INFERENTIAL PROCEDURES BASED ON THE DOUBLE BOOTSTRAP FOR LOG LOGISTIC REGRESSION MODEL WITH CENSORED DATA

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ABSTRACT   Traditional inferential procedures based on the asymptotic normality assumption such as the Wald often produce misleading inferences when dealing with censored data and small samples. Alternative estimation techniques such as the jackknife and bootstrap percentile allow us to construct the interval estimates without relying on any classical assumptions. Recently, the double bootstrap became preferable as it is not only free from any classical assumptions, but also has higher order of accuracy. In this paper, we compare the performances of the interval estimates based on the double bootstrap without pivot with the Wald, jackknife and bootstrap percentile interval estimates for the parameters of the log logistic model with right censored data and covariates via a coverage probability study. Based on the results of the study, we concluded that the double bootstrap without pivot technique works better than the other interval estimation techniques, even when sample size is 25. The double bootstrap without pivot technique worked well with real data on hypernephroma patients.

(**Keywords**: censored data, coverage probability study, double bootstrap, interval estimation, log logistic)

INTRODUCTION

In survival analysis, large sample interval estimation based on the asymptotic normality assumptions (also known as Wald interval) is often used as a technique to construct confidence interval for parameters when censored data are involved. Literature shows that misleading inferences could arise when dealing with censored observations and small sample sizes, see [1], [2], [3], [4] and [5]. Jackknife and bootstrap are resampling techniques that do not rely on asymptotic normality assumption and therefore are able to produce more reliable interval estimates.

Jackknife technique was first introduced for bias estimation of a statistic of interest in small sample [6], [7]. The technique later was expanded for estimating standard errors and constructing reasonably reliable confidence interval estimates [8]. A complete review on the jackknife technique and its application can be found in [9]. The bootstrap technique was first introduced by Efron [10] who proposed the bootstrap percentile (B-p) interval. It constructs interval estimates based on the percentiles of the bootstrap distribution of a statistics.

The B-p interval estimation technique is popular due to its simplicity and ability to produce accurate results without having the knowledge of normalizing transformations [11]. More discussion on bootstrap confidence intervals can be obtained in [12], [13], [14], [15] and [16].

Double bootstrap (DB) is a sampling procedure that involves resampling from the bootstrap samples. This technique was originally suggested by Efron [17]. The theory of DB confidence intervals was developed by Hall [18], Beran [19], Loh [20] and Martin [21]. Theoretically DB produces better interval estimation than ordinary or single bootstrap as it has higher order of accuracy. DB reduces the error in the ordinary bootstrap by estimating an error and using it to adjust the ordinary bootstrap according to [22] and [23]. Chernick [24] provided a complete literature on bootstrap interval estimation techniques. The application of the DB confidence interval involving censored and truncated data can be found in [25]. The authors compared the performance of single and double bootstrap interval estimation techniques and highlighted that the latter works better.

In this research, we investigate the performance of the Wald, jackknife, B-p and DB without pivot (DB-p) techniques via coverage probability study at two nominal error probability levels for the parameters of log logistic regression model with right censored data. Moderate and small samples will be focused in our study. Each sample will be investigated at two

censoring proportions. A real data set is analyzed and some concluding remarks are made at the end of this paper.

THE MODEL

The log logistic is a popular parametric distribution in the survival analysis due to its ability to accommodate nonmonotonic hazard functions. Examples of nonmonotonic hazard function are given in the lung cancer trial [26], the curability of breast cancer study [27] and the AIDS infection rate study [28]. Several authors have discussed the log logistic distribution. Bennett [29] presented the linear model for the log odds on survival. Other authors that also made contribution are [30], [31], [32], [33] and [25].

