-1}^{*})\right]$, $z_{ij}^{*} = \left[\log(a_j) - \mathbf{x}_i^{*T}\right]/\sigma$, $z_{ij-1}^{*} = \left[\log(a_{j-1}) - \mathbf{x}_i^{*T}\right]/\sigma$, and $\mathbf{x}_i^{*T} = \beta_1 x_{i1} + \cdots + \beta_t(x_{it} + \omega_i S_x) + \cdots + \beta_p x_{ip}$. We omit the matrix $\boldsymbol{\Delta} = (\boldsymbol{\Delta}_{\varphi}^T, \boldsymbol{\Delta}_{\sigma}^T, \boldsymbol{\Delta}_{\boldsymbol{\beta}}^T)^T$ in this work.

4. APPLICATIONS

4.1. Simulation Study

We conduct Monte Carlo simulation studies to assess the finite sample behavior of the MLEs of φ, σ, β_0, and β_1. The sample sizes were generated by taking $n = 20$, $n = 75$, and $n = 150$. The log-lifetimes denoted by $\log(T_1), \ldots, \log(T_n)$ were generated from the log-Burr XII distribution (3) by considering the reparameterization $\gamma = \sigma^{-1}$ and $\lambda = \exp(\mu)$ and by assuming $\mu_i = \beta_0 + \beta_1 x_i$, where x_i was generated from a uniform [0, 1] distribution. The true parameter values used in the data-generating processes are $\varphi = 1$, $\sigma = 0.25$, $\beta_0 = 2$, and $\beta_1 = 3$. The censoring times denoted by $C_1, \ldots, C_n$ were generated from a uniform distribution $[0, \tau]$, where τ was adjusted until censoring percentage of 0.30. Then we fix the number of intervals at $k = 5$ and $k = 10$ for $n = 20$, and $k = 5$, $k = 10$, and $k = 20$ for $n = 75$ and $n = 150$. To construct the intervals, we consider the minimum and maximum log-lifetime generated to be the extremes of the interval. Sorting the log-lifetimes that were not censored, we obtained the remaining values to compose each interval.

For each configuration of n and k, all results were obtained from 1000 Monte Carlo replications and the simulations were carried out using the Ox matrix programming language. In each replication, a random sample of size n is drawn from the log-Burr XII regression model (4) for survival grouped data and the BFGS method (see, e.g., Press et al., 1992) was used for maximizing the total log-likelihood function $l(\boldsymbol{\theta})$. For each fit, the mean estimates, standard errors (SEs), and mean square errors (MSEs) were calculated.

The figures in Table 1 indicate that the biases, SEs, and MSEs of the MLEs of φ, σ, β_0, and β_1 decrease toward zero as the sample size n increases, as expected. Future research should be conducted to obtain the bias corrections for these estimators.

4.2. Vitamin A Data

We consider a data set provided by the Instituto de Saúde Coletiva–Universidade Federal da Bahia. This data set was designed to assess the effect of vitamin A supplementation on recurrent diarrheal episodes in small children; see, for example, Barreto et al. (1994) and Silva et al. (2008). The data from a randomized community trial were designed to assess the effect of vitamin A supplementation on

Table 1 Mean estimates, standard errors, and mean squared errors of the MLEs $\hat{\varphi}$, $\hat{\sigma}$, $\hat{\beta}_0$, and $\hat{\beta}_1$ in the log-Burr XII regression model for grouped survival data

