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Interval Estimations for Parameters of Gompertz Model with Time-Dependent Covariate and Right Censored Data

(Anggaran Selang Keyakinan bagi Parameter Model Gompertz dengan Kovariat yang Berubah Mengikut Masa dan Data Tertapis Kanan)

KAVEH KIANI*, JAYANTHI ARASAN & HABSHAH MIDI

ABSTRACT

There are numerous parametric models for analyzing survival data such as exponential, Weibull, log-normal and gamma. One of such models is the Gompertz model which is widely used in biology and demography. Most of these models are extended to new forms for accommodating different types of censoring mechanisms and different types of covariates. In this paper the performance of the Gompertz model with time-dependent covariate in the presence of right censored data was studied. Moreover, the performance of the model was compared at different censoring proportions (CP) and sample sizes. Also, the model was compared with fixed covariate model. In addition, the effect of fitting a fixed covariate model wrongly to a data with time-dependent covariate was studied. Finally, two confidence interval estimation techniques, Wald and jackknife, were applied to the parameters of this model and the performance of the methods was compared.

Keywords: Gompertz model; jackknife; right censored; time-dependent covariate

ABSTRAK

Terdapat banyak model parametrik untuk menganalisis data mandirian seperti, eksponen, Weibull, Log-normal dan gamma. Salah satu model tersebut adalah model Gompertz yang digunakan secara meluas dalam biologi dan demografik. Sebahagian besar daripada model ini dikembangkan kepada bentuk-bentuk baru untuk menampung pelbagai jenis data tertapis dan kovariat. Dalam makalah ini kebolehan model Gompertz dengan kovariat yang berubah dengan masa dengan data tertapis dikaji. Selain itu, prestasi model ini pada kadaran data tertapis dan saiz sampel yang berbeza dibandingkan. Juga, model ini dibandingkan dengan model kovariat tetap. Di samping itu, kesan menggunakan model kovariat tetap untuk data dengan kovariat yang berubah dengan masa dikaji. Akhirnya, dua kaedah selang keyakinan, Wald dan jackknife diaplikasikan pada parameter model ini dan prestasinya dibandingkan.

Kata kunci: Data tertapis kanan; jackknife*; kovariat bergantung masa; model Gompertz*

INTRODUCTION

The statistical analysis and modeling of lifetime data are usually done by applying various kinds of parametric, semi-parametric or non-parametric models. In this paper the performance of the Gompertz model with fixed and time-dependent covariate in the presence of right censored data was studied. The Gompertz model was introduced by Gompertz in 1825 as a model for human mortality. Recently, it has found more application in fields such as biology and demography. The hazard function of the Gompertz model is:

$$h(t) = \lambda exp(\gamma t), t \geq 0, \lambda > 0, \gamma > 0,$$

where is the non-negative continuous random variable which denotes the individual's life time. The scale parameter is λ and the shape parameter is γ. The survivor function of the model is

$$S(t) = exp\left[\frac{\lambda}{\gamma}\left(1 - e^{\gamma t}\right)\right],$$

and the probability density function is:

$$f(t) = \lambda\, exp\left[yt + \frac{\lambda}{\gamma}\left(1 - e^{\gamma t}\right)\right].$$

The properties of the Gompertz distribution are presented in Johnson et al. (1995). Recently many authors have done studies on different characteristics and statistical methodology of Gompertz distribution; for instance, Makany (1991) and Chen (1997). Garg et al. (1970) obtained maximum likelihood estimate (MLE) of the parameters of Gompertz distribution. Wu et al. (2004) proposed unweighted and weighted least squares estimates for parameters of the Gompertz distribution under the complete data and first failure-censored data. Fixed covariates are measured at the start of study and stay constant over the study's duration, for example, gender or race. Time-dependent covariates vary over time such as age and blood pressure. Following Kalbfleisch and Prentice (1973, 2002), Lachin (2000) and Sparling (2002) the history of a time-dependent covariate process up to time may be incorporated into the model to assess the effect of the covariate on the relative risk of the event over time. Cox (1975) suggested using time-dependent covariates in the proportional hazards regression models and gave the partial likelihood analysis and also generated the partial likelihood function for censored data. Petersen (1986) introduced an algorithm for estimating parameters of parametric models in the presence of time-dependent covariates. Sparling et al. (2006) proposed a parametric family of survival regression models for left, right and interval-censored data with both fixed and time-dependent covariates. Arasan and Lunn (2009) extended the bivariate exponential model to incorporate a time-dependent covariate. A complete review on the jackknife and its application was done by Miller (1974). Also, Arasan and Lunn (2008) investigated several alternative methods of constructing confidence interval (CI) estimates for a parallel two-component model with dependent failure and a time-dependent covariate.

The objective of this study was to extend the Gompertz model to incorporate a time-dependent covariate in the presence of right censored data and to obtain a confidence interval estimation method for the parameters of this model. Firstly, we conducted a simulation study to evaluate the performance of the model by checking the value of bias, standard error (SE) and root mean square error (RMSE), of the parameter estimates at different sample sizes and censoring proportions (CP). Then, we assessed the performance of two confidence interval estimation methods, the jackknife and Wald, via a coverage probability study at different nominal error probabilities and CP levels. In this research, all the codes for the simulation studies were written in FORTRAN® (FTN95) programming language.