Let T be a random variable representing the lifetimes that follow the log logistic distribution, $\mathbf{x}' = (x_0, x_1, \ldots, x_p)$ be the vector of covariates where $x_0 = 1$, $\boldsymbol{\beta}' = (\beta_0, \beta_1 \ldots, \beta_p)$ be the vector of unknown parameters and $\sigma > 0$. If $Y = \log(T)$ and $z = (y - \boldsymbol{\beta}'\mathbf{x})/\sigma$ the probability density and survival functions could be expressed respectively as

$$f(t, \mathbf{x}, \boldsymbol{\beta}, \sigma) = \frac{1}{\sigma} \exp(z)[1 + \exp(z)]^{-2}, \qquad (1)$$

$$S(t, \mathbf{x}, \boldsymbol{\beta}, \sigma) = [1 + \exp(z)]^{-1}. \qquad (2)$$

There are both censored and uncensored lifetimes for $i = 1, 2, \ldots, n$ observations and p covariates. The indicator variable δ_i is equal to 1 when t_i is uncensored and 0 when t_i is censored.

The likelihood function for the full sample of n independent observations of time and p covariates is,

$$L(\boldsymbol{\beta}, \sigma) = \prod_{i=1}^{n} \left(\frac{1}{\sigma} \exp(z_i)[1 + \exp(z_i)]^{-2} \right)^{\delta_i} \times \qquad (3)$$
$$\left([1 + \exp(z_i)]^{-1} \right)^{1-\delta_i}.$$

The log-likelihood function is given as follows,

$$\ell(\boldsymbol{\beta}, \sigma) = \sum_{i=1}^{n} \left\{ \delta_i(-\log \sigma - 2\log[1 + \exp(z_i)] + z_i) - (1 - \delta_i)\log[1 + \exp(z_i)] \right\}. \qquad (4)$$

Let us define $A_i = \exp(z_i)[1 + \exp(z_i)]^{-1}$, where $i = 1, 2, \ldots, n$. For $j, k = 0, 1, \ldots, p$ and $x_{i0} = 1$, the first and second derivatives of the log-likelihood function are,

$$\frac{\partial \ell(\boldsymbol{\beta}, \sigma)}{\partial \beta_j} = \sum_{i=1}^{n} \frac{x_{ij}}{\sigma} \left\{ -\delta_i + (1 + \delta_i)A_i \right\}, \qquad (5)$$

$$\frac{\partial \ell(\boldsymbol{\beta}, \sigma)}{\partial \sigma} = \sum_{i=1}^{n} \frac{1}{\sigma} \left\{ -\delta_i(1 + z_i) + (1 + \delta_i)z_i A_i \right\}, \qquad (6)$$

$$\frac{\partial^2 \ell(\boldsymbol{\beta}, \sigma)}{\partial \beta_j \partial \sigma} = \sum_{i=1}^{n} \frac{x_{ij}}{\sigma} \left\{ -\delta_i \left(\frac{1}{\sigma} \right) + (1 + \delta_i)A_i \times \right. \qquad (7)$$
$$\left. [1 + z_i(1 + A_i)] \right\},$$

$$\frac{\partial^2 \ell(\boldsymbol{\beta}, \sigma)}{\partial \beta_j \partial \beta_k} = \sum_{i=1}^{n} \frac{x_{ij} x_{ik}}{\sigma^2} (1 + \delta_i)A_i(A_i - 1), \qquad (8)$$

$$\frac{\partial^2 \ell(\boldsymbol{\beta}, \sigma)}{\partial \sigma^2} = \sum_{i=1}^{n} \frac{1}{\sigma^2} \left\{ -\delta_i(1 + 2z_i) - (1 + \delta_i) \times \right. \qquad (9)$$
$$\left. z_i^2 A_i \left(1 + \frac{1}{\sigma^2} A_i \right) \right\}.$$

CONFIDENCE INTERVAL ESTIMATION PROCEDURES

In this section, we discuss Wald, jackknife, B-p and DB-p techniques for constructing the confidence interval for the parameters of the log logistic regression model in the presence of right censored data. We consider one covariate in the model. The model involves three parameters, β_0, β_1 and σ. The bootstrap samples were generated using the nonparametric bootstrap resampling technique.

