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On Parametric Linear Transformation Model with Left-Truncated and Interval-Censored Data

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Abstract:
In this paper, a parametric linear transformation model is considered with left truncated and interval censored case I data. The maximum likelihood estimators of the regression parameters are computed. The testing of hypotheses regarding to the parameters are also performed. An extensive Monte Carlo simulation technique was used to compute the proposed estimators along with some of their properties.

1. Introduction:

Let T be the survival time of patient and Z be a q-dimensional vector of covariates. The Linear Transformation Model (LTM) assumes that the effect of Z on the response variable T is given by

$$H(T) = -\beta^T Z + \epsilon,$$

Here, H(.) is a monotone increasing function, β is q-dimensional regression parameter and ϵ is the error term which is assumed to follow a known distribution function F_ϵ, free of the covariate Z. The conditional survival function of T given Z of linear transformation model has the form

$$S_T(t|Z) = P(T > t|Z) = S_\epsilon\,(H(t) + \beta^T Z\,|Z)$$

or

$$S_T(t|Z) = e^{\wedge_\epsilon(H(t) + \beta^T Z\,|Z)}$$

where $\underset{\epsilon}{\wedge}(.\,|Z)$ is the conditional cumulative hazard function of ϵ given Z.

The LTM has two important special cases, namely: proportional hazard model or Cox model (PHM) when ϵ follows the extreme value distribution and proportional odd model (POM) when ϵ follows the logistic distribution (Cheng et. al., (1995).and Murphy, (1997)). Censoring in the collected data occurs when we observe incomplete data rather than exact data due to some reasons. Censoring are frequently occurring in survival data and the most common reasons are:

loss follow up when the patient may decide to move elsewhere, with drawal from the study and termination of the study.

If the cause of the censoring is independent of the time of event then we call this case as noninformative censoring scheme, otherwise it is called informative censoring. Left censoring occurs when the event has already occurred at a time before the observation time while

right censoring occurs when the event has not occurred at or before the observation time.
The event may or may not happen after the observation time. Interval censoring case I (or current status) is a combination of left and right censored observations that is every observation either
is left censored or right censored.
%For example, suppose that we are interested in the the age at HIV infection in a certain population. We follow the people in a sample for 1 year, and administrate an HIV test to each subject within this period. Based on the results of this test, an HIV infection either observed to occur of the subject (left-censored) or not observed yet (right-censored).
Another form of missing information can be represented by truncation. Truncation occurs when the missing information on the data is due to the design of the experiment. The main difference between censoring and truncation is that censored object can be observed while the object cannot be observed in the case of truncation. Left truncation occurs when we can only observe those individuals whose event time is
greater than some truncation threshold. For some examples of left-truncated and interval-censored data, we refer to examples given in (Sun, (2010)).
McLain and Ghosh (2013) considered time transformation models and used the sieve method through Bernstein polynomial to find the maximum likelihood of the unknown monotonic transformation of survival time. The asymptotic properties of the obtained estimators were investigated. Zhang, et. al (2013) considered the linear transformation model as a model of failure time data with current status data. Xiang and Hu (2016) proposed a class of semiparametric transformation cure models for analyzing interval-censored data in the presence of a cure function. A class of semiparametric transformation cure model is proposed Zeng and Lin (2016) The effects of common variables that depend on the likely time of a controlled failure time have been formulated through a broad category of quasi-parametric conversion models that include relative risks and relative probability models. The non-parametric maximum probability of this category of models has also been assessed with an arbitrary number of monitoring times for each subject. An EM-type algorithm that meets consistently, even in the presence of covariates based on time, has been used to show that estimates of regression parameters are consistent, naturally refined, and effectively consistent with the estimation of the common variation matrix easily. Finally, it was demonstrated that our actions were performed through simulation studies and applied to the **HIV/AIDS** study conducted in Thailand. Lum, et. al (2018) suggested an efficient penalized estimation method for a semi-parametric linear transformation model with current status data. They used B-Spline technique and improved an efficient hybrid algorithm involving the Fisher scoring algorithm and the isotonic regression. Xu, et. al (2018) proposed a non-mixture Cox regression cure rate model and adopted the semiparametric spline-based sieve maximum likelihood approach to analyze such data.Shen(2014a) analyzed left truncated and right censored data using additive hazard modele.He used the integrated square error to select an optimal bandwidth least-squared estimator .He also consider a semiparametric approach for the case when the distribution of the left-truncated variable is parameterized.A simulation study was conducted to asses the performance of the proposed estimators .Shen (2014c) considered a semiparametric transformation model where the truncation time is both a truncated variable and a predictor of the time to failure. Simulation studies are conducted to investigate finite sample performance of the proposed estimator. He also applied his methods to bone marrow and heart transplant data. **(Kim (2003))** studied the maximum likelihood estimator (MLE) for the proportional hazards
model with left-truncated and current status censored data. He proved that the MLE of the regression parameter is asymptotically normal with a $\sqrt{n}$ convergence rate and achieved the information

bound and proved the MLE of the baseline cumulative hazard function converges only at rate $n^{\frac{1}{3}}$.