n	Interval (k)	Parameters	Mean	SE	MSE
20	5	φ	0.589	0.012	0.313
		σ	0.170	0.170	0.015
		β_0	2.063	0.012	0.148
		β_1	2.766	0.019	0.415
	10	φ	0.568	0.010	0.287
		σ	0.155	0.002	0.013
		β_0	2.028	0.010	0.101
		β_1	2.738	0.021	0.509
75	5	φ	0.767	0.011	0.175
		σ	0.212	0.002	0.005
		β_0	2.075	0.007	0.055
		β_1	2.780	0.010	0.148
	10	φ	0.831	0.010	0.128
		σ	0.217	0.002	0.005
		β_0	1.998	0.006	0.036
		β_1	2.926	0.008	0.069
	20	φ	0.799	0.010	0.140
		σ	0.211	0.002	0.006
		β_0	1.966	0.006	0.037
		β_1	2.941	0.009	0.084
150	5	φ	0.793	0.010	0.143
		σ	0.221	0.002	0.005
		β_0	2.095	0.006	0.045
		β_1	2.743	0.007	0.115
	10	φ	0.903	0.009	0.090
		σ	0.231	0.001	0.001
		β_0	2.017	0.004	0.016
		β_1	2.932	0.005	0.030
	20	φ	0.905	0.009	0.090
		σ	0.231	0.001	0.001
		β_0	1.990	0.004	0.016
		β_1	2.969	0.005	0.026

diarrheal episodes in 1207 pre-school children, aged 6–48 months at the baseline, who received either placebo or vitamin A in a small city in the northeast of Brazil from December 1990 to December 1991. The total time was defined as the time from the first dose of vitamin A until the occurrence of an episode of diarrhea. An episode of diarrhea was defined as a sequence of days with diarrhea, and a day with diarrhea was defined when 3 or more liquid or semiliquid movements were reported in a 24-hour period. The information on the occurrence of diarrhea collected at each visit corresponds to a recall period of 48–72 hours. The number of liquid and semiliquid movements per 24 hours was recorded. It was observed that of the 1207 children under study, 925 showed a diarrheal episode, which means that 282 children showed censored times. The explanatory variables considered in the models are: x_{i1}: age at

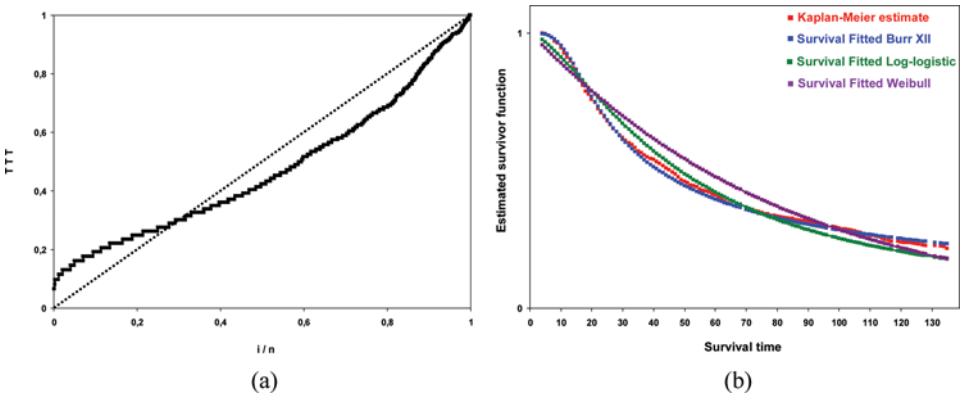


Figure 2 (a) TTT plot on vitamin A data. (b) Estimated survival function by fitting the Burr XII, log-logistic, and Weibull distributions and the empirical survival function for vitamin A data. (Color figure available online.)

baseline (in months); x_{i2}: treatment (0 = placebo, 1 = vitamin A); and x_{i3}: gender (0 = girl, 1 = boy).

In many applications, there is qualitative information about the failure rate function shape which can help us in selecting a particular model. In this context, a device called the total time on test (TTT) plot (Aarset, 1987) is useful. The TTT plot is obtained by plotting $G(r/n) = [(\sum_{i=1}^{r} T_{i:n}) + (n-r)T_{r:n}]/(\sum_{i=1}^{n} T_{i:n})$ against r/n, where $r = 1, \ldots, n$ and $T_{i:n}$, $i = 1, \ldots, n$, are the order statistics of the sample (Mudholkar et al., 1995). The TTT plot for these data given in Fig. 2(a) indicates a unimodal-shaped failure rate function. In order to assess whether the distribution is appropriate, the plot comparing the empirical survival function and the estimated survival function by fitting the Burr XII, log-logistic, and Weibull models is given in Fig. 2(b). Based on Fig. 2(b), it is reasonable to consider that the logarithms of the times to events follow the log-Burr XII distribution.