Asymptotic Normality (Wald)

Let $\hat{\boldsymbol{\theta}}$ be the maximum likelihood estimate (MLE) for the vector of parameters $\boldsymbol{\theta}$. Cox and Hinkley [34] showed that under mild regularity conditions, $\hat{\boldsymbol{\theta}}$ is asymptotically normally distributed with mean $\boldsymbol{\theta}$ and covariance matrix $I(\boldsymbol{\theta})^{-1}$, where $I(\boldsymbol{\theta})$ is the Fisher information matrix evaluated at $\boldsymbol{\theta}$. The matrix $I(\boldsymbol{\theta})$ can be estimated by the observed information matrix $i(\hat{\boldsymbol{\theta}})$. The estimate of $\text{var}(\hat{\theta}_j)$ is then given by the jth diagonal element of the inverse of $i(\hat{\boldsymbol{\theta}})$. If $z_{1-\alpha/2}$ is the $1 - \alpha/2$ quantile of the standard normal distribution, then the $100(1 - \alpha)\%$ confidence interval for θ_j could be expressed as

$$\hat{\theta}_j \pm z_{1-\frac{\alpha}{2}} \sqrt{\hat{\text{var}}(\hat{\theta}_j)}. \qquad (10)$$

Jackknife

The jackknife is a resampling technique where each subsample removes one observation from the original sample [11]. If we have a sample $\mathbf{y} = (y_1, y_2, \ldots, y_n)$,

then the ith jackknife sample will be $\mathbf{y}_{(i)} = (y_1, y_2, \ldots, y_{i-1}, y_{i+1}, \ldots, y_n)$ for $i = 1, 2, \ldots, n$. Let $\hat{\theta}$ be the MLE for parameter θ, then $\hat{\theta}_{(i)}$ will be the jackknife replication of $\hat{\theta}$ obtained from the ith jackknife sample. The jackknife estimate of the parameter θ and jackknife estimate of standard error is then calculated by using

$$\hat{\theta}_{\text{jack}} = \hat{\theta} - (n-1)(\hat{\theta}_{(\cdot)} - \hat{\theta}), \qquad (11)$$

$$\hat{se}(\hat{\theta})_{\text{jack}} = \left[\frac{n-1}{n} \sum_{i=1}^{n} (\hat{\theta}_{(i)} - \hat{\theta}_{(\cdot)}) \right]^{\frac{1}{2}}, \qquad (12)$$

where $\hat{\theta}_{(\cdot)} = \sum_{i=1}^{n} \hat{\theta}_{(i)} / n$.

If $t_{(1 - \alpha/2, \, n - 1)}$ is the $1 - \alpha/2$ quantile of the student's t distribution at $n - 1$ degrees of freedom, then the $100(1 - \alpha)\%$ jackknife confidence interval for θ could be expressed as

$$\hat{\theta}_{\text{jack}} \pm t_{\left(1 - \frac{\alpha}{2}, n-1\right)} \hat{se}(\hat{\theta})_{\text{jack}}. \qquad (13)$$

Bootstrap Percentile

The B-p interval is constructed from the percentiles of the bootstrap distribution of the MLE for parameter θ. For the sample $\mathbf{y} = (y_1, y_2, \ldots, y_n)$, we first generate B independent bootstrap samples, $\mathbf{y}^{*1}, \mathbf{y}^{*2}, \ldots, \mathbf{y}^{*B}$. Then we compute the MLE, $\hat{\theta}_b^*$ from the bootstrap sample, $\mathbf{y}^{*b}$ for $b = 1, 2, \ldots, B$. Following that, we sort the $\hat{\theta}_b^*$ in the ordered list, which we will have $\hat{\theta}_{[1]}^*, \hat{\theta}_{[2]}^*, \ldots, \hat{\theta}_{[B]}^*$. The $100(1 - \alpha)\%$ bootstrap percentiles confidence interval for θ could be expressed as

$$\hat{\theta}_{[B \cdot (\alpha/2)]}^* < \hat{\theta} < \hat{\theta}_{[B \cdot (1-\alpha/2)]}^*. \qquad (14)$$

The value of B is chosen such that values of $B \cdot (\alpha/2)$ and $B \cdot (1 - \alpha/2)$ are integers.