GOMPERTZ MODEL WITH RIGHT CENSORED DATA AND FIXED COVARIATE

The effect of covariates on survival time can be incorporated to the hazard function by allowing the parameter λ to be a function of the covariates. Covariates can be either fixed or time-dependent. For a data set with a fixed covariate x_i where $i = 1, 2,\ldots, n$, the hazard function for i^{th} subject can be expressed as;

$$h(t_i) = \lambda_i \, exp(\gamma t_i) = exp(\beta_0 + \beta_1 x_i + \gamma t_i),$$

where $\lambda_i = exp\ (\beta_0 + \beta_1 x_i)$ and vector of parameters is $\theta = (\beta_0, \beta_1, \gamma)$. The parameters of this model can be estimated by the method of maximum likelihood. If there are no consored observation, then the likelihood function for the full sample is:

$$L(\theta) = \prod_{i=1}^{n} f(t_i) = \prod_{i-1}^{n} \left\{ e^{\beta_0+\beta_1 x_i+\gamma t_i}\, exp\left[\frac{e^{(\beta_0+\beta_1 x_i)}}{\gamma}\left(1-e^{\gamma t_i}\right)\right]\right\}.$$

In order to incorporate right censored data to the likelihood function we need to define a censoring indicator variable denoted as S. For the i^{th} observation:

$$s_i = \begin{cases} 1, & \text{observation is not consored;} \\ 0, & \text{observation is right censored.} \end{cases}$$

If t_i is the observed survival time for the i^{th} subject then the likelihood function will be

$$\begin{aligned} L(\theta) &= \prod_{i=1}^{n} \{f(t_i)\}^{S_i} \{S(t_i)\}^{1-S_i} \\ &= \prod_{i=1}^{n} \left\{ e^{\beta_0+\beta_1 x_i+\gamma t_i}\, exp\left[\frac{e^{(\beta_0+\beta_1 x_i)}}{\gamma}\left(1-e^{\gamma t_i}\right)\right]\right\}^{S_i} \left\{ exp\left[\frac{e^{(\beta_0+\beta_1 x_i)}}{\gamma}\left(1-e^{\gamma t_i}\right)\right]\right\}^{1-s_i} \end{aligned}$$

and log-likelihood function is:

$$l(\theta) = \sum_{i=1}^{n} s_i \left\{ \left(\beta_0 + \beta_1 x_i + \gamma t_i\right) + \frac{e^{(\beta_0+\beta_1 x_i)}}{\gamma}\left(1-e^{\gamma t_i}\right)\right\} + (1-s_i)\left\{\frac{e^{(\beta_0+\beta_1 x_i)}}{\gamma}\left(1-e^{\gamma t_i}\right)\right\}.$$

The first and second derivatives of the log-likelihood function would be as follows:

$$\frac{\partial l(\theta)}{\partial \beta_j} = \sum_{i=1}^{n} x_i^j \left(S_i + \frac{\lambda_i - h(t_i)}{\gamma}\right), \quad j = 0,1,$$

$$\frac{\partial^2 l(\theta)}{\partial \beta_j \partial \beta_k} = \sum_{i=1}^{n} x_i^{j+k} \left(\frac{\lambda_i - h(t_i)}{\gamma}\right), \quad j = 0,1 \quad k = 0,1,$$

$$\frac{\partial^2 l(\theta)}{\partial \beta_j \partial \gamma} = \sum_{i=1}^{n} -x_i^j \left(\frac{t_i h(t_i)}{\gamma} + \frac{\lambda_i - h(t_i)}{\gamma^2}\right), \quad j = 0,1,$$

$$\frac{\partial^2 l(\theta)}{\partial \gamma^{1+j}} = \sum_{i=1}^{n} -\left(\frac{-2}{\gamma}\right)^j \left(\frac{t_i h(t_i)}{\gamma} + \frac{\lambda_i h(t_i)}{\gamma^2}\right) - \left(\frac{t_i^2 h(t_i)}{\gamma}\right)^j + (t_i S_i)^{1-j} - (-1)^{1-j}, \quad j = 0,1.$$

The inverse of the observed information matrix, which can be obtained from the second partial derivatives of the log-likelihood function evaluated at $\widehat{\beta}_0$, $\widehat{\beta}_1$ and $\hat{\gamma}$, provides us with the estimates for the variance and covariance of $\widehat{\theta}$.

$$\widehat{var}(\theta) = \left[i\left(\widehat{\beta}_0, \widehat{\beta}_1, \hat{\gamma}\right)\right]^{-1}.$$

The MLE of the parameters can be obtained by using the Newton-Raphson iterative procedure.

SIMULATION STUDY AND RESULTS

A simulation study using 1000 samples each with n=50 and n=100 was conducted for this model for both censored and uncensored observations and one fixed covariate. The covariate values were simulated independently from the standard normal distribution. The values of 0.04 ,0.02 and 0.03 were chosen as the parameters of β_0, β_1 and γ. Random numbers, u_i's, from the uniform distribution on the interval (0,1) were generated to produce t_i's. The censoring times or c_i's were generated from $\exp(\mu)$ distribution, where the value of μ would be adjusted to obtain the desired approximate CP in the data. There are two possible types of data. The first is when $t_i \le c_i$ which means t_i is uncensored. The second is when $t_i > c_i$ which means t_i is censored. The t_i's were generated by:

$$t_i = \frac{1}{\gamma} ln\left[1 - \frac{\gamma \, ln\, u_i}{\lambda_i}\right].$$

Table 1 shows the bias, SE and RMSE, $\sqrt{SE^2 + bias^2}$, of the parameter estimates at different CP levels and sample sizes. CP means 10 percent of data are right censored. We can clearly see that the bias, SE and RMSE values increase with the increase in CP and decrease in sample size, which means higher CP and small sample size make estimates less efficient and rather inaccurate.

GOMPERTZ MODEL WITH RIGHT CENSORED DATA AND TIME-DEPENDENT COVARIATE

In the model with time-dependent covariates, we are dealing with covariates whose value changes over time and not fixed throughout the study. Let x_{aij} represent a time-dependent covariate which changes over update times a_{ij} where $i = 1,2,\ldots, n$ and $j = 0,1,\ldots, k$. Here a_{i0} is the time origin or $a_{i0} = 0$. The hazard function can be expressed as:

$$h\left(t_i \middle| x_{aij}\right) = \lambda_{ij}\, exp\left(\gamma t_i\right) = exp\left(\beta_0 + \beta_1 x_{aij} + \gamma t_i\right).$$

It assumed the x_{aij} follows a step function which means within the interval a_{ij} to $a_{i(j+1)}$, x stays constant at x_{aij} and change to $x_{ai(j+1)}$ at $a_{i(j+1)}$ in the following interval. The vector of parameters is $\theta = (\beta_0, \beta_1, \gamma)$.

