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Modeling of Parametric Bayesian Cure Rate Survival for Pulmonary Tuberculosis Data Analysis

Statistics

KEYWORDS : Cure fraction, Frailty, MCMC, Prior

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ABSTRACT

The cure fraction refers to the proportion of patients who are cured of disease constituting long-term survivors. The study of cure fraction gives a useful measure of disease control and provides better predictions of long term survival rates to researchers and policy makers. In this article we study the parametric Bayesian cure rate model for right-censored data for population with a surviving fraction relating to two cases namely with and without frailty. We assume normal prior for covariates and Gamma prior for shape parameter. The estimates of the parameters are obtained using the Markov chain Monte Carlo (MCMC) technique. A real dataset from a pulmonary tuberculosis clinical trial is used in this research paper. Distributions including Exponential, Exponentiated Exponential, Weibull, Log-Logistic, Gamma and Log-Normal have been considered and a comparison of the results is presented.

1. Introduction

Cure rate models which include a cure fraction in survival models are becoming very popular in analyzing data from in areas such as health, criminology, reliability and economics. In recent years, there has been an increasing interest in modeling survival data with long term survivors. This may arise from clinical trials, in which, even after an extended follow-up, no further events of interest are observed and some of them may be considered as cured. Failing to account for such cured subjects would lead to incorrect inferences and researchers may be interested in estimating the cure fraction. The first cure rate models developed by Boag (1949) were to estimate the proportion of patients cured among those who were receiving treatment for cancer of mouth and throat, cervix, uteri and breast and later developed by Berkson and Gage (1952). It was called the mixture model and also known as the standard cure rate model. An alternative mixture model was developed by Yakovlev et al., (1993) and this model is known as the bounded cumulative hazard model. Bayesian formulation of cure rate model is given in Chen et al., (1999) and discussed by Ibrahim et al., (2001). A SAS macro for parametric and semi-parametric mixture cure models worked by Corbière and Joly (2007), Cure fraction model with random effects for regional variation in cancer survival analyzed by Seppä et al., (2009), Cure Models for Estimating Hospital-Based Breast Cancer Survival was analyzed by Rama et al., (2010). Zhao et al., (2014) had developed Bayesian random threshold estimation in a Cox proportional hazards cure model.

The Exponentiated Exponential (*EE*) distribution has been studied extensively for complete data set by Gupta and Kundu (1999, 2001a, 2001b, 2002, 2003a, 2003b, 2004) and Kundu and Gupta (2008) for both the Bayesian and Non-Bayesian methods. Recently Sundaram and Venkatesan (2012) have studied the two parameters *EE* distribution for Bayesian and non Bayesian survival model with censored data and the results are compared with Exponential (*E*), Weibull (*W*), Log-Logistic (*LL*), Gamma (*G*) and Log-Normal (*LN*). This research paper is focused on the study of cure fraction from different distributions both in with and without frailty of parametric Bayesian cure rate survival model. The parametric Bayes estimators, random-effect (i.e., frailty) and cure fraction are estimated using MCMC technique with the help of SAS based on the information provided by empirical data set.

Cure rate models are consisting of a cured (non-susceptible) fraction and an uncured (susceptible) fraction. It is assumed that the survival function for the entire population $S(t)$ is a mixture of cured and uncured subjects. Hence this model is known as a mixture cure rate model and can be written as

$$S(t) = \phi S_c(t) + (1-\phi)S_{uc}(t) \qquad (1)$$

where ϕ is a proportion of patients cured on treatment and $1-\phi$ is the proportion of patients uncured and with respect to the cure rate model we can assume a particular distribution for the survival function of the cured groups $S_c(t)$ and survival function of the uncured groups $S_{uc}(t)$. Since those who fall into the cured part of the equation (1) will never experience the event of interest, the $lim_{t\to\infty}S_c(t) = 1$, and the survival distribution function $S(t)$ for the entire population of patients, this leads to a parametric survival model. The popular distributions considered are Exponential, Exponentiated Exponential, Weibull, Log-Logistic, Gamma and Log-Normal and it becomes,

$$S(t) = \phi + (1-\phi)S_{uc}(t). \qquad (2)$$

The probability mixture density function corresponding to the above equation (2) is

$$f(t) = (1-\phi)f_{uc}(t) \qquad (3)$$

and the hazard function of the population of patients from equations (2) and (3) is

$$h(t) = \frac{(1-\phi)f_{uc}(t)}{\phi + (1-\phi)S_{uc}(t)}. \qquad (4)$$

The mixture model may be parametric or non-parametric depending on whether $f_{uc}(t)$ is specified or not. Suppose there are n patients entering to a clinical study. Let t_i, $i=1,2,\dots,n$ be the observed survival time for the i^{th} patient and let δ_i be a censoring indicator defined such that

$$\delta_i = \begin{cases} 1 \; if \; t_i \; is \; censored \\ 0 \; otherwise \end{cases}$$