The paper is proceeding as follows. In Section 1, we calculate the maximum likelihood estimators of the regression parameters. Section 2 focuses on testing of the hypotheses using likelihood ratio, Rao score and Wald tests. In Section 3, we conducted a simulation study to asses the performance of the proposed estimators.

Maximum Likelihood Estimation:

Assume that for each subject there is an examination time (C). The lifetime of the subject (T) is only known to occur before (T< C) (left-censored) or after (T>C) (right-censored) the examination time. Assume also, L is the left-truncation random variable such that T cannot be obsereved unless T>L.

Since the life-time cannot be observed exactly, then our observation will consist of X=(L,C,Δ,Z), where L is the left-truncation random variable, C is the examination (monitoring) time random variable, Δ=I(T≤ C) is the censored indicator random variable and Z is q-dimensional vector of covariates. Suppose that given Z, T and (L,C) are independent and the distribution L and C do not include β.

The log likelihood of β based on a sample of n independent observations X_i=(L_i, C_i, Δ_i, Z_i), i=1,2,...,n, can be written (up to terms do not involve β) as

$$l_n(\beta)=\sum_{i=1}^{n}\left(\Delta_i \log(1-s_i)+(1-\Delta_i)\log(s_i)\right)$$

where s_i=s(c_i| z_i)/s(l_i| z_i). and s(c_i| z_i)= S_ϵ (H(c_i) + β^TZ |Z), s(l_i| z_i)= S_ϵ (H(l_i) + β^TZ |Z)$ Following (McLain and Ghosh (2013)),let

$$S(t|z)=(1+re^{H(t)+\beta Z})^{\frac{-1}{r}}$$

Notice that r=0,1 correspond to PHM and POM, respectively. Now,

$$s_i=s(c_i|\, z_i)/s(l_i|\, z_i)$$

$$=\left(\frac{1+re^{H(\,l_i)+\beta Z}}{1+re^{H(\,c_i)+\beta Z}}\right)^{\frac{1}{r}}=\left(\frac{g_1}{g_2}\right)$$

where

$$g_1=(1+re^{H(\,l_i)+\beta Z})^{\frac{1}{r}} \quad \text{and} \quad g_2=(1+re^{H(\,c_i)+\beta Z})^{\frac{1}{r}}$$

The score function of β is computed by taking the first derivative of l_n with respect to β_j , j=1,2,… ,q as

$$k_{r,j}(c,l,\delta,z;\beta)=\frac{\partial l_n(\beta)}{\partial \beta_j}=\sum_{i=1}^{n}\left(\frac{-\delta_i}{1-s_i}+\frac{(1-\delta_i)}{s_i}\right)\frac{\partial s_i}{\partial \beta_j}$$

where

$$\frac{\partial s_i}{\partial \beta_j}=\frac{g_2\frac{\partial g_1}{\partial \beta_j}-g_1\frac{\partial g_2}{\partial \beta_j}}{g_2^2}$$

$$\frac{\partial g_1}{\partial \beta_j}=z_j\, e^{H(\,l_i)+\beta Z}(1+re^{H(\,l_i)+\beta Z})^{\frac{1-r}{r}}$$

and

$$\frac{\partial g_2}{\partial \beta_j}=z_j\, e^{H(\,c_i)+\beta Z}(1+re^{H(\,c_i)+\beta Z})^{\frac{1-r}{r}}$$

Hence, the maximum likelihood estimator (mle) $\widehat{\beta_n}$ is the value of β satisfies $k_{r,j}$(c,l,δ,z; β)=0. for all j=1,2 ….,q To find the variance of the mle, we use the observed information matrix $I(\beta)$ at $\hat{\beta}$ where

$$I(\beta)=\begin{pmatrix} -\frac{\partial^2 l_n}{\partial \beta_1^2} & \cdots & -\frac{\partial^2 l_n}{\partial \beta_1 \partial \beta_q} \\ \cdots & \cdots & \cdots \\ -\frac{\partial^2 l_n}{\partial \beta_q \partial \beta_1} & \cdots & -\frac{\partial^2 l_n}{\partial \beta_q^2} \end{pmatrix}$$

where the second derivative with respect to β_j and β_k , j,k=1,2,… ,q is given by

