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PARAMETER ESTIMATION FOR THE EXPONENTIATED RAYLEIGH MODEL WITH COVARIATES UNDER RIGHT CENSORED

(*Anggaran Parameter untuk Model Rayleigh Eksponen dengan Kovariat bawah Penapisan Kanan*)

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ABSTRACT

In this study, the exponentiated Rayleigh (ER) model is extended to include covariates in the presence of right censored data. The maximum likelihood estimation (MLE) for the parameter estimates were assessed using the bias, standard error (SE) and root mean square error (RMSE) of the parameter estimates at various sample sizes and censoring proportion (cp) via simulation study. Additionally, the coverage probability study is conducted to compare three methods of constructing confidence intervals: Wald, jackknife and bootstrap-t method. The coverage probability study showed that the best confidence interval estimation technique for parameters β_0 and β_1 is the bootstrap-t method. However, for the parameter γ, at $\alpha = 0.05$ ($\alpha = 0.1$) the bootstrap-t (Wald) method is preferred. The model is then applied to preclinical data on refractory F98 glioma and compared to the Kaplan-Meier estimate. The Akaike information criterion (AIC) is used to evaluate the performances of the exponential, Weibull and log-logistic regression models against the extended ER model. Based on the AIC value, the extended ER model is the best fitting model for the data. The analysis shows that treating treatment groups in the data as a covariate in the extended ER model is significant. Hence, it is concluded that different treatments affect the survival times of rats in the data.

Keywords: bootstrap; covariates; exponentiated Rayleigh; jackknife; right censored

ABSTRAK

Dalam kajian ini, model ER dilanjutkan untuk menambahkan kovariat bagi data yang tertapis kanan. Anggaran parameter menggunakan MLE dinilai berdasarkan bias, SE, dan RMSE bagi parameter pada pelbagai saiz sampel dan cp melalui kajian simulasi. Selain itu, kajian kebarangkalian liputan dijalankan untuk membandingkan tiga kaedah pembinaan selang keyakinan: kaedah Wald, jackknife dan bootstrap-t. Kajian kebarangkalian liputan menunjukkan bahawa teknik penganggaran selang keyakinan terbaik untuk parameter β_0 dan β_1 adalah kaedah bootstrap-t. Manakala, untuk parameter γ, pada $\alpha = 0.05$ ($\alpha = 0.1$) kaedah bootstrap-t (Wald) lebih sesuai. Model ini kemudiannya digunakan untuk data praklinikal berkaitan glioma F98 refraktori dan dibandingkan dengan anggaran Kaplan-Meier. AIC digunakan untuk menilai prestasi model antara regresi eksponen, Weibull dan log-logistik terhadap model ER lanjutan. Berdasarkan nilai AIC, model ER lanjutan menunjukkan kesesuaian terbaik untuk data. Analisis menunjukkan bahawa kumpulan rawatan dalam data sebagai kovariat dalam model lanjutan ER adalah signifikan. Maka, disimpulkan bahawa rawatan yang berbeza mempengaruhi masa kemandirian tikus dalam data.

Kata kunci: bootstrap; jackknife; kovariat; Rayleigh eksponen; tertapis kanan

1. Introduction

Survival analysis is fundamentally the analysis of time to an event of interest, the goal is often to estimate the time until an event of interest occurs. The key difference that separates survival analysis from ordinary data analysis is the occurrence of censoring in survival data. According to Turkson *et al.* (2021) if not handled cautiously, censoring could introduce biased results and affect the power of a statistical analysis. Kleinbaum and Klein (1996) describe censoring as the event in which the exact time to event of interest is not known. There are three different censoring, namely left censored, right censored and interval censored. Left censored data is where the exact time to event is less than or equal to the observed time to event. Right censored is where the exact time to event is equal to or greater than the observed time to event. Interval censored is where the exact time to event is within an interval. Lee and Wang (2003) explained that right censored data can be further divided into type I, type II and type III censoring. Type I censoring is when the number of censored observations is a random variable and there is a fixed censoring time. Type II censoring occurs when there is a fixed number of censored observation. Type III censoring is when the censoring is random because of staggered entry and unequal follow-up.

When fitting a model to survival data, the three main approaches are the parametric, non-parametric and semi-parametric model. The parametric model is more efficient but also stricter with the assumptions. Some common distributions used to fit survival data are the exponential, Weibull and log-logistics distribution (Kartsonaki 2016). Whereas, the non-parametric model is less rigid with assumptions but may not be as efficient. The most widespread non-parametric method is the Kaplan-Meier estimates (Rudolph *et al.* 2018). Semi-parametric model is an intermediate between parametric and non-parametric models. It relies on some assumptions but provides more flexibility compared to the parametric model. The Cox proportional hazards model first introduced by Cox (1972) is an example of a semi-parametric model that assumes proportional hazards. Covariates are variables that may influence the outcome of the primary variable of interest. The method of incorporating covariates in parametric models was first discussed by Feigl and Zelen (1965).

The Weibull distribution, first introduced by Weibull (1939) is of the commonly used distributions in survival analysis. It is able to fit data with constant, monotonic decreasing or monotonic increasing hazard rates. However, it is unable to fit non-monotonic hazard rates hence, extensions of the Weibull distribution was introduced. The exponentiated Weibull (EW) model was proposed by Mudholkar and Srivastava (1993) as an alternative to the Weibull distribution as it offers unimodal and bathtub hazard rates. Mudholkar *et al.* (1995) showed the flexibility of the EW distribution by fitting it to censored data that exhibits non-Weibull hazard rates. The study concluded that the Weibull distribution showed a poor fit for said data, while the EW provides a much better fit. Khan (2018) introduced the exponentiated Weibull regression (EWR) distribution that incorporates the effect of covariates into the EW distribution.

Alharbi *et al.* (2021) extended the generalized exponential model (GEM) to include covariates in the presence of right-censored data. The authors evaluated the maximum likelihood estimates of the GEM using the bias, SE and RMSE and found that the SE and RMSE decreases (increases) when the sample size (cp) increases (decreases). Ismail *et al.* (2024) extended the two-parameter bathtub hazard model and compared the Wald and likelihood interval estimates of the model using coverage probability study. The study found that both the Wald and likelihood method performs better at larger sample size but the Wald method produced more asymmetrical intervals. Loh *et al.* (2017) compared the Wald, likelihood ratio and jackknife interval estimates for the parameters of the log logistic model with doubly interval censored data. From the coverage probability study, the Wald method outperformed the likelihood ratio and jackknife inferential procedures. Arasan and Lunn (2008) compared the Wald, Jackknife and likelihood ratio confidence interval construction methods for the parameters of the bivariate exponential model with time varying covariates using coverage probability study. At a low (high) confidence level, the likelihood ratio (jackknife) method is preferred. Manoharan *et al.* (2015) compared the performance of the Wald, likelihood ratio and jackknife confidence intervals estimates for the parameters of the log-normal model with fixed covariates through a coverage probability study. The results show that the Wald, likelihood ratio and jackknife intervals performed well when no truncation or censoring is present in the data.

In the field of survival analysis, many commonly used models such as exponential, Weibull, log-logistic are extended to incorporate censored data and covariates. This study aims to obtain the exponentiated Rayleigh regression (ERR) model by including covariates in the ER model under right censored data. Following that, a simulation study was conducted to compare the performance of the ERR model parameter estimates at various sample sizes and cp by assessing the bias, SE and RMSE. The performance of three different confidence interval construction methods, namely Wald, jackknife and bootstrap-t were compared using coverage probability study by analyzing the number of conservative (C), anticonservative (AC) and asymmetry (AS) intervals produced by each method at different sample sizes, cp and nominal error (α). Lastly, the proposed ERR model is fit to real preclinical data on refractory F98 glioma. The AIC value is used to compare the performance of the proposed ERR model on the data against common parametric regression models in the field of survival analysis.

2. Methodology

The Weibull model consists of two parameters, a scale parameter λ and shape parameter β. It is able to fit data with constant, monotonic increasing and monotonic decreasing hazard rates but unable to fit non-monotonic hazard rates. The Rayleigh model is a special case of the Weibull model when the shape parameter β is two. The two-parameter ER distribution is able to fit data with constant, monotonic and non-monotonic hazard rates. It has a scale parameter, λ and a shape parameter γ. As discussed by Surles and Padgett (2001), the probability distribution function (PDF), cumulative distribution function (CDF), survival and hazard functions of the ER model are given by Eq. (1) - Eq. (4).

$$f(t) = 2\gamma\lambda^2 t(1 - e^{-(\lambda t)^2})^{\gamma-1} e^{-(\lambda t)^2}. \tag{1}$$

$$F(t) = (1 - e^{-(\lambda t)^2})^{\gamma}. \tag{2}$$

$$S(t) = 1 - (1 - e^{-(\lambda t)^2})^{\gamma}. \tag{3}$$

$$h(t) = \frac{2\gamma\lambda^2 t(1 - e^{-(\lambda t)^2})^{\gamma-1} e^{-(\lambda t)^2}}{1 - (1 - e^{-(\lambda t)^2})^{\gamma}}, \tag{4}$$

where $t > 0, \lambda > 0, \gamma > 0$.

In this study, the ERR model is proposed to allow the inclusion of covariates into the ER model. p covariates were incorporated into the model by letting the scale parameter be $\lambda = e^{-\boldsymbol{\beta}'\mathbf{x}}$ where $\boldsymbol{\beta}' = (\beta_0, \beta_1, \beta_2, ..., \beta_p)$ is a vector of the p parameters and $\mathbf{x} = (x_0, x_1, x_2, ..., x_p)$ is a vector of the p covariate values. Hence the PDF, CDF, survival and hazard function are shown in Eq. (5) - Eq. (8).

$$f(t) = 2\gamma(e^{-\boldsymbol{\beta}'\mathbf{x}})^2 t(1 - e^{-(e^{-\boldsymbol{\beta}'\mathbf{x}}t)^2})^{\gamma-1} e^{-(e^{-\boldsymbol{\beta}'\mathbf{x}}t)^2}. \tag{5}$$

$$F(t) = (1 - e^{-(e^{-\boldsymbol{\beta}'\mathbf{x}}t)^2})^{\gamma}. \tag{6}$$

$$S(t) = 1 - (1 - e^{-(e^{-\boldsymbol{\beta}'\mathbf{x}}t)^2})^{\gamma}. \tag{7}$$

$$h(t) = \frac{2\gamma(e^{-\boldsymbol{\beta}'\mathbf{x}})^2 t\big(1 - e^{-(e^{-\boldsymbol{\beta}'\mathbf{x}}t)^2}\big)^{\gamma-1} e^{-(e^{-\boldsymbol{\beta}'\mathbf{x}}t)^2}}{1 - (1 - e^{-(e^{-\boldsymbol{\beta}'\mathbf{x}}t)^2})^{\gamma}}. \tag{8}$$

The inverse transform method is used to generate the i^{th} random variate from the ERR model as shown in Eq. (9),

$$t_i = \frac{(-\log[1 - u_i^{\frac{1}{\gamma}}])^{\frac{1}{2}}}{e^{-\boldsymbol{\beta}'\mathbf{x}_i}}, \tag{9}$$

where $u \sim U(0,1)$.