Likelihood for the mixture cure model, which was initially introduced by De Angelis et al., (1997) is given by

$$L(t_i,\theta_i) = \prod_{i=1}^{n} \{(1-\phi_i)f_{uc}(t_i)\}^{\delta_i}$$

$$\{\phi_i + (1-\phi_i)S_{uc}(t)\}^{1-\delta_i}. \qquad (5)$$

Note, the ϕ_i are estimated by use of a link function, usually the *log-log*, *Identity*, *Logit* or *Probit* functions (Andersson, 2007; Lambert et al., 2007).

The rest of this paper is organized as follows: The concepts of parametric Bayesian cure rate survival model explained in section 2. In section 3, the parametric Bayesian cure rate survival model with frailty concepts are presented. A real database is presented in section 4. In section 5, results and discussions are presented. Finally our summary and conclusion of study models are stated in section 6.

2. Parametric Bayesian cure rate survival model

The survival function for *T*, and the survival function for the population using equation (2), we get

$$S_{pop}(t) = exp(-\theta) + (1-exp(-\theta))S_{uc}(t),$$

where $S_{pop}(t)$ is standard cure rate model with cure rate equal to $\phi = exp(-\theta)$ and survival function for the non-cured population is $S_{uc}(t)$. If the covariates depend on θ through the relationship $\theta = exp(x'\beta)$, where x is a p x *1* vector of regression coefficients for the cured and non-cured group. For the cured group, the sign of regression coefficients affects the cure fraction. Thus a negative regression coefficient leads to a larger cure fraction, when the corresponding covariate takes a positive value. For the non-cured group, the regression coefficients affect the hazard function. Specifically, a negative regression coefficient leads to a larger hazard, whereas a positive regression coefficient leads to a smaller hazard, when the corresponding covariate takes a positive value.

Let t_i denote the survival time for subject i,which may be right censored, and let δ_i denote the censoring indicator, which equals 1 if t_i is a failure time and 0 if it is right censored. The observed data are given by $D_{obs} = (n, t, \delta)$, where $t = (t_1, t_2, \dots, t_n)'$, and $\delta = (\delta_1, \delta_2, \dots, \delta_n)'$. Also, let $N = (N_1, N_2, \dots, N_n)'$. The complete data are given by D = *(n, t, δ, N)*, where *N* is an unobserved vector of latent variables. The complete data likelihood function of the parameters (ψ, θ) can then be written as

$$L(\theta, \psi/D) = \left(\prod_{i=1}^{n} S(t_i|\psi)^{N_i-\delta_i}(N_i f(t_i|\psi)^{\delta_i}\right) \text{x}$$
$$exp\left(\sum_{i=1}^{n}(N_i \, log(\theta) - log(N_i!)) - n\theta\right). \quad (6)$$

Let $x_i' = (x_{i1}, \dots, x_{ip})$ denote the p x 1 vector of covariates for the ith subject, and let $\beta = (\beta_1, \dots, \beta_p)'$ denote the corresponding vector of regression coefficients and θ to the covariates by $\theta_i \equiv \theta(x_i'\beta) = exp(x_i'\beta)$, so that the cure rate for subject i is $exp(-\theta_i) = exp\left(-exp(x_i'\beta)\right), i = 1,2, \dots, n.$ This relationship between θ_i and β is equivalent to a canonical link for θ_i in the setting of generalized linear models. In this context we can write the complete data likelihood of (β, ψ) as

$$L(\beta, \psi/D) = \left(\prod_{i=1}^{n} S(t_i|\psi)^{N_i-\delta_i}(N_i f(t_i|\psi)^{\delta_i}\right) \text{x}$$
$$exp\left(\sum_{i=1}^{n}(N_i x_i'\beta - log(N_i!)) - exp(x_i'\beta))\right). \quad (7)$$