$$\frac{\partial^2 l_{n(\beta)}}{\partial \beta_j \partial \beta_k}=\sum_{i=1}^{n}\left(\frac{\partial^2 s_i}{\partial \beta_j \partial \beta_k}\left(\frac{-\delta_i}{1-s_i}+\frac{(1-\delta_{i)}}{s_i}\right)--\frac{\partial s_i}{\partial \beta_j}\frac{\partial s_i}{\partial \beta_k}\left(\frac{s_i}{(1-s_i)^2}+\frac{(1-\delta_{i)}}{s_i^2}\right)\right)$$

and

$$\frac{\partial^2 s_i}{\partial \beta_j \partial \beta_k}=\frac{g_2(g_2\frac{\partial^2 g_1}{\partial \beta_j \partial \beta_k}+\frac{\partial g_1 \partial g_2}{\partial \beta_k \partial \beta_j}-g_1\frac{\partial^2 g_2}{\partial \beta_j \partial \beta_k}-\frac{\partial g_1 \partial g_2}{\partial \beta_k \partial \beta_j}}{g_2^3}$$

$$\frac{\partial^2 g_1}{\partial \beta_j \partial \beta_k}=z_j z_k e^{H(\ l_i)+\beta Z}\ (1+re^{H(\ l_i)+\beta Z})^{\frac{1-r}{r}}\ [(1-r)\ (1+re^{H(\ l_i)+\beta Z})^{-1}+1]$$

$$\frac{\partial^2 g_2}{\partial \beta_j \partial \beta_k}=z_j z_k e^{H(\ c_i)+\beta Z}\ (1+re^{H(\ c_i)+\beta Z})^{\frac{1-r}{r}}\ [(1-r)\ (1+re^{H(\ c_i)+\beta Z})^{-1}+1]$$

The first special case of LTM; is PHM. It is known that LTM with r=0 reduces to PHM and hence substituting r=0 in (5) gives us the survival function

$$s(t)=\lim_{r\to 0}(1+re^t)^{\frac{-1}{r}}=e^{-e^t}$$

The score function of β_j in this case is given by

$$k_{0,j}(c,l,\delta,z;\beta)=\frac{\partial l_n(\beta)}{\partial \beta_j}=\sum_{i=1}^{n}\left(\frac{-\delta_i}{1-s_i}+\frac{(1-\delta_i}{s_i}\right)\frac{\partial s_i}{\partial \beta_j}.\quad j=1,2\ldots,q$$

where

$$s_i=\frac{e^{e^{H(\ l_i)+\beta Z}}}{e^{e^{H(\ c_i)+\beta Z}}}=\frac{g_1}{g_2},\ \text{(say)}$$

$$\frac{\partial s_i}{\partial \beta_j}=\frac{g_2\frac{\partial g_1}{\partial \beta_j}-g_1\frac{\partial g_2}{\partial \beta_j}}{g_2^2}$$

$$\frac{\partial g_1}{\partial \beta_j}=z_j e^{H(\ l_i)+\beta Z}e^{e^{H(\ l_i)+\beta Z}}$$

$$\frac{\partial g_2}{\partial \beta_j}=z_j e^{H(\ c_i)+\beta Z}e^{e^{H(\ c_i)+\beta Z}}$$

and

The second derivative of l_n with respect to $\beta_j$andβ_k, j,k=1,2,…,q is given by

$$\frac{\partial^2 l_{n(\beta)}}{\partial \beta_j \partial \beta_k}=\sum_{i=1}^{n}\left(\frac{\partial^2 s_i}{\partial \beta_j \partial \beta_k}\left(\frac{-\delta_i}{1-s_i}+\frac{(1-\delta_{i)}}{s_i}\right)--\frac{\partial s_i}{\partial \beta_j}\frac{\partial s_i}{\partial \beta_k}\left(\frac{s_i}{(1-s_i)^2}+\frac{(1-\delta_{i)}}{s_i^2}\right)\right)$$

and

$$\frac{\partial^2 g_1}{\partial \beta_j \partial \beta_k}=z_k z_j e^{H(\ l_i)+\beta Z}e^{e^{H(\ l_i)+\beta Z}}(e^{H(\ l_i)+\beta Z}+1)$$

$$\frac{\partial^2 g_1}{\partial \beta_j \partial \beta_k}=z_k z_j e^{H(\ c_i)+\beta Z}e^{e^{H(\ c_i)+\beta Z}}(e^{H(\ c_i)+\beta Z}+1)$$

The second special case of LTM; namely POM. Clearly, LTM with r=1 reduces to PHM and substituting r=1 in(5) gives us the survival function $s(t)=(1+e^t)^{-1}$

The score function in this case is given by

$$k_{1,j}(c,l,\delta,z;\beta)=\frac{\partial l_n(\beta)}{\partial \beta_j}=\sum_{i=1}^{n}\left(\frac{-\delta_i}{1-s_i}+\frac{(1-\delta_i}{s_i}\right)\frac{\partial s_i}{\partial \beta_j}.\quad j=1,2\ldots,q$$

where

$s_i = \frac{1+e^{H(\,l_i)+\beta Z}}{1+e^{H(\,c_i)+\beta Z}} = \frac{g_1}{g_2}$, (say)