The MLE technique is used for the parameter estimation of the ERR model. As demonstrated by Patti *et al.* (2007), to incorporate right censored data into the likelihood function, a censoring indicator variable is added to the likelihood function such that for the i^{th} observation,

$$c_i = \begin{cases} 1, & \text{for uncensored,} \\ 0, & \text{for censored.} \end{cases}$$

The likelihood function of right censored data is given by Eq. (10).

$$L(\boldsymbol{\beta}, \gamma) = \prod_{i=1}^{n} [f(t_i)]^{c_i} [S(t_i)]^{1-c_i}. \tag{10}$$

Hence the likelihood and loglikelihood function for the ERR model in the presence of right censored data are shown in Eq. (11) - Eq. (12).

$$\begin{aligned} L(\boldsymbol{\beta}, \gamma) = \prod_{i=1}^{n} & \Big[2\gamma (e^{-\boldsymbol{\beta}'\mathbf{x}_i})^2 t_i (1 - e^{-((e^{-\boldsymbol{\beta}'\mathbf{x}_i})t_i)^2})^{\gamma-1} e^{-((e^{-\boldsymbol{\beta}'\mathbf{x}_i})t_i)^2} \Big]^{c_i} \\ & \times \Big[1 - \big(1 - e^{-(e^{-\boldsymbol{\beta}'\mathbf{x}_i} t_i)^2}\big)^{\gamma} \Big]^{1-c_i}. \end{aligned} \tag{11}$$

$$\begin{aligned} l(\boldsymbol{\beta}, \gamma) = \sum_{i=1}^{n} & c_i \big\{ \log[2\gamma (e^{-\boldsymbol{\beta}'\mathbf{x}_i})^2 t_i] + (\gamma - 1)\log[1 - e^{-((e^{-\boldsymbol{\beta}'\mathbf{x}_i})t_i)^2}] - ((e^{-\boldsymbol{\beta}'\mathbf{x}_i})t_i)^2 \big\} \\ & + (1 - c_i)\log[1 - (1 - e^{-((e^{-\boldsymbol{\beta}'\mathbf{x}_i})t_i)^2})^{\gamma}]. \end{aligned} \tag{12}$$

Since the likelihood equations of the ERR model is nonlinear, the Newton-Raphson (NR) method is used to solve the nonlinear equations.

First introduced by Fisher (1925), the variance for the parameter estimates is estimated using the inverse Fisher Information. Since the Fisher Information is hard to obtain, it is estimated with the observed Fisher information. The observed information matrix of an ERR model with one covariate and three parameters is given by Eq. (13).

$$\mathbf{i}(\beta_0, \beta_1, \gamma) = - \left. \begin{bmatrix} \frac{\partial^2 l}{\partial \beta_0^2} & \frac{\partial^2 l}{\partial \beta_0 \partial \beta_1} & \frac{\partial^2 l}{\partial \beta_0 \partial \gamma} \\ \frac{\partial^2 l}{\partial \beta_1 \partial \beta_0} & \frac{\partial^2 l}{\partial \beta_1^2} & \frac{\partial^2 l}{\partial \beta_1 \partial \gamma} \\ \frac{\partial^2 l}{\partial \gamma \partial \beta_0} & \frac{\partial^2 l}{\partial \gamma \partial \beta_1} & \frac{\partial^2 l}{\partial \gamma^2} \end{bmatrix} \right|_{\beta_0 = \hat{\beta}_0,\ \beta_1 = \hat{\beta}_1,\ \gamma = \hat{\gamma}} \tag{13}$$

As proven by Wald (1940), the $100(1-\alpha)\%$ Wald confidence interval for θ_j is given by Eq. (14),

$$\hat{\theta}_j \pm z_{1-\frac{\alpha}{2}} \sqrt{i^{-1}(\hat{\theta})_{jj}}, \tag{14}$$

where $i^{-1}(\hat{\theta})_{jj}$ refers to the diagonal element of the observed information matrix.

In their book, Efron (1982) illustrated sampling using jackknife and bootstrap method. To obtain the jackknife samples, each observation is removed from the original sample one after another. Hence, an original sample of n observations will have n jackknife samples, where the i^{th} sample will have $n-1$ observations, with the i^{th} observation removed. The parameter estimate of the jackknife sample is given by Eq. (15),

$$\hat{\theta}_{jack} = \hat{\theta} - (n-1)\{\hat{\theta_{(.)}} - \hat{\theta}\}. \tag{15}$$

and the SE of the jackknife estimates are given by Eq. (16),

$$\hat{se}(\hat{\theta})_{jack} = \sqrt{\frac{n-1}{n}\sum_{i=1}^{n}\left\{\hat{\theta}_{(i)} - \hat{\theta}_{(.)}\right\}^2}, \tag{16}$$

where $\hat{\theta}_{(.)} = \sum_{i=1}^{n} \frac{\hat{\theta}_{(i)}}{n}$.
The $100(1-\alpha)\%$ jackknife confidence interval is defined as Eq. (17),

$$\hat{\theta}_{jack} \pm t_{(1-\frac{\alpha}{2}, n-1)}\hat{se}(\hat{\theta})_{jack}, \tag{17}$$

where t stands for the Student's t distribution.

In parametric bootstrap, B samples of size n are generated from the presumed distribution of the original sample. For each bootstrap sample, the standardized value of the parameter estimate is calculated using Eq. (18),

$$Z(\hat{\theta}^b) = \frac{\hat{\theta}^b - \hat{\theta}}{\hat{se}(\hat{\theta^b})}, \tag{18}$$

where $\hat{\theta}^b$ is the parameter estimate of the b^{th} sample for $b = 1, 2, ..., B$ and $\hat{\theta}$ is the parameter estimate from the original sample.
The SE of the b^{th} bootstrap parameter estimates, $\hat{se}(\hat{\theta^b})$ is obtained using the inverse of the observed Fisher information of the b^{th} bootstrap sample. $Z(\hat{\theta}^b)$ is sorted in ascending order to obtain $[Z(\hat{\theta}^b)]_k = [Z(\hat{\theta}^b)]_1, [Z(\hat{\theta}^b)]_2, ..., [Z(\hat{\theta}^b)]_B$. The $100(1-\alpha)\%$ bootstrap-t confidence interval is obtained using Eq. (19),

$$\left\{\hat{\theta} - [Z(\hat{\theta}^b)]_{B.(1-\frac{\alpha}{2})}\hat{se}(\hat{\theta}), \hat{\theta} - [Z(\hat{\theta}^b)]_{B.(\frac{\alpha}{2})}\hat{se}(\hat{\theta})\right\}, \tag{19}$$

where $\hat{se}(\hat{\theta})$ is obtained using the observed Fisher information of the original sample.
If $B.(1-\frac{\alpha}{2})$ or $B.\frac{\alpha}{2}$ are not integers, they are to be rounded to the nearest highest or lower integers.

3. Simulation Study and Results

Two simulation studies were conducted in this study, the first simulation study evaluated the performance of the maximum likelihood estimates of the ERR model at different sample sizes n and cp by computing the bias, SE and RMSE of the parameter estimates. The performance of the parameter estimates are considered ideal if the bias, SE and RMSE are close to zero.

The second simulation study, known as the coverage probability study compared the performance of confidence interval construction method namely, Wald, jackknife and bootstrap-t at different n, cp and nominal error (α) by evaluating the number of C, AC and AS intervals and computing the estimated left and right error probabilities of the three methods. A confidence interval construction method is considered ideal if it produces minimal number of C, AC and AS intervals and the left and right error probabilities are close to the nominal error divided by two. Both simulations were conducted using R software.

The first simulation was conducted for $N = 1000$ replications at $n = 30, 50, 80, 120, 150, 200$

and $cp = 0\%, 5\%, 10\%, 20\%, 30\%$. The value of the three parameters in the ERR model are $\beta_0 = 0.9$, $\beta_1 = 0.5$ and $\gamma = 1.1$. The values were chosen as such to replicate the observations of the preclinical data on refractory F98 glioma (Klein & Moeschberger 2003).

The steps in the first simulation are as follows:

(1) Draw random values, u_i from a standard uniform distribution to produce survival times, t_i from the ERR model using the inverse transform method.
(2) Generate random values, x_i from the standard normal distribution to mimic covariate values.
(3) Obtain censoring times, c_i from an exponential distribution with parameter λ, where λ is varied according to the desired cp.
(4) The survival time, t_i is said to be right censored if $t_i > c_i$.

Table 1: Bias, SE and RMSE of $\hat{\beta}_0$, $\hat{\beta}_1$, $\hat{\gamma}$

		$\hat{\beta}_0$			$\hat{\beta}_1$			$\hat{\gamma}$		
cp	n	Bias	SE	RMSE	Bias	SE	RMSE	Bias	SE	RMSE
0%	30	0.04839	0.12353	0.13267	-0.00320	0.09711	0.09716	0.17369	0.38376	0.42124
	50	-0.02277	0.08974	0.09258	-0.00255	0.07165	0.07170	0.07474	0.24082	0.25215
	80	-0.01694	0.07280	0.07474	0.00004	0.05705	0.05705	0.05851	0.18633	0.19530
	120	-0.01051	0.05772	0.05867	0.00225	0.04638	0.04643	0.03931	0.14514	0.15037
	150	-0.00801	0.05335	0.05395	0.00091	0.03976	0.03977	0.02519	0.12722	0.12969
	200	-0.00911	0.04329	0.04424	0.00023	0.03521	0.03521	0.02500	0.10888	0.11171
5%	30	-0.04791	0.12480	0.13368	-0.00217	0.09741	0.09743	0.17420	0.38412	0.42177
	50	-0.02263	0.09018	0.09298	-0.00176	0.07215	0.07217	0.07562	0.24136	0.25293
	80	-0.01723	0.07309	0.07509	0.00034	0.05740	0.05740	0.05918	0.18751	0.19663
	120	-0.01056	0.05818	0.05913	0.00213	0.04677	0.04682	0.03943	0.14617	0.15139
	150	-0.00830	0.05411	0.05474	0.00071	0.04029	0.04030	0.02562	0.12765	0.13020
	200	-0.00936	0.04360	0.04459	0.00023	0.03548	0.03548	0.02526	0.10918	0.11206
10%	30	-0.04832	0.12549	0.13447	-0.00203	0.09823	0.09825	0.17555	0.38430	0.42250
	50	-0.02301	0.09069	0.09356	-0.00173	0.07263	0.07265	0.07678	0.24390	0.25570
	80	-0.01719	0.07323	0.07522	0.00073	0.05776	0.05776	0.05908	0.18801	0.19707
	120	-0.01071	0.05893	0.05990	0.00216	0.04695	0.04700	0.03964	0.14696	0.15221
	150	-0.00855	0.05459	0.05526	0.00051	0.04067	0.04067	0.02602	0.12850	0.13111
	200	-0.00959	0.04408	0.04511	0.00007	0.03594	0.03594	0.02560	0.10995	0.11289
20%	30	-0.04984	0.12751	0.13690	-0.00217	0.09977	0.09979	0.18439	0.39917	0.43970
	50	-0.02322	0.09235	0.09522	-0.00152	0.07440	0.07442	0.07891	0.24944	0.26162
	80	-0.01792	0.07377	0.07592	0.00066	0.05876	0.05876	0.06095	0.18969	0.19924
	120	-0.01087	0.06004	0.06102	0.00202	0.04813	0.04817	0.03998	0.14715	0.15248
	150	-0.00854	0.05552	0.05617	0.00051	0.04137	0.04137	0.02685	0.12979	0.13254
	200	-0.00960	0.04475	0.04577	0.00037	0.03681	0.03681	0.02603	0.11044	0.11347
30%	30	-0.04926	0.13292	0.14175	-0.00150	0.10235	0.10236	0.18842	0.40961	0.45087
	50	-0.02440	0.09352	0.09665	-0.00142	0.07653	0.07654	0.08119	0.25263	0.26536
	80	-0.01694	0.07596	0.07783	0.00197	0.06024	0.06027	0.06119	0.19165	0.20118
	120	-0.01141	0.06113	0.06219	0.00193	0.04933	0.04937	0.04143	0.14945	0.15509
	150	-0.00845	0.05677	0.05740	0.00059	0.04222	0.04222	0.02673	0.13094	0.13364
	200	-0.00954	0.04631	0.04728	0.00063	0.03717	0.03718	0.02661	0.11222	0.11533

Table 1 shows the bias, SE and RMSE values for the parameter estimates of the ERR model using the MLE technique at different cp and n. It is observed that when cp is fixed, the SE and RMSE decreases as n increases. Hence the performance of the parameter estimate increases when n increases. This property holds true for all three parameters of the ERR model and at every cp level. For a fixed n, the SE and RMSE increase as the cp increases. Hence, the performance of the parameter estimate decreases as cp increases.