If we assume independent priors for (β, ψ), then the posterior distributions of (β, ψ) are also independent. The above complete data likelihood equation (7) involving β looks like a Poisson generalized linear model with a canonical link, with the *N$_i$'s* being the observables. We consider the joint non-informative prior $\phi(\beta, \psi) \propto \phi(\psi)$ where $\psi = (\alpha, \lambda)'$ are the Weibull parameters in $f(t|\psi)$. This non-informative prior implies that β and ψ are independent a priori and $\phi(\beta) \propto 1$ is a uniform improper prior. We assume that

$$\phi(\psi) = \phi(\alpha|\delta_0, \tau_0)\phi(\lambda),$$

where

$$\phi(\alpha|\delta_0, \tau_0) \propto \alpha^{\delta_0 - 1} exp(-\tau_0 \alpha),$$

and δ_0 and τ_0 are two specified hyper parameters. The posterior distribution of (β, ψ) based on the observed data $D_{obs} = (n, t, X, \delta)$ is given by

$$\phi(\beta, \psi|D_{obs}) \propto \left(\sum_{N} L(\beta, \psi|D)\right)\phi(\alpha|\delta_0, \tau_0)\phi(\lambda), \quad (8)$$

where the sum in equation (8) extends over all possible values of the vector *N* (Ibrahim et al., 2001).

In this circumstance using equations (6), (7) and (8) we present the Bayesian cure rate with canonical link function in the setting of generalized linear models for *E*, *EE, W, LL, G* and *LL* distributions using a survival data set and the results have been compared via DIC.

3. Parametric Bayesian cure rate survival model with frailty

In this section the researcher has extended the previously proposed parametric Bayesian cure rate survival model. One can incorporate random-effects (RE) to fit life time data set. We apply this method to examine patterns of clinical trials using survival data. Models for frailty in multivariate cure fraction models considered by Yin (2008). Thus for times t_{ij} observed on subjects i and events j, Yin proposed multiplicative frailty at subject level combined with Poisson regression for θ_{ij} in the cure fraction s$exp(-\theta_{ij})$. One option takes

$$S_{uc}(t_{ij}) = exp\left(-\theta_{ij} Z_i F(t_{ij})\right), \quad (9)$$

with hazard rates

$$h_{uc}(t_{ij}) = \theta_{ij} Z_i f(t_{ij}). \quad (10)$$

In this context using the above two equations in (6), (7) and (8) we present the Bayesian cure rate frailty with canonical link function in the setting of generalized linear models for *E, EE, W, LL, G* and *LN* distributions using a survival data set and the results have been compared via DIC.

4. Databases

The aim of the study is to assess the response time to an 8 month treatment regimen consisting of Ethambutol, Rifampicin, Isoniazid and Pyrazinamide thrice a week for first two months followed by Isoniazid and Ethambutol daily for next 6 months. The primary outcome variable is sputum culture conversion time. A total 467 patients were included in the analysis. Out of these, 90% had favourable response and 10% had not responded or lost which constitute the censored observations. Four important covariates were considered for model comparison. The other details can be found from TRC-ICMR (2007).

5. Results and Discussion

In this section are presented the applications of life time pulmonary tuberculosis data set for the empirical comparisons using parametric Bayesian cure rate and parametric Bayesian cure rate with frailty survival model. The parameters estimates are obtained using the Markov chain Monte Carlo (MCMC) technique. The results are compared with DIC and also compared with Bayesian *EE* cure rate survival model with and without frailty. We carried out the following two sub sections studies to examine the model.

5.1 Parametric Bayesian cure rate survival model

This section presents the modeling of censored survival data for parametric Bayesian cure rate model using Exponential, Exponentiated Exponential, Weibull, Log-Logistic, Gamma and Log-Normal distributions. This model is fitted to the survival data set described in section 4. The estimated values of the parameters, the regression coefficients, SD, MCSE, cure rate and percentiles are presented in tables 1 - 6.

In the parametric Bayesian cure rate survival model, we used Normal prior for covariates (β) and Gamma prior for alpha (α) with 20000 and 40000 iterations and obtained the posterior summaries of covariates. It can be seen from tables 1-6, the covariates *age, weight* and % *doses* are significant for *LN* (at 20000 iterations), the covariates *age* and % *doses* are significant for *LN* (at 40000 iterations). Bayesian *W* cure rate survival model gave the smaller MC standard error compared to other models. Bayesian *LN* cure rate survival model (at 20000 and 40000 iterations) is better fit than the other parametric Bayesian cure rate survival model based on DIC value (tables 1 - 6). Figures.1 - 14 show the trace plots of the MC samples, autocorrelation and marginal posterior densities of covariates. It is noticed that for the Bayesian cure rate survival model, the plots indicate that the MC samples are mixing well at 20000 and 40000 iterations It is observed that the Bayesian *LN* cure rate survival model performs better than the other models (*E, EE, W, LL, G*). Moreover, the cure rate of Bayesian *EE* cure survival model is higher than the other models for pulmonary tuberculosis data.