The likelihood and log-likelihood functions for both censored and uncensored observations are given by:

Let us consider this model with at most two levels of the covariate for each subject, so $j = 0,1$. Here, in order to incorporate two levels of the covariate to the likelihood function we need to define a covariate updating indicator variable denoted as L. For the i^{th} observation:

$$l_i = \begin{cases} 1, & \text{covariate is updated;} \\ 0, & \text{covariate is not updated.} \end{cases}$$

Then the hazard function before and after updating is:

$$h_{i0}\left(t_i\right) = h\left(t_i \middle| x_{a_{io}}\right) = exp\left(\beta_0 + \beta_1 x_{a_{io}} + \gamma t_i\right),$$
$$h_{i1}\left(t_i\right) = h\left(t_i \middle| x_{a_{il}}\right) = exp\left(\beta_0 + \beta_1 x_{a_{il}} + \gamma t_i\right).$$

TABLE 1. Bias, SE and RMSE of the estimates for fixed covariate model

		$\widehat{\beta_0}$		$\widehat{\beta_1}$		$\widehat{\gamma}$	
	CP	n=50	n=100	n=50	n=100	n=50	n=100
	0	-0.0733	-0.0413	-0.0029	-0.0009	0.1094	0.0543
	10	-0.0784	-0.0439	-0.0025	-0.0013	0.1223	0.0588
	20	-0.0789	-0.0471	-0.0042	-0.0013	0.1258	0.0649
Bias	30	-0.0809	-0.0473	-0.0032	-0.0015	0.1358	0.0712
	40	-0.0843	-0.0496	-0.0047	-0.0032	0.1410	0.0794
	50	-0.0949	-0.0532	-0.0066	-0.0070	0.1665	0.0876
	0	0.2091	0.1442	0.2193	0.1429	0.1890	0.1204
	10	0.2225	0.1522	0.2292	0.1497	0.2243	0.1372
	20	0.2364	0.1636	0.2504	0.1624	0.2592	0.1678
SE	30	0.2553	0.1769	0.2701	0.1761	0.3192	0.2084
	40	0.2793	0.1925	0.2909	0.1911	0.3973	0.2673
	50	0.3261	0.2115	0.3297	0.2080	0.5430	0.3408
	0	0.2216	0.1499	0.2193	0.1429	0.2184	0.1321
	10	0.2359	0.1584	0.2292	0.1497	0.2555	0.1492
	20	0.2492	0.1702	0.2504	0.1624	0.2881	0.1799
RMSE	30	0.2679	0.1831	0.2702	0.1761	0.3469	0.2202
	40	0.2918	0.1988	0.2910	0.1911	0.4216	0.2789
	50	0.3396	0.2181	0.3298	0.2081	0.5680	0.3519

So, the log-likelihood function will be:

$$l(\theta)=\sum_{i=1}^{n} s_i\left(1-l_i\right)\left[ln\left(h_{io}\left(t_i\right)\right)+\frac{\lambda_{i0}}{\gamma}\left(1-e^{\gamma t_i}\right)\right]+\left(1-s_i\right)\left(1-l_i\right)\left[\frac{\lambda_{i0}}{\gamma}\left(1-e^{\gamma t_i}\right)\right]$$

$$+s_i l_i\left[ln\left(h_{il}\left(t_i\right)\right)+\frac{\lambda_{i0}}{\gamma}\left(1-e^{\gamma t_i}\right)+\frac{\lambda_{i1}}{\gamma}\left(e^{\gamma i1}-e^{\gamma t_i}\right)\right]$$

$$+\left(1-s_i\right)l_i\left[\frac{\lambda_{io}}{\gamma}\left(1-e^{\gamma t_i}\right)+\frac{\lambda_{i1}}{\gamma}\left(e^{\gamma a_{i1}}-e^{\gamma t_i}\right)\right].$$

The first and second derivatives of the log-likelihood function would be as follows:

$$\frac{\partial l(\theta)}{\partial\beta_0}=\sum_{i=1}^{n}\left(s_i+\left(1-1_i\right)\left\{\frac{\lambda_{i0}-h_{i0}\left(t_i\right)}{\gamma}\right\}+l_i\left\{\frac{\lambda_{i0}-h_{i0}\left(a_{i1}\right)+h_{i1}\left(a_{i1}\right)-h_{i1}\left(t_i\right)}{\gamma}\right\}\right),$$

$$\frac{\partial l(\theta)}{\partial\beta_1}=\sum_{i=l}^{n}\left(l_i s_i\left(x_{a_{i1}}-x_{a_{io}}\right)+s_i x_{a_{i0}}+\left(1-l_i\right)x_{a_{i0}}\left\{\frac{\lambda_{i0}-h_{i0}\left(t_i\right)}{\gamma}\right\}\right.$$
$$\left.+l_i\left\{\frac{x_{a_{i0}}\left(\lambda_{i0}-h_{i0}\left(a_{i1}\right)\right)+x_{a_{i1}}\left(h_{i1}\left(a_{i1}\right)-h_{i1}\left(t_i\right)\right)}{\gamma}\right\}\right)$$

$$\frac{\partial l(\theta)}{\partial\gamma_0}=\sum_{i=1}^{n}\left(s_i t_i-\left(1-l_i\right)\left\{\frac{\lambda_{i0}-h_{i0}\left(t_i\right)}{\gamma^2}+\frac{t_i h_{i0}\left(t_i\right)}{\gamma}\right\}\right)$$
$$-l_i\left\{\frac{\lambda_{i0}-h_{io}\left(a_{i1}\right)+h_{i1}\left(a_{i1}\right)-h_{i1}\left(t_i\right)}{\gamma^2}\right\}$$
$$+\frac{a_{i1}\left(h_{i0}\left(a_{i1}\right)-h_{i1}\left(a_{i1}\right)\right)+t_i h_{i1}\left(t_i\right)}{\gamma}$$