In order to have an idea about the behavior of the vitamin A data, Fig. 3 gives a histogram of the times of diarrhea. It shows a high frequency of observations at the initial time and near the end of the study. It can also be seen from Fig. 3 that the minimum value for the response variable is 4 and the maximum value is 185. This fact indicates that a significant number of ties exist, and also that the log-Burr XII model can fit these data. For this reason, the log-Burr XII regression model for grouped data is an interesting alternative to model the vitamin A data. The lifetimes were categorized in eight intervals $\{(4, 21], (21, 38], \ldots, (126, 185]\}$. No criterion exists to establish the number of intervals. The only assumption is the presence of at least one failure in each interval. Hence, for the sake of convenience, $k = 8$ intervals was adopted. Table 2 lists the lifetime logarithms in intervals, and the numbers of failures, censoring, and individuals at risk in each of the eight intervals.

Maximum Likelihood and Jackknife Estimation. The MLEs of the parameters in the log-Burr XII regression model fitted to the grouped survival data were computed using the subroutine MaxBFGS in Ox and the results are given in Table 3. In addition, in Table 3 we report the jackknife estimates of the model parameters.

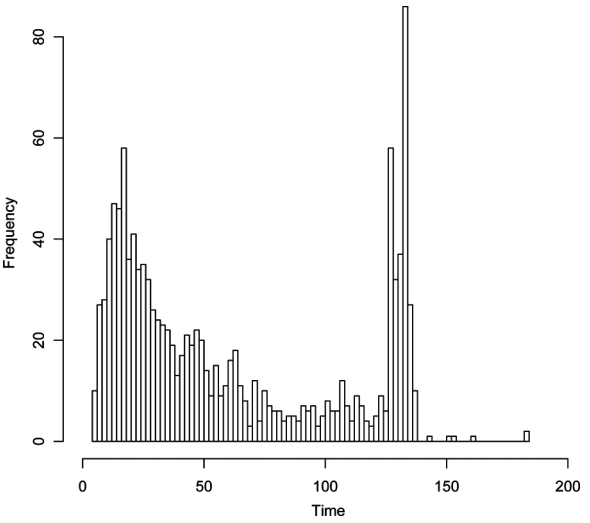


Figure 3 Histogram of the vitamin A data.

The figures in Table 3 indicate that the explanatory variable treatment (x_2) is significant in the log-Burr XII model for grouped survival data at the level of 6%. On the other hand, the explanatory variable x_3 is not significant in the model at the level of 5%. For the sake of illustration, Table 4 shows the tests to compare the survival curves by the log-rank and Wilcoxon nonparametric tests by considering the explanatory variable "treatment." Results similar to those obtained in Table 3 can be observed.

Global Influence Analysis. In this section, we use Ox to compute the case-deletion measures $GD_i(\boldsymbol{\theta})$ and $LD_i(\boldsymbol{\theta})$ presented in section 3.1. The results of such influence measure index plots are displayed in Fig. 4. From this figure, we note that the cases 461 and 1030 are possible influential observations.

Local and Total Influence Analysis. In this section, we perform an analysis of local influence for the vitamin A data using the log-Burr XII regression model for grouped survival data. By applying the local influence theory developed in

Table 2 Life table for vitamin A data

Interval I_j	Number of failures	Number of censoring	Number at risk
[4, 21)	292	0	1207
[21, 38)	243	4	915
[38, 55)	138	6	668
[55, 73)	101	2	524
[73, 90)	46	3	421
[90, 108)	49	6	372
[108, 126)	46	11	317
[126, 185)	10	250	260

Table 3 Maximum likelihood and jackknife estimates for the parameters of the log-Burr XII model for grouped survival data fitted to vitamin A data