Table 1 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Exponential cure rate survival model for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda} = 0.2682; \hat{\alpha} = 1.000$; DIC = 1841						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	1.3162	0.1883	0.0106	1.1915	1.3140	1.4386	20000
Sex (β_1)	0.1332	0.1369	0.0060	0.0396	0.1349	0.2264	20000
Age (β_2)	0.0757	0.1220	0.0054	-0.0055	0.0753	0.1581	20000
Weight (β_3)	-0.0723	0.1128	0.0047	-0.1469	-0.0735	0.0049	20000
% Doses (β_4)	-0.2922	0.1657	0.0091	-0.3990	-0.2904	-0.1828	20000
Cure rate	0.0125	0.0095	0.0005	0.0059	0.0101	0.0165	20000
Intercept (β_0)	1.3311	0.1904	0.0079	1.2032	1.3321	1.4583	40000
Sex (β_1)	0.1309	0.1360	0.0041	0.0387	0.1325	0.2251	40000
Age (β_2)	0.0695	0.1232	0.0041	-0.0117	0.0709	0.1519	40000
Weight (β_3)	-0.0712	0.1149	0.0035	-0.1484	-0.0709	0.0088	40000
% Doses (β_4)	-0.3036	0.1670	0.0070	-0.4121	-0.3034	-0.1939	40000
Cure rate	0.0121	0.0092	0.0003	0.0057	0.0098	0.0160	40000

Table 2 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Exponentiated Exponential cure rate survival model for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda} = 0.5220; \hat{\alpha} = 2.5627$; DIC = 1772						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	0.2537	0.1295	0.0130	0.1584	0.2252	0.3244	20000
Sex (β_1)	0.0461	0.0399	0.0020	0.0219	0.0423	0.0694	20000
Age (β_2)	0.0182	0.0336	0.0016	-0.0014	0.0167	0.0392	20000
Weight (β_3)	-0.0107	0.0312	0.0013	-0.0290	-0.0095	0.0081	20000
% Doses (β_4)	-0.0711	0.0508	0.0024	-0.1001	-0.0658	-0.0363	20000
Cure rate	0.2545	0.0474	0.0049	0.2257	0.2625	0.2896	20000
Intercept (β_0)	0.2408	0.1285	0.0096	0.1458	0.2144	0.3090	40000
Sex (β_1)	0.0452	0.0377	0.0014	0.0210	0.0422	0.0669	40000
Age (β_2)	0.0186	0.0324	0.0011	-0.0005	0.0174	0.0385	40000
Weight (β_3)	-0.0102	0.0307	0.0009	-0.0280	-0.0093	0.0087	40000
% Doses (β_4)	-0.0686	0.0511	0.0024	-0.0965	-0.0631	-0.0344	40000
Cure rate	0.2591	0.0474	0.0037	0.2302	0.2680	0.2944	40000

Table 3 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Weibull cure rate survival model for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda} = 0.5050; \hat{\alpha} = 1.7088$; DIC = 1696						
Covariates	Mean	SD	MCSE	Percentiles			Iteration
				25%	50%	75%	
Intercept (β_0)	0.6831	0.0753	0.0028	0.6280	0.6809	0.7339	20000
Sex (β_1)	0.0743	0.0444	0.0014	0.0442	0.0740	0.1043	20000
Age (β_2)	0.0234	0.0388	0.0012	-0.0038	0.0224	0.0504	20000
Weight (β_3)	-0.0177	0.0381	0.0012	-0.0435	-0.0178	0.0085	20000
% Doses (β_4)	-0.1076	0.0628	0.0023	-0.1499	-0.1061	-0.0640	20000
Cure rate	0.1135	0.0178	0.0006	0.1012	0.1134	0.1257	20000
Intercept (β_0)	0.6844	0.0747	0.0019	0.6310	0.6813	0.7334	40000
Sex (β_1)	0.0736	0.0443	0.0010	0.0440	0.0735	0.1035	40000
Age (β_2)	0.0230	0.0387	0.0008	-0.0034	0.0220	0.0490	40000
Weight (β_3)	-0.0176	0.0390	0.0009	-0.0434	-0.0174	0.0091	40000
% Doses (β_4)	-0.1081	0.0631	0.0016	-0.1498	-0.1059	-0.0637	40000
Cure rate	0.1134	0.0178	0.0004	0.1013	0.1135	0.1255	40000