$\frac{\partial s_i}{\partial \beta_j} = \frac{g_2\frac{\partial g_1}{\partial \beta_j} - g_1\frac{\partial g_2}{\partial \beta_j}}{g_2^2}$

$\frac{\partial g_1}{\partial \beta_j} = z_j e^{H(\,l_i)+\beta Z}$

and

$\frac{\partial g_2}{\partial \beta_j} = z_j e^{H(\,c_i)+\beta Z}$

The second derivative with respect β_j and β_k, j,k=1,2,…,q is given by

$\frac{\partial^2 l_{n(\beta)}}{\partial \beta_j \partial \beta_k} = \sum_{i=1}^{n}\left(\frac{\partial^2 s_i}{\partial \beta_j \partial \beta_k}\left(\frac{-\delta_i}{1-s_i} + \frac{(1-\delta_{i)}}{s_i}\right) - \frac{\partial s_i}{\partial \beta_j}\frac{\partial s_i}{\partial \beta_k}\left(\frac{s_i}{(1-s_i)^2} + \frac{(1-\delta_{i)}}{s_i^2}\right)\right)$

where

$\frac{\partial^2 s_i}{\partial \beta_j \partial \beta_k} = \frac{g_2\left(g_2\frac{\partial^2 g_1}{\partial \beta_j \partial \beta_k} + \frac{\partial g_1 \partial g_2}{\partial \beta_k \partial \beta_j} - g_1\frac{\partial^2 g_2}{\partial \beta_j \partial \beta_k} - \frac{\partial g_1 \partial g_2}{\partial \beta_k \partial \beta_j}\right.}{g_2^3}$

and

$\frac{\partial^2 g_1}{\partial \beta_j \partial \beta_k} = z_k z_j e^{H(\,l_i)+\beta Z}$ $\quad \frac{\partial^2 g_1}{\partial \beta_j \partial \beta_k} = z_k z_j e^{H(\,c_i)+\beta Z}$

Testing of Hypothesis

Letβ^T =(β_1^T, β_2^T)\$,where β_1^T andβ_2^T are components of β with dimensions k and q-k, respectively.

We like to test the hypothesisH_0: β_1=β_{01}.

First, consider the Likelihood Ratio Test (LRT).

It is well-known. (Buse. (1982)) that T_L=-2(log(L(β_{01},$\hat{\beta}_2$))- log(L(,$\hat{\beta}_n$)))$\xrightarrow{D} \chi_k^2$

where L(.)the likelihood function and $\hat{\beta}_n$ is the maximum likelihood estimated of β and $\hat{\beta}_2$the maximum likelihood estimated of β_2

We reject H_0 with significance leve α if

$T_L \geq \chi_{k,1-\alpha}^2$. Second, consider the Rao's Score Test. It is known that (Yanqing and Xikui (2011))

$T_R = S_1^T(x;\beta_{01};\widehat{\beta_2})I^{11}(\beta_{01};\widehat{\beta_2})S_1(x;\beta_{01};\widehat{\beta_2}) \xrightarrow{D} \chi_k^2$

where S_1^T is the score function of β_1 given by

$S_1(x;\beta) = \frac{\partial \log(f(x;\beta))}{\partial \beta_1^T}$

I is the information of β is

$$\mathrm{I}(\beta) = \begin{pmatrix} I_{11} & I_{12} \\ I_{21} & I_{22} \end{pmatrix} \equiv \begin{pmatrix} -E\left(\frac{\partial^2 \log(f(x;\beta))}{\partial \beta_1^T \partial \beta_1}\right) & -E\left(\frac{\partial^2 \log(f(x;\beta))}{\partial \beta_1^T \partial \beta_2}\right) \\ -E\left(\frac{\partial^2 \log(f(x;\beta))}{\partial \beta_2^T \partial \beta_1}\right) & -E\left(\frac{\partial^2 \log(f(x;\beta))}{\partial \beta_2^T \partial \beta_2}\right) \end{pmatrix}$$

and

I^{11} the sub matrix of$I^{-1}(\beta)$ corresponding with β_1.\$

We reject H_0 with significance leve α if

$T_R \geq \chi_{k,1-\alpha}^2$. Third, we consider Wald test. It is known. (Shao. J (1999))

T_W=($\hat{\beta}_{01}$; β_{01})I($\hat{\beta}_n$)($\hat{\beta}_{01}$; $\beta_{01})^T \xrightarrow{D} \chi_\kappa^2$

We reject H_0 with significance leve α if

$T_W \geq \chi_{k,1-\alpha}^2$.