A coverage probability study was conducted for $N = 1000$ times with $n = 30, 50, 80, 120, 150, 200$ and $cp = 0\%, 5\%, 10\%, 20\%, 30\%$. The nominal error values included are $\alpha = 0.05, 0.1$.

Coverage probability is the probability that the true parameter falls within the estimated confidence interval. The performance of the confidence interval estimates of different methods can be measured by using the left and right error probabilities. As shown in their study, Arasan & Lunn (2008) described the left(right) error probability can be estimated by summing the number of times the true parameter is lesser(greater) than the left(right) endpoint of the confidence interval divided by the total number of repetitions, N. Ideally, both the left and right error probabilities should be equal or close to the nominal error probability divided by two. The total error probability is the sum of the left and right error probability.

As used by Kiani and Arasan (2018) and Alharbi *et al.* (2022), the estimated error probabilities for the Wald confidence intervals are given by Eq. (20) - Eq. (21),

$$\text{Left Error} = \frac{\#\left\{\theta < \hat{\theta} - z_{1-\frac{\alpha}{2}}\sqrt{v\hat{a}r(\hat{\theta})}\right\}}{N}. \tag{20}$$

$$\text{Right Error} = \frac{\#\left\{\theta > \hat{\theta} + z_{1-\frac{\alpha}{2}}\sqrt{v\hat{a}r(\hat{\theta})}\right\}}{N}. \tag{21}$$

the jackknife confidence intervals are shown in Eq. (22) - Eq. (23),

$$\text{Left Error} = \frac{\#\left\{\theta < \hat{\theta}_{jack} - t_{(1-\frac{\alpha}{2},n-1)}\hat{se}(\hat{\theta})_{jack}\right\}}{N}. \tag{22}$$

$$\text{Right Error} = \frac{\#\left\{\theta > \hat{\theta}_{jack} + t_{(1-\frac{\alpha}{2},n-1)}\hat{se}(\hat{\theta})_{jack}\right\}}{N}. \tag{23}$$

and the bootstrap-t confidence intervals are given by Eq. (24) - Eq. (25).

$$\text{Left Error} = \frac{\#\left\{\theta < \hat{\theta} - [Z(\hat{\theta}^b)]_{B.(1-\frac{\alpha}{2})}\hat{se}(\hat{\theta})\right\}}{N}. \tag{24}$$

$$\text{Right Error} = \frac{\#\left\{\theta > \hat{\theta} - [Z(\hat{\theta}^b)]_{B.(\frac{\alpha}{2})}\hat{se}(\hat{\theta})\right\}}{N}. \tag{25}$$

The performance of confidence interval estimates can also be assessed using the number of C, AC and AS intervals produced. An interval estimate is C if the coverage probability is lesser than the nominal confidence level, AC if the coverage probability is greater than the nominal confidence level and AS if the probability of the true parameter laying below the lower limit of the interval estimate and above the upper limit of the interval estimate is significantly different. According to Doganaksoy and Schmee (1993), a method is AC if the total probability is greater than $\alpha + 2.58 \times SE(\hat{\alpha})$ and C if the total probability is less than $\alpha - 2.58 \times SE(\hat{\alpha})$. A method is AS if the larger value of the left or right error probability is more than 1.5 times the smaller error probability.

In this study, the performance of the three confidence interval construction methods are evaluated by tabulating the number of C, AC and AS intervals produced for different parameters of the ERR model at different n, cp and α. In Tables 2-7, a confidence interval construction method will be marked as "1" if either a C, AC or AS interval was produced, and "0" otherwise.

From Tables 2 and 3, the Wald method performed the poorest for parameter β_0 with the most amount of AS and AC interval estimates. The jackknife method produced many AS interval estimates. The bootstrap-t method outperforms the Wald and jackknife method.

Table 2: Performance of the Wald, jackknife and bootstrap-t method for β_0 at $\alpha = 0.05$

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
0%	30	0	1	1	0	0	1	0	0	0
	50	0	1	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	1	0	0	0
	150	0	1	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0
5%	30	0	1	1	0	0	1	0	0	0
	50	0	0	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	1
	120	0	0	1	0	0	1	0	0	0
	150	0	0	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0
10%	30	0	1	1	0	0	1	0	0	0
	50	0	0	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	1	0	0	0
	150	0	0	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0
20%	30	0	1	1	0	0	1	0	0	0
	50	0	0	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	1	0	0	0
	150	0	1	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0
30%	30	0	1	1	0	0	1	0	0	0
	50	0	0	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	1	0	0	0
	150	0	1	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0

Table 3: Performance of the Wald, jackknife and bootstrap-t method for β_0 at $\alpha = 0.1$

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
0%	30	0	1	1	0	0	1	0	0	0
	50	0	1	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	0	0	0	0
	150	0	0	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0
5%	30	0	1	1	0	0	1	0	0	0
	50	0	1	1	0	0	1	0	0	0

Table 3 (Continued)

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	0	0	0	0
	150	0	0	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0
10%	30	0	1	1	0	0	1	0	0	0
	50	0	1	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	0	0	0	0
	150	0	0	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0
20%	30	0	1	1	0	0	1	0	0	0
	50	0	1	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	1	0	0	0
	150	0	0	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0
30%	30	0	1	1	0	0	1	0	0	0
	50	0	0	1	0	0	1	0	0	0
	80	0	0	1	0	0	1	0	0	0
	120	0	0	1	0	0	1	0	0	0
	150	0	1	1	0	0	1	0	0	0
	200	0	0	1	0	0	0	0	0	0

Table 4 and 5 shows that for the parameter β_1, the Wald method consistently produces AC intervals at small sample size $n = 30$. The jackknife method had AS interval estimates for smaller (larger) sample sizes at $\alpha = 0.05$ ($\alpha = 0.1$). The bootstrap-t method performed the best.

Table 4: Performance of the Wald, jackknife and bootstrap-t method for β_1 at $\alpha = 0.05$

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
0%	30	0	1	0	0	0	0	0	0	0
	50	0	0	0	0	0	1	0	0	0
	80	0	0	0	0	0	1	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	0	0	0	0
5%	30	0	1	0	0	1	0	0	0	0
	50	0	0	0	0	0	1	0	0	0
	80	0	0	0	0	0	1	0	0	1
	120	0	0	0	0	0	0	0	0	0
	150	0	0	1	0	0	1	0	0	0
	200	0	0	0	0	0	0	0	0	0
10%	30	0	1	0	0	1	0	0	0	0
	50	0	0	0	0	0	1	0	0	0
	80	0	0	0	0	0	1	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	0	0	0	0	0	0	0

Table 4 (Continued)

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
	200	0	0	0	0	0	0	0	0	0
20%	30	0	1	0	0	1	0	0	0	0
	50	0	0	0	0	0	1	0	0	0
	80	0	0	0	0	0	0	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	1	0	0	0	1	0	0
	200	0	0	0	0	0	1	0	0	0
30%	30	0	1	0	0	1	0	0	0	0
	50	0	0	0	0	0	1	0	0	0
	80	0	0	0	0	0	0	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	1	0	0	0	0	0	0
	200	0	0	0	0	0	0	0	0	0

Table 5: Performance of the Wald, jackknife and bootstrap-t method for β_1 at $\alpha = 0.1$

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
0%	30	0	1	0	0	0	0	0	0	0
	50	0	0	0	0	0	0	0	0	0
	80	0	0	0	0	0	0	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
5%	30	0	1	0	0	0	0	0	0	0
	50	0	0	1	0	0	0	0	0	0
	80	0	0	0	0	0	0	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
10%	30	0	1	0	0	0	0	0	0	0
	50	0	0	0	0	0	0	0	0	0
	80	0	0	0	0	0	0	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	0	0	0	0	0	0	0
	200	0	0	0	0	0	1	0	0	0
20%	30	0	1	0	0	0	0	0	0	0
	50	0	0	0	0	0	0	0	0	0
	80	0	0	0	0	0	0	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	0	0	0	0	0	0	0
	200	0	0	0	0	0	0	0	0	0
30%	30	0	1	0	0	0	0	0	0	0
	50	0	0	0	0	0	0	0	0	0
	80	0	0	0	0	0	0	0	0	0
	120	0	0	0	0	0	0	0	0	0
	150	0	0	0	0	0	0	1	0	0
	200	0	0	0	0	0	0	0	0	0

The interval estimates for the parameter γ are shown in Tables 6 and 7. The jackknife method performed the worst as all the interval estimates were AS. At $\alpha = 0.05$ ($\alpha = 0.1$), the bootstrap-t (Wald) method performed the best with the least C, AC and AS intervals across all cp and n.

