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# Optimal B-Robust Estimation for the Parameters of the Marshall-Olkin Extended Burr XII Distribution with an Application to Pharmacokinetics

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Abstract:

- Parameters of Marshall-Olkin Extended Burr XII (MOEBXII) distribution are usually estimated using maximum likelihood (ML) and least squares (LS) estimation methods. However, these estimators are not robust to the outliers which are often encountered in practice. The purpose of this paper is to obtain robust estimators for the parameters of MOEBXII distribution using optimal B robust estimation method. A simulation study is provided to show the performance of the proposed estimators over ML, LS and robust M estimators. Further, a real data example from a pharmacokinetics study is also given to illustrate the modeling capacity of the MOEBXII distribution when the parameters are properly estimated.

Key-Words:

- *Least squares estimator; Marshall-Olkin extended Burr XII (MOEBXII) distribution; maximum likelihood estimator; optimal B-robust estimator.*

AMS Subject Classification:

- 62F35, 65C60



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## 1. INTRODUCTION

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Burr [4] introduced a family of continuous distributions that includes twelve types of cumulative distribution functions with different shapes. Since then, Burr XII distribution has attracted attention in many different fields [15, 20, 2, 22, 21, 16, 10]. The Burr distribution has relationship with several distributions and some of them are summarized by Rodriguez [23] and Tadikamalla [26]. Because of its flexibility for modeling data, several generalizations of the Burr XII distribution have been introduced in literature. One of these generalizations is based on the Marshall-Olkin transformation which further improves the flexibility of the Burr XII distribution. Marshall and Olkin [19] introduced a method of obtaining a family of distributions with an additional parameter  $\alpha$ . Let  $F(x)$  and  $\bar{F}(x) = 1 - F(x)$  be the cumulative distribution function (cdf) and the survival function of the baseline distribution, respectively. Then, a Marshall-Olkin (MO) extended distribution can be defined with the following survival function

$$(1.1) \quad \bar{F}_\alpha(x) = \frac{\alpha \bar{F}(x)}{1 - \bar{\alpha} \bar{F}(x)}$$

where  $\alpha > 0$  is an additional parameter and  $\bar{\alpha} = 1 - \alpha$ . When  $\alpha = 1$ , we get the baseline distribution. Using the transformation given in (1.1) several generalized distributions are defined in the literature. One of these generalizations is the Marshall-Olkin extended Burr type XII (MOEBXII) distribution introduced by Al-Saiari et al. [3].

Several researchers have considered parameter estimation of the Burr XII distribution. For instance, Wingo [28, 29] has considered estimating the parameters of the Burr XII distribution using the ML estimation method. Malinowska et al. [17] have provided the minimum variance linear unbiased estimators (MVLUE), the best linear invariant estimators (BLIE) and the ML estimators based on  $n$ -selected generalized order statistics for the parameters of the Burr XII distribution. Shao [24] has given a complete investigation on the behaviors of the ML estimates based on uncensored and right-censored data. Wang and Cheng [27] have used a robust regression method to estimate the parameters of the Burr XII distribution. Dogru and Arslan [6, 7] have proposed estimators based on the M estimation and the optimal B-robust (OBR) estimation methods to estimate the parameters of Burr XII distribution. However, concerning the MOEBXII distribution a small number of researchers have been considered to estimate the parameters of the MOEBXII distribution in the literature. For example, Al-Saiari et al. [3] have used the ML and Bayes estimation methods to estimate the parameters of the MOEBXII distribution. Since ML estimators may be spoiled when there are outliers in the data, robust estimation methods can be used to estimate the parameters of MOEBXII distribution. Recently, Guney and Arslan [9] and Ozdemir et al. have explored the robust estimation methods to

estimate the parameters of MOEBXII distribution if robustness is a concern. The aim of this paper is twofold. First, alternative to the robust estimation methods used in the paper by Güney and Arslan [9] and Özdemir et al., we propose to use the OBR estimation method to estimate the parameters of the MOEBXII distribution. By doing this, we gain robustness against to the outliers in the data. The second aim of this study is to use the MOEBXII distribution to model the pharmacokinetics data using the robust estimators which has not been tried before.

Note that, the pharmacokinetics properties of the drug are among the most important drug characteristics for optimal treatment after the selection of the appropriate drug in the treatment of a disease. The most appropriate daily dose to achieve the effective plasma level is determined by these features. Among these properties one of the most important pharmacokinetics property is plasma drug concentration. The maximum concentration ( $C_{max}$ ) and the time taken to reach the maximum concentration ( $T_{max}$ ) are also important variables for the pharmacokinetics studies. These variables can be easily estimated by using the right distribution. However, to obtain the reliable estimates of  $C_{max}$  and  $T_{max}$ , trustfully modeling of the plasma drug concentration is necessary (For more details see [1]).

The remainder of the paper is organized as follows. In Section 2, we briefly recall the MOEBXII distribution. In Section 3, we first summarize the ML, LS and robust M estimation methods, and then we give the OBR estimators for the parameters of the MOEBXII distribution. Section 4 and Section 5 are dedicated to the simulation study and a real data from pharmacokinetics study to compare the performance of the OBR estimation method with the ML, LS and robust M estimation methods. Finally, conclusions and discussions are given in Section 6.

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## 2. MARSHALL-OLKIN EXTENDED BURR XII DISTRIBUTION

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The probability density function (pdf) and the cdf of Burr XII distribution are

$$(2.1) \quad f(x; c, k) = ck \frac{x^{(c-1)}}{(1+x^c)^{k+1}}, x \geq 0,$$

$$(2.2) \quad F(x; c, k) = 1 - \frac{1}{(1+x^c)^k}, x \geq 0$$

where  $c$  and  $k > 0$  are the shape parameters. Substituting the cdf of the Burr XII distribution given in (2.2) into the transformation equation given in (1.1) the Marshall-Olkin Extended Burr XII distribution ( $\text{MOEBXII}(\alpha, c, k)$ ) is obtained with the following pdf and cdf, respectively

$$(2.3) \quad f(x; \alpha, c, k) = \alpha ck \frac{x^{(c-1)} (1+x^c)^{-(k+1)}}{\left[1 - (1-\alpha)(1+x^c)^{-k}\right]^2}, x \geq 0,$$

$$(2.4) \quad F(x; \alpha, c, k) = \frac{1 - (1+x^c)^{-k}}{1 - (1-\alpha)(1+x^c)^{-k}}, x \geq 0$$

where  $\alpha, c$  and  $k > 0$  are the shape parameters [3]. When  $\alpha = 1$  the Burr XII distribution is recovered with two parameters  $c$  and  $k$ . The MOEBXII distribution contains distributions with different shapes for the different values of the parameters. For example we get, bell-shaped, right-skewed or L-shaped distributions when we set different values for  $\alpha, c$  and  $k$ . This makes crucial advantage of flexibility for this distribution to fit data sets with several different shapes. One can see [3] for further details about the MOEBXII distribution.

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### 3. PARAMETER ESTIMATION

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In this section, the ML, LS, robust M and the OBR estimation methods to estimate the parameters of the MOEBXII distribution.

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#### 3.1. Maximum Likelihood Estimation

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Let  $x = (x_1, x_2, \dots, x_n)$  be a random sample of size  $n$  from the MOEBXII( $\alpha, c, k$ ) distribution with the unknown parameters  $\alpha, c$  and  $k$ . The log-likelihood function is

$$(3.1) \quad l(\alpha, c, k) = n \log(\alpha ck) + (c-1) \sum_{i=1}^n \log x_i - (k+1) \sum_{i=1}^n \log(1+x_i^c) \\ - 2 \sum_{i=1}^n \log(1 - (1-\alpha)(1+x_i^c)^{-k}).$$

Taking the derivatives of this function with respect to  $\alpha, c$  and  $k$ , we get the following score functions

$$(3.2) \quad s_\alpha = \frac{n}{\alpha} - 2 \sum_{i=1}^n \frac{(1+x_i^c)^{-k}}{1 - (1-\alpha)(1+x_i^c)^{-k}},$$

$$(3.3) \quad s_c = \frac{n}{c} + \sum_{i=1}^n \log x_i - (k+1) \sum_{i=1}^n \frac{x_i^c \log(x_i)}{1+x_i^c} \\ - 2k(1-\alpha) \sum_{i=1}^n \frac{(1+x_i^c)^{-(k+1)} x_i^c \log(x_i)}{1 - (1-\alpha)(1+x_i^c)^{-k}},$$

$$(3.4) \quad s_k = \frac{n}{k} - \sum_{i=1}^n \log(1 + x_i^c) - 2(1 - \alpha) \sum_{i=1}^n \frac{(1+x_i^c)^{-k} \log(1+x_i^c)}{1 - (1-\alpha)(1+x_i^c)^{-k}}.$$

The ML estimators of the parameters can be obtained by setting the score functions to zero and solving them simultaneously with respect to  $\alpha$ ,  $c$  and  $k$ . Since the likelihood equations ( $s_\alpha = 0$ ,  $s_c = 0$ ,  $s_k = 0$ ) cannot be solved analytically, we need to use some numeric methods to obtain the estimates of the parameters.