Table 4 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Log-Logistic cure rate survival model for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda} = 0.4130; \hat{\alpha} = 3.2229$; DIC = 1577						
Covariates	Mean	SD	MCSE	Percentiles			Iteration
				25%	50%	75%	
Intercept (β_0)	0.8843	0.0955	0.0034	0.8201	0.8820	0.9468	20000
Sex (β_1)	0.0811	0.0629	0.0022	0.0369	0.0798	0.1242	20000
Age (β_2)	0.0763	0.0574	0.0020	0.0373	0.0755	0.1145	20000
Weight (β_3)	-0.0244	0.0546	0.0018	-0.0608	-0.0246	0.0119	20000
% Doses (β_4)	-0.1547	0.0867	0.0031	-0.2122	-0.1535	-0.0941	20000
Cure rate	0.0600	0.0149	0.0005	0.0495	0.0592	0.0694	20000
Intercept (β_0)	0.8838	0.0950	0.0024	0.8192	0.8823	0.9461	40000
Sex (β_1)	0.0821	0.0618	0.0016	0.0395	0.0818	0.1240	40000
Age (β_2)	0.0753	0.0562	0.0014	0.0375	0.0747	0.1127	40000
Weight (β_3)	-0.0245	0.0539	0.0012	-0.0606	-0.0247	0.0118	40000
% Doses (β_4)	-0.1545	0.0868	0.0021	-0.2118	-0.1537	-0.0965	40000
Cure rate	0.0601	0.0150	0.0003	0.0495	0.0593	0.0695	40000

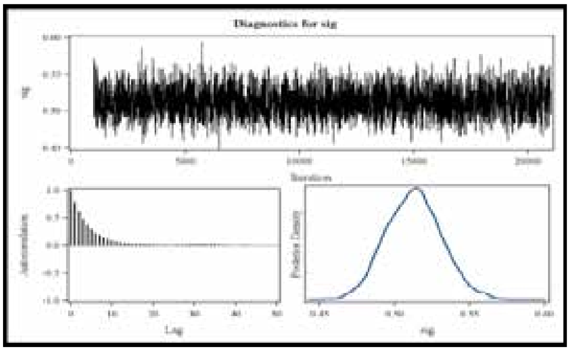
Table 5 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Gamma cure rate survival model for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda}$ = 1.7538; $\hat{\alpha}$ = 1.4066; DIC = 1828						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	0.3994	0.1224	0.0052	0.3183	0.3978	0.4790	20000
Sex (β_1)	0.0294	0.0757	0.0025	-0.0199	0.0308	0.0799	20000
Age (β_2)	0.0218	0.0617	0.0022	-0.0199	0.0204	0.0626	20000
Weight (β_3)	0.0265	0.0608	0.0023	-0.0141	0.0255	0.0662	20000
% Doses (β_4)	0.0794	0.0882	0.0028	0.0181	0.0759	0.1358	20000
Cure rate	0.2093	0.0350	0.0018	0.1850	0.2079	0.2323	20000
Intercept (β_0)	0.4018	0.1193	0.0034	0.3203	0.3995	0.4790	40000
Sex (β_1)	0.0304	0.0730	0.0017	-0.0179	0.0313	0.0792	40000
Age (β_2)	0.0220	0.0612	0.0015	-0.0183	0.0219	0.0625	40000
Weight (β_3)	0.0261	0.0622	0.0017	-0.0148	0.0245	0.0670	40000
% Doses (β_4)	0.0765	0.0866	0.0019	0.0178	0.0727	0.1323	40000
Cure rate	0.2081	0.0342	0.0010	0.1847	0.2080	0.2309	40000

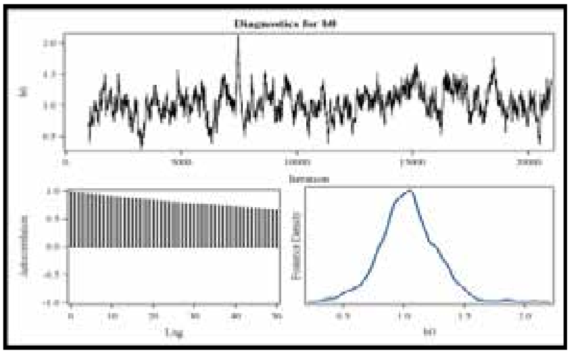
Table 6 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Log-Normal cure rate survival model for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda}$ = 0.3560; $\hat{\alpha}$ = 0.5129; DIC = **1444**						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	1.0327	0.2249	0.0251	0.8937	1.0284	1.1730	20000
Sex (β_1)	-0.1854	0.1605	0.0140	-0.2937	-0.1827	-0.0696	20000
Age (β_2)**	-0.0926	0.1389	0.0083	-0.1855	-0.0907	0.0056	20000
Weight (β_3)*	0.0051	0.1310	0.0086	-0.0872	-0.0006	0.0863	20000
% Doses (β_4)*	0.1408	0.1913	0.0209	0.0142	0.1440	0.2619	20000
Cure rate	0.1238	0.0457	0.0040	0.0895	0.1199	0.1525	20000
Intercept (β_0)	1.0485	0.2267	0.0183	0.9007	1.0406	1.1983	40000
Sex (β_1)	-0.1771	0.1594	0.0098	-0.2845	-0.1731	-0.0648	40000
Age (β_2)$	-0.1061	0.1382	0.0066	-0.1991	-0.1060	-0.0095	40000
Weight (β_3)	0.0052	0.1306	0.0062	-0.0860	0.0018	0.0916	40000
% Doses (β_4)***	0.1244	0.1949	0.0152	-0.0104	0.1326	0.2574	40000
Cure rate	0.1217	0.0470	0.0031	0.0864	0.1189	0.1530	40000