	MLEs				Jackknife estimates		
$\boldsymbol{\theta}$	Estimate	SE	p-Value	95% CI	Estimate	SE	95% CI
φ	1.049	0.347	—	(0.370; 1.729)	0.893	0.430	(0.049; 1.737)
σ	0.829	0.115	—	(0.603; 1.055)	0.828	0.144	(0.545; 1.111)
β_0	2.602	0.328	<0.001	(1.960; 3.245)	2.577	0.350	(1.890; 3.264)
β_1	0.042	0.005	0.000	(0.033; 0.051)	0.042	0.006	(0.030; 0.054)
β_2	0.174	0.090	0.053	(−0.002; 0.350)	0.178	0.092	(−0.002; 0.358)
β_3	0.071	0.089	0.425	(−0.103; 0.245)	0.072	0.089	(−0.103; 0.247)

Table 4 Testing for homogeneity of survival curves for treatment to vitamin A data

Test	Chi-squares	Degrees of freedom	p-Value
Log-rank	3.7559	1	0.0526
Wilcoxon	3.0021	1	0.0832

section 3.2, where case-weight perturbation is used, the value $C_{\mathbf{d}_{max}} = 1.80$ was obtained as a maximum curvature. Figure 5(a) plots the eigenvector corresponding to $|\mathbf{d}_{max}|$, and the total influence C_i is shown in Fig. 5(b). The observation 461 is very distinguished in relation to the others.

The perturbation of the vector for the explanatory variable age (x_1) is investigated here. For perturbation of the explanatory variable age, the value $C_{\mathbf{d}_{max}} = 0.43$ was obtained as a maximum curvature. Plots of $|\mathbf{d}_{max}|$ and the total local influence C_i against the observation index are shown in Figs. 6(a) and 6(b), respectively. In these two plots, we can see no influential observation.

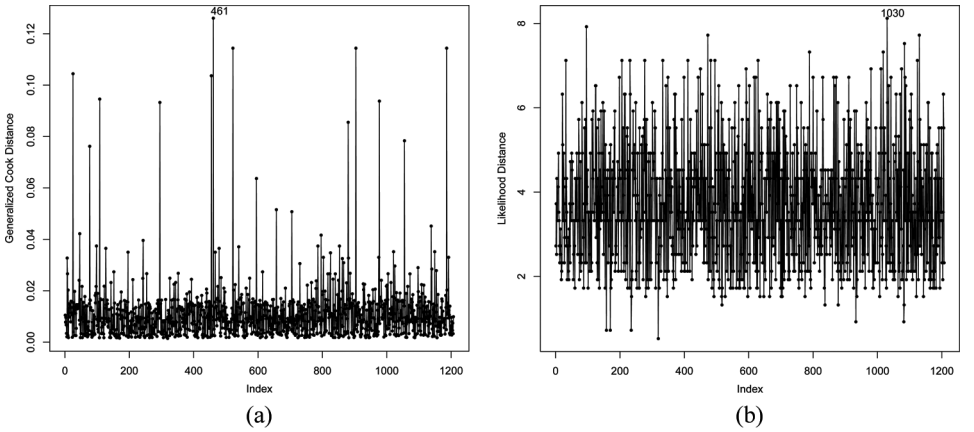
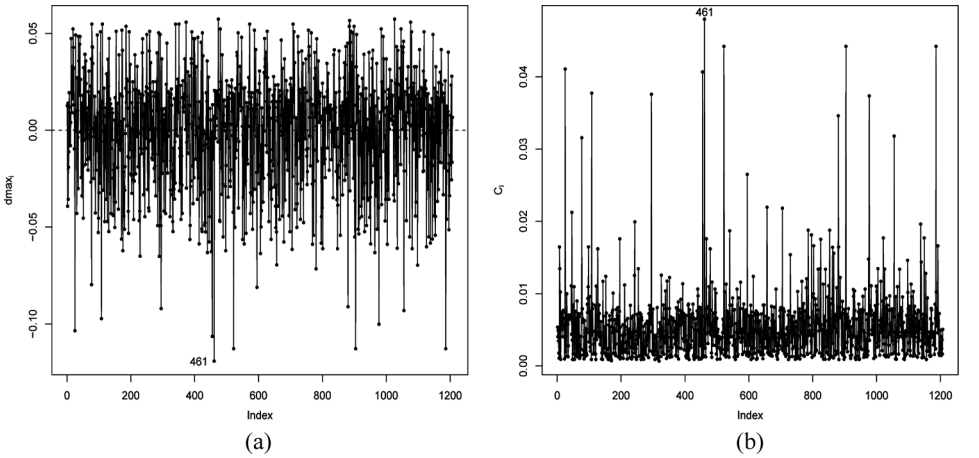