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### 3.2. Least Squares Estimation

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LS estimation method was used to estimate the parameters of the Burr distribution [13] and the MOEBXII distribution [9]. The LS estimation method to estimate the parameters of the MOEBXII distribution can be summarized as follows. It is basically based on minimizing the following function.

$$(3.5) \quad \begin{aligned} S(\alpha, c, k) &= \sum_{i=1}^n \left( \hat{F}(x_i) - F(x_i) \right)^2 \\ &= \sum_{i=1}^n \left( \hat{F}(x_i) - \frac{1 - (1+x_i^c)^{-k}}{1 - (1-\alpha)(1+x_i^c)^{-k}} \right)^2. \end{aligned}$$

Since the cdf of the MOEBXII distribution is a non-linear function, the minimization of equation (3.5) is not easy to obtain. To handle this problem,  $\log \left( \frac{1}{1-F(x)} \right)$  transformation can be used.

Let  $y_{(i)} = \log \left( \frac{1}{1-\hat{F}(x_{(i)})} \right)$  and  $u_{(i)} = \log \left( \frac{1}{1-F(x_{(i)})} \right)$  with

$$(3.6) \quad \hat{F}(x_{(i)}) = \frac{i - 0.5}{n}, i = 1, 2, \dots, n.$$

Here  $x_{(i)}$  denotes the  $i$ . order statistics of the sample from the MOEBXII distribution. Thus, the LS estimates of the parameters can be obtained by minimizing the following objective function

$$(3.7) \quad S(\alpha, c, k) = \sum_{i=1}^n (y_{(i)} - u_{(i)})^2.$$

To obtain the LS estimates, the following equations should be solved with respect to  $\alpha, c$  and  $k$ .

$$(3.8) \quad \sum_{i=1}^n (y_{(i)} - u_{(i)}) \frac{1 - (1 + x_{(i)}^c)^{-k}}{\alpha \left[ 1 - (1 - \alpha) (1 + x_{(i)}^c)^{-k} \right]} = 0,$$

$$(3.9) \quad \sum_{i=1}^n (y_{(i)} - u_{(i)}) \frac{kx_{(i)}^c \log(x_{(i)})}{(1 + x_{(i)}^c) \left[ 1 - (1 - \alpha) (1 + x_{(i)}^c)^{-k} \right]} = 0,$$

$$(3.10) \quad \sum_{i=1}^n (y_{(i)} - u_{(i)}) \frac{\log(1 + x_{(i)}^c)}{\left[ 1 - (1 - \alpha) (1 + x_{(i)}^c)^{-k} \right]} = 0.$$

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### 3.3. M Estimation

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Guney and Arslan [9] have been proposed to estimate the parameters of the MOEBXII distribution using M estimation method ([14]). The method is based on minimizing the following objective function with respect to the parameters of interest

$$(3.11) \quad Q(\alpha, c, k) = \sum_{i=1}^n \rho(y_i - u_i).$$

Here  $\rho$  is more resistant than the square function in LS method to the outliers in data set. It is also non-negative, symmetric function and  $\rho(0) = 0$ . In this study, we consider the Tukey's  $\rho$  function given as

$$(3.12) \quad \rho(x) = \begin{cases} 1 - (1 - (x/b)^2)^3, & |x| \leq b \\ 1, & |x| > b \end{cases}$$

$$(3.13) \quad \rho'(x) = \Psi(x) = \begin{cases} x(1 - (x/b)^2)^2, & |x| \leq b \\ 0, & |x| > b \end{cases}$$

with the robustness tuning constant  $b$  (see Maronna et al., [18], pp:29). Here the tuning constant  $b$  determines if an observation is an outlier or not. Tukey's biweight function truncates the residuals that are larger than  $b$ . Therefore, small values of  $b$  imply higher robustness while large values of  $b$  provide higher efficiency.

In literature the suggested choice of  $b$  is 4.685 to achieve 95% asymptotic efficiency at the standard normal distribution [18].

Since  $\rho$  is differentiable, M estimates can be obtained by solving the following non-linear equations based on the derivatives of objective function (3.11).

$$(3.14) \quad \log \hat{\alpha} = \frac{\sum_{i=1}^n \omega_i (y_i - k \log(1 + x_i^c) - \log h_i) \left( \frac{1 - (1 + x_i^c)^{-k}}{\alpha h_i} \right)}{\sum_{i=1}^n \omega_i \left( \frac{1 - (1 + x_i^c)^{-k}}{\alpha h_i} \right)},$$

$$(3.15) \quad \hat{k} = \frac{\sum_{i=1}^n \omega_i (y_i + \log(\alpha) - \log h_i) \frac{\log(1 + x_i^c)}{h_i}}{\sum_{i=1}^n \omega_i \frac{(\log(1 + x_i^c))^2}{h_i}},$$

$$(3.16) \quad \sum_{i=1}^n \omega_i (y_i - u_i) \frac{x_i^c \log(x_i) (1 - (1 + x_i^c)^{-k})}{(1 + x_i^c)^{-k} h_i} = 0,$$

where  $h_i = 1 - (1 - \alpha)(1 + x_i^c)^{-k}$  and the weights are

$$(3.17) \quad \omega_i = \left( 1 - \left( \frac{y_i - u_i}{b} \right)^2 \right)^2 I(|y_i - u_i| \leq b).$$

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#### 3.4. Optimal B-Robust Estimation

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The class of the OBR estimators was defined by Hampel et al. [11]. The OBR estimation method is a robust alternative modification of M estimation method with bounded influence function. It is also the most efficient one in the class of robust M-estimators. In literature, Victoria-Feser [30] and Victoria-Feser and Ronchetti [31] introduced the OBR estimation method to estimate the parameters of the Pareto and the gamma distributions. Dogru and Arslan [7] introduced the OBR estimation method for the Burr XII distribution. Dogru and Arslan [8] also proposed robust estimators by using the OBR estimation method for the parameters of the generalized half-normal distribution.

According to Hampel et al. [11], there are two ways of defining the optimal B-robust estimation. The first one is the minimax approach defined by Huber [14]. The second one is called the infinitesimal approach introduced by Hampel



et al. [11]. In this paper, we will use the second approach that aims to find M-estimators with bounded influence function (IF) and minimum asymptotic variance.

IF can be defined as follows. For a sample of  $n$  observations,  $\underline{x} = (x_1, x_2, \dots, x_n)$ , the empirical distribution function  $F_n(x)$  is

$$(3.18) \quad F_n(x) = \frac{1}{n} \sum_{i=1}^n \delta_{x_i}(x)$$

where  $\delta_{x_i}$  denotes a point mass in  $x$ . For a parametric model  $\{F_\theta : \theta \in \Theta \subset R^p\}$ , estimator of  $\theta$ ;  $T_n$  can be represented as a statistical functional of the empirical distribution, i.e.  $T_n(x_1, x_2, \dots, x_n) = T_n(F_n)$ . In our case  $\theta = (\alpha, c, k)$ . Then, the IF of  $T_n$  is given by

$$(3.19) \quad IF(x, T_n, F_\theta) = \lim_{\epsilon \rightarrow 0} \frac{T_n((1 - \epsilon)F_\theta + \epsilon\delta_x) - T_n(F_\theta)}{\epsilon}.$$

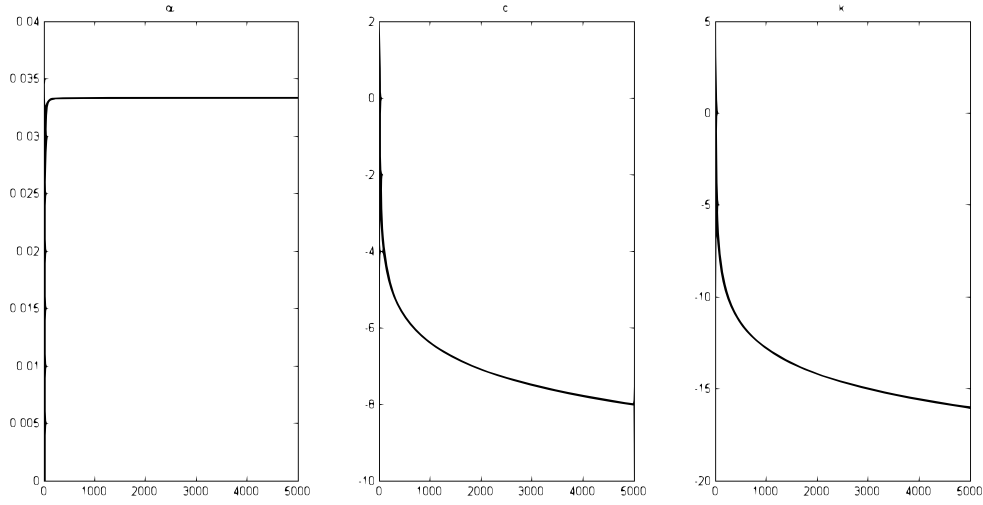
The IF describes the relative influence of individual observations toward the value of an estimate [11]. When the IF is unbounded, an outlier can have an overriding influence on the estimate. The IF of the ML estimator is

$$(3.20) \quad IF = J(\theta)^{-1} s(x, \theta)$$

where  $J(\theta)$  is the Fisher information matrix and  $s(x, \theta) = \frac{\partial}{\partial \theta} \log f(x, \theta)$  is the vector of score functions. It is clear that the IF of the ML estimator will not be bounded if the score function is not bounded.