Simulation:

In this section, the performance of the proposed estimators obtained in Section 2 are investigated through a Monte-Carlo simulation techniques using R language. To generate a random variate of the failure time T from the LTM when the survival function given by $S(t|z) = (1 + re^{H(t)+\beta Z})^{\frac{-1}{r}}$, we use inverse distribution function method as given in the following algorithm.

- **Step.1** Generate u~ U(0,1).
- **Step.2** If r=0, compute T by

$t = H^{-1}(\log(-\log(u)) - \beta^T Z)$

and if 0<r≤ 1, compute T as $t = H^{-1}(\log(\frac{u^{-r}-1}{r}) - \beta^T Z)$

In this study, we we consider q=3, i.e. $\beta^T = (\beta_1^T, \beta_2^T, \beta_2^T)$ with covariates Z_1~Binomial(1,0.5) $and\ Z_2$ ~Norm(0,1),

Z_3~Norm(−1,1).

Take H(t)= log(t). We assume that the left-truncation L and the monitoring time C to follow the uniform distributions U (0,1) and L+1.5U (0,1), respectively. The results given below are for n=100 and n=200, n=400 with 500 replications. Table 1 shows the results obtained based on data simulation for $\hat{\beta}_n$, \$ the maximum likelihood of β_0 with β_0=$(-1,0.5,1)^T$ and β_0=$(-1.5,-0.5,0.5)^T$ for the case r= 0,1. The results of the table include the bias (BIAS) which is the average of estimate $\hat{\beta}_n$ minus the true value, the sample standard deviation (SSD) of $\hat{\beta}_n$, and the average of the estimated standard error (ESD) using the observation information matrix, 95% confidence interval, the empirical coverage probability (CP) and the percentage of right censored observations.

R	n	β	Bias	SSD	ESD	CI	CP%	RC
		-1	0.030	0.461	0.439	(-1.891, 0.169)	93	0.748
	100	0.5	-0.013	0.289	0.289	(-0.054, 1.080)	94	0.748
		1	-0.039	0.262	0.250	(0.547 ,1.531)		0.748
							94	
		-1		0.239	0.236	(-1.467, -0.539)	94	0.713
	200	0.5	0.003	0.157	0.156	(0.207, 0.821)	94	0.713
		1	-0.014	0.137	0.142	(0.741 , 1.300)	96	0.713
			-0.021					
r=0		-1	-0.005	0.165	0.164	(-1.317, -	95	0.669
	400	0.5	-0.007	0.104	0.108	0.671)	95	0.669
		1	-0.012	0.100	0.099	(0.294, 0.719)	95	0.669
						(0.817 ,1.207)		
		-1.5	0.062	0.364	0.346	(-2.242, -0.883)	94	0.668
	100	- 0.5	0.027	0.225	0.214	(-0.948, -0.107)	93	0.668
		0.5	-0.016	0.168	0.159	(0.204 , 0.828)	93	0.668
		-1.5	0.018	0.244	0.236	(-1.981, -1.055)	94	0.667
	200	-0.5	0.018	0.146	0.145	(-0.803, -	95	0.667
		0.5	-0.005	0.111	0.109	0.233)	94	0.667
						(0.290 , 0.719)		
		-1.5	0.009	0.169	0.165	(-1.832, -1.185)	94	0.777
	400	-0.5	0.002	0.102	0.101	(-0.701, -0.304)	95	0.777
		0.5	-	0.075	0.076	(0 .350 , 0.649)	94	0.777
			0.0003					

$Table\ 1$: $Simulation\ results\ of\ Maximum\ Likelihood\ Estimators\ of\ \beta\ for\ r = 0, 1$

	n	β	Bias	SSD	ESD	CI	CP%	RC
		-1	0.037	0.564	0.532	(-2.081 ,0.006)	93	0.777
	100	0.5	-0.047	0.381	0.354	(-0.148, 1.242)	92	0.777
		1	-0.076	0.314	0.297	(0.494 ,1.658)		0.777
							93	
r=1		-1	0.008	0.350	0.366	(-1.714, -0.302)	95	0.775
	200	0.5	-0.019	0.242	0.237	(0.053,0.985)	93	0.775
		1	-0.024	0.200	0.199	(0.633,1.415)	95	0.775
		-1	0.008	0.252	0.249	(-1.498, -0.518)	94	0.775
	400	0.5	-0.012	0.154	0.164	(0.189 ,0.834)	96	0.775
		1	-0.009	0.140	0.138	(0.738 ,1.281)	95	0.775
		-1.5	0.068	0.524	0.504	(-2.557, -0.576)	93	0.774
	100	- 0.5	0.035	0.369	0.339	(-1.201 ,0.130)	93	0.774
		0.5	-0.032	0.265	0.254	(0.033 ,1.031)	94	0.774
		-1.5	0.015	0.347	0.342	(-2.186, -0.844)	95	0.774
	200	-0.5	0.014	0.233	0.228	(-0.962, -0.066)	93	0.774
		0.5	-0.020	0.173	0.173	(0.181 , 0.859)	95	0.774
		-1.5	0.012	0.237	0.237	(-1.978, -1.046)	94	0.777
	400	-0.5	0.006	0.152	0.158	(-0.816, -0.196)	95	0.777
		0.5	-0.003	0.113	0.119	(0.268 , 0.738)	94	0.777