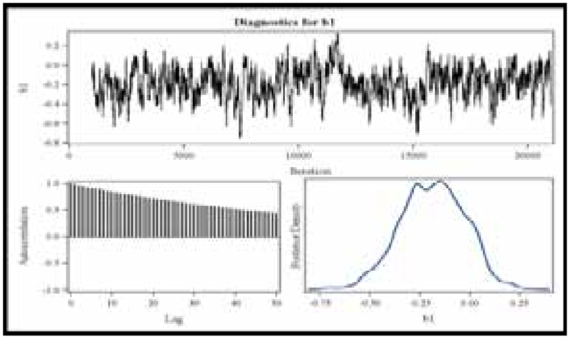
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; \$ $p < 0.0001$



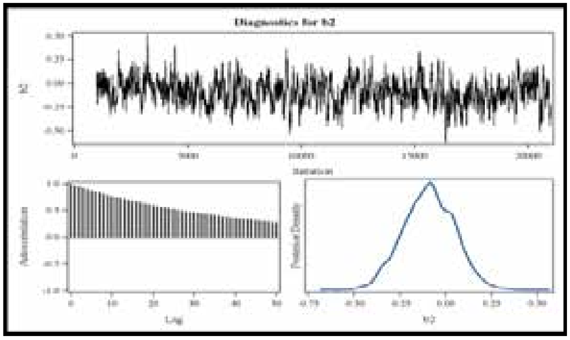
1. Sig-Shape



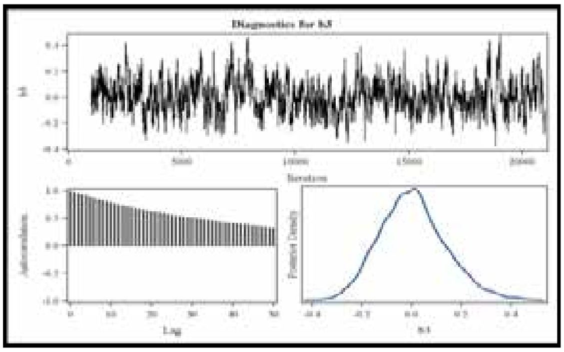
2.b0-Intercept



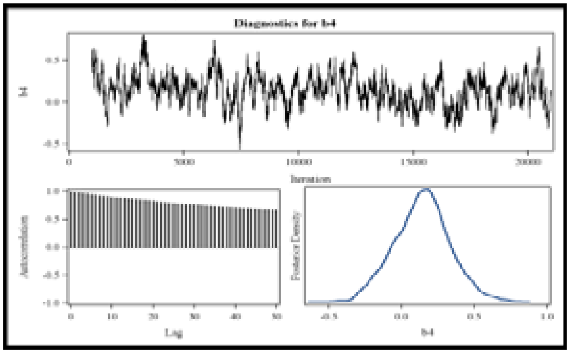
3. b1-Sex



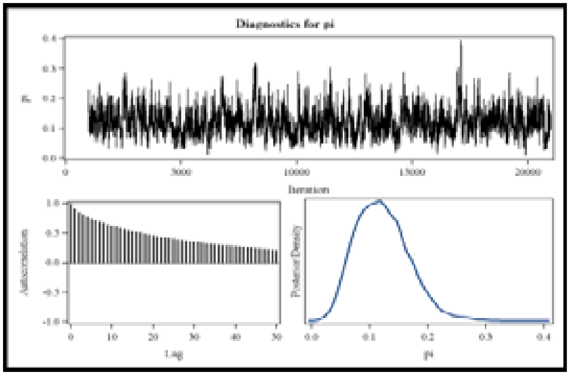
4.b2-Age



5. b3-Weight

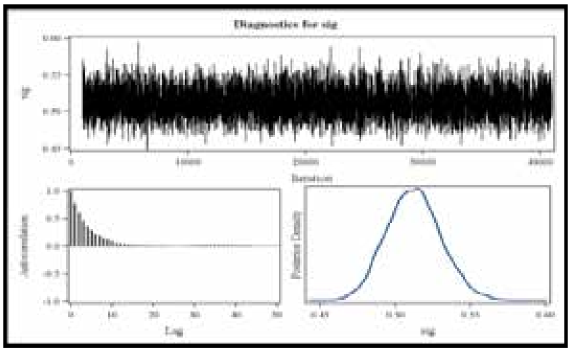


6.b4-%Doses

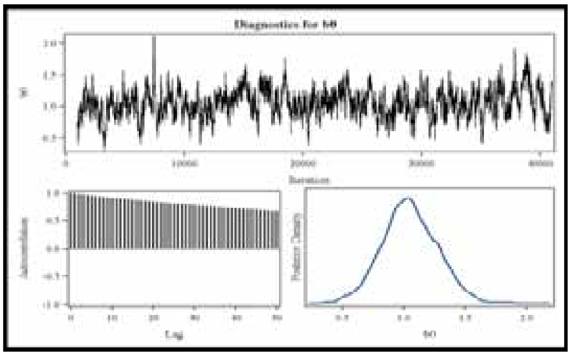


7. pi – Cure rate

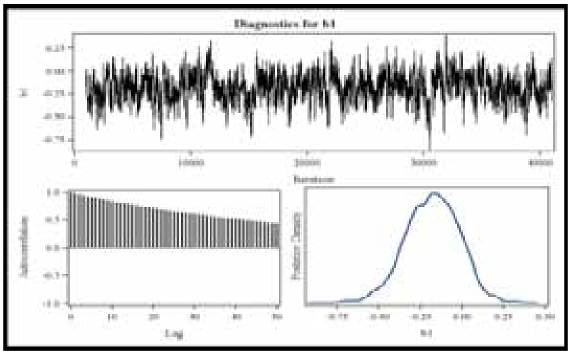
Figure 1-7 Trace plots, Autocorrelations and Marginal posterior densities of coefficients using Bayesian Log-Normal cure rate survival model after 20000 iterations for Pulmonary Tuberculosis data