Table 6: Performance of the Wald, jackknife and bootstrap-t method for γ at $\alpha = 0.05$

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
0%	30	1	0	1	0	0	1	0	0	0
	50	0	0	0	0	0	1	0	0	1
	80	0	0	0	0	0	1	0	0	0
	120	0	0	0	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
5%	30	0	0	1	0	0	1	0	1	1
	50	0	0	0	0	0	1	0	1	1
	80	0	0	0	0	0	1	0	0	0
	120	0	0	0	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
10%	30	1	0	1	0	0	1	0	1	1
	50	0	0	0	0	0	1	0	0	0
	80	0	0	0	0	0	1	0	0	0
	120	0	0	0	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
20%	30	1	0	1	0	0	1	0	0	1
	50	0	0	1	0	0	1	0	1	0
	80	0	0	0	0	0	1	0	0	0
	120	0	0	1	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
30%	30	1	0	1	0	0	1	0	0	1
	50	1	0	1	1	0	1	0	0	0
	80	0	0	0	0	0	1	0	0	0
	120	0	0	1	0	0	1	0	1	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0

Table 7: Performance of the Wald, jackknife and bootstrap-t method for γ at $\alpha = 0.1$

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
0%	30	0	0	0	1	0	1	0	0	0
	50	0	0	0	1	0	1	0	0	0
	80	0	0	0	1	0	1	0	0	0
	120	0	0	0	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
5%	30	0	0	0	1	0	1	0	0	0

Table 7 (Continued)

		Wald			Jackknife			Bootstrap-t		
cp	n	C	AC	AS	C	AC	AS	C	AC	AS
	50	0	0	0	1	0	1	0	0	0
	80	0	0	0	1	0	1	0	0	0
	120	0	0	0	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
10%	30	0	0	0	1	0	1	0	1	0
	50	0	0	0	1	0	1	0	0	0
	80	0	0	0	1	0	1	0	0	0
	120	0	0	0	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
20%	30	1	0	0	1	0	1	0	0	1
	50	0	0	0	1	0	1	0	0	0
	80	0	0	0	0	0	1	0	0	0
	120	0	0	0	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0
30%	30	0	0	0	1	0	1	0	0	0
	50	0	0	0	1	0	1	0	0	0
	80	0	0	0	0	0	1	0	0	0
	120	0	0	0	0	0	1	0	0	0
	150	0	0	0	0	0	1	0	0	0
	200	0	0	0	0	0	1	0	0	0

The detailed estimated left error (LE), right error (RE) and total error (TE) probabilities for the Wald, jackknife and bootstrap-t methods are given in Tables 8-13. Figures 1-6 illustrates the trends of the error probabilities of the interval estimates across different cp, n and α. An ideal interval estimate has left and right error probabilities that are close to $\frac{\alpha}{2}$.

Table 8: Estimated error probabilities of Wald, jackknife and bootstrap-t of β_0 at $\alpha = 0.05$

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
0%	30	0.006	0.086	0.092	0.014	0.042	0.056	0.025	0.034	0.059
	50	0.003	0.067	0.070	0.011	0.042	0.053	0.021	0.028	0.049
	80	0.005	0.054	0.059	0.016	0.039	0.055	0.030	0.025	0.055
	120	0.006	0.041	0.047	0.014	0.033	0.047	0.025	0.024	0.049
	150	0.011	0.058	0.069	0.016	0.043	0.059	0.030	0.029	0.059
	200	0.016	0.049	0.065	0.023	0.034	0.057	0.018	0.022	0.040
5%	30	0.007	0.087	0.094	0.015	0.041	0.056	0.028	0.036	0.064
	50	0.005	0.062	0.067	0.012	0.036	0.048	0.023	0.034	0.057
	80	0.005	0.059	0.064	0.015	0.040	0.055	0.028	0.018	0.046
	120	0.008	0.038	0.046	0.012	0.032	0.044	0.028	0.021	0.049
	150	0.010	0.056	0.066	0.017	0.042	0.059	0.028	0.029	0.057
	200	0.018	0.043	0.061	0.025	0.028	0.053	0.017	0.024	0.041
10%	30	0.007	0.091	0.098	0.013	0.045	0.058	0.032	0.030	0.062
	50	0.005	0.061	0.066	0.011	0.036	0.047	0.022	0.028	0.050
	80	0.006	0.059	0.065	0.017	0.036	0.053	0.024	0.029	0.053
	120	0.008	0.039	0.047	0.012	0.032	0.044	0.025	0.028	0.053

Table 8 (Continued)

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
	150	0.011	0.054	0.065	0.019	0.040	0.059	0.032	0.027	0.059
	200	0.015	0.039	0.054	0.030	0.031	0.061	0.023	0.023	0.046
20%	30	0.009	0.083	0.092	0.013	0.043	0.056	0.026	0.026	0.052
	50	0.007	0.058	0.065	0.012	0.037	0.049	0.023	0.032	0.055
	80	0.005	0.050	0.055	0.017	0.037	0.054	0.029	0.024	0.053
	120	0.004	0.039	0.043	0.010	0.031	0.041	0.023	0.022	0.045
	150	0.011	0.057	0.068	0.018	0.043	0.061	0.031	0.026	0.057
	200	0.014	0.035	0.049	0.022	0.026	0.048	0.019	0.019	0.038
30%	30	0.007	0.086	0.093	0.010	0.044	0.054	0.026	0.027	0.053
	50	0.004	0.063	0.067	0.014	0.032	0.046	0.023	0.032	0.055
	80	0.005	0.051	0.056	0.017	0.038	0.055	0.026	0.030	0.056
	120	0.005	0.045	0.050	0.015	0.033	0.048	0.021	0.019	0.040
	150	0.010	0.058	0.068	0.020	0.043	0.063	0.035	0.028	0.063
	200	0.017	0.036	0.053	0.020	0.024	0.044	0.021	0.020	0.041

Table 9: Estimated error probabilities of Wald, jackknife and bootstrap-t of β_0 at $\alpha = 0.1$

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
0%	30	0.018	0.129	0.147	0.040	0.073	0.113	0.053	0.046	0.099
	50	0.015	0.118	0.133	0.037	0.072	0.109	0.042	0.048	0.090
	80	0.016	0.097	0.113	0.036	0.072	0.108	0.056	0.043	0.099
	120	0.029	0.072	0.101	0.039	0.056	0.095	0.053	0.049	0.102
	150	0.025	0.089	0.114	0.038	0.070	0.108	0.059	0.048	0.107
	200	0.038	0.078	0.116	0.049	0.063	0.112	0.047	0.044	0.091
5%	30	0.016	0.129	0.145	0.036	0.074	0.110	0.050	0.063	0.113
	50	0.015	0.117	0.132	0.038	0.073	0.111	0.045	0.058	0.103
	80	0.018	0.095	0.113	0.036	0.071	0.107	0.052	0.038	0.090
	120	0.028	0.074	0.102	0.043	0.055	0.098	0.042	0.047	0.089
	150	0.028	0.074	0.102	0.041	0.068	0.109	0.056	0.046	0.102
	200	0.037	0.076	0.113	0.050	0.059	0.109	0.044	0.045	0.089
10%	30	0.015	0.131	0.146	0.036	0.076	0.112	0.054	0.064	0.118
	50	0.015	0.114	0.129	0.034	0.070	0.104	0.050	0.051	0.101
	80	0.017	0.093	0.110	0.032	0.072	0.104	0.052	0.044	0.096
	120	0.028	0.071	0.099	0.038	0.056	0.094	0.048	0.053	0.101
	150	0.028	0.093	0.121	0.044	0.067	0.111	0.056	0.050	0.106
	200	0.036	0.078	0.114	0.047	0.060	0.107	0.045	0.043	0.088
20%	30	0.016	0.128	0.144	0.039	0.072	0.111	0.047	0.050	0.097
	50	0.017	0.112	0.129	0.039	0.067	0.106	0.052	0.055	0.107
	80	0.018	0.083	0.101	0.029	0.065	0.094	0.060	0.043	0.103
	120	0.025	0.072	0.097	0.033	0.053	0.086	0.045	0.045	0.090
	150	0.026	0.094	0.120	0.043	0.070	0.113	0.058	0.047	0.105
	200	0.036	0.081	0.117	0.052	0.059	0.111	0.046	0.044	0.090
30%	30	0.018	0.126	0.144	0.042	0.071	0.113	0.050	0.047	0.097
	50	0.015	0.109	0.124	0.036	0.066	0.102	0.050	0.055	0.105
	80	0.020	0.095	0.115	0.032	0.063	0.095	0.058	0.050	0.108
	120	0.021	0.075	0.096	0.037	0.056	0.093	0.049	0.046	0.095
	150	0.036	0.100	0.136	0.044	0.077	0.121	0.060	0.055	0.115

Table 9 (Continued)

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
	200	0.028	0.075	0.103	0.045	0.050	0.095	0.047	0.046	0.093

Table 10: Estimated error probabilities of Wald, jackknife and bootstrap-t of β_1 at $\alpha = 0.05$

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
0%	30	0.035	0.042	0.077	0.033	0.034	0.067	0.025	0.028	0.053
	50	0.026	0.037	0.063	0.023	0.042	0.065	0.024	0.023	0.047
	80	0.027	0.034	0.061	0.023	0.036	0.059	0.030	0.025	0.055
	120	0.023	0.019	0.042	0.024	0.022	0.046	0.019	0.021	0.040
	150	0.025	0.021	0.046	0.030	0.018	0.048	0.023	0.024	0.047
	200	0.025	0.032	0.057	0.022	0.032	0.054	0.028	0.021	0.049
5%	30	0.035	0.043	0.078	0.033	0.035	0.068	0.021	0.025	0.046
	50	0.027	0.035	0.062	0.019	0.041	0.060	0.026	0.026	0.052
	80	0.029	0.029	0.058	0.023	0.038	0.061	0.031	0.018	0.049
	120	0.024	0.018	0.042	0.025	0.021	0.046	0.015	0.021	0.036
	150	0.028	0.018	0.046	0.029	0.019	0.048	0.021	0.021	0.042
	200	0.026	0.032	0.058	0.024	0.035	0.059	0.024	0.020	0.044
10%	30	0.034	0.038	0.072	0.033	0.035	0.068	0.025	0.020	0.045
	50	0.026	0.036	0.062	0.019	0.042	0.061	0.025	0.022	0.047
	80	0.028	0.029	0.057	0.020	0.032	0.052	0.026	0.022	0.048
	120	0.025	0.020	0.045	0.026	0.023	0.049	0.018	0.016	0.034
	150	0.027	0.019	0.046	0.026	0.019	0.045	0.020	0.024	0.044
	200	0.026	0.034	0.060	0.024	0.034	0.058	0.022	0.023	0.045
20%	30	0.038	0.039	0.077	0.033	0.036	0.069	0.027	0.025	0.052
	50	0.023	0.032	0.055	0.019	0.036	0.055	0.025	0.022	0.047
	80	0.032	0.034	0.066	0.023	0.032	0.055	0.026	0.022	0.048
	120	0.025	0.023	0.048	0.027	0.027	0.054	0.017	0.021	0.038
	150	0.031	0.019	0.050	0.029	0.020	0.049	0.017	0.015	0.032
	200	0.024	0.032	0.056	0.020	0.033	0.053	0.022	0.020	0.042
30%	30	0.037	0.043	0.080	0.034	0.034	0.068	0.030	0.021	0.051
	50	0.024	0.029	0.053	0.021	0.032	0.053	0.027	0.025	0.052
	80	0.031	0.029	0.060	0.025	0.025	0.050	0.032	0.024	0.056
	120	0.027	0.024	0.051	0.028	0.022	0.050	0.021	0.025	0.046
	150	0.033	0.019	0.052	0.029	0.022	0.051	0.019	0.018	0.037
	200	0.024	0.029	0.053	0.021	0.031	0.052	0.024	0.019	0.043

Table 11: Estimated error probabilities of Wald, jackknife and bootstrap-t of β_1 at $\alpha = 0.1$

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
0%	30	0.067	0.066	0.133	0.053	0.060	0.113	0.052	0.057	0.109
	50	0.042	0.061	0.103	0.043	0.061	0.104	0.053	0.051	0.104
	80	0.054	0.057	0.111	0.048	0.056	0.104	0.059	0.046	0.105
	120	0.054	0.046	0.100	0.057	0.045	0.102	0.040	0.044	0.084
	150	0.057	0.038	0.095	0.055	0.035	0.090	0.047	0.043	0.090