Double Bootstrap without Pivot

The DB-p confidence interval was proposed by Shi [35] and discussed by Letson and McCullough [23]. This technique is particularly useful when pivotal information is not available. The steps to obtain the DB-p confidence interval for parameter θ are as follows,

1. Obtain the MLE $\hat{\theta}$ based on the sample $\mathbf{y} = (y_1, y_2, \ldots, y_n)$.

2. Generate B independent bootstrap samples, $\mathbf{y}^{*1}, \mathbf{y}^{*2}, \ldots, \mathbf{y}^{*B}$ from the original sample.

3. Compute $\hat{\theta}_b^*$, MLE from the bootstrap sample, $\mathbf{y}^{*b}$ for $b = 1, 2, \ldots, B$.

4. Sort the $\hat{\theta}_b^*$ in an ascending order to obtain $\hat{\theta}_{[1]}^*$, $\hat{\theta}_{[2]}^*, \ldots, \hat{\theta}_{[B]}^*$.

5. Draw another C bootstrap resamples for each $\mathbf{y}^{*b}$, $b = 1, 2, \ldots, B$.

6. Compute the $\hat{\theta}_{bc}^{**}$, MLE from the bootstrap resample for $b = 1, 2, \ldots, B$ and $c = 1, 2, \ldots, C$.

7. For each c, calculate the total number of $\hat{\theta}_{bc}^{**}$ that is less than or equal to $\hat{\theta}$ and divide by numbers of bootstrap resamples, C,

$$Q_b = \frac{\#(\hat{\theta}_{bc}^{**} \leq \hat{\theta})}{C}.$$

8. Sort the Q_b in an ascending order to obtain $Q_{[1]}$, $Q_{[2]}, \ldots, Q_{[B]}$.

9. Calculate the values, $l = B \cdot Q_{[B \cdot (\alpha/2)]}$ and $u = B \cdot Q_{[B \cdot (1 - \alpha/2)]}$.

10. The $100(1 - \alpha)\%$ DB-p confidence interval for parameter θ will be

$$\hat{\theta}_{[l]}^* < \hat{\theta} < \hat{\theta}_{[u]}^*. \qquad (15)$$

COVERAGE PROBABILITY STUDY

Study Design

We conducted a simulation study with $N = 1000$ for sample sizes, $n = 25, 30, 40, 50$ and 60 to compare the performance of the confidence interval estimates at two nominal error probabilities, $\alpha = 0.05$ and 0.10. Two levels of approximate censoring proportions (cp) = 5% and 10% were used. We generated observations from the log logistic distribution with 4.4, -0.03 and 0.6 as the true values for parameters β_0, β_1 and σ respectively to replicate data usually seen in the lung cancer studies [26].

The covariate x_i were generated from $N(0,1)$. We generated random numbers u_i from $U(0,1)$ to produce t_i where $t_i = \exp\{\beta_0 + \beta_1 x_i + \sigma \log[(1 - u_i)/ u_i]\}$. In order to obtain censored observations, we simulate the censoring time, $c_i \sim \exp(\lambda)$ where the value of λ can be adjusted to obtain the desired approximate censoring proportion in our data. We generated $B = 1000$ bootstrap samples to construct the B-p and DB-p intervals. $C = 150$ bootstrap resamples were generated from each bootstrap sample for the DB-p interval.