Concerning the score functions for the MOEBXII distribution given in (3.2)-(3.4), one can easily observe that the score function for  $\alpha$  is bounded but the score functions for  $c$  and  $k$  are unbounded functions of  $x$  as in the Burr XII distribution. That is, we have  $\lim_{x \rightarrow \infty} s_c = -\infty$  and  $\lim_{x \rightarrow \infty} s_k = -\infty$ . These unbound- edness of score functions for the parameter  $c$  and  $k$  can also be easily observed in Figure 1.

If  $\alpha$ ,  $c$  and  $k$  are estimated by using the ML and LS estimation methods, these estimators may suffer from possible outliers. Therefore, instead of using the ML and LS methods we will propose to use the OBR estimation method in the presence of outliers.

Figure 1: Plots of the score functions with  $(\alpha, c, k) = (30, 2, 1)$ 

Consider the following standardized OBR estimating equation

$$(3.21) \quad \sum_{i=1}^n \Psi_b(A(\theta)(s(\theta, x_i) - a(\theta))) = \sum_{i=1}^n W(\theta, x_i, c_B)(s(\theta, x_i) - a(\theta)) = 0$$

where

$$(3.22) \quad W(\theta, x_i, c_B) = \min \left( 1, \frac{c_B}{\|A(\theta)(s(\theta, x_i) - a(\theta))\|} \right),$$

$\Psi_b$  is the derivative of  $\rho_b$ , is  $c_B \geq \sqrt{\dim(\theta)}$  is a tuning parameter,  $\|\cdot\|$  denoted the Euclidean norm,  $s(\cdot)$  is the score function,  $A(\theta)$  is a  $\dim(\theta) \times \dim(\theta)$  scaling matrix and  $a(\theta)$  is a  $\dim(\theta)$  centering vector determined by

$$(3.23) \quad E[\Psi_b(x)\Psi_b(x)^T] = [A(\theta)^T A(\theta)]^{-1},$$

$$(3.24) \quad E[\Psi_b(s(\theta, x) - a(\theta))] = 0.$$

The OBR estimates for the parameter  $\theta$  will be the solution of this equation. The OBR estimator keeps a level of efficiency close to the ML estimator because of the score function. The constant  $c_B$ , robustness constant, is typically fixed by setting the amount of efficiency loss and a bound on the IF. For higher

values of  $c_B$  the estimator gains efficiency, but lose robustness and vice versa. If the bound on the IF is removed, i.e, choose  $c_B = \infty$  the OBR estimation method reduces to the ML estimation method. To compute the OBR estimates of the parameters, we follow an algorithm proposed by Victoria-Feser and Ronchetti [31].

*OBRE Algorithm:*

1. Fix the precision threshold  $\eta$  and the initial value for  $\theta_{(0)}$  (we can take the ML estimates as the initial values).

Take initial values  $\mathbf{a} = \mathbf{0}$ , and  $A = \left([J^{-1}]^T\right)^{1/2}$  where

$$(3.25) \quad J = \int s(\theta, x) s(\theta, x)^T dF_\theta(x)$$

is the Fisher Information Matrix.

2. Solve the following equations with respect to  $\mathbf{a}$  and  $A$

$$(3.26) \quad A^T A = M_2^{-1}$$

$$(3.27) \quad \mathbf{a} = \frac{\int W(\theta, x, c_B) s(\theta, x) dF_\theta(x)}{\int W(\theta, x, c_B) dF_\theta(x)}$$

where

$$(3.28) \quad M_k = \int W(\theta, x, c_B)^k [s(\theta, x) - \mathbf{a}(\theta)] [s(\theta, x) - \mathbf{a}(\theta)]^T dF_\theta(x), \\ k = 1, 2.$$

The current values of  $\theta$ ,  $\mathbf{a}$  and  $A$  are used as initial values to solve the given equations.

3. Now compute  $M_1$  and

$$(3.29) \quad \Delta\theta = M_1^{-1} \left( \frac{1}{n} \sum_{i=1}^n W(\theta, x_i, c_B)^k [s(\theta, x_i) - a(\theta)] \right).$$

4. If  $\|\Delta\theta\| > \nu$  then  $\theta \rightarrow \theta + \Delta\theta$  and return to step 2, otherwise terminate the algorithm.

Victoria-Feser and Ronchetti [30] mentioned that: “The algorithm is convergent provided the starting point is near to the solution” in their study. Therefore, we used different initial points for the first step of the algorithm. Then we observed that there are no significant differences between the estimates according to the different initial points. In this study, the ML estimates are used as an initial points.

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#### 4. SIMULATION STUDY

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A Monte Carlo simulation study was conducted based on various scenarios for the number of observations and outliers to examine the performance of the estimation methods; the ML, LS, robust M estimation with Tukey and the OBR estimation methods. The superiority of the estimates was assessed by using the performance measures, bias and Root-mean-square error (RMSE) defined as

$$(4.1) \quad Bias(\hat{\theta}) = \frac{1}{N} \sum_{i=1}^N (\hat{\theta}_i - \theta),$$

$$(4.2) \quad RMSE(\hat{\theta}) = \sqrt{\frac{1}{N} \sum_{i=1}^N (\hat{\theta}_i - \theta)^2}.$$

We generated  $N = 100$  replications from the MOEBXII distribution with the sample sizes  $n = 25$ ,  $n = 50$  and  $n = 100$ . We consider the following parameter values  $(\alpha, c, k) = (3, 1, 1)$ ,  $(3, 1, 2)$ ,  $(3, 2, 1)$ ,  $(3, 2, 2)$ ,  $(3, 3, 3)$ ,  $(5, 1, 1)$ ,  $(5, 1, 2)$ ,  $(5, 2, 1)$  and  $(5, 2, 2)$ . (One can find the details for generating data set from the MOEBXII distribution in [9]). In this study, the outliers are generated by multiplying the largest observations in the data by 5.

To obtain the M estimations in the simulation study, we determine the tuning constant  $b = 4.685$  for Tukey's  $\rho$  function. For the OBR estimation method, robustness parameter  $c_B$  and precision threshold  $\nu$  were taken as 3 and  $10^{-6}$  respectively.

The simulation results in all cases are summarized in Tables 1-8. In these tables, the bias and RMSE values calculated by using the equations (4.1)-(4.2) are reported for the ML, LS, M estimation with Tukey's  $\rho$  function and the OBR methods.

Tables 1-3 present the results from the case without outlier. From these tables, we can observe that the OBR estimation method has superiority in terms of bias and RMSE in all simulation scenarios for small sample sizes. For moderate sample size we can still observe the better performance of the OBR estimators in most of the cases. However, when sample size increases, the superiority of the ML estimation method in terms of RMSE can be easily observed from Table 3, which is an expected performance of the ML estimation method.

It is obvious from Table 1 that the OBR estimation method has the best performance in terms of RMSE for all parameters for the small sample size ( $n =$

25). The biases of the OBR estimates are lower than that of other methods for most of the values of the parameters. Table 2 shows that the OBR and the ML estimation methods are compatible according to the RMSE values under the assumption of moderate sample sizes ( $n = 50$ ). According to the results given in Table 3, as the sample size increases, the ML estimation method seems superior to the other methods in terms of RMSE in most of the cases as expected.

We recreated the simulation for the same scenarios with outliers and the results are summarized in Tables 4-7. We generate one outlier to see the performance of the estimators in case there is an outlier in the data, for all the sample sizes. Further, to see the behavior of the estimators under the condition that there are more than one outlier, we conduct an additional simulation which we use four outliers in sample size 50. It is already mentioned that the four outliers are generated by multiplying the four largest observation with 5.