Table 11(Continued)

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
	200	0.043	0.061	0.104	0.041	0.062	0.103	0.049	0.050	0.099
5%	30	0.064	0.072	0.136	0.055	0.058	0.113	0.050	0.051	0.101
	50	0.039	0.062	0.101	0.044	0.062	0.106	0.055	0.053	0.108
	80	0.051	0.060	0.111	0.046	0.055	0.101	0.054	0.038	0.092
	120	0.055	0.049	0.104	0.055	0.046	0.101	0.044	0.049	0.093
	150	0.055	0.049	0.104	0.059	0.037	0.096	0.045	0.043	0.088
	200	0.044	0.063	0.107	0.040	0.063	0.103	0.044	0.048	0.092
10%	30	0.065	0.069	0.134	0.056	0.057	0.113	0.051	0.045	0.096
	50	0.041	0.060	0.101	0.045	0.066	0.111	0.049	0.055	0.104
	80	0.053	0.056	0.109	0.046	0.056	0.102	0.061	0.049	0.110
	120	0.053	0.047	0.100	0.052	0.047	0.099	0.041	0.036	0.077
	150	0.057	0.038	0.095	0.052	0.039	0.091	0.047	0.043	0.090
	200	0.046	0.060	0.106	0.038	0.067	0.105	0.049	0.049	0.098
20%	30	0.064	0.071	0.135	0.056	0.056	0.112	0.054	0.058	0.112
	50	0.044	0.052	0.096	0.042	0.058	0.100	0.048	0.051	0.099
	80	0.055	0.054	0.109	0.050	0.053	0.103	0.058	0.045	0.103
	120	0.044	0.053	0.097	0.050	0.052	0.102	0.043	0.046	0.089
	150	0.057	0.039	0.096	0.055	0.040	0.095	0.045	0.034	0.079
	200	0.049	0.059	0.108	0.040	0.059	0.099	0.042	0.059	0.101
30%	30	0.062	0.063	0.125	0.059	0.057	0.116	0.057	0.050	0.107
	50	0.045	0.057	0.102	0.047	0.061	0.108	0.045	0.050	0.095
	80	0.053	0.051	0.104	0.048	0.049	0.097	0.057	0.046	0.103
	120	0.048	0.051	0.099	0.051	0.050	0.101	0.045	0.048	0.093
	150	0.060	0.045	0.105	0.057	0.043	0.100	0.035	0.035	0.070
	200	0.043	0.054	0.097	0.037	0.054	0.091	0.045	0.047	0.092

Table 12: Estimated error probabilities of Wald, jackknife and bootstrap-t of γ at $\alpha = 0.05$

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
0%	30	0.008	0.024	0.032	0.002	0.035	0.037	0.034	0.024	0.058
	50	0.017	0.023	0.040	0.004	0.033	0.037	0.037	0.024	0.061
	80	0.015	0.020	0.035	0.006	0.031	0.037	0.025	0.035	0.060
	120	0.019	0.026	0.045	0.011	0.041	0.052	0.034	0.032	0.066
	150	0.018	0.027	0.045	0.011	0.033	0.044	0.033	0.029	0.062
	200	0.023	0.023	0.046	0.012	0.028	0.040	0.024	0.028	0.052
5%	30	0.008	0.025	0.033	0.001	0.038	0.039	0.044	0.024	0.068
	50	0.017	0.022	0.039	0.004	0.032	0.036	0.046	0.029	0.075
	80	0.016	0.021	0.037	0.006	0.030	0.036	0.019	0.027	0.046
	120	0.017	0.025	0.042	0.011	0.040	0.051	0.030	0.027	0.057
	150	0.019	0.028	0.047	0.011	0.033	0.044	0.034	0.028	0.062
	200	0.021	0.024	0.045	0.012	0.029	0.041	0.023	0.026	0.049
10%	30	0.008	0.021	0.029	0.001	0.039	0.040	0.045	0.027	0.072
	50	0.016	0.021	0.037	0.004	0.031	0.035	0.034	0.025	0.059
	80	0.016	0.020	0.036	0.005	0.031	0.036	0.027	0.035	0.062
	120	0.018	0.026	0.044	0.011	0.039	0.050	0.032	0.032	0.064
	150	0.018	0.027	0.045	0.012	0.032	0.044	0.031	0.027	0.058
	200	0.022	0.023	0.045	0.010	0.030	0.040	0.025	0.027	0.052

Table 12 (Continued)

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
20%	30	0.009	0.022	0.031	0.001	0.039	0.040	0.037	0.019	0.056
	50	0.014	0.024	0.038	0.003	0.036	0.039	0.041	0.029	0.070
	80	0.019	0.020	0.039	0.005	0.031	0.036	0.026	0.031	0.057
	120	0.018	0.030	0.048	0.010	0.037	0.047	0.028	0.036	0.064
	150	0.022	0.028	0.050	0.012	0.033	0.045	0.031	0.030	0.061
	200	0.021	0.024	0.045	0.009	0.035	0.044	0.022	0.025	0.047
30%	30	0.007	0.024	0.031	0.001	0.026	0.027	0.036	0.022	0.058
	50	0.012	0.020	0.032	0.002	0.030	0.032	0.039	0.027	0.066
	80	0.016	0.020	0.036	0.005	0.030	0.035	0.023	0.033	0.056
	120	0.017	0.028	0.045	0.010	0.029	0.039	0.038	0.034	0.072
	150	0.023	0.026	0.049	0.012	0.033	0.045	0.029	0.028	0.057
	200	0.025	0.022	0.047	0.011	0.036	0.047	0.025	0.023	0.048

Table 13: Estimated error probabilities of Wald, jackknife and bootstrap-t of γ at $\alpha = 0.1$

		Wald			Jackknife			Bootstrap-t		
cp	n	LE	RE	TE	LE	RE	TE	LE	RE	TE
0%	30	0.038	0.042	0.080	0.003	0.065	0.068	0.056	0.049	0.105
	50	0.045	0.038	0.083	0.013	0.061	0.074	0.059	0.044	0.103
	80	0.041	0.039	0.080	0.015	0.055	0.070	0.047	0.060	0.107
	120	0.034	0.046	0.080	0.019	0.057	0.076	0.060	0.054	0.114
	150	0.048	0.044	0.092	0.020	0.062	0.082	0.057	0.062	0.119
	200	0.057	0.043	0.100	0.036	0.065	0.101	0.050	0.050	0.100
5%	30	0.039	0.040	0.079	0.002	0.063	0.065	0.063	0.048	0.111
	50	0.044	0.036	0.080	0.013	0.058	0.071	0.066	0.049	0.115
	80	0.043	0.041	0.084	0.014	0.057	0.071	0.046	0.053	0.099
	120	0.037	0.045	0.082	0.019	0.062	0.081	0.055	0.055	0.110
	150	0.037	0.045	0.082	0.021	0.064	0.085	0.057	0.065	0.122
	200	0.057	0.042	0.099	0.034	0.062	0.096	0.048	0.049	0.097
10%	30	0.037	0.042	0.079	0.002	0.065	0.067	0.073	0.054	0.127
	50	0.042	0.038	0.080	0.011	0.059	0.070	0.058	0.044	0.102
	80	0.039	0.042	0.081	0.012	0.059	0.071	0.046	0.057	0.103
	120	0.039	0.043	0.082	0.019	0.064	0.083	0.057	0.055	0.112
	150	0.057	0.044	0.101	0.020	0.064	0.084	0.054	0.063	0.117
	200	0.056	0.041	0.097	0.033	0.062	0.095	0.049	0.048	0.097
20%	30	0.033	0.042	0.075	0.002	0.064	0.066	0.064	0.042	0.106
	50	0.040	0.040	0.080	0.010	0.053	0.063	0.064	0.052	0.116
	80	0.044	0.041	0.085	0.014	0.062	0.076	0.045	0.055	0.100
	120	0.041	0.046	0.087	0.019	0.064	0.083	0.052	0.056	0.108
	150	0.051	0.048	0.099	0.027	0.073	0.100	0.054	0.060	0.114
	200	0.057	0.045	0.102	0.035	0.063	0.098	0.040	0.048	0.088
30%	30	0.034	0.044	0.078	0.002	0.064	0.066	0.060	0.045	0.105
	50	0.046	0.037	0.083	0.009	0.047	0.056	0.061	0.053	0.114
	80	0.043	0.040	0.083	0.018	0.064	0.082	0.055	0.062	0.117
	120	0.042	0.040	0.082	0.019	0.067	0.086	0.061	0.057	0.118
	150	0.054	0.047	0.101	0.028	0.069	0.097	0.055	0.064	0.119
	200	0.055	0.045	0.100	0.032	0.064	0.096	0.049	0.049	0.098

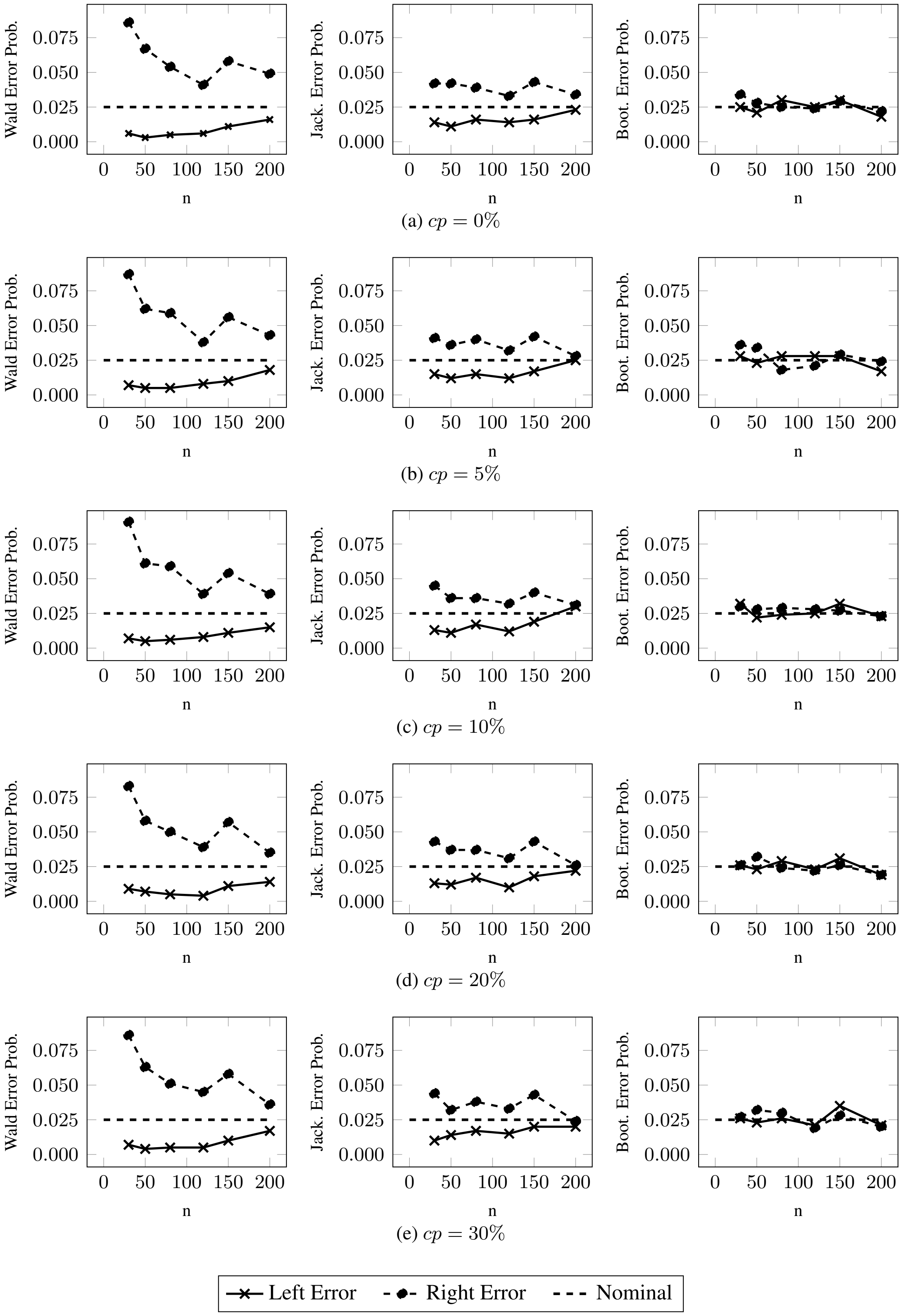


Figure 1: Estimated error probabilities of Wald, jackknife and bootstrap-t of β_0 at $\alpha = 0.05$