The coverage probability error of a confidence interval is the probability that the true value of the parameter falls outside the interval. We obtained the estimated coverage probability error by summing up the numbers of interval that did not contain the true parameter value divided by the total number of samples. The estimated left (right) error probability was obtained by summing up the numbers for the left (right) endpoint was more (less) than the true parameter value divided by the total number of samples. We calculated the left, right and total error probabilities for each parameter.

As given in [36], if $\hat{\alpha}$ is the estimated coverage error probability, then its standard error is approximately $se(\hat{\alpha}) = [\alpha(1-\alpha)/N]^{1/2}$. The interval is called anticonservative if the total error probability is more than $\alpha + 2.58se(\hat{\alpha})$. If the total error probability is less than $\alpha - 2.58se(\hat{\alpha})$, the interval is called conservative. The interval is called symmetric when the larger of the left or right error probability is less than 1.5 times the smaller one. The simulation study was performed using the R programming language.

Study Results and Discussions

The performances of these interval estimation techniques were evaluated based on the total numbers of anticonservative (AC), conservative (C) and asymmetrical (AS) intervals. When $\alpha = 0.05$, at $n \leq 30$, the DB-p and jackknife techniques performed the best

compared to the Wald and B-p (Table 1). The DB-p is slightly better than the jackknife as it produces the least numbers of AC and AS intervals. However, it produces C interval when the data are censored. When $n > 30$, the DB-p performs the best followed by the jackknife, B-p and Wald as it did not produce any AC or C intervals.

When $\alpha = 0.10$, the DB-p performs the best even at $n \leq 30$ because it does not produce any AC, C or AS intervals (Table 2). This is followed by the jackknife, Wald and B-p where these techniques are still producing AC and AS intervals. When $n > 30$, the DB-p technique is the preferred technique as it only produces one AC interval, followed by the jackknife, Wald and B-p.

Hence, overall the DB-p performs the best at all nominal levels, sample sizes and censoring proportions. The jackknife performs well by producing few AC intervals. The B-p and Wald techniques did not perform well as they produced too many AC and AS intervals. In addition, the left and right error probabilities for DB-p technique are much closer to the $\alpha/2$ as compared to the Wald, jackknife and B-p techniques. The summary of interval estimation at $\alpha = 0.05$ and 0.10 for each parameter is given in Table 3 and Table 4. An example of graphical display of the left and right error probabilities for the interval estimation techniques is given in Figure $1 - 3$.

Table 1. Performance of the interval estimation techniques at different *n* for $\alpha = 0.05$

n	Technique	Uncensored			cp = 5%			cp = 10%		
		AC	C	AS	AC	C	AS	AC	C	AS
25	Wald	3	0	1	3	0	1	2	0	1
	Jackknife	2	0	1	1	0	2	1	0	1
	B-p	1	0	2	1	0	2	1	0	2
	DB-p	1	0	1	1	1	1	1	1	1
30	Wald	3	0	1	3	0	1	3	0	1
	Jackknife	0	0	1	1	0	1	0	0	1
	B-p	2	0	1	2	0	2	2	0	2
	DB-p	0	0	1	0	0	1	0	0	1
40	Wald	1	0	1	1	0	1	1	0	2
	Jackknife	0	0	1	1	0	1	1	0	2
	B-p	2	0	1	1	0	1	1	0	1
	DB-p	0	0	0	0	0	0	0	0	0
50	Wald	2	0	1	2	0	1	1	0	1
	Jackknife	0	0	2	0	0	1	0	0	1
	B-p	1	0	1	1	0	1	1	0	2
	DB-p	0	0	0	0	0	0	0	0	1
60	Wald	1	0	2	1	0	2	1	0	3
	Jackknife	0	0	2	0	0	1	0	0	2
	B-p	1	0	1	1	0	1	1	0	1
	DB-p	0	0	1	0	0	1	0	0	1