The second part consists of testing the hypotheses about the true values of β_0 .Let the true value of β is denoted by β_0^T =($\beta_{01}, \beta_{02}, \beta_{03}$) and define e_i is a 3-dimensional vector whose the element of the i-th position equals to 1 and the rest are zero. First, consider the hypothesis H_0:β_i =β_{0i} where i=1,2,3. The likelihood ratio test (LRT) of size α for testing H_0 is given by

Reject H_0 with size α if $T_L \geq \chi^2_{1,1-\alpha}$,

where T_L test statistic is defined by

$$T_L = -2(\log(L(\hat{\beta}_n - e_{i\beta_{0i}}) - \log(L(\hat{\beta}_n)).$$

The Rao score test (RST) of size α for testing $H_0$is given by

Reject H_0 with size α if $T_R \geq \chi^2_{1,1-\alpha}$,

where

$$T_R = S_i^2(x; \hat{\beta}_n - e_i\beta_{0i})I^{ii}(\hat{\beta}_n - e_i\beta_{0i})$$

I^{ii} the sub matrix of I^{-1} (β) corresponding with β_i,

S_i is the score function of β_i given by

$$S_i(x;\beta) = \frac{\partial \log(f(x;\beta))}{\partial \beta_i}$$

and I is the information of β.

The Wald test (WT) of size α for testing $H_0$is given by

Reject H_0 with size α if $T_W \geq \chi^2_{1,1-\alpha}$,

where

$$T_W = \left(\hat{\beta}_i - \beta_{0i}\right)^2 I_{ii}(\hat{\beta}_n)$$

and I_{ii} the sub matrix of I(β) corresponding with β_i.

Second, consider the hypothesis H_0: $\beta = \beta_0$.

The likelihood ratio test (LRT) of size α for testing H_0 is

Reject H_0 with size α if $T_L \geq \chi^2_{1,1-\alpha}$,

where T_L test statistic is defined by

$$T_L = -2(\log(\beta_0) - \log(\hat{\beta}_n))$$

The Rao score test (RST) of size α for testing H_0 is given by

Reject H_0 with size α if $T_R \geq \chi^2_{1,1-\alpha}$,

where

$$T_R = S^T(x;\beta_0)I^{-1}(\beta_0)S(x;\beta_0)$$

The Wald test (WT) of size α for testing H_0 is given by

Reject H_0 with size α if $T_W \geq \chi^2_{1,1-\alpha}$,

where

$$T_W = \left(\hat{\beta}_n - \beta_0\right)^T I(\hat{\beta}_n)(\hat{\beta}_n - \beta_0)$$

From the Table 1, it is clear that the results show that the amount of bias (Bias) of the obtained estimators are small for all cases and the estimated standard errors (ESD) are close to the sample standard deviations (SSD). Therefore, one can say that the proposed estimators seem to be unbiased and the variance estimation also seem to be reasonable. Also, the estimation results seem to be consistent with respect to the percentage of the interval censored observation. With respect to true model i.e. with respect to the value of r, it is clear that the bias and standard error go up when the true model moves away from the proportional hazards model. The probabilities of the simulation results covering the true values (PC) are in average 94%. Figure 1 and Figure 2 presented the distributions of the proposed estimators and obviously the estimators are approximately normal. Tables 2-3 show the results of testing the hypotheses about $\hat{\beta}_n$ for r=0,1. These results include the likelihood ratio test, the Rao score test the and the Wald test with significance level α =0.05.