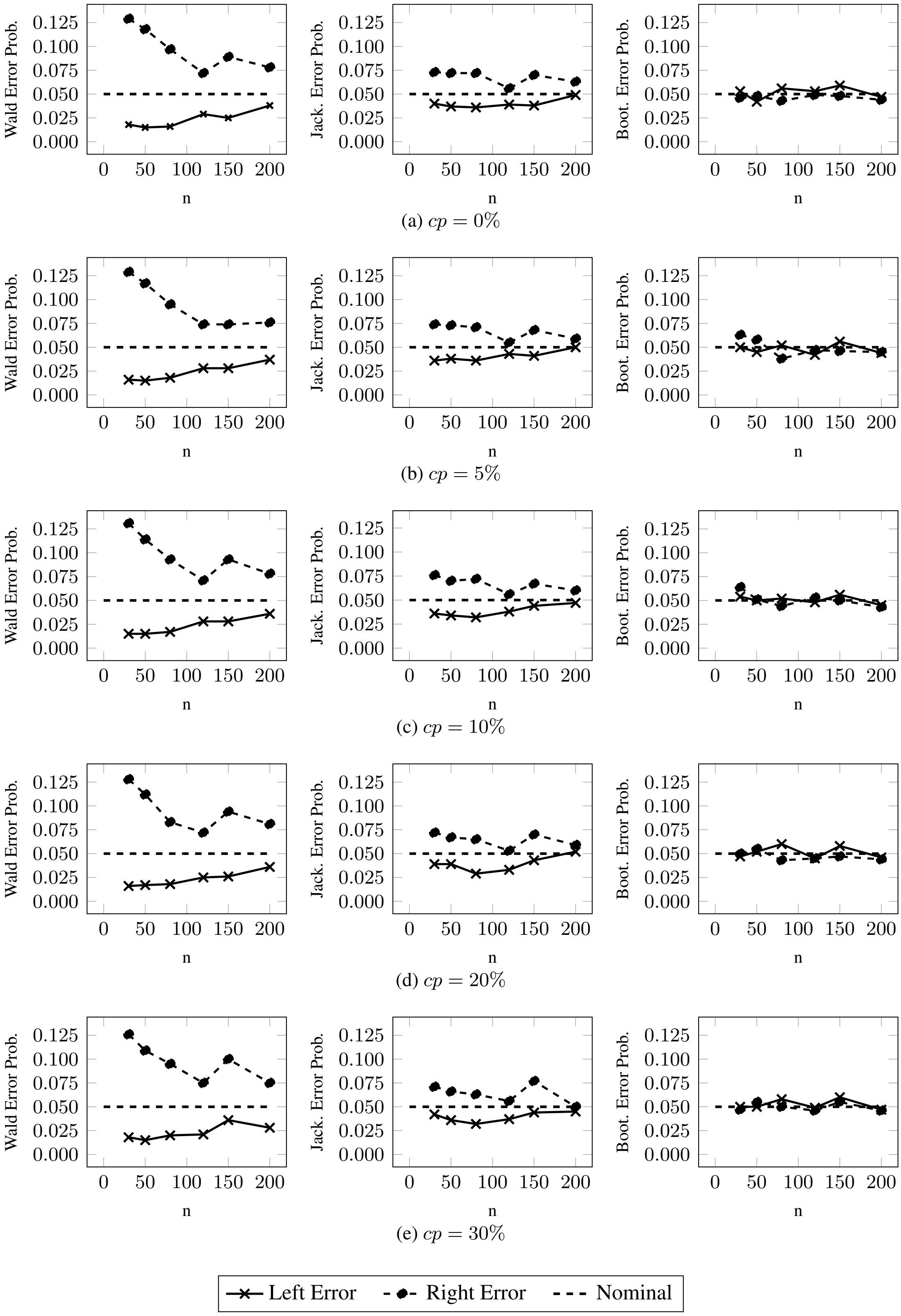


Figure 2: Estimated error probabilities of Wald, jackknife and bootstrap-t of β_0 at $\alpha = 0.1$

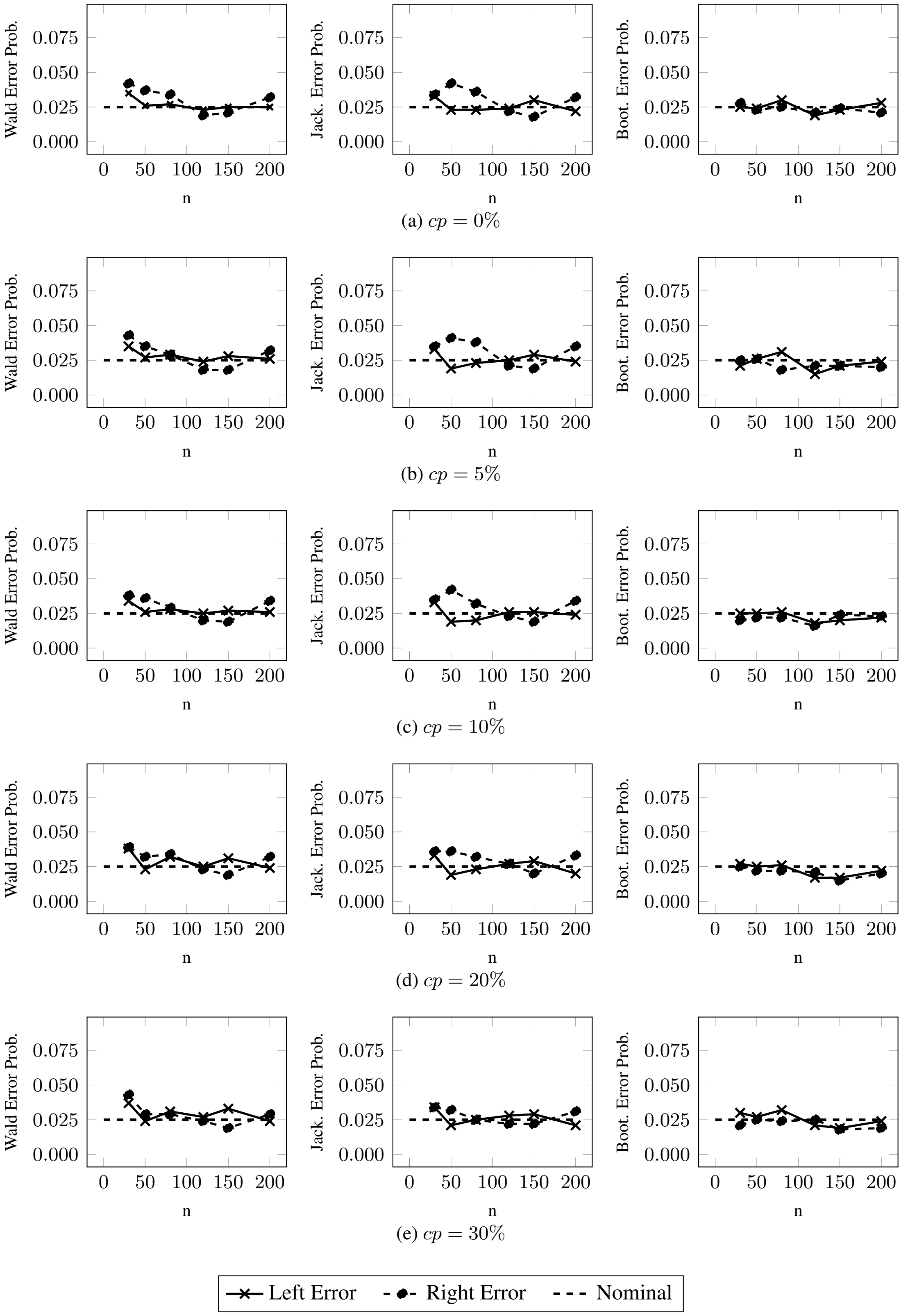


Figure 3: Estimated error probabilities of Wald, jackknife and bootstrap-t of β_1 at $\alpha = 0.05$