Table 2. Performance of the interval estimation techniques at different *n* for $\alpha = 0.10$

n	Technique	Uncensored			cp = 5%			cp = 10%		
		AC	C	AS	AC	C	AS	AC	C	AS
25	Wald	2	0	1	2	0	1	2	0	1
	Jackknife	1	0	1	1	0	1	0	0	1
	B-p	1	0	1	1	0	1	1	0	2
	DB-p	0	0	0	0	0	0	0	0	0
30	Wald	2	0	1	2	0	1	2	0	1
	Jackknife	0	0	1	0	0	1	1	0	1
	B-p	2	0	1	2	0	2	2	0	1
	DB-p	0	0	0	0	0	0	0	0	0
40	Wald	1	0	1	1	0	1	1	0	1
	Jackknife	0	0	1	0	0	1	0	0	1
	B-p	1	0	1	1	0	1	1	0	1
	DB-p	1	0	0	0	0	0	0	0	0
50	Wald	0	0	1	1	0	1	0	0	1
	Jackknife	0	0	1	0	0	1	0	0	1
	B-p	1	0	1	1	0	1	1	0	1
	DB-p	0	0	0	0	0	0	0	0	0
60	Wald	1	0	2	1	0	1	1	0	1
	Jackknife	0	0	2	0	0	1	0	0	1
	B-p	1	0	1	1	0	1	1	0	1
	DB-p	0	0	0	0	0	0	0	0	0
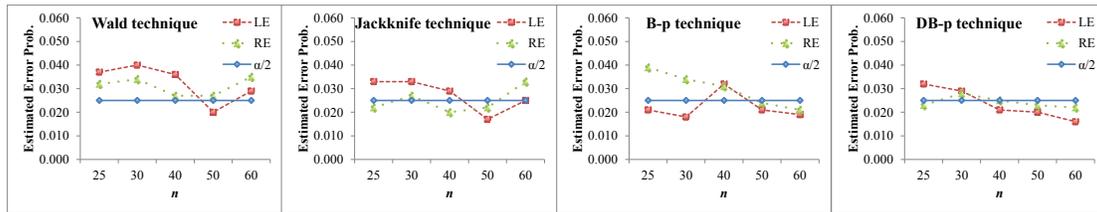
Figure 1. Interval estimates for parameter β_0 at $\alpha = 0.05$ and cp = 5%
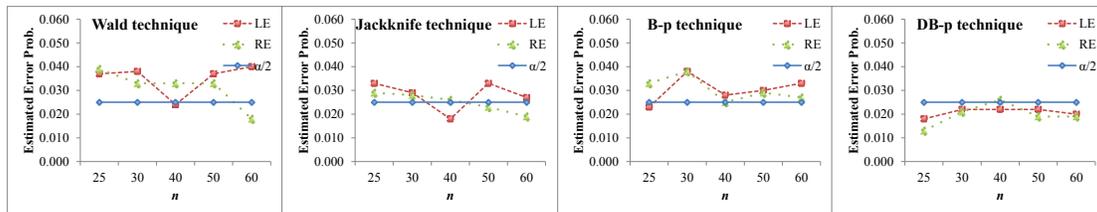
Figure 2. Interval estimates for parameter β_1 at $\alpha = 0.05$ and cp = 5%
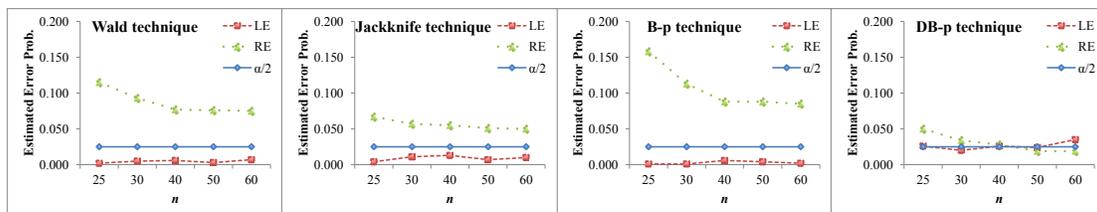
Figure 3. Interval estimates for parameter σ at $\alpha = 0.05$ and cp = 5%