Table 4 shows the simulation results for the sample size  $n = 25$  with one outlier. We observe that outlier induces a large influence on the bias and RMSE of the ML and the LS estimators whereas it has a smaller impact on the robust estimators. If the M and the OBR estimation methods are compared with each other, the OBR estimation method is superior to the M estimation method in terms of the RMSE.

Table 5 shows the simulation results with one outlier with the sample size 50. When the data include outlier, the ML and the LS estimators are drastically worsen which is reflected to the higher RMSE and biases. However, the M and the OBR estimators still have better performance.

Table 6 represents the simulation results with one outlier with the sample size 100. According to Table 6, the OBR estimation method outperforms in terms of bias and RMSE values for the most values of the parameters among the others.

The results given in Table 7 are similar to the results reported in Table 4-6. The OBR estimator seems superior to the other estimators in terms of bias and RMSE values.

To sum up, all of these results show that the amount of efficiency we lose by using the OBR estimation method is negligible in comparison to the other estimation methods in most of the cases.

According to a anonymous referee's suggestion, we conduct an additional simulation study to confirm the results of real data example considered in the next section. In this simulation design we generate 50 observations from the MOEBXII distribution by using the following initial parameters  $(\alpha, c, k) = (30, 2, 1)$ . We consider two outlier cases about this simulation design, first we add one outlier and then we add four outliers. The results of this simulation are given in Table 8. According to Table 8, the OBR and the ML methods show similar performances when the data set has no outliers. Considering the RMSE values, the OBR and ML estimators show better performance than the LS and the M estimators. On

the other hand, when we create one outlier in the data, the performances of the ML and LS estimators are drastically worsen in terms of the RMSE and the bias values. Unlike the ML and the LS estimates, M estimates do not affected from the outlier. Considering the OBR estimator, we observe that it has the best performance among all the estimators we considered. If the data set has four outliers, then the OBR estimator has the best performances and it is followed by the M estimator. In this case, the ML and the LS estimators are worse according to bias and RMSE values.

In summary, when there are potential outliers in the data the OBR estimation method outperforms among the others in terms of the bias and RMSE values.

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## 5. REAL DATA EXAMPLE

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In this section the application of the MOEBXII distribution to a real data set is discussed to illustrate the performance of the proposed parameter estimation method. We use a data set from a pharmacy study of Canaparo et al.[5]. The sample size is  $n = 65$ . The data is related to the ibuprofen which is widely available as an over-the-counter treatment for pain and fever. It represents the mean plasma concentration–time profile of Ibuprofen (S) in all healthy subjects after a single 400 mg oral dose of racemic Ibuprofen. Ibuprofen blood plasma levels are were computed at various time points using data from pharmacokinetics trials.

We use the MOEBXII distribution to fit the data. We consider the ML, LS, M and the OBR estimators to obtain the parameter estimates. The following steps are used to obtain the OBR estimates of the parameters:

- (i) Obtain the ML estimate.
- (ii) Take  $c_B = 3$ , the ML estimate as an initial estimate and calculate the OBR estimate.
- (iii) Take  $c_B = 3$ , the OBR estimate obtained in step (ii) as a new initial estimate and calculate the OBR estimate again [11].

Note that one can see [11] and [31] for further details about the selection of the robustness tuning constant [8].

To further see the performance of the estimator, we consider adding one and four outliers to the data. The parameter estimates for the real data are given in Table 9. In this table, we summarize the results for the cases outliers and without outliers. The fitted densities obtained from the ML, the LS, the

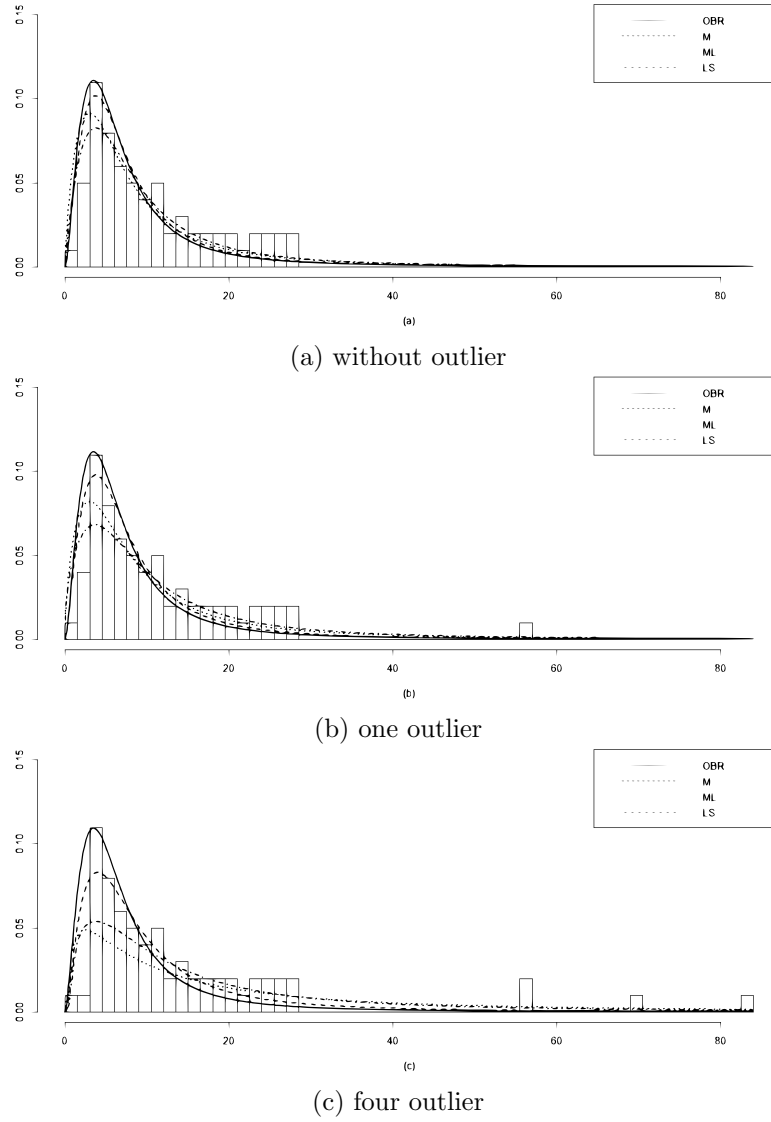


Figure 2: Histogram of Ibuprofen data and the fitted densities with the ML, LS, robust M and OBR estimates

robust M and the OBR estimates in case of outliers and without outliers, and histogram of the ibuprofen data are shown in Figure 2.

Figure 2(a) illustrates the fitted densities when there is no outlier in the data. From Figure 2(a), it can be seen that the MOEBXII distribution is suitable to model the mean plasma concentration of ibuprofen. All of the mentioned estimators are in good agreement in terms of fitting data in the tail. However, the ML and LS are not provided a good fit in the central portion of the data. The fitted density obtained from the robust estimator based on Tukey's  $\rho_b$  function shows better fit than the ML and LS fits in the central portion of the data. In particular, the model obtained from the OBR estimates performs fairly well to describe the central part of the data set. The fitted densities obtained from the

ML, LS estimates don't seem catch  $C_{max}$ , the pick of the data. Therefore these estimators can not give reasonable estimate for  $T_{max}$ , the time taken to reach the maximum concentration.

Figure 2(b) shows the fitted densities when there is one outlier in the data set. From this figure, the OBR and M estimators seem not to be affected from one outlier. In addition, From Table 9, it is clear that the estimates obtained from the OBR and M estimation with one outlier is closer to the estimates obtained without outlier. Similar comments can be made for the ML estimates. Adding one outlier causes a small difference on the ML estimation. However, it does not still provides better fit than the OBR and M estimators do. The fitted density obtained from the ML estimates seems not catching the pick of the data. Concerning the LS estimator, it can be seen that only one outlier has an significant effect on LS estimator. This can also be observed from Table 9.

Finally, in Figure 2(c) we display the histogram of the data with four outliers along with the fitted densities. From this figure, we can clearly see that the best fitted density is obtained from the OBR estimation method. The OBR is followed by the M estimator. This figure demonstrates how outliers could potentially distort the ML and the LS estimates. The performance of the ML and the LS estimators are worse than the OBR and M estimator. Results from Table 9 is also supported this outcome.

From these results, we can conclude that if we have some outliers in the data, the OBR estimation method can be used safely because the OBR estimation method are not affected from the outliers as the other methods do. To sum up, we can clearly observe that the OBR estimation method can be used to find better fits for the data sets that may have some outliers.