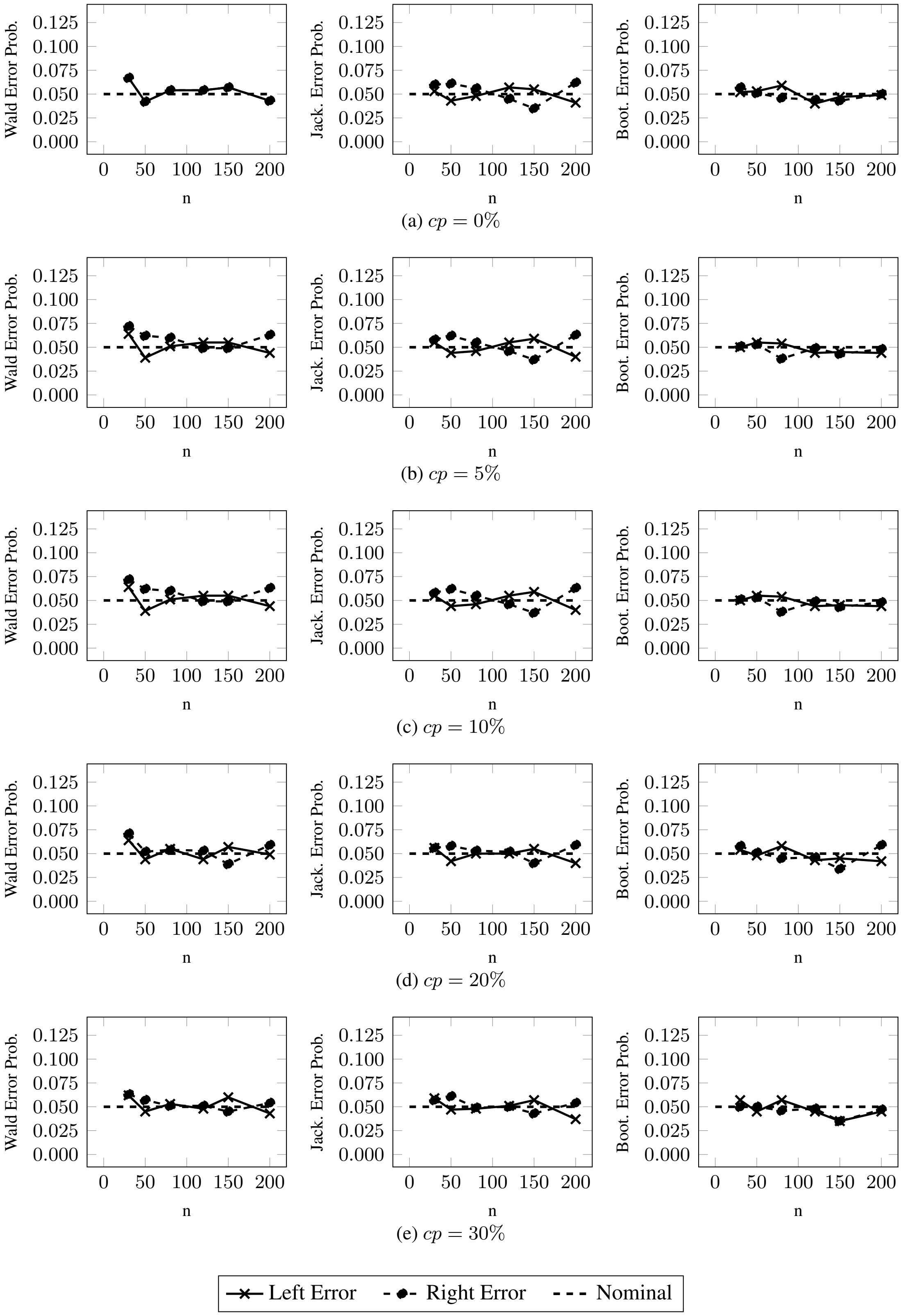


Figure 4: Estimated error probabilities of Wald, jackknife and bootstrap-t of β_1 at $\alpha = 0.1$

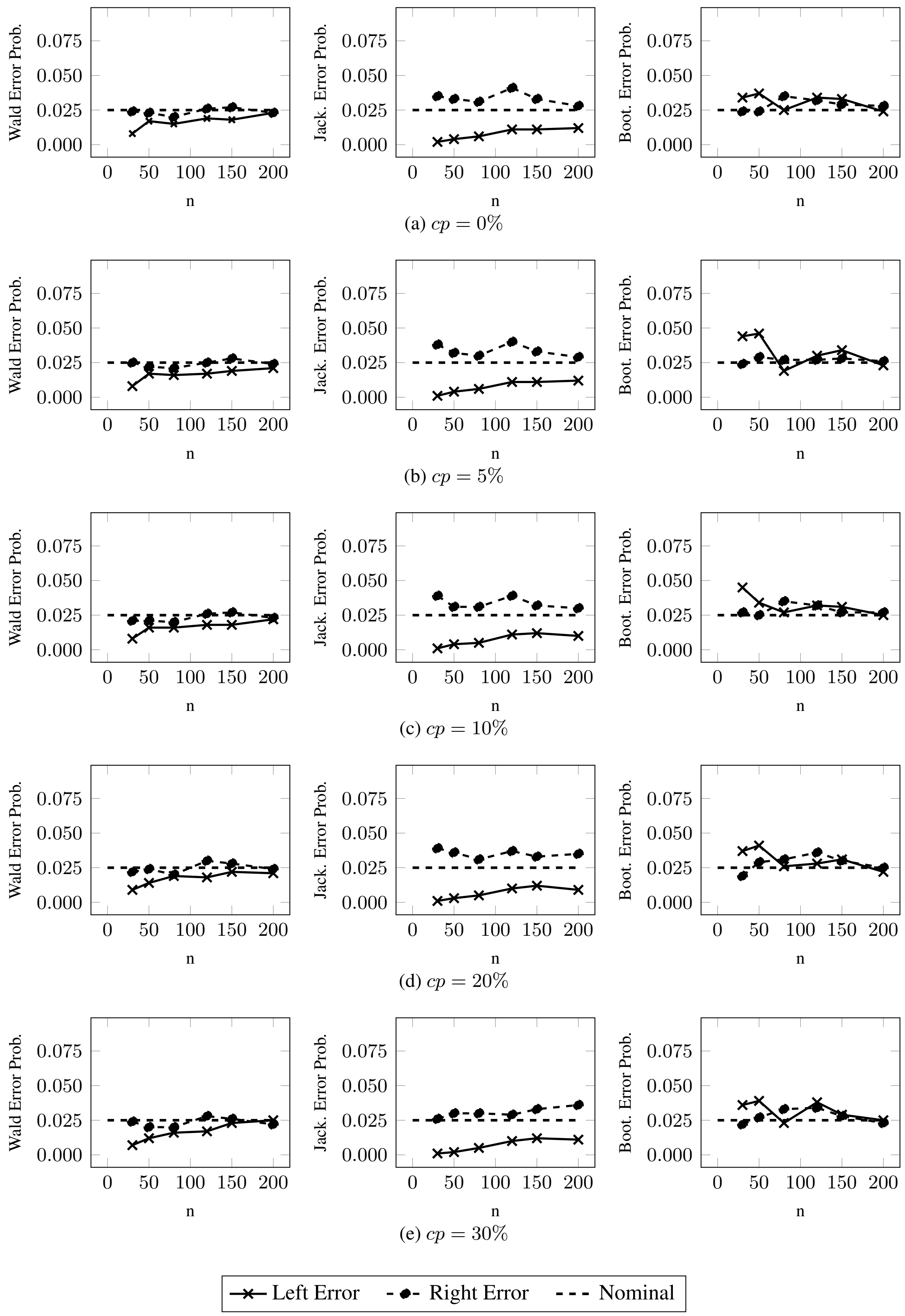


Figure 5: Estimated error probabilities of Wald, jackknife and bootstrap-t of γ at $\alpha = 0.05$

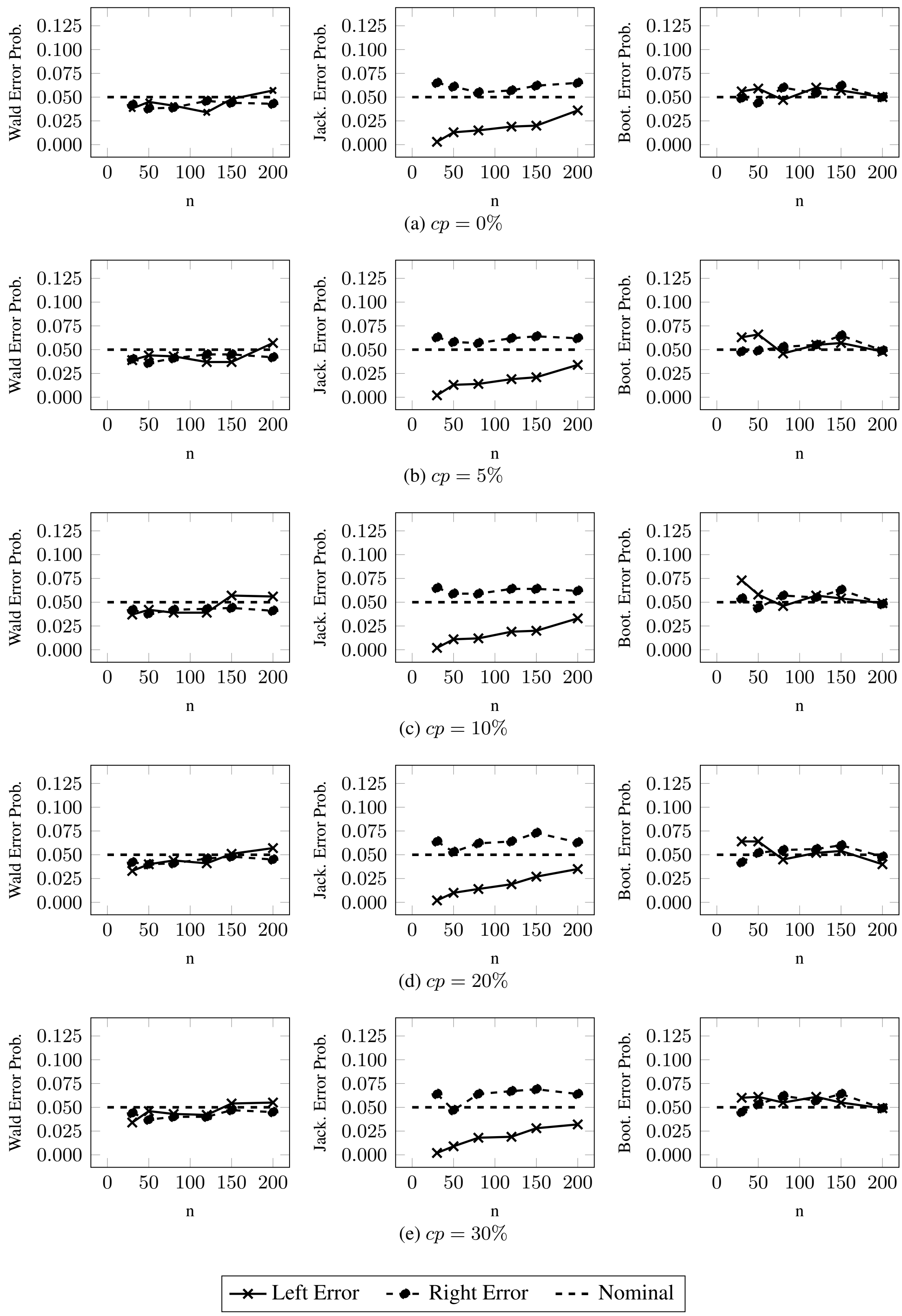


Figure 6: Estimated error probabilities of Wald, jackknife and bootstrap-t of γ at $\alpha = 0.1$

For β_0, Figures 1 and 2 show the Wald method has a converging tendency towards the nominal level $\frac{\alpha}{2}$ as n increases but performs poorly at smaller sample sizes $n = 30, 50, 80$. The jackknife method produces left and right error probabilities that are much closer to the nominal error as compared to the Wald method and converges to the nominal level nearing $n = 120$. The bootstrap-t method shows the best performance as the error probabilities are closest to the nominal level across all cp and n.

Based on Figures 3 and 4 for the parameter β_1, the Wald method produced error probabilities close to the nominal level except at small sample size $n = 30$. The jackknife method shows deviation tendencies nearing $n = 200$. The bootstrap-t method performed the best as the error probabilities are consistently close to the nominal level.

For parameter γ, Figures 5 and 6 showed that generally the error probabilities of the Wald and bootstrap-t method are close to the nominal level. The jackknife method has right error probabilities that are mostly close to the nominal error while the left error probabilities converge as n increases.

Based on the coverage probability study, the best confidence interval estimation technique for parameters β_0 and β_1 is the bootstrap-t method. However, for the parameter γ, at $\alpha = 0.05$ $(\alpha = 0.1)$ the bootstrap-t (Wald) method is preferred.