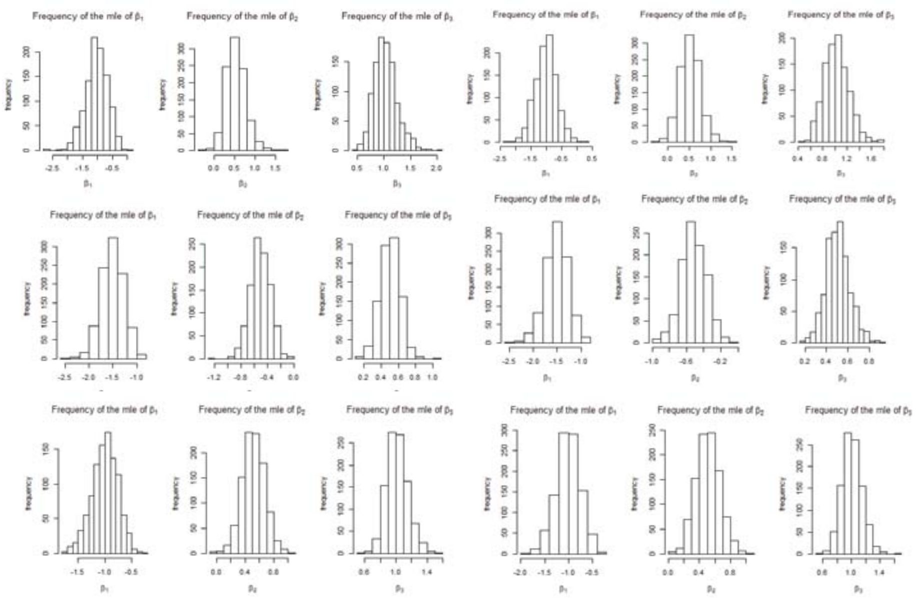
For the one-parameter test, H_0 is rejected if test statistics is grater than 3.84 and for the three-parameter test, H_0 is rejected if the test statistic is grater than 7.81 or equivalently the p-value is less that 0.05 for the both cases. Clearly, there is no significance difference between the estimated values and the true values for all as the studied cases at 0.05 significance level.

Table 2: Testing Hypotheses of H_0

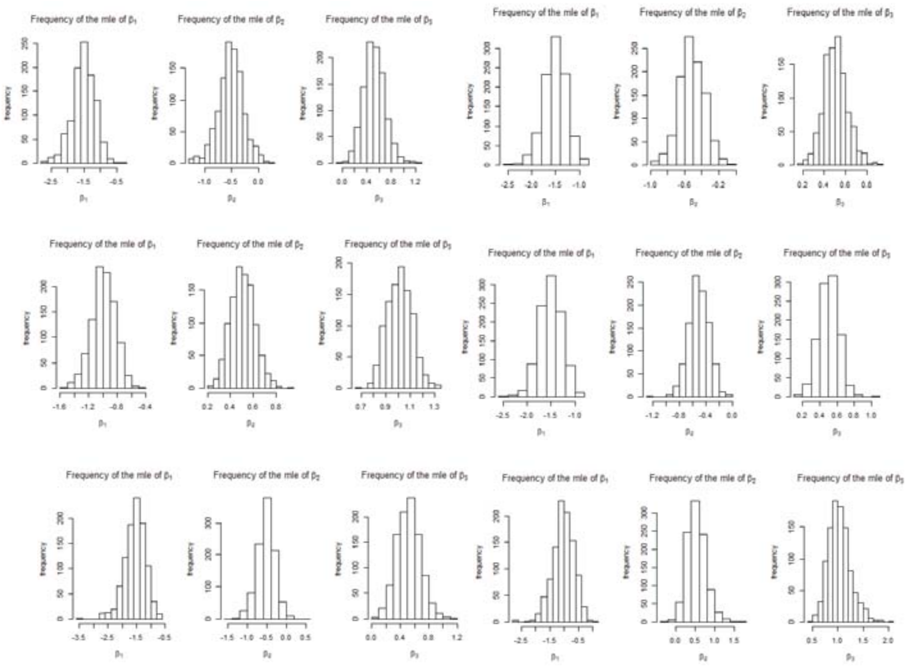
n	β	H_0	LRT(p-value)	RST(p-value)	WT(p-value)
	-1	=-1β_1	1.290(0.256)	1.776(0.182)	0.990(0.319)
	0.5	=0.5β_2	1.029(0.310)	1.089(0.269)	0.905(0.341)
100	1	= 1β_3	1.322(0.250)	1.286(0.256)	0.894(0.344)
	-1	=-1β_1	1.161(0.281)	1.408(0.235)	1.000(0.317)
	0.5	=0.5β_2	1.089(0.296)	1.170(0.279)	0.984(0.321)
200	1	= 1β_3	1.092(0.296)	1.286(0.256)	0.894(0.344)
	-1	=-1β_1	1.127(0.288)	1.307(0.252)	0.989(0.320)
	0.5	=0.5β_2	1.000(0.317)	1.069(0.301)	0.916(0.338)
400	1	= 1β_3	1.221(0.269)	1.429(0.231)	1.026(0.311)
	-1.5	=-1.5β_1	1.286(0.256)	2.189(0.139)	0.982(0.321)
	-0.5	=-0.5β_2	1.165(0.280)	1.236(0.266)	1.023(0.311)
100	0.5	= 0.5β_3	1.280(0.257)	1.485(0.223)	1.054(0.304)
	-1.5	=-1.5β_1	1.258(0.262)	2.18990.139)	0.982(0.321)
	-0.5	=-0.5β_2	1.080 (0.298)	1.236(0.266)	1.023(0.311)
200	0.5	= 0.5β_3	1.160(0.281)	1.485(0.223)	1.054(0.304)
	-1.5	=-1.5β_1	1.199(0.273)	1.460(0.226)	1.022(0.311)
	-0.5	=-0.5β_2	1.081(0.298)	1.144(0.284)	1.012(0.314)
400	0.5	= 0.5β_3	1.091(0.296)	1.247(0.264)	0.961(0.326)
100	(-1,0.5,1)	(-1,0.5,1)$\beta =$	3.027(0.387)	2.982(0.394)	2.82(0.420)
200	(-1,0.5,1)	=(-1,0.5,1)β	2.943(0.400)	2.911(0.405)	2.903(0.406)
400	(-1,0.5,1)	=(-1,0.5,1)β	2.939(0.401)	2.926(0.403)	2.922(0.403)
100	(-1.5,-0.5,0.5)	(-1.5,-$\beta =$ 0.5,0.5)	3.123(0.373)	3.026(0.387)	2.997(0.392)
200	(-1.5,-0.5,0.5)	(-1.5,-$\beta =$ 0.5,0.5)	3.123(0.373)	3.026(0.387)	2.997(0.392)
400	(-1.5,-0.5,0.5)	(-1.5,-$\beta =$ 0.5,0.5)	2.971(0.396)	2.971(0.396)	2.969(0.396)