Table 3. Summary of the performance of the interval estimates for all the parameters at $\alpha = 0.05$

cp	Technique	β_0			β_1			σ		
		AC	C	AS	AC	C	AS	AC	C	AS
Uncensored	Wald	2	0	0	3	0	1	5	0	5
	Jackknife	0	0	1	1	0	1	1	0	5
	B-p	1	0	1	1	0	0	5	0	5
	DB-p	0	0	0	0	0	0	1	0	3
5%	Wald	2	0	0	3	0	1	5	0	5
	Jackknife	0	0	1	0	0	0	3	0	5
	B-p	0	0	2	1	0	0	5	0	5
	DB-p	0	0	0	0	1	0	1	0	3
10%	Wald	1	0	1	2	0	2	5	0	5
	Jackknife	0	0	1	0	0	1	2	0	5
	B-p	0	0	3	1	0	0	5	0	5
	DB-p	0	0	0	0	1	0	1	0	3

Table 4. Summary of the performance of the interval estimates for all the parameters at $\alpha = 0.10$

cp	Technique	β_0			β_1			σ		
		AC	C	AS	AC	C	AS	AC	C	AS
Uncensored	Wald	1	0	0	1	0	1	4	0	5
	Jackknife	0	0	0	0	0	1	1	0	5
	B-p	0	0	0	1	0	0	5	0	5
	DB-p	0	0	0	0	0	0	1	0	0
5%	Wald	1	0	0	2	0	0	4	0	5
	Jackknife	0	0	0	0	0	0	1	0	5
	B-p	0	0	1	1	0	0	5	0	5
	DB-p	0	0	0	0	0	0	0	0	0
10%	Wald	0	0	0	2	0	0	4	0	5
	Jackknife	0	0	0	0	0	0	1	0	5
	B-p	0	0	1	1	0	0	5	0	5
	DB-p	0	0	0	0	0	0	0	0	0

REAL DATA ANALYSIS

Survival times of 29 hypernephroma patients with nephrectomy were obtained from [37]. Here, the age group was chosen as the covariate and 13.8% of the data is censored. Figure 4 shows that the log logistic hazard plot is rather linear, suggesting the log logistic distribution is a reasonable fit to the data. Table 5 gives the parameter estimates when the data were fitted to the log logistic regression model. The 95% confidence interval using the Wald, jackknife, B-p and DB-p interval estimation techniques were also given.

Figure 5 gives the histogram of 1000 bootstrap replications of parameter estimates $\hat{\beta}_0, \hat{\beta}_1$ and $\hat{\sigma}$. The sampling distribution for all parameters are rather skewed and not normally distributed when tested via the Kolmogorov-Smirnov test at $\alpha = 0.05$. Therefore, the Wald interval based on the asymptotic normality assumptions of the MLEs might not be reliable and alternative interval estimation may produce more desirable results.