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## 6. CONCLUSION

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Two objectives have been considered in this study. First we have proposed to use the OBR estimation method to estimate the parameters of the MOEBXII distribution proposed by Al-Saiari et al. [3] with the advantage of flexibility to fit the data sets with various shapes. Second, we have considered the modeling the data sets from pharmacokinetics studies represent the changes in plasma concentrations of drugs with the MOEBXII distribution. When the estimation problem is addressed, from both the simulation study and the real data example we observe that the OBR estimator exhibits strong robustness in presence of observations discordant with the assumed model. These results show that not only the OBR estimate achieves smaller RMSE for the small sample sizes but also its RMSE is smaller for the outlier cases for each sample sizes than those of the ML, LS and robust M estimators. The simulation results of the ML and LS estimators for the outlier cases are quite different from the cases without



outlier. The existence of outliers in data results in striking differences in RMSE of ML and LS estimates, in contrast to robust estimates, especially the OBR estimates. A general inspection of the table shows that a comparison of the OBR with the ML, LS and robust M estimation methods reveals the superiority of the new estimate in the outlier case and/or small sample case. When we consider the real world data analysis, modeling pharmacokinetics data set with the MOEBXII distribution, from the real data example we can observe that the MOEBXII distribution with the OBR estimates can be a good choice for modeling the changes in plasma concentrations of drugs which is an important pharmacokinetics variable. Because estimating the parameters with the OBR estimation method would be more reliable in estimating other variables such as  $C_{max}$  and  $T_{max}$  other pharmacokinetics variables.

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Table 1: The bias and RMSE (Parenthesis) for n=25.

Parameter $\alpha$					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	0.1081 (0.2221)	-0.4797 (0.6033)	-0.0864 (0.0623)	-0.0845	<b>(0.0464)</b>
(3,1,2)	0.0118 (0.2294)	0.3000 (0.3205)	-0.0938 (0.1003)	0.0069	<b>(0.0165)</b>
(3,2,1)	0.1761 (0.2195)	-0.0871 (0.4903)	-0.0431 (0.2034)	-0.0011	<b>(0.0032)</b>
(3,2,2)	0.1778 (0.2142)	0.1685 (0.2696)	0.1198 (0.1808)	0.0100	<b>(0.0036)</b>
(3,3,3)	0.0525 (0.1987)	0.1937 (0.1947)	-0.0778 (0.1537)	0.0101	<b>(0.0039)</b>
(5,1,1)	0.0328 (0.2173)	-0.0641 (0.6265)	-0.0990 (0.2846)	-0.0495	<b>(0.1965)</b>
(5,1,2)	-0.0668 (0.1981)	-0.4701 (0.1622)	-0.4683 (0.5792)	-0.0102	<b>(0.1415)</b>
(5,2,1)	-0.0606 (0.2083)	-0.4757 (0.5291)	0.0095 (0.1544)	0.0088	<b>(0.0039)</b>
(5,2,2)	-0.0269 (0.2111)	-0.0653 (0.7695)	-0.4989 (0.6140)	0.0087	<b>(0.0193)</b>
Parameter $c$					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	0.1229 (0.1026)	0.3267 (0.2359)	0.3239 (0.2059)	0.0690	<b>(0.0841)</b>
(3,1,2)	0.1073 (0.0555)	0.2684 (0.1663)	0.2711 (0.1606)	-0.0005	<b>(0.0150)</b>
(3,2,1)	0.1180 (0.1370)	0.4928 (0.4435)	0.4513 (0.3848)	-0.0012	<b>(0.0039)</b>
(3,2,2)	0.0801 (0.1123)	0.3417 (0.3475)	0.3760 (0.3220)	-0.0011	<b>(0.0001)</b>
(3,3,3)	0.0198 (0.1421)	0.3733 (0.4870)	0.3993 (0.4264)	-0.0034	<b>(0.0003)</b>
(5,1,1)	0.0645 (0.0888)	0.3310 (0.3067)	0.4119 (0.3607)	0.1541	<b>(0.0271)</b>
(5,1,2)	0.0947 (0.0531)	0.3728 (0.2557)	0.2709 (0.1452)	0.0010	<b>(0.0007)</b>
(5,2,1)	0.0333 (0.1558)	0.2107 (0.5419)	0.1893 (0.3722)	-0.0028	<b>(0.0002)</b>
(5,2,2)	0.1550 (0.1154)	0.1436 (0.5794)	0.4771 (0.3996)	-0.0016	<b>(0.0004)</b>
Parameter $k$					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	-0.0403 (0.0739)	0.4731 (0.3267)	-0.1742 (0.1155)	-0.0320	<b>(0.0635)</b>
(3,1,2)	-0.0305 (0.1011)	-0.3271 (0.4601)	-0.1788 (0.1281)	0.0026	<b>(0.0020)</b>
(3,2,1)	-0.0068 (0.0497)	0.2188 (0.3604)	-0.1080 (0.1292)	0.0006	<b>(0.0023)</b>
(3,2,2)	0.0312 (0.0941)	-0.2834 (0.3071)	-0.2902 (0.2239)	0.0025	<b>(0.0037)</b>
(3,3,3)	-0.0025 (0.1321)	-0.1886 (0.2640)	-0.0999 (0.2113)	0.0045	<b>(0.0709)</b>
(5,1,1)	-0.2456 (0.1743)	-0.3374 (0.4375)	-0.3855 (0.3544)	0.0067	<b>(0.0570)</b>
(5,1,2)	-0.0290 (0.0966)	-0.9483 (0.9097)	-0.9361 (0.8912)	-0.0017	<b>(0.0078)</b>
(5,2,1)	0.0013 (0.0479)	-0.5580 (0.3312)	-0.5309 (0.2920)	0.0018	<b>(0.0012)</b>
(5,2,2)	-0.0521 (0.0893)	-0.0616 (0.1308)	-0.0527 (0.1543)	0.0020	<b>(0.0009)</b>

Table 2: The bias and RMSE (Parenthesis) for n=50.

Parameter $\alpha$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.0988 (0.2140)	-0.3154 (0.1141)	-0.0477 (0.0240)	-0.0127 ( <b>0.0047</b> )
(3,1,2)	-0.0183 (0.2215)	-0.3803 (0.1631)	-0.1934 (0.0724)	-0.0066 ( <b>0.0628</b> )
(3,2,1)	0.0435 ( <b>0.0188</b> )	-0.2936 (0.1646)	-0.0262 (0.0495)	-0.0442 (0.0950)
(3,2,2)	-0.0083 (0.2069)	0.0970 (0.1246)	-0.1616 (0.0687)	0.0156 ( <b>0.0666</b> )
(3,3,3)	-0.0537 ( <b>0.0210</b> )	-0.0713 (0.1523)	-0.0840 (0.0774)	0.1114 (0.3523)
(5,1,1)	-0.0260 (0.2289)	-0.4694 (0.2311)	-0.4008 (0.2362)	-0.0178 ( <b>0.0745</b> )
(5,1,2)	-0.0579 (0.2139)	-0.1342 (0.2093)	-0.4957 (0.2457)	-0.0263 ( <b>0.0214</b> )
(5,2,1)	-0.0264 (0.2139)	0.0147 (0.2217)	-0.4142 (0.2188)	-0.0259 ( <b>0.0013</b> )
(5,2,2)	-0.0481 (0.1915)	0.0584 (0.2048)	-0.4999 (0.2500)	-0.0331 ( <b>0.0727</b> )
Parameter $c$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.0466 (0.0479)	0.2047 (0.0652)	0.1930 (0.0645)	0.0015 ( <b>0.0184</b> )
(3,1,2)	0.0267 (0.0423)	0.1867 (0.0529)	0.1461 (0.0529)	0.0011 ( <b>0.0096</b> )
(3,2,1)	0.0477 (0.0710)	0.3217 (0.1453)	0.2983 (0.1346)	0.0054 ( <b>0.0512</b> )
(3,2,2)	0.0501 (0.0359)	0.3102 (0.1353)	0.2588 (0.1226)	-0.0024 ( <b>0.0021</b> )
(3,3,3)	0.0307 (0.0582)	0.3692 (0.1865)	0.3227 (0.1811)	-0.0287 ( <b>0.0215</b> )
(5,1,1)	0.0505 ( <b>0.0342</b> )	0.1857 (0.0528)	0.2200 (0.0804)	0.0016 (0.0469)
(5,1,2)	0.0227 ( <b>0.0146</b> )	0.1026 (0.0547)	0.3426 (0.1504)	0.0012 (0.0648)
(5,2,1)	0.0592 (0.0816)	0.1588 (0.1661)	0.3253 (0.1614)	0.0043 ( <b>0.0387</b> )
(5,2,2)	0.0613 (0.0893)	0.1208 (0.0954)	0.4289 (0.2160)	0.0024 ( <b>0.0342</b> )
Parameter $k$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	-0.0218 (0.0198)	-0.0982 (0.0281)	-0.2219 (0.0605)	-0.0026 ( <b>0.0179</b> )
(3,1,2)	0.0469 (0.0505)	0.1787 (0.0472)	-0.1068 (0.0315)	-0.0021 ( <b>0.0059</b> )
(3,2,1)	0.0032 (0.0659)	-0.0263 (0.0565)	-0.0805 ( <b>0.0558</b> )	-0.0049 (0.0613)
(3,2,2)	0.0104 ( <b>0.0461</b> )	-0.2862 (0.1539)	-0.1492 (0.0642)	0.0069 (0.0086)
(3,3,3)	-0.0239 (0.0933)	-0.1003 (0.1198)	-0.2754 (0.1172)	0.0456 ( <b>0.0650</b> )
(5,1,1)	-0.0299 (0.0239)	-0.4980 (0.2481)	-0.4967 (0.2468)	-0.0023 ( <b>0.0012</b> )
(5,1,2)	-0.0134 ( <b>0.0330</b> )	-0.0235 (0.0946)	-0.4470 (0.2499)	-0.0049 (0.0771)
(5,2,1)	-0.0006 ( <b>0.0210</b> )	0.0010 (0.0487)	-0.4959 (0.2462)	-0.0033 (0.0246)
(5,2,2)	-0.0033 ( <b>0.0242</b> )	0.0197 (0.0909)	-0.4989 (0.2489)	-0.0051 (0.0279)