$$\frac{\partial^2 l(\theta)}{\partial\beta_j\partial\beta_k}=\sum_{i=l}^{n}\left(1-l_i\right)x_{a_{i0}}^{j+k}\left\{\frac{\lambda_{i0}-h_{i0}\left(t_i\right)}{\gamma}\right\}$$
$$+l_i\left\{\frac{x_{a_{i0}}^{j+k}\left(\lambda_{i0}-h_{i0}\left(a_{i1}\right)\right)+x_{a_{i1}}^{j+k}\left(h_{i1}\left(a_{i1}\right)-h_{i1}\left(t_i\right)\right)}{\gamma}\right\},$$

$$j=0,1\ k=0,1.$$

$$\frac{\partial^2 l(\theta)}{\partial\beta_j\partial\gamma}=\sum_{i=1}^{n}\left(-\left(1-l_i\right)x_{a_{i0}}^{j}\left\{\frac{\lambda_{i0}-h_{i0}\left(t_i\right)}{\gamma^2}+\frac{t_i h_{i0}\left(t_i\right)}{\gamma}\right\}\right.$$
$$-l_i\left\{\frac{x_{a_{i0}}^{j}\left(\lambda_{i0}-h_{i0}\left(a_{i1}\right)\right)+x_{a_{i1}}^{j}\left(h_{i1}\left(a_{i1}\right)-h_{i1}\left(t_i\right)\right)}{\gamma^2}\right.$$
$$\left.\left.+\frac{x_{a_{i0}}^{j}a_{i1}\left(h_{i0}\left(a_{i1}\right)-h_{i1}\left(a_{i1}\right)\right)+x_{ai1}^{j}t_i h_{i1}\left(t_i\right)}{\gamma}\right\}\right),j=0,1,$$

$$\frac{\partial^2 l(\theta)}{\partial\gamma^2}=\sum_{i=1}^{n}\left(\left(1-l_i\right)\left\{\frac{2\left(\lambda_{i0}-h_{i0}\left(t_i\right)\right)}{\gamma^3}+\frac{2t_i h_{i0}\left(t_i\right)}{\gamma^2}-\frac{t_i^2 h_{i0}\left(t_i\right)}{\gamma}\right\}\right.$$
$$+l_i\left\{\frac{2\left(\lambda_{i0}-h_{i0}\left(a_{i1}\right)+h_{i1}\left(a_{i1}\right)-h_{i1}\left(t_i\right)\right)}{\gamma^3}\right.$$
$$+\frac{2\left[a_{i1}\left(h_{i0}\left(a_{i1}\right)-h_{i1}\left(a_{i1}\right)\right)+t_i h_{i1}\left(t_i\right)\right]}{\gamma^2}$$
$$\left.\left.\frac{a_{i1}^2\left(h_{i0}\left(a_{i1}\right)-h_{i1}\left(a_{i1}\right)\right)+t_i^2 h_{i1}\left(t_i\right)}{\gamma}\right\}\right).$$

The MLE of the parameters can be obtained by using the Newton-Raphson iterative procedure.

Simulation Study and Results

A simulation study using 1000 samples each with n=50 and n=100 was conducted for this model for both censored and uncensored observations and one time-dependent covariate. Two levels of the covariate were simulated independently from the standard normal distribution. The values of 0.04, 0.02 and 0.03 were chosen as the parameters of β_0, β_1 and γ. Random numbers, u_i's, from the uniform distribution on the interval (0,1) were generated to produce t_i's. The censoring times or c_i's were generated from $\exp(\mu)$ distribution, where the value of μ would be adjusted to obtain the desired approximate CP in the data. The update times or a_{i1}'s were generated from $\exp(v)$distribution where the value of v can be adjusted to obtain larger or smaller values of a_{i1}. Here v was chosen as 1. There are four possible types of data. The first is when $t_i < c_i$ and $t_i < a_{i1}$ which means the survival time is uncensored and covariate is not updated. The second is when $t_i < c_i$ and $t_i \geq a_{i1}$ which means survival time is uncensored and covariate is updated. The third is when $t_i \geq c_i$ and $c_i < a_{i1}$ or survival time is censored and covariate is not updated and finally, $t_i \geq c_i$ and $c_i \geq a_{i1}$ which means survival time is censored and covariate is updated. The t_i's were generated by:

$$\text{if } u_i \geq exp\left\{\frac{\lambda_{i0}}{\gamma}\left[1-exp\left(\gamma a_{i1}\right)\right]\right\}\text{ then, }\quad t_i=\frac{1}{\gamma}ln\left[1-\frac{\gamma\, ln\, u_i}{\lambda_{i0}}\right],$$

$$\text{if } u_i < exp\left\{\frac{\lambda_{i0}}{\gamma}\left[1-exp\left(\gamma a_{il}\right)\right]\right\}\text{ then, }$$

$$t_i=\frac{1}{\gamma}ln\left[\frac{\lambda_{i0}-\lambda_{i0}\ exp\left(\gamma a_{i1}\right)+\lambda_{i1}\ exp\left(\gamma a_{i1}\right)u_i}{\lambda_{i1}}\right].$$

The simulation study was done to assess the bias, SE and RMSE of the estimates at different CP levels and sample sizes. From Table 2 we can clearly see that the bias, SE and RMSE values increase with the increase in CP and decrease in sample size.

Table 3 gives RMSE values of the estimates when a fixed covariate model was fitted wrongly to a data set with time-dependent covariate. The results indicate that, when the interval is very wide (close), which means at small (large) value of v, the RMSE values between time-dependent covariate model and fixed covariate model are very close. This is expected because as intervals become very wide (close), the time-dependent covariate become closer to a fixed covariate. But, when the interval takes a medium size, RMSE values of the wrong model increase substantially. As a result, if a time-dependent covariate data is fitted to a fixed covariate model, the accuracy and efficiency of the estimates will be highly affected, thus the model will be completely unreliable.