Figure 4 (a) Index plot of $GD_i(\boldsymbol{\theta})$ (generalized Cook's distance) and (b) index plot of $LD_i(\boldsymbol{\theta})$ (likelihood distance) from the fit of the log-Burr XII model to vitamin A data.

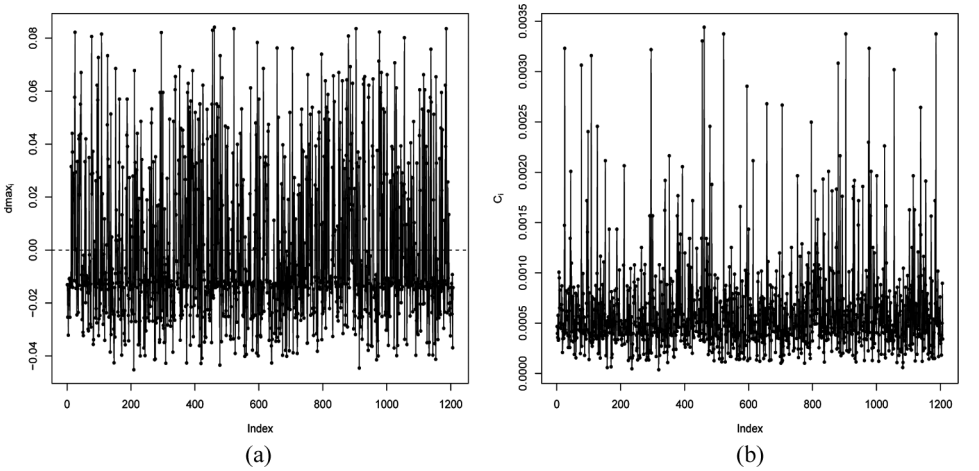


(a) (b)

Figure 5 (a) Index plot of $\mathbf{d}_{max}$ for $\boldsymbol{\theta}$ (case-weight perturbation) and (b) total local influence for $\boldsymbol{\theta}$ (case-weight perturbation) from the fit of the log-Burr XII model to vitamin A data.

4.3. Impact of the Detected Influential Observations

From the diagnostics analysis (global and local influence) we can consider the observations 461 and 1030 as possibly influential points. Observation 461 represents the individual grouped in the eighth interval; she is a female and shows one of the youngest ages in the set of observations that were censored when receiving treatment with placebo. Observation 1030 represents the individual grouped in the seventh interval with one of the youngest ages in the group treated with placebo and being a female, nevertheless belonging to the set of observations that failed.



(a) (b)

Figure 6 (a) Index plot of $\mathbf{d}_{max}$ for $\boldsymbol{\theta}$ (age explanatory variable perturbation) and (b) total local influence on estimate $\hat{\boldsymbol{\theta}}$ (age explanatory variable perturbation) from the fit of the log-Burr XII model to vitamin A data.