Table 3: The bias and RMSE (Parenthesis) for n=100.

Parameter $\alpha$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.0097 ( <b>0.0355</b> )	-0.2899 (0.1072)	-0.0607 (0.0397)	-0.1376 (0.2175)
(3,1,2)	-0.0191 ( <b>0.0368</b> )	-0.3663 (0.1805)	-0.2242 (0.0980)	0.0879 (0.2121)
(3,2,1)	0.0325 ( <b>0.0347</b> )	-0.3331 (0.1830)	-0.0721 (0.0711)	0.0540 (0.1974)
(3,2,2)	0.0249 ( <b>0.0365</b> )	0.0373 (0.1226)	-0.1339 (0.0878)	-0.0457 (0.2264)
(3,3,3)	-0.0006 ( <b>0.0328</b> )	-0.1143 (0.1465)	-0.1815 (0.1187)	-0.0452 (0.2125)
(5,1,1)	-0.0487 ( <b>0.0357</b> )	-0.4458 (0.2158)	-0.3646 (0.2165)	-0.0300 (0.2173)
(5,1,2)	-0.0168 ( <b>0.0349</b> )	-0.1446 (0.1883)	-0.4709 (0.2435)	-0.0504 (0.2126)
(5,2,1)	0.0293 ( <b>0.0354</b> )	0.0118 (0.2107)	-0.3618 (0.2227)	0.0597 (0.2211)
(5,2,2)	0.0137 ( <b>0.0368</b> )	-0.0741 (0.2187)	-0.4960 (0.2468)	0.0701 (0.1997)
Parameter $c$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.0315 ( <b>0.0164</b> )	0.2066 (0.0980)	0.2044 (0.0986)	0.0557 (0.0492)
(3,1,2)	0.0254 ( <b>0.0134</b> )	0.1471 (0.0566)	0.1561 (0.0598)	0.0115 (0.0177)
(3,2,1)	-0.0001 ( <b>0.0282</b> )	0.2233 (0.1595)	0.2116 (0.1534)	0.0666 (0.1013)
(3,2,2)	0.0034 ( <b>0.0203</b> )	0.3162 (0.1652)	0.3160 (0.1594)	0.1252 (0.0733)
(3,3,3)	0.0232 ( <b>0.0288</b> )	0.3041 (0.1628)	0.2714 (0.1573)	0.1005 (0.1030)
(5,1,1)	0.2304 (0.0941)	0.1675 (0.0636)	0.0613 (0.0446)	0.0152 ( <b>0.0211</b> )
(5,1,2)	0.0318 ( <b>0.0154</b> )	0.0833 (0.0476)	0.3125 (0.1322)	0.0323 (0.0344)
(5,2,1)	0.3095 ( <b>0.1688</b> )	0.0565 (0.1553)	0.0231 (0.0306)	0.1173 (0.1171)
(5,2,2)	0.0069 ( <b>0.0290</b> )	0.0375 (0.0949)	0.3916 (0.1986)	0.0320 (0.0849)
Parameter $k$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.0071 (0.0218)	-0.0794 (0.0507)	-0.2181 (0.0733)	-0.0462 ( <b>0.0118</b> )
(3,1,2)	-0.0088 (0.0514)	0.1005 (0.0536)	-0.1030 (0.0447)	-0.0233 ( <b>0.0287</b> )
(3,2,1)	0.0049 ( <b>0.0128</b> )	0.0109 (0.0759)	-0.1993 (0.0722)	-0.0009 (0.0382)
(3,2,2)	-0.2288 (0.0843)	-0.2906 (0.1341)	-0.0071 ( <b>0.0223</b> )	-0.0313 (0.0732)
(3,3,3)	-0.0237 ( <b>0.0302</b> )	-0.1285 (0.1235)	-0.1397 (0.1128)	-0.0007 (0.0958)
(5,1,1)	0.0130 ( <b>0.0226</b> )	-0.4924 (0.2428)	-0.4952 (0.2455)	-0.0218 (0.0363)
(5,1,2)	-0.0045 ( <b>0.0230</b> )	-0.0171 (0.1301)	-0.4933 (0.2456)	-0.0490 (0.0512)
(5,2,1)	0.0153 ( <b>0.0106</b> )	0.0231 (0.0478)	-0.4908 (0.2415)	-0.0143 (0.0306)
(5,2,2)	0.0152 ( <b>0.0215</b> )	-0.0074 (0.0779)	-0.4995 (0.2495)	0.0207 (0.0566)

Table 4: The bias and RMSE (Parenthesis) for n=25 with one outlier.

Parameter $\alpha$					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	0.5260 (0.7583)	0.3937 (0.6005)	0.0648 (0.0974)	0.0675	<b>(0.0334)</b>
(3,1,2)	0.7677 (1.0733)	-0.2801 (0.9506)	0.2737 (0.3186)	0.1322	<b>(0.1359)</b>
(3,2,1)	0.6696 (0.8518)	0.7122 (0.5237)	0.0598 (0.0664)	0.0693	<b>(0.0384)</b>
(3,2,2)	0.9541 (0.9890)	-0.3073 (0.2022)	0.2807 (0.5148)	0.1792	<b>(0.1211)</b>
(3,3,3)	0.3557 (0.1608)	0.8745 (0.8261)	0.1740 (0.2903)	0.0327	<b>(0.0782)</b>
(5,1,1)	0.7769 (0.8408)	0.6287 (0.5721)	0.3778 (0.2233)	0.1630	<b>(0.0783)</b>
(5,1,2)	0.8666 (0.9375)	0.7299 (0.7325)	0.4934 (0.2456)	0.0133	<b>(0.0215)</b>
(5,2,1)	0.6980 (0.9422)	0.5848 (0.5159)	0.3630 (0.2123)	-0.0127	<b>(0.0257)</b>
(5,2,2)	0.9814 (0.9669)	0.8705 (0.8508)	0.4707 (0.7286)	0.2630	<b>(0.2471)</b>
Parameter $c$					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	-0.2184 (0.1522)	-0.3247 (0.2277)	-0.2399 (0.1012)	-0.0170	<b>(0.0016)</b>
(3,1,2)	-0.1275 (0.0787)	-0.3053 (0.2022)	-0.2481 (0.1208)	-0.0298	<b>(0.0158)</b>
(3,2,1)	-0.2308 (0.3010)	-0.4433 (0.4108)	-0.2805 (0.1529)	-0.0303	<b>(0.0039)</b>
(3,2,2)	0.0665 (0.1365)	-0.2382 (0.2869)	-0.1332 (0.1106)	-0.0491	<b>(0.0328)</b>
(3,3,3)	0.4780 (0.3820)	-0.2563 (0.3921)	-0.4035 (0.3110)	-0.1655	<b>(0.1587)</b>
(5,1,1)	-0.2185 (0.2043)	-0.4727 (0.3573)	-0.2399 (0.1081)	-0.0214	<b>(0.0015)</b>
(5,1,2)	-0.0734 (0.1097)	-0.3024 (0.1942)	-0.3290 (0.1483)	0.0227	<b>(0.0528)</b>
(5,2,1)	-0.2499 (0.4091)	-0.5456 (0.5562)	-0.1779 (0.1339)	-0.0251	<b>(0.0810)</b>
(5,2,2)	-0.0615 (0.2139)	-0.5764 (0.5222)	-0.3317 (0.1961)	-0.0728	<b>(0.0270)</b>
Parameter $k$					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	0.2541 (0.1131)	-0.3756 (0.3442)	0.3033 (0.1241)	0.0213	<b>(0.0048)</b>
(3,1,2)	0.4746 (0.3717)	0.4407 (0.5491)	0.2398 (0.1200)	0.0637	<b>(0.0899)</b>
(3,2,1)	0.2620 (0.1153)	-0.5760 (0.4492)	0.2638 (0.1155)	0.0170	<b>(0.0019)</b>
(3,2,2)	0.5505 (0.3801)	0.5809 (0.3841)	0.2605 (0.1061)	0.0583	<b>(0.0551)</b>
(3,3,3)	0.9466 (0.9067)	0.7017 (0.5734)	0.4727 (0.4533)	0.2293	<b>(0.1271)</b>
(5,1,1)	0.2190 (0.1047)	0.6239 (0.4033)	0.4945 (0.2448)	0.0280	<b>(0.0026)</b>
(5,1,2)	0.2445 (0.3798)	0.9613 (0.9299)	0.4976 (0.9480)	0.2095	<b>(0.2479)</b>
(5,2,1)	0.1730 (0.1975)	0.5925 (0.3678)	0.4706 (0.2271)	-0.0004	<b>(0.0538)</b>
(5,2,2)	0.4730 (0.3290)	0.9820 (0.9687)	0.4554 (0.2455)	0.0791	<b>(0.0385)</b>