Table 3: Testing of Hypotheses (Likelihood Ratio Test,Ros'e Score Test,Wald Test) for H_0

n	β	H_0	LRT(p-value)	RST(p-value)	WT(p-value)
	-1	=-1β_1	1.325(0.249)	2.009(0.156)	0.942(0.331)
	0.5	=0.5β_2	1.229(0.267)	1.310(0.252)	1.028 (0.310)
100	1	= 1β_3	1.267(0.260)	1.401(0.236)	1.761(0.184)
	-1	=-1β_1	1.161(0.281)	1.515(0.218)	0.898(0.343)
	0.5	=0.5β_2	1.057(0.303)	0.898(0.343)	0.969 (0.324)
200	1	= 1β_3	1.603(0.205)	0.950 (0.329)	0.969 (0.324)
	-1	=-1β_1	1.251(0.263)	1.594(0.206)	0.991(0.319)
	0.5	=0.5β_2	0.905(0.341)	0.926(0.335)	0.858 (0.354)
400	1	= 1β_3	1.586(0.207)	0.996(0.318)	0.858 (0.354)
	-1.5	=-1.5β_1	1.313(0.251)	2.023(0.154)	0.925(0.336)
	-0.5	=-0.5β_2	1.197(0.273)	1.246 (0.264)	1.016(0.313)
100	0.5	= 0.5β_3	1.306(0.253)	1.650(0.198)	0.927(0.335)
	-1.5	=-1.5β_1	1.274(0.258)	1.722(0.189)	0.971(0.324)
	-0.5	=-0.5β_2	1.038 (0.302)	1.058(0.303)	0.960 (0.327)
200	0.5	= 0.5β_3	1.241(0.265)	1.533 (0.215)	0.947 (0.330)
	-1.5	=-1.5β_1	1.228(0.267)	1.579(0.208)	0.967(0.325)
	-0.5	=-0.5β_2	0.954(0.328)	0.974(0.323)	0.915(0.338)
400	0.5	= 0.5β_3	1.110(0.292)	1.371(0.241)	0.879 (0.348)
100	(-1,0.5,1)	(-1,0.5,1)$\beta =$	3.162 (0.367)	3.162(0.367)	2.772(0.428)
200	(-1,0.5,1)	=(-1,0.5,1)β	2.945 (0.400)	2.914 (0.405)	2.798(0.423)
400	(-1,0.5,1)	=(-1,0.5,1)β	2.921(0.403)	2.905(0.406)	2.846(0.415)
100	(-1.5,-0.5,0.5)	(-1.5,-$\beta =$ 0.5,0.5)	3.119(0.373)	3.008(0.390)	2.744(0.432)
200	(-1.5,-0.5,0.5)	(-1.5,-$\beta =$ 0.5,0.5)	2.992(0.392)	2.945(0.400)	2.810(0.421)
400	(-1.5,-0.5,0.5)	(-1.5, -$\beta =$ 0.5,0.5)	2.864(0.413)	2.847(0.415)	2.786(0.425)



Histogram of Maximum Likelihood Estimators for r=0



Histogram of Maximum Likelihood Estimators for r=1

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