Table 5 Relative changes (RC, %), estimates, and the associated p-values in parentheses for the regression coefficients to explain the log-survival time from the fit of the model to vitamin A data

Dropping	$\hat{\varphi}$	$\hat{\sigma}$	$\hat{\beta}_0$	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$
None	—	—	—	—	—	—
	1.049	0.829	2.602	0.042	0.174	0.071
	(—)	(—)	(0.000)	(0.000)	(0.053)	(0.425)
Set I_1	[−6]	[−2]	[−2]	[0]	[−3]	[−4]
	1.115	0.847	2.647	0.042	0.180	0.074
	(—)	(—)	(0.000)	(0.000)	(0.045)	(0.403)
Set I_2	[0]	[0]	[0]	[0]	[−2]	[−6]
	1.052	0.829	2.593	0.042	0.177	0.075
	(—)	(—)	(0.000)	(0.000)	(0.049)	(0.401)
Set I_3	[−7]	[−2]	[−1]	[−2]	[−6]	[−10]
	1.119	0.847	2.638	0.043	0.184	0.078
	(—)	(—)	(0.000)	(0.000)	(0.041)	(0.379)

In order to reveal the impact of these two observations on the parameter estimates, we refitted the model under some situations. First, we individually eliminate each one of these two cases. Next, we remove the totality of potentially influential observations from the original data set. In Table 5, we give the relative changes (in percentages) of the parameter estimates defined by $RC_{\boldsymbol{\theta}_j} = [(\hat{\boldsymbol{\theta}}_j - \hat{\boldsymbol{\theta}}_j(I))/\hat{\boldsymbol{\theta}}_j] \times 100$, and the corresponding p-values, where $\hat{\boldsymbol{\theta}}_j(I)$ denotes the MLE of $\boldsymbol{\theta}_j$ after "set I" of observations being removed. Note that in Table 5 the sets are $I_1 = \{\sharp 461\}$, $I_2 = \{\sharp 1030\}$ and $I_3 = \{\sharp 461, \sharp 1030\}$.

From Table 5, we note that the MLEs from the log-Burr XII regression model for grouped survival data are not highly sensitive under deletion of the outstanding observations. In general, the significance of the parameter estimates does not change (at the level of 5%) after removing set I.

Final Model. The LR statistic for testing the null hypothesis H_0: $\beta_3 = 0$ versus H_1: $\beta_3 \neq 0$, that is, to verify the contribution effects of the explanatory variable x_3, is $w = 0.392$ (p-value $= 0.996$), and then we conclude that the parameter β_3 is not significant for the model. Based on this analysis, we conclude that the log-Burr XII regression model for grouped survival data is more appropriate for

Table 6 Maximum likelihood estimates from the log-Burr XII regression model for grouped survival data fitted to the final vitamin A data (final model)

	MLEs			
$\boldsymbol{\theta}$	Estimate	SE	p-Value	95% CI
φ	1.071	0.358	—	(0.368, 1.774)
σ	0.836	0.116	—	(0.608, 1.064)
β_0	2.661	0.328	<0.001	(2.018, 3.305)
β_1	0.042	0.005	0.000	(0.033, 0.051)
β_2	0.176	0.090	0.050	(0.000, 0.352)

fitting these data. The MLEs of the parameters in the final model are given in Table 6.

From the fitted log-Burr XII regression model, we note that the explanatory variables "age" x_1 and "treatment" x_2 are significant at (5%). According to the final model, one possible interpretation is that there is a significant difference between "placebo" and "vitamin A" for survival times.

5. CONCLUDING REMARKS

In this article, we propose a log-Burr XII regression model for grouped survival data as an alternative to model lifetime data in the presence of many ties. We use the matrix programming language Ox (MaxBFGS subroutine) to obtain the maximum likelihood estimates (MLEs), and asymptotic tests are performed for the parameters based on the likelihood ratio (LR) statistics. On the other hand, as an alternative analysis, we discuss the use of the jackknife estimator in the log-Burr XII regression model for grouped survival data. In the application to a real data set, we observe that both estimators present similar results. We also discuss applications of influence diagnostics in the log-Burr XII regression models for grouped survival data. Further, we perform a general model checking analysis that makes it a very attractive option for modeling grouped survival data. Also, we discuss the robustness aspects of the MLE from the fitted log-Burr XII regression model for grouped survival data through sensitivity analysis.