The 95% DB-p confidence intervals for all parameters are widest compared to other methods because they need to accommodate the bias and adjust the error in the ordinary bootstrap procedure (Table 5). The DB-p interval for σ is the narrowest among the three parameters which agrees with the histogram in Figure 5 where bootstrap replication of $\hat{\sigma}$ is less skewed. Although the jackknife, Wald and B-p produce narrower intervals, they may not be reliable as they may fail to include the true parameters value, as indicated by our simulation studies.
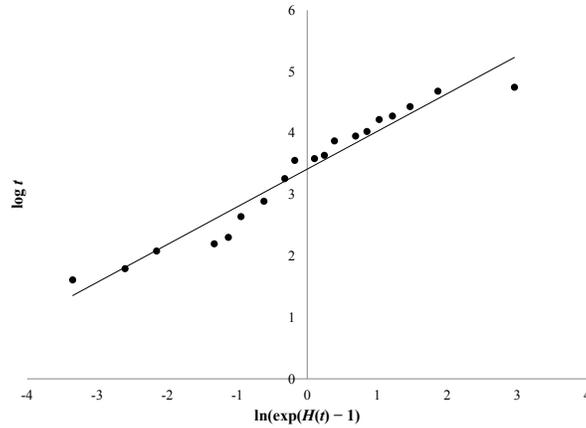
Figure 4. Log logistic hazard plot of the survival time of 29 hypernephroma patients with nephrectomy
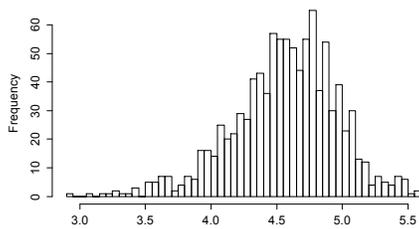
(a) Bootstrap replication of $\hat{\beta}_0$
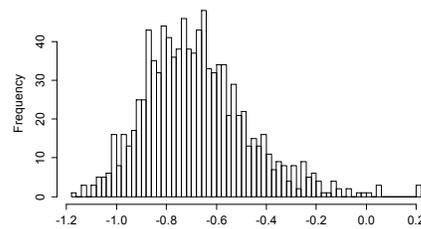
(b) Bootstrap replication of $\hat{\beta}_1$
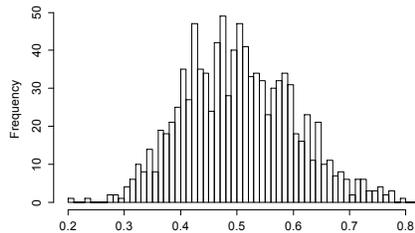
(c) Bootstrap replication of $\hat{\sigma}$

Figure 5. 1000 bootstrap replication of $\hat{\beta}_0$, $\hat{\beta}_1$ and $\hat{\sigma}$ for hypernephroma patients with nephrectomy data

Table 5. MLE of hypernephroma patients with nephrectomy data and 95% confidence intervals

θ	β_0	β_1	σ
$\hat{\theta}$	4.58	-0.69	0.53
se	0.397	0.221	0.089
Wald	(3.799,5.354)	(-1.125,-0.257)	(0.351,0.700)
Jackknife	(3.856,5.388)	(-1.117,-0.326)	(0.330,0.752)
B-p	(3.641,5.300)	(-1.020,-0.203)	(0.329,0.715)
DB-p	(3.525,5.247)	(-1.041,-0.111)	(0.368,0.865)

CONCLUSION

Based on the coverage probability studies, we would recommend the DB-p technique to be employed as the preferred method for the interval estimation for the parameters of log logistic regression model especially when n is small. It works well when the data is either uncensored or censored. This result varies from the result obtained by Arasan and Adam [25] for the model without covariate when data is truncated, which actually did not recommend the DB-p method. The jackknife technique could be used as an alternative method for the model as it performs as good as the DB-p. The Wald technique starts to work well when $n > 30$, as expected. However, it produces quite a number of anticonservative and asymmetric intervals.

Skewed distributions are common in the survival analysis even when the data is uncensored. When we bootstrap the sample with censored observations, it is possible to have highly skewed bootstrap replications of parameter estimates. In this case, the B-p technique is more likely to fail as it uses the empirical distribution based on the bootstrap replication of the data in hand. The performance of the B-p interval does not seem to be significantly better than the other interval estimation techniques. Therefore, we will not recommend B-p interval for this model.

In this research, we considered only small to moderate samples with low censoring proportions. Larger sample sizes and higher censoring proportions could be considered in future. Other double bootstrap interval estimation techniques such as DB-t can also be considered for the parameters of log logistic regression model in future.

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