TABLE 2. Bias, SE and RMSE of the estimates for time-dependent covariate model

		$\widehat{\beta_0}$		$\widehat{\beta_1}$		$\widehat{\gamma}$	
	CP	n=50	n=100	n=50	n=100	n=50	n=100
Bias	0	-0.0732	-0.0406	-0.0033	-0.0006	0.1088	0.0534
	10	-0.0792	-0.0428	-0.0017	0.0002	0.1223	0.0572
	20	-0.0785	-0.0453	-0.0013	0.0005	0.1245	0.0624
	30	-0.0805	-0.0462	-0.0037	-0.0002	0.1345	0.0688
	40	-0.0825	-0.0490	-0.0135	0.0002	0.1363	0.0776
	50	-0.0891	-0.0508	-0.0165	0.0018	0.1547	0.0836
SE	0	0.2074	0.1448	0.2154	0.1374	0.1905	0.1197
	10	0.2207	0.1522	0.2253	0.1458	0.2253	0.1362
	20	0.2206	0.1634	0.2439	0.1563	0.2610	0.1665
	30	0.2557	0.1756	0.2680	0.1715	0.3177	0.2067
	40	0.2806	0.1904	0.2841	0.1851	0.3989	0.2603
	50	0.3229	0.2093	0.3125	0.2024	0.5603	0.3393
RMSE	0	0.2200	0.1503	0.2154	0.1374	0.2194	0.1311
	10	0.2345	0.1581	0.2253	0.1458	0.2564	0.1477
	20	0.2479	0.1696	0.2439	0.1563	0.2892	0.1778
	30	0.2681	0.1816	0.2681	0.1715	0.3450	0.2067
	40	0.2925	0.1967	0.2841	0.1851	0.3989	0.2717
	50	0.3350	0.2154	0.3129	0.2024	0.5603	0.3494

TABLE 3. RMSEs of wrong and correct fitted model to time-dependent data

		$\nu = 0.05$		$\nu = 5.5$		$\nu = 13$	
CP		Wrong	Correct	Wrong	Correct	Wrong	Correct
10	$\widehat{\beta_0}$	0.16	0.16	2.17	0.15	0.16	0.16
	$\widehat{\beta_1}$	0.16	0.15	2.39	0.15	0.16	0.15
	$\widehat{\gamma}$	0.14	0.15	2.52	0.16	0.14	0.15
30	$\widehat{\beta_0}$	0.18	0.18	4.21	0.17	0.19	0.18
	$\widehat{\beta_1}$	0.18	0.18	3.89	0.17	0.23	0.18
	$\widehat{\gamma}$	0.21	0.21	6.15	0.20	0.26	0.21

CONFIDENCE INTERVAL ESTIMATES

In this section we compared two methods of constructing confidence intervals for the parameters of the time-dependent model. The first method is asymptotic normality confidence interval or the Wald interval and the second is alternative computer based technique known as the jackknife. For discussions in following sections we will use β_1 as our example and similar procedure would then apply for the rest of the parameters.

ASYMPTOTIC NORMALITY CONFIDENCE INTERVAL (WALD)

Let $\hat{\theta}$ be the maximum likelihood estimator for the vector of parameters θ and $l(\theta)$ the log-likelihood function of θ. Following Cox and Hinkley (1974), under mild regularity conditions, $\hat{\theta}$ is asymptotically normally distributed with mean θ and covariance matrix $I^{-1}(\theta)$ where $I(\theta)$ is the Fisher information matrix evaluated at the true value of the θ. The matrix $I(\theta)$ can be estimated by the observed information matrix $I(\hat{\theta})$. The $\widehat{var}(\hat{\beta}_1)$ is the $(2,2)^{th}$ element of matrix $I(\hat{\theta})$. If $z_{1-\frac{\alpha}{2}}$ is the $(1-\alpha/2)$ quantile of the standard normal distribution the 100 (1- α)% confidence interval for β_1 is:

$$\hat{\beta}_1 - z_{1-\frac{\alpha}{2}}\sqrt{\widehat{var}\left(\hat{\beta}_1\right)} < \beta_1 < \hat{\beta}_1 + z_{1-\frac{\alpha}{2}}\sqrt{\widehat{var}\left(\hat{\beta}_1\right)}$$

JACKKNIFE CONFIDENCE INTERVAL

Let us say that $\hat{\beta}_1$ is the MLE of the parameter β_1 obtained from the original dataset $x=(x_1, x_2, \ldots, x_n)$. The jackknife estimate of bias and SE are computed from the jackknife samples. For a data set with n observations, the i^{th} jackknife sample is defined to be x with the i^{th} observation removed. So, the jackknife sample would consist of $(n-1)$ observations, all except the i^{th} observation.

$$x_{(i)}=(x_1, x_2, \ldots, x_{i-1}, x_{i+1}, \ldots, x_n).$$

Let $\hat{\beta}_{1(i)}$ be the MLE of the parameter based on the jackknife sample, then, the new estimate, $\hat{\beta}_{1(jack)}$ is defined by

$$\hat{\beta}_{1(jack)} = \hat{\beta}_1 - (n-1)\left(\hat{\beta}_{1(\cdot)} - \hat{\beta}_1\right),$$

where

$$\hat{\beta}_{1(\cdot)} = \sum_{i=1}^{n} \frac{\hat{\beta}_{1(i)}}{n}.$$

The jackknife estimate of the SE is:

$$\widehat{SE}_{jack}\left(\hat{\beta}_1\right) = \sqrt{\frac{n-1}{n}\sum_{i=1}^{n}\left(\hat{\beta}_{1(i)} - \hat{\beta}_{1(\cdot)}\right)^2}.$$

If $t_{\left(1-\frac{\alpha}{2},n-1\right)}$ is the (1− α/2)quantile of the student's t distribution at (n-1) degrees of freedom, the100(1−α)% confidence interval for β_1 is:

$$\hat{\beta}_{1(jack)} - t_{\left(1-\frac{\alpha}{2},n-1\right)} \widehat{SE}_{jack}\left(\hat{\beta}_1\right) < \beta_1 < \hat{\beta}_{1(jack)}$$
$$+ t_{\left(1-\frac{\alpha}{2},n-1\right)} \widehat{SE}_{jack}\left(\hat{\beta}_1\right).$$