APPENDIX MATRIX OF THE SECOND DERIVATIVES $\ddot{\mathbf{L}}(\boldsymbol{\theta})$

Here we derive the necessary formulas to obtain the second order partial derivatives of the log-likelihood function. After some algebraic manipulation, we obtain:

$$\ddot{\mathbf{L}}_{\varphi\varphi} = -\sum_{j=1}^{k}\sum_{i\in F_j}\log(b_{ij})^2\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-\varphi}\left[\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-\varphi}+1\right]$$

$$\ddot{\mathbf{L}}_{\varphi\sigma} = \sum_{j=1}^{k}\left\{\sum_{i\in F_j}[\dot{b_{ij}}]_{\sigma}\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-(\varphi+1)}\left[-\left(1-b_{ij}^{-\varphi}\right)^{-1}\varphi b_{ij}^{-(2\varphi+1)}\log(b_{ij})\right.\right.$$
$$\left.\left.+1-\varphi\log(b_{ij})\right]-\sum_{i\in R_j}\left(\frac{[\dot{b_{ij}}]_{\sigma}}{b_{ij}}\right)-\sum_{i\in C_j}\left(\frac{[\dot{b_{ij}}]_{\sigma}}{b_{ij}}\right)\right\}$$

$$\ddot{\mathbf{L}}_{\varphi\beta_m} = \sum_{j=1}^{k}\left\{\sum_{i\in F_j}[\dot{b_{ij}}]_{\beta_m}\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-(\varphi+1)}\left[-\left(1-b_{ij}^{-\varphi}\right)^{-1}\varphi b_{ij}^{-(2\varphi+1)}\log(b_{ij})\right.\right.$$
$$\left.\left.+1-\varphi\log(b_{ij})\right]-\sum_{i\in R_j}\left(\frac{[\dot{b_{ij}}]_{\beta_m}}{b_{ij}}\right)-\sum_{i\in C_j}\left(\frac{[\dot{b_{ij}}]_{\beta_m}}{b_{ij}}\right)\right\}$$

$$\ddot{\mathbf{L}}_{\sigma\sigma} = \sum_{j=1}^{k}\left\{\sum_{i\in F_j}\varphi\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-(\varphi+1)}\left[-\varphi\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-(\varphi+1)}[\dot{b_{ij}}]_{\sigma}^2-(\varphi+1)b_{ij}^{-1}[\dot{b_{ij}}]_{\sigma}^2\right.\right.$$

$$+\ [\ddot{b}_{ij}]_{\sigma\sigma}\Big] - \varphi \sum_{i\in R_j}\left(\frac{[\ddot{b}_{ij}]_{\sigma\sigma}b_{ij} - [\dot{b}_{ij}]_{\sigma}^2}{b_{ij}^2}\right) - \frac{\varphi}{2}\sum_{i\in C_j}\left(\frac{[\ddot{b}_{ij}]_{\sigma\sigma}b_{ij} - [\dot{b}_{ij}]_{\sigma}^2}{b_{ij}^2}\right)\Bigg\}$$

$$\ddot{\mathbf{L}}_{\sigma\beta_m} = \sum_{j=1}^{k}\Bigg\{\sum_{i\in F_j}\varphi\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-(\varphi+1)}\Big[-\varphi\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-(\varphi+1)}[\dot{b}_{ij}]_{\beta_m}[\dot{b}_{ij}]_{\sigma}$$

$$-(\varphi+1)b_{ij}^{-1}[\dot{b}_{ij}]_{\beta_m}[\dot{b}_{ij}]_{\sigma} + [\ddot{b}_{ij}]_{\sigma\beta_m}\Big] - \varphi\sum_{i\in R_j}\left(\frac{[\ddot{b}_{ij}]_{\sigma\beta_m}b_{ij} - [\dot{b}_{ij}]_{\beta_m}[\dot{b}_{ij}]_{\sigma}}{b_{ij}^2}\right)$$

$$-\frac{\varphi}{2}\sum_{i\in C_j}\left(\frac{[\ddot{b}_{ij}]_{\sigma\beta_m}b_{ij} - [\dot{b}_{ij}]_{\beta_m}[\dot{b}_{ij}]_{\sigma}}{b_{ij}^2}\right)\Bigg\}$$