4. Real Data Analysis

4.1. *Introduction*

In this study, the ERR model was fitted to real preclinical data and the interval estimates of the parameters were calculated. The data provided by Klein and Moeschberger (2003) was collected from a study on the efficacy of boron neutron capture therapy (BNCT) in treating the therapeutically refractory F98 glioma, using boronophenylalanine (BPA) as the capture agent. The study involved implanting F98 glioma cells into the brains of rats. Three treatment was considered in the study. Treatment one, the rats were untreated, treatment two, the rats were treated only with radiation, and treatment three, the rats received radiation plus an appropriate concentration of BPA.

The data consists of the treatment type, survival time and censoring indicator. There are 30 observation for the survival time of rats in days. Each treatment group consists 10 observations. $(1 =$ untreated, $2 =$ radiated, $3 =$ radiated $+$ BPA). The censoring indicator is 1 if the rat is dead and 0 if the rat is alive up until the last follow-up. There are 3 out of 30 censored observation, hence the data has a cp of 10%. The data is analyzed to investigate the effect of treatments on the survival times of rats.

4.2. *Preliminary study*

Descriptive statistics such as the number of observations, mean, standard deviation, first quantile, median and third quantile were analyzed as a whole and by treatment. The censored data were removed when performing preliminary analysis.

Table 14: Descriptive statistics of uncensored survival times

Treatment	**N**	**Mean**	**Std. Dev.**	**Q1**	**Median**	**Q3**
Overall	27	29.56	5.04	26	30	32
1	10	24.9	3.11	23.2	25	26.8
2	9	29.6	1.81	29	30	31
3	8	35.4	2.92	33.5	35.5	38

As shown in Table 14, the overall mean survival time of the data is 29.56 days and the median is 30 days. The mean survival times of rats for treatment 1 is 24.9 days, treatment 2 is

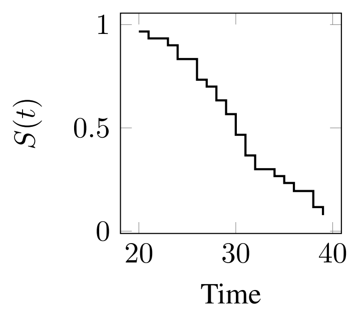


Figure 7: Kaplan-Meier curve of overall survival times

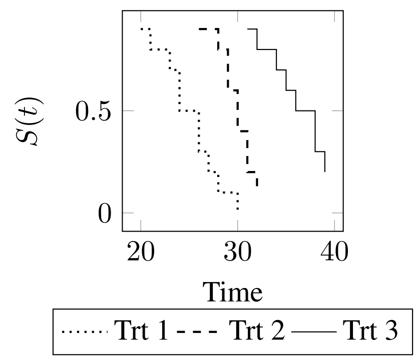


Figure 8: Kaplan-Meier curves of different treatment survival times

29.6 days and treatment 3 is 35.4 days. A longer mean survival time, suggests a more effective treatment method. Hence, from the preliminary study, treatment 3 using radiation and BPA appears to be most effective as rats from the group had the longest mean survival time.

4.3. *Non-parametric approach*

The Kaplan-Meier curve summarizes the survival times of the rats implanted with F98 glioma cells as a whole and by individual treatment groups. The non overlapping Kaplan-Meier curves for each treatment suggests a statistically significant differences in the survival times across the treatments. To formally test the significance of the difference between the survival times, the log-rank test is performed.

Figure 7 summarizes the Kaplan-Meier curve of the overall survival times of the rats implanted with F98 glioma cells. From Figure 8, the Kaplan-Meier curves of each individual treatment are different from one another. This aligns with the assumption that different treatments affect the survival time of rats made in the preliminary study stage.

The log-rank test is used to test the assumption that the survival times of rats are different for at least 1 treatment group.

$H_0 : S_1(t) = S_2(t) = S_3(t)$

H_1 : At least 1 $S_i(t) \neq S_j(t)$ for $i, j = 1, 2, 3$

Using Table 15, the Chi-Square test statistics is $\chi^2 = 33.4$ and the corresponding p-value is < 0.001. The p-value is less than 0.05, hence the null hypothesis is rejected. At $\alpha = 0.05$ significance level, there is sufficient evidence to show that the survival function for at least 1 treatment group is different. It is concluded that different treatments significantly affect the survival times.

Table 15: Log-rank test statistics of treatment

	n_{1j}	d_{1j}	e_{1j}	$\frac{(d_{1j}-e_{1j})^2}{e_{1j}}$	$\frac{(d_{1j}-e_{1j})^2}{v_{1j}}$
Treatment = 1	10	10	2.66	20.300	27.365
Treatment = 2	10	9	7.60	0.258	0.431
Treatment = 3	10	8	16.74	4.566	16.587
Total	30	27	27		

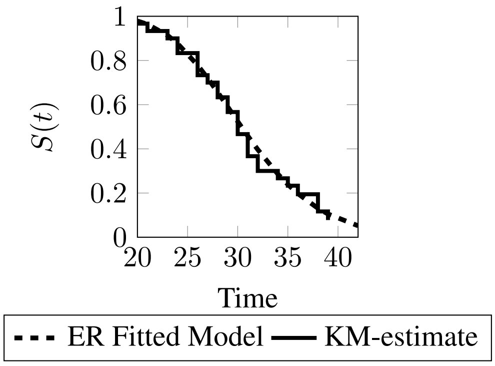


Figure 9: Comparison of Kaplan-Meier estimate and ERR model without covariates

4.4. *Data analysis with ERR model*

Since the treatment type is significant in the survival times of rats implanted with F98 glioma cells. The ERR model with covariates is fitted to the data and compared with the Kaplan-Meier estimate. Following that, the parameters β_0, β_1, γ are estimated using MLE. The ER model without covariates is first fitted to the data and compared to the non-parametric Kaplan-Meier curve. If the survival curves are close to each other, the proposed model is considered to be suitable for the data. From Figure 9 the survival curve of the ER model is close to the Kaplan-Meier estimate. The ER model is a good fit for the data. Proceeding that, the ERR model with covariates is fitted to the model and compared with the Kaplan-Meier estimate for each individual treatment. From Figure 10, all three plots show a close fit between the survival curve of the ERR model and Kaplan-Meier estimate, hence the ERR model fits the data well. The plots suggest treatment 3 to be the most effective treatment as the survival times of rats are longest.

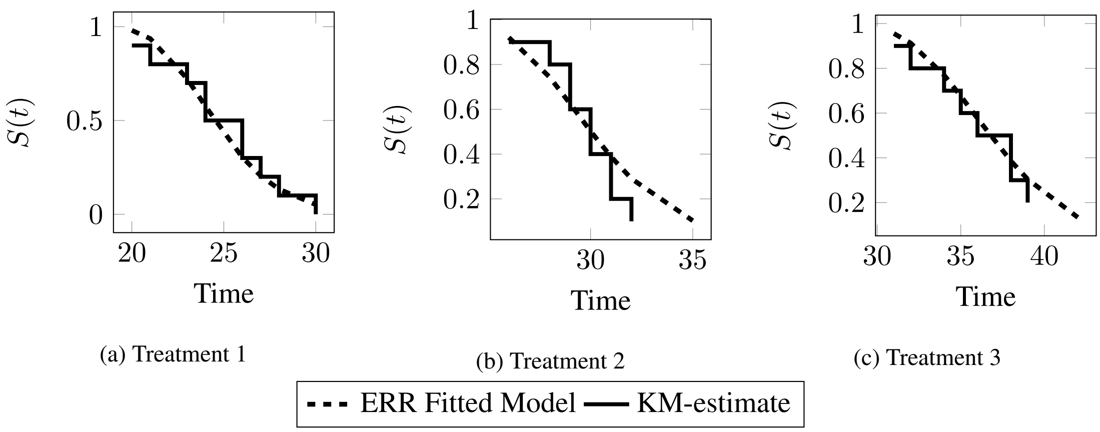
Table 16 show the descriptive statistics of the parameter estimates of the ERR model. The p-value of all three parameters are less than 0.05, hence they are all significant in the model.

To assess the performance of the ERR model, it is compared to common regression models in survival analysis, namely the exponential regression, Weibull regression and log-logistic regression model. A high value for the maximum loglikelihood and a low value for the AIC means that the model is a good fit to the data.

From Table 17, the ERR model has the highest maximum loglikelihood and lowest AIC value among the models compared. Hence,the ERR model is the best fitting model for the data.

Table 16: Descriptive statistics of parameter estimates of the ERR model

	Estimate	Standard Error	Test Statistic	p-value
β_0	2.17613	0.05338	40.763	< 0.001
β_1	0.20271	0.02440	8.309	< 0.001
γ	120.35396	9.02737	13.332	< 0.001



(a) Treatment 1 (b) Treatment 2 (c) Treatment 3

Figure 10: Comparison of Kaplan-Meier estimate and ERR model with covariates

Table 17: Comparison of the AIC of different regression models

Regression Models	Maximum Loglikelihood	No. of Parameters	AIC
Exponential	-122.18231	2	248.3646
Weibull	-92.48697	3	190.9739
Log-logistic	-90.23902	3	186.4780
Exponentiated Rayleigh	-72.91355	3	151.8271

5. Conclusion and Future Work

5.1. *Conclusion*

In this study the ER model is extended to include one covariate to obtain the ERR model under right censored data. The parameter estimates were obtained using MLE method and NR iterative procedure. The performance of the maximum likelihood estimates of the ERR model is evaluated using the bias, SE and RMSE. The performance of parameter estimates are ideal when the bias, SE and RMSE are close to zero. From the analysis, when sample size n is constant and cp increases, the SE and RMSE increases. Hence the performance of parameter estimates decreases. Whereas, when the cp is constant and n increases, the SE and RMSE of the parameter estimate decreases. Hence the performance of the parameter estimate increases.

The coverage probability study is used to compare the performance of the Wald, jackknife and bootstrap-t confidence interval construction methods by evaluating the number of C, AC and AS intervals produced by each method at different n, cp and α. The performance of the interval estimation method is best if it produces the least amount of C, AC and AS intervals. From the coverage probability study, the best confidence interval estimation technique for parameters β_0 and β_1 is the bootstrap-t method. However, for the parameter γ, at $\alpha = 0.05$ $(\alpha = 0.1)$ the bootstrap-t (Wald) method is preferred.

The preliminary study of the real data showed the mean survival times of rats are different for the three treatment groups. To test the assumption, non-parametric methods like the Kaplan-Meier curve and log-rank test are performed. Results from the non-parametric approach showed that the difference in survival times of the three treatments is statistically significant. Hence the ERR model (with covariates) was proposed to fit the data. To evaluate the performance of the ERR model, it was compared to common regression models (exponential, Weibull, log-logistic) using the maximum loglikelihood and AIC value. The ERR model has the highest maximum loglikelihood and lowest AIC value hence it is concluded to be the best fitting model for the data.

5.2. *Future work*

In this research, the ERR model was fitted solely to right censored data. Future studies may include the application of the ERR model to datasets with left censored or interval censored data. Only three methods for constructing confidence intervals were discussed. Future research could compare other interval construction methods for the parameters of the ERR model, such as the likelihood ratio method and the bootstrap percentile method to assess their performance. The data analyzed in this research contained only one covariate. Future research can involve extending the Rayleigh model to multiple covariates. Furthermore, only fixed covariates were considered in this study. An extension of the Rayleigh model to accommodate time-varying covariates can be a valuable direction for future work.

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