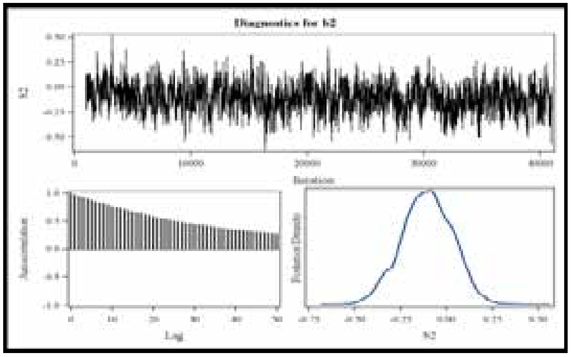
8. Sig-Shape



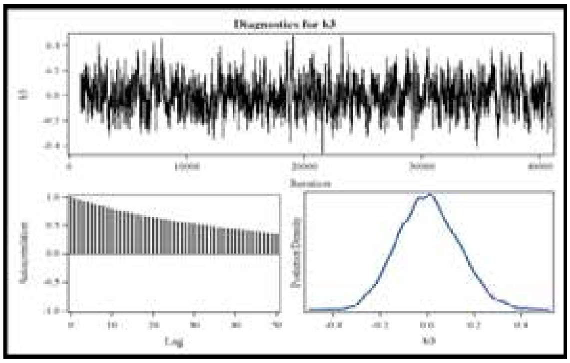
9.b0-Intercept



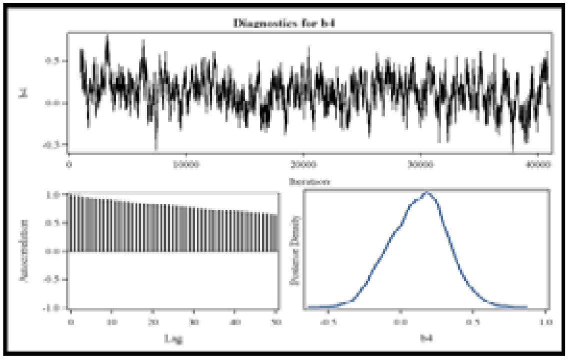
10. b1-Sex



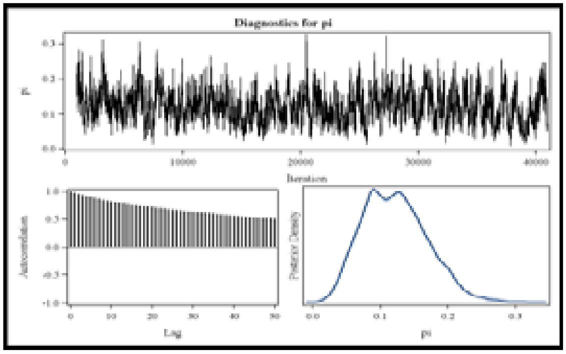
11.b2-Age



12 b3-Weight



13 b4-% Doses



14 pi - Cure rate

Figure 8-14 Trace plots, Autocorrelations and Marginal posterior densities of coefficients using Bayesian Log-Normal cure rate survival model after 40000 iterations for Pulmonary Tuberculosis data

5.2.1 Parametric Bayesian cure rate survival model with frailty

This section considers the modeling of censored survival data for parametric Bayesian cure rate with frailty using Exponential, Exponentiated Exponential, Weibull, Log-Logistic, Gamma and Log-Normal distributions. This model is fitted to the life time pulmonary tuberculosis data set described in section 4 and the results are compared with DIC. The estimated values of the parameters, the regression coefficients, SD, MCSE and percentiles are presented in tables 7 - 12.

In the parametric Bayesian cure rate survival model with frailty, the researcher used Normal prior for random effect (Z) and covariates (β) and Gamma prior for alpha (α) with 20000 and 40000 iterations and obtained the posterior summaries of covariates. We observed from tables 7 - 12, the covariates *age,* and '*% doses'* are significant for *EE* (at 20000 iterations)*,* and the covariates *age* is significant for *LN* (at 20000 iterations). Bayesian *W* cure rate survival model with frailty gave the smaller MC standard error compared to other models. We noticed that from Tables 7 - 12, the Bayesian *LN* cure rate survival model with frailty has smaller DIC at 20000 and 40000 iterations. Figures 15 – 30 show the trace plots of the MC samples, autocorrelation and marginal posterior densities of covariates. It is noticed that for the Bayesian cure rate survival model with frailty, the plots indicate that the MC samples are mixing well at 20000 and 40000 iterations. It is observed that the performance of Bayesian *LN* cure rate survival model with frailty is better fit compared to other models.