$$\ddot{\mathbf{L}}_{\beta_m\beta_s} = \sum_{j=1}^{k}\Bigg\{\sum_{i\in F_j}\varphi\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-(\varphi+1)}\Big[-\varphi\left(1-b_{ij}^{-\varphi}\right)^{-1}b_{ij}^{-(\varphi+1)}[\dot{b}_{ij}]_{\beta_m}[\dot{b}_{ij}]_{\beta_s}$$

$$-(\varphi+1)b_{ij}^{-1}[\dot{b}_{ij}]_{\beta_m}[\dot{b}_{ij}]_{\beta_s} + [\ddot{b}_{ij}]_{\beta_m\beta_s}\Big] - \varphi\sum_{i\in R_j}\left(\frac{[\ddot{b}_{ij}]_{\beta_m\beta_s}b_{ij} - [\dot{b}_{ij}]_{\beta_m}[\dot{b}_{ij}]_{\beta_s}}{b_{ij}^2}\right)$$

$$-\frac{\varphi}{2}\sum_{i\in C_j}\left(\frac{[\ddot{b}_{ij}]_{\beta_m\beta_s}b_{ij} - [\dot{b}_{ij}]_{\beta_m}[\dot{b}_{ij}]_{\beta_s}}{b_{ij}^2}\right)\Bigg\}$$

where

$$b_{ij} = \frac{1+\exp(z_{ij})}{1+\exp(z_{ij-1})},\quad z_{ij} = \frac{\log(a_j)-\mathbf{x}_i^T\boldsymbol{\beta}}{\sigma},\quad z_{ij-1} = \frac{\log(a_{j-1})-\mathbf{x}_i^T\boldsymbol{\beta}}{\sigma}$$

$$[\dot{b}_{ij}]_{\sigma} = -\left[\frac{z_j\exp(z_j) - b_{ij}z_{j-1}\exp(z_{j-1})}{\sigma[1+\exp(z_{j-1})]}\right],\quad [\dot{b}_{ij}]_{\beta_m} = -x_{im}\left[\frac{\exp(z_j) - b_{ij}\exp(z_{j-1})}{\sigma[1+\exp(z_{j-1})]}\right]$$

$$[\ddot{b}_{ij}]_{\sigma\sigma} = \frac{z_j\exp(z_j)(1+z_j-v_{ij}) - z_{j-1}\exp(z_{j-1})\left[b_{ij}(1+z_{j-1}-v_{ij}) - \sigma[\dot{b}_{ij}]_{\sigma}\right]}{\sigma^2[1+\exp(z_{j-1})]}$$

$$-\sigma^{-1}[\dot{b}_{ij}]_{\sigma}$$

$$[\ddot{b}_{ij}]_{\sigma\beta_m} = \frac{x_{im}\left\{\exp(z_j)(z_j-v_{ij}) - \exp(z_{j-1})\left[b_{ij}(z_{j-1}-v_{ij}) - \sigma[\dot{b}_{ij}]_{\sigma}\right]\right\}}{\sigma^2[1+\exp(z_{j-1})]} - \sigma^{-1}[\dot{b}_{ij}]_{\beta_m}$$

$$[\ddot{b}_{ij}]_{\beta_m\beta_s} = \frac{x_{im}x_{is}\left\{\exp(z_j)(1-z_{j-1}^{-1}v_{ij}) - \exp(z_{j-1})\left[b_{ij}(1-z_{j-1}^{-1}v_{ij}) - \sigma x_{is}^{-1}[\dot{b}_{ij}]_{\beta_s}\right]\right\}}{\sigma^2[1+\exp(z_{j-1})]}$$

$$[\dot{b}_{ij}]_{\beta_s} = -x_{is}\left[\frac{\exp(z_j) - b_{ij}\exp(z_{j-1})}{\sigma[1+\exp(z_{j-1})]}\right]\quad\text{and}\quad v_{ij} = \frac{z_{j-1}\exp(z_{j-1})}{1+\exp(z_{j-1})}$$

where $m, s = 1, 2, \ldots, p$.

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