COVERAGE PROBABILITY STUDY AND RESULTS

A coverage probability study using 2000 samples each with *n*=20, 30, 40, 50, 100, 150, 200, 250 and 350 and two CP levels of 10% and 30% was conducted to compare the performance of the confidence interval estimates at different sample sizes and CP levels. The nominal error probabilities were chosen as 0.05 and 0.1. Left and right error probabilities were estimated and total error probability was calculated. Following Arasan (2006), the estimated left(right) error probability is calculated by adding the number of times the left (right) endpoint was more (less) than the true parameter value divided by the total number of samples, N. Following Doganaksoy and Schmee (1993), if the total error probability is greater than α + 2.58 × SE ($\hat{\alpha}$), then the method is termed anti-conservative; if the total error probability is less than α + 2.58 × SE ($\hat{\alpha}$), then the method is termed conservative, and if the larger error probability is more than 1.5 times the smaller one, then the method is termed asymmetrical. Standard error of estimated error probability is approximately, $SE(\hat{\alpha}) = \sqrt{\alpha(1-\alpha)/N}$.

The overall performance of the different methods of constructing confidence intervals are judged based on the total number of anti-conservative, conservative and asymmetrical intervals. Also, behavior of the methods at different nominal error probabilities α and CP levels is of interest. By comparing the two methods of computing confidence interval estimates, we found that Wald method gives better interval estimates of β_0 and jackknife method gives better interval estimates of β_1 and γ . Overall, the jackknife method seems to perform better than the Wald method.

Tables 4 and 5 show estimated left, right and total error probabilities of parameters at different sample sizes and CP levels for Wald and jackknife methods where the nominal error probability α is 0.05 . The estimated total error probabilities of both methods are close to the nominal error probability but some intervals have asymmetric left and right estimated error probabilities.

Table 6 shows the summary of the results obtained from the coverage probability study. The jackknife method produces fewer anti-conservative intervals compared to the Wald method. However, it generates many conservative intervals whereas the Wald method does not produce any conservative interval. Having many conservative intervals is not very desirable because it produces intervals wider than they need to be. The Wald also produces many asymmetrical intervals. Both methods appear to perform slightly better at α = 0.05 and also at higher CP level.

Tables 7 and 8 show the total conservative, anti-conservative and asymmetrical intervals at α = 0.05 level. We can clearly see that a large portion of the asymmetrical intervals are produced by β_0 and γ. Also anti-conservative intervals are produced by the Wald method only for β_0 and

TABLE 4. Estimated error probabilities of Wald method (α = 0.05)

		Left error		Right error		Total error	
	n	CP=10	CP=30	CP=10	CP=30	CP=10	CP=30
β_0	20	0.019	0.016	0.036	0.032	0.055	0.048
	30	0.018	0.025	0.034	0.036	0.052	0.061
	40	0.018	0.024	0.030	0.035	0.047	0.059
	50	0.016	0.017	0.035	0.036	0.051	0.053
	100	0.016	0.020	0.030	0.036	0.046	0.056
	150	0.022	0.022	0.030	0.030	0.051	0.051
	200	0.019	0.022	0.034	0.028	0.053	0.050
	250	0.020	0.024	0.038	0.032	0.058	0.055
	350	0.020	0.021	0.031	0.027	0.051	0.048
β_1	20	0.028	0.029	0.038	0.042	0.065	0.071
	30	0.035	0.030	0.031	0.032	0.065	0.062
	40	0.034	0.030	0.031	0.030	0.064	0.059
	50	0.029	0.028	0.033	0.031	0.061	0.060
	100	0.028	0.032	0.029	0.025	0.057	0.056
	150	0.017	0.020	0.030	0.028	0.046	0.048
	200	0.028	0.025	0.023	0.021	0.051	0.046
	250	0.023	0.022	0.022	0.019	0.045	0.041
	350	0.027	0.030	0.027	0.025	0.054	0.054
γ	20	0.088	0.008	0.002	0.001	0.090	0.081
	30	0.067	0.070	0.025	0.004	0.069	0.074
	40	0.069	0.062	0.004	0.005	0.073	0.067
	50	0.064	0.064	0.030	0.005	0.067	0.068
	100	0.048	0.046	0.040	0.005	0.052	0.051
	150	0.045	0.041	0.008	0.012	0.053	0.051
	200	0.040	0.035	0.011	0.011	0.051	0.045
	250	0.042	0.039	0.007	0.013	0.050	0.052
	350	0.043	0.041	0.013	0.016	0.056	0.057

TABLE 5. Estimated error probabilities of jackknife method (α = 0.05)

	n	Left error CP=10	Left error CP=30	Right error CP=10	Right error CP=30	Total error CP=10	Total error CP=30
β_0	20	0.007	0.005	0.043	0.044	0.050	0.049
	30	0.008	0.004	0.043	0.047	0.051	0.051
	40	0.008	0.006	0.035	0.039	0.043	0.045
	50	0.009	0.007	0.037	0.042	0.046	0.049
	100	0.010	0.011	0.033	0.046	0.043	0.057
	150	0.013	0.015	0.032	0.029	0.045	0.044
	200	0.017	0.017	0.036	0.034	0.053	0.051
	250	0.016	0.019	0.036	0.032	0.052	0.051
	350	0.017	0.021	0.033	0.028	0.050	0.049
β_1	20	0.014	0.017	0.012	0.014	0.014	0.026
	30	0.012	0.021	0.017	0.019	0.029	0.040
	40	0.016	0.015	0.015	0.018	0.031	0.033
	50	0.023	0.022	0.022	0.021	0.045	0.057
	100	0.016	0.017	0.019	0.021	0.035	0.038
	150	0.016	0.019	0.030	0.023	0.046	0.042
	200	0.021	0.018	0.023	0.022	0.044	0.040
	250	0.022	0.021	0.024	0.018	0.046	0.039
	350	0.020	0.021	0.027	0.028	0.047	0.049
γ	20	0.045	0.036	0.011	0.009	0.056	0.045
	30	0.037	0.036	0.016	0.017	0.053	0.053
	40	0.034	0.034	0.023	0.022	0.057	0.056
	50	0.035	0.033	0.033	0.023	0.068	0.056
	100	0.026	0.026	0.041	0.029	0.067	0.055
	150	0.019	0.029	0.046	0.037	0.065	0.066
	200	0.023	0.021	0.033	0.035	0.056	0.056
	250	0.024	0.022	0.041	0.034	0.064	0.056
	350	0.027	0.020	0.039	0.041	0.066	0.060