Table 5: The bias and RMSE (Parenthesis) for n=50 with one outlier.

Parameter $\alpha$					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	0.7658 (0.7925)	0.2757 (0.5942)	0.0844 (0.0336)	0.0972	<b>(0.0192)</b>
(3,1,2)	0.9122 (0.9377)	-0.2170 (0.1263)	0.2961 (0.1128)	0.0691	<b>(0.0969)</b>
(3,2,1)	0.8448 (0.8977)	0.7232 (0.5303)	0.0696 (0.0452)	0.0194	<b>(0.0203)</b>
(3,2,2)	0.9860 (0.9818)	-0.2744 (0.1613)	0.1150 (0.1290)	0.3149	<b>(0.0935)</b>
(3,3,3)	0.9464 (0.9216)	0.2705 (0.2294)	0.3848 (0.1637)	-0.0039	<b>(0.0482)</b>
(5,1,1)	0.5430 (0.8791)	0.6820 (0.5746)	0.3746 (0.2256)	0.1248	<b>(0.0341)</b>
(5,1,2)	0.8018 (0.9470)	0.9043 (0.8835)	0.4865 (0.2431)	0.1075	<b>(0.2400)</b>
(5,2,1)	0.8957 (0.9413)	0.6427 (0.5411)	0.4286 (0.2280)	0.0585	<b>(0.1521)</b>
(5,2,2)	0.9518 (0.9853)	0.9194 (0.8797)	0.4780 (0.2481)	0.1677	<b>(0.2322)</b>
Parameter c					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	-0.1187 (0.1086)	-0.2660 (0.1783)	-0.1984 (0.0917)	-0.0161	<b>(0.0004)</b>
(3,1,2)	-0.0095 (0.0199)	-0.1356 (0.0502)	-0.1181 (0.0473)	-0.0036	<b>(0.0008)</b>
(3,2,1)	-0.1724 (0.2018)	-0.2910 (0.2963)	-0.1612 (0.1244)	-0.0281	<b>(0.0024)</b>
(3,2,2)	-0.1955 (0.1236)	-0.2882 (0.2294)	0.0101 (0.0581)	-0.0290	<b>(0.0045)</b>
(3,3,3)	0.5491 (0.3680)	-0.2338 (0.2683)	-0.0770 (0.1276)	-0.0786	<b>(0.0182)</b>
(5,1,1)	-0.1099 (0.0960)	-0.3937 (0.2707)	-0.2269 (0.1000)	-0.0159	<b>(0.0004)</b>
(5,1,2)	-0.0081 (0.0340)	-0.3363 (0.1934)	-0.3118 (0.1338)	-0.0102	<b>(0.0010)</b>
(5,2,1)	-0.1651 (0.2883)	-0.5914 (0.5327)	-0.3109 (0.1790)	-0.0341	<b>(0.0034)</b>
(5,2,2)	0.1245 (0.1309)	-0.5378 (0.4875)	-0.3568 (0.1874)	-0.0336	<b>(0.0051)</b>
Parameter k					
	ML	LS	M (Tukey)	OBR	
(3,1,1)	0.2419 (0.1065)	-0.3498 (0.3793)	0.2529 (0.0928)	0.0223	<b>(0.0009)</b>
(3,1,2)	0.5264 (0.3272)	0.5314 (0.4231)	0.2287 (0.0853)	0.0217	<b>(0.0074)</b>
(3,2,1)	0.2877 (0.1012)	-0.5686 (0.3724)	0.2880 (0.1090)	0.0161	<b>(0.0011)</b>
(3,2,2)	0.6017 (0.4020)	0.6141 (0.4017)	0.2857 (0.1095)	0.0346	<b>(0.0075)</b>
(3,3,3)	0.9529 (0.9132)	0.6530 (0.4790)	0.2459 (0.1222)	0.0912	<b>(0.0250)</b>
(5,1,1)	0.1709 (0.0692)	0.6144 (0.3888)	0.4969 (0.2470)	0.0198	<b>(0.0008)</b>
(5,1,2)	0.3460 (0.1854)	0.9919 (0.9857)	0.4437 (0.2444)	0.0243	<b>(0.0083)</b>
(5,2,1)	0.2067 (0.0796)	0.6092 (0.3788)	0.4968 (0.2470)	0.0118	<b>(0.0081)</b>
(5,2,2)	0.4108 (0.2310)	0.9936 (0.9879)	0.4991 (0.2491)	0.0377	<b>(0.0080)</b>



Table 6: The bias and RMSE (Parenthesis) for n=100 with one outlier.

Parameter $\alpha$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.8537 (0.9116)	0.7543 (0.6559)	0.0566 (0.0316)	0.0104 ( <b>0.0018</b> )
(3,1,2)	0.9586 (0.9905)	-0.3791 (0.2258)	0.2690 (0.1110)	0.0130 ( <b>0.0016</b> )
(3,2,1)	0.9976 (0.9954)	0.8250 (0.6824)	0.0300 (0.0309)	0.0137 ( <b>0.0290</b> )
(3,2,2)	0.4103 (0.1894)	-0.2510 (0.1249)	0.3399 (0.1359)	0.0192 ( <b>0.0018</b> )
(3,3,3)	0.9669 (0.9403)	-0.2345 (0.1484)	0.4405 (0.1998)	0.0393 ( <b>0.0753</b> )
(5,1,1)	0.9206 (0.9225)	0.8001 (0.8085)	0.4078 (0.2375)	0.0153 ( <b>0.0003</b> )
(5,1,2)	0.9836 (0.9710)	0.9266 (0.8986)	0.4604 (0.2496)	0.0318 ( <b>0.0386</b> )
(5,2,1)	0.9471 (1.0099)	0.7665 (0.6802)	0.4633 (0.2418)	0.0180 ( <b>0.0407</b> )
(5,2,2)	0.4346 (0.2033)	0.9036 (0.8763)	0.4800 (0.2500)	0.0268 ( <b>0.0034</b> )
Parameter $c$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	-0.0742 (0.4301)	-0.1888 (0.6320)	-0.1622 (0.0572)	-0.0013 ( <b>0.0231</b> )
(3,1,2)	-0.0144 (0.0093)	-0.1600 (0.4116)	-0.1358 (0.0390)	-0.0015 ( <b>0.0012</b> )
(3,2,1)	-0.2041 (0.1376)	-0.4140 (0.3012)	-0.2573 (0.1460)	-0.0035 ( <b>0.0155</b> )
(3,2,2)	0.0852 (0.0584)	-0.2921 (0.1768)	-0.1749 (0.0913)	-0.0036 ( <b>0.0451</b> )
(3,3,3)	0.5257 (0.3139)	-0.3673 (0.3133)	-0.1820 (0.1206)	-0.0102 ( <b>0.0600</b> )
(5,1,1)	-0.0490 (0.0431)	-0.3632 (0.2194)	-0.2476 (0.1015)	-0.0014 ( <b>0.0245</b> )
(5,1,2)	0.0414 (0.0126)	-0.2780 (0.1118)	-0.2837 (0.1087)	-0.0020 ( <b>0.0012</b> )
(5,2,1)	-0.1072 (0.1860)	-0.6308 (0.5946)	-0.3055 (0.1529)	-0.0031 ( <b>0.0117</b> )
(5,2,2)	0.3992 (0.0753)	-0.5101 (0.3795)	-0.3966 (0.1878)	-0.0032 ( <b>0.0343</b> )
Parameter $k$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.2783 (0.0949)	-0.9356 (1.0459)	0.2708 (0.0819)	0.0020 ( <b>0.0576</b> )
(3,1,2)	0.5343 (0.3174)	0.6186 (0.4029)	0.2308 (0.1867)	0.0040 ( <b>0.0915</b> )
(3,2,1)	0.3315 (0.1188)	-1.1387 (1.3363)	0.3016 (0.0988)	0.0025 ( <b>0.0857</b> )
(3,2,2)	0.5936 (0.3715)	0.5878 (0.3550)	0.2493 (0.1933)	0.0050 ( <b>0.1096</b> )
(3,3,3)	0.9831 (0.9681)	0.8888 (0.8074)	0.2834 (0.1353)	0.0124 ( <b>0.0084</b> )
(5,1,1)	0.1908 (0.0588)	0.6082 (0.3774)	0.4993 (0.2493)	0.0019 ( <b>0.0458</b> )
(5,1,2)	0.3245 (0.1361)	0.9955 (0.9914)	0.4971 (0.2472)	0.0055 ( <b>0.0107</b> )
(5,2,1)	0.2006 (0.0638)	0.6048 (0.3712)	0.4987 (0.2488)	0.0021 ( <b>0.0549</b> )
(5,2,2)	0.3428 (0.1376)	0.9992 (0.9985)	0.3428 (0.1376)	0.0041 ( <b>0.0679</b> )