TABLE 6. Summary of the performance of Wald and jackknife methods

α	CP	Conservative Wald	Conservative Jackknife	Anti-conservative Wald	Anti-conservative Jackknife	Asymmetrical Wald	Asymmetrical Jackknife
0.05	10	0	4	7	5	19	15
	30	0	2	5	1	13	14
0.1	10	0	5	7	0	17	16
	30	0	5	7	0	15	12

TABLE 7. Performance of Wald method at α = 0.05

	CP=10									CP=30								
	Conservative			Anti-conservative			Asymmetrical			Conservative			Anti-conservative			Asymmetrical		
n	β_0	β_1	γ	β_0	β_1	γ	β_0	β_1	γ	β_0	β_1	γ	β_0	β_1	γ	β_0	β_1	γ
20					*	*	*		*					*	*	*		*
30					*	*	*		*						*			*
40					*	*	*		*						*		*	*
50						*	*		*						*	*		*
100							*		*							*		*
150								*	*									*
200							*		*									*
250							*		*									*
350							*	*	*									*
Subtotal	0	0	0	0	3	4	8	2	9	0	0	0	0	1	4	3	1	9
Total		0			7			19			0			5			13	

TABLE 8. Performance of jackknife method at α = 0.05

	CP=10									CP=30								
	Conservative			Anti-conservative			Asymmetrical			Conservative			Anti-conservative			Asymmetrical		
n	β_0	β_1	γ	β_0	β_1	γ	β_0	β_1	γ	β_0	β_1	γ	β_0	β_1	γ	β_0	β_1	γ
20		*					*		*		*					*		*
30		*					*									*		*
40		*					*		*		*					*		*
50		*				*	*									*		
100						*	*		*							*		
150						*	*	*	*						*	*		
200							*									*		*
250						*	*		*							*		*
350						*	*											*
Subtotal	0	4	0	0	0	5	9	1	5	0	2	0	0	0	1	8	0	6
Total		4			5			15			2			1			14	

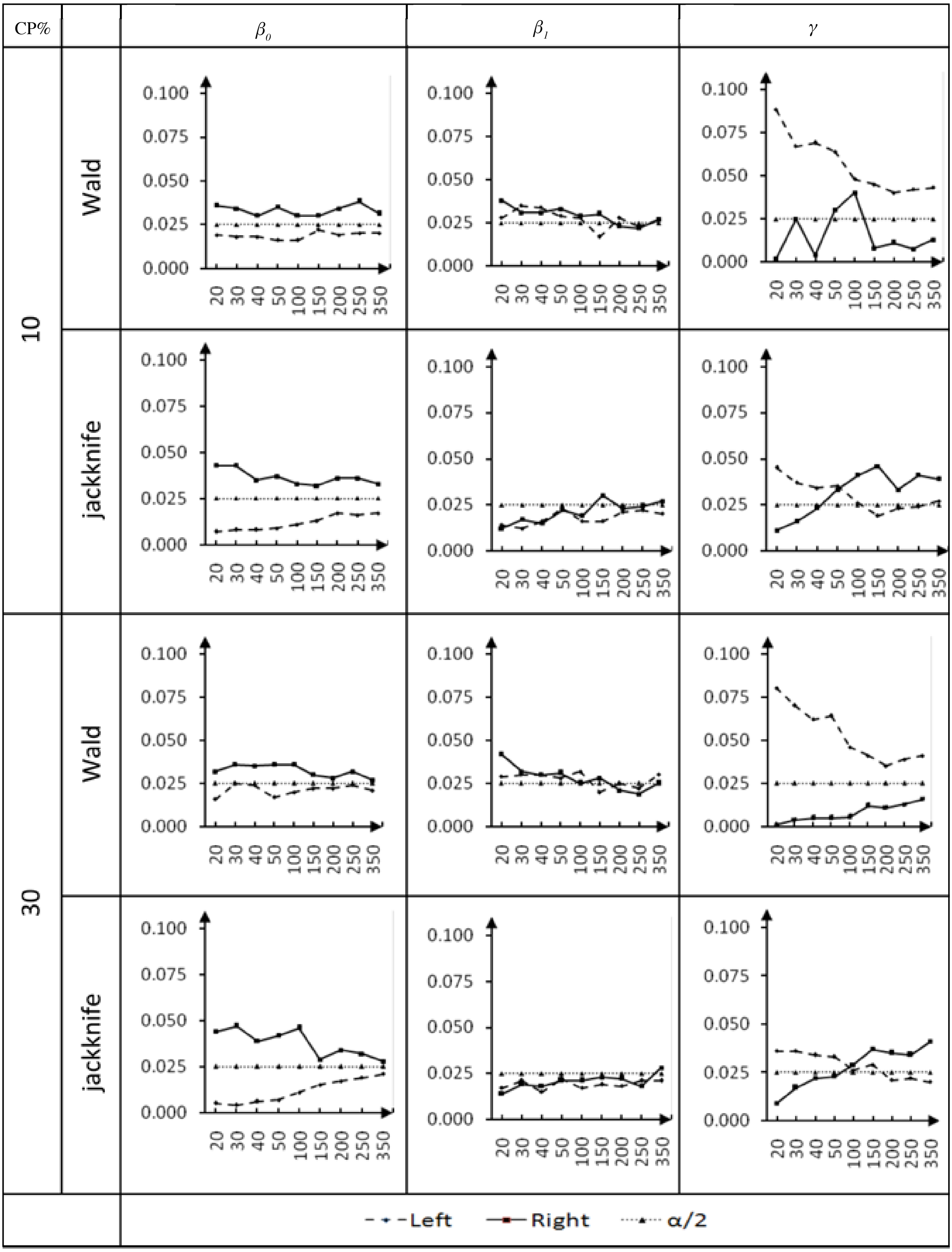

FIGURE 1. Estimated error probabilities of Wald and jackknife methods at $\alpha = 0.05$

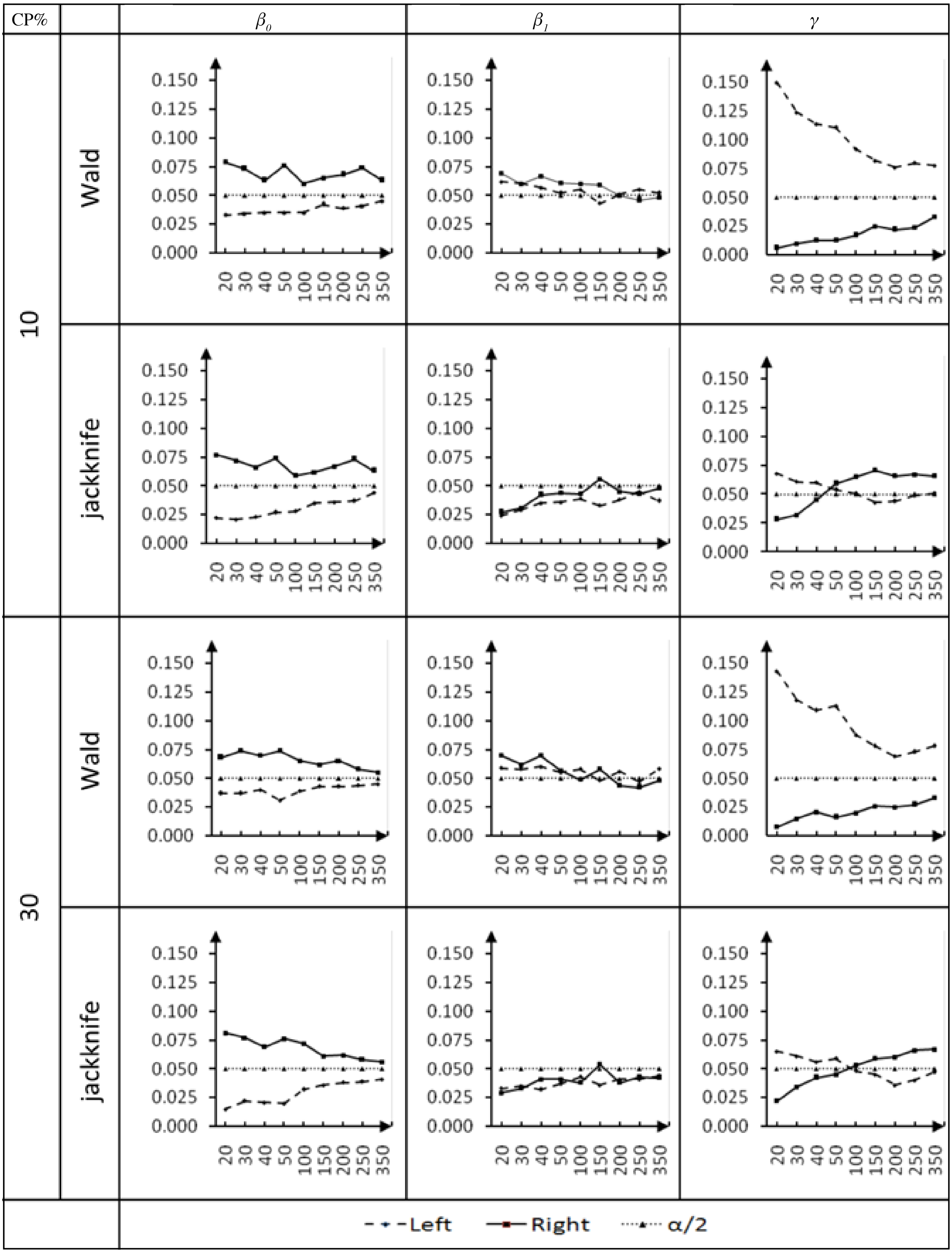

FIGURE 2. Estimated error probabilities of Wald and jackknife methods at $\alpha = 0.1$

for γ small sample sizes (<50). For the jackknife method, anti-conservative intervals is observed for large sample sizes (>100). If we look at Figures 1 and 2, for β_1 the jackknife method works better for all sample sizes, since most of the estimated left and right errors are approximately equal and are closer to $\alpha/2$. For β_0, the Wald method is slightly better especially for small sample sizes (<50). Finally, for γ, the jackknife method performs better than the Wald method for small and large sample sizes and very well for medium sample sizes (n=50, 100)

CONCLUSION

In this paper the MLE for the parameters of the Gompertz model with both fixed and time-dependent covariate were obtained. It was shown that the bias, SE and RMSE increase substantially when CP increases and sample size decreases. Also, it was shown that the jackknife method gave better interval estimations for the parameters than the Wald method. The Wald method is known to produce many asymmetrical intervals (Arasan & Lunn 2008). So, other confidence interval estimation methods like bootstrap-t confidence interval could also be developed for the parameters of this model. Both asymptotic and alternative confidence interval estimations should be investigated. The time-dependent model discussed here should be investigated further to include other types of censored data such as interval and doubly interval-censored data. The model could also be extended to include more covariates to see its performance when dealing with more or different types of covariates.

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Kaveh Kiani*
Laboratory of Computational Statistics and Operations Research
Institute for Mathematical Research
Universiti Putra Malaysia
43400 Serdang, Selangor D.E.
Malaysia

Jayanthi Arasan & Habshah Midi
Department of Mathematics
Faculty of Science
Universiti Putra Malaysia
43400 Serdang, Selangor D.E.
Malaysia

*Corresponding author; email: kaveh@inspem.upm.edu.my

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