Table 7: The bias and RMSE (Parenthesis) for  $n=50$  with four outliers.

Parameter $\alpha$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	1.8192 (1.6599)	0.8780 (0.7723)	0.1795 (0.0634)	0.0834 ( <b>0.0116</b> )
(3,1,2)	2.3995 (2.9045)	0.4393 (0.2599)	0.4573 (0.2555)	0.1753 ( <b>0.0405</b> )
(3,2,1)	2.1213 (2.6922)	0.8396 (0.7130)	0.2445 (0.1116)	0.1012 ( <b>0.0123</b> )
(3,2,2)	2.6898 (2.2763)	0.3345 (0.1911)	0.4635 (0.2822)	0.1896 ( <b>0.0679</b> )
(3,3,3)	2.9292 (2.5814)	0.3273 (0.1249)	0.5968 (0.3730)	0.2891 ( <b>0.1190</b> )
(5,1,1)	2.9800 (3.0851)	0.8503 (0.7336)	0.2737 (0.1275)	0.1125 ( <b>0.0160</b> )
(5,1,2)	3.9945 (4.3873)	0.9993 (0.9986)	0.9991 (0.9982)	0.2696 ( <b>0.1125</b> )
(5,2,1)	3.7069 (3.1097)	0.9545 (0.9885)	0.3372 (0.1666)	0.1335 ( <b>0.0220</b> )
(5,2,2)	3.5945 (4.1334)	0.9853 (0.9761)	0.9940 (0.9898)	0.2896 ( <b>0.1202</b> )
Parameter $c$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.2709 (0.1274)	0.2205 (0.0778)	0.2232 (0.0878)	0.0150 ( <b>0.0005</b> )
(3,1,2)	0.3592 (0.1972)	0.1978 (0.0636)	0.1986 (0.0697)	0.0167 ( <b>0.0004</b> )
(3,2,1)	0.7857 (1.1572)	0.5197 (0.6674)	0.3933 (0.2462)	0.0329 ( <b>0.0015</b> )
(3,2,2)	0.9072 (1.1683)	0.3664 (0.2268)	0.3465 (0.1961)	0.0417 ( <b>0.0044</b> )
(3,3,3)	1.3173 (2.0957)	0.3082 (0.1525)	0.3728 (0.2224)	0.0800 ( <b>0.0098</b> )
(5,1,1)	0.3561 (0.2606)	0.3810 (0.2948)	0.3490 (0.2166)	0.0128 ( <b>0.0002</b> )
(5,1,2)	0.4625 (0.3055)	0.2670 (0.1102)	0.2925 (0.1343)	0.0162 ( <b>0.0004</b> )
(5,2,1)	0.9675 (1.4720)	0.8075 (1.0989)	0.5793 (0.4692)	0.0352 ( <b>0.0017</b> )
(5,2,2)	0.9994 (1.2173)	0.4066 (0.2439)	0.4501 (0.3097)	0.0402 ( <b>0.0025</b> )
Parameter $k$				
	ML	LS	M (Tukey)	OBR
(3,1,1)	0.5637 (0.3516)	1.8390 (1.6041)	0.3359 (0.1325)	0.0196 ( <b>0.0008</b> )
(3,1,2)	1.4464 (2.1420)	0.8282 (0.7011)	0.3686 (0.2293)	0.0474 ( <b>0.0031</b> )
(3,2,1)	0.6755 (0.4794)	1.4009 (2.7706)	0.3795 (0.1661)	0.0210 ( <b>0.0006</b> )
(3,2,2)	1.6785 (2.8440)	0.8418 (0.7197)	0.5169 (0.3583)	0.0521 ( <b>0.0067</b> )
(3,3,3)	2.8503 (3.1275)	0.8355 (0.7122)	0.3288 (0.1913)	0.0926 ( <b>0.0129</b> )
(5,1,1)	0.5399 (0.3318)	0.6267 (0.4037)	0.6583 (0.4414)	0.0159 ( <b>0.0003</b> )
(5,1,2)	1.4151 (2.0741)	0.9999 (0.9998)	0.7133 (0.7656)	0.0454 ( <b>0.0032</b> )
(5,2,1)	0.6832 (0.4851)	0.6485 (0.4277)	0.6753 (0.4605)	0.0205 ( <b>0.0006</b> )
(5,2,2)	1.6970 (1.8872)	0.9983 (0.9967)	0.1379 (0.1287)	0.0497 ( <b>0.0038</b> )

Table 8: The Bias and RMSE (Parenthesis) for  $n=50$  with  $(\alpha, c, k) = (30, 2, 1)$ .

No outlier				
	ML	LS	M (Tukey)	OBR
$\alpha$	-0.0911 ( <b>0.0189</b> )	0.1513 (0.1769)	0.0941 (0.1980)	0.0728 (0.0185)
$c$	0.0297 (0.0177)	-0.2540 (0.2389)	-0.1555 (0.2224)	0.0064 ( <b>0.0083</b> )
$k$	-0.0355 (0.0334)	-0.1736 (0.2788)	-0.2290 (0.1051)	0.0034 ( <b>0.0027</b> )
One outlier				
	ML	LS	M (Tukey)	OBR
$\alpha$	0.4326 (0.5467)	0.9932 (0.9774)	0.2994 (0.1121)	0.1264 ( <b>0.0404</b> )
$c$	-0.3290 (0.2696)	0.9540 (0.9310)	0.2066 (0.0912)	0.0828 ( <b>0.0024</b> )
$k$	0.2182 (0.1020)	0.6785 (0.5012)	0.1924 (0.0469)	0.0478 ( <b>0.0079</b> )
Four outliers				
	ML	LS	M (Tukey)	OBR
$\alpha$	0.6399 (0.9130)	1.0653 (1.8696)	0.5462 (0.3189)	0.1545 ( <b>0.0821</b> )
$c$	0.7921 (1.1059)	0.7132 (0.8086)	0.5152 (0.2921)	0.0095 ( <b>0.0003</b> )
$k$	0.3678 (0.2183)	0.5893 (0.5048)	0.1863 (0.0461)	0.0547 ( <b>0.0095</b> )

Table 9: The ML, LS, M and OBR estimates for ibuprofen data.

	without outlier			with one outlier			with four outliers		
	$\hat{\alpha}$	$\hat{c}$	$\hat{k}$	$\hat{\alpha}$	$\hat{c}$	$\hat{k}$	$\hat{\alpha}$	$\hat{c}$	$\hat{k}$
ML	23.7002	1.7654	0.9243	24.7562	1.5853	0.9899	20.1377	2.2483	0.4986
LS	37.002	1.8365	0.9726	38.1051	1.3580	1.2221	35.8070	3.8365	0.3769
M(Tukey)	41.1842	2.2900	0.8721	40.1748	2.3886	0.8160	41.8742	2.9751	0.6129
OBR	34.5757	2.5723	0.7726	34.7176	2.5421	0.7853	34.8430	2.4720	0.8013