Table 7 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Exponential cure rate survival model with frailty for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda} = 1.9947; \hat{\alpha} = 1.0000$; DIC = 1841						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	-0.6905	1.2508	0.2603	-1.5214	-0.8977	0.1663	20000
Sex (β_1)	0.1239	0.1295	0.0073	0.0356	0.1270	0.2105	20000
Age (β_2)	0.0701	0.1205	0.0059	-0.0090	0.0720	0.1521	20000
Weight (β_3)	-0.0675	0.1177	0.0061	-0.1515	-0.0721	0.0106	20000
% Doses (β_4)	-0.3170	0.1654	0.0097	-0.4256	-0.3128	-0.2120	20000
Z (RE)	2.0362	1.2444	0.2604	1.1853	2.2294	2.8804	20000
Cure rate	0.0118	0.0098	0.0005	0.0055	0.0095	0.0149	20000
Intercept (β_0)	-1.4339	2.2800	0.3523	-2.0809	-0.8933	0.1348	40000
Sex (β_1)	0.1275	0.1291	0.0049	0.0401	0.1290	0.2142	40000
Age (β_2)	0.0675	0.1219	0.0041	-0.0138	0.0700	0.1499	40000
Weight (β_3)	-0.0733	0.1137	0.0051	-0.1520	-0.0781	0.0020	40000
% Doses (β_4)	-0.3123	0.1622	0.0065	-0.4201	-0.3097	-0.2048	40000
Z (RE)	2.7762	2.2702	0.3515	1.2198	2.2024	3.4216	40000
Cure rate	0.0118	0.0092	0.0003	0.0056	0.0095	0.0153	40000

Table 8 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Exponentiated Exponential cure rate survival model with frailty for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda} = 0.0143; \hat{\alpha} = 2.7276$; DIC = 1770						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	-1.5564	1.0421	0.2270	-2.2665	-1.5067	-1.0701	20000
Sex (β_1)	0.0448	0.0360	0.0024	0.0214	0.0412	0.0622	20000
Age (β_2)*	0.0164	0.0299	0.0024	0.0005	0.0172	0.0341	20000
Weight (β_3)	-0.0109	0.0299	0.0021	-0.0288	-0.0097	0.0088	20000
% Doses (β_4)***	-0.0682	0.0471	0.0043	-0.0926	-0.0616	-0.0370	20000
Z (RE)	1.7843	1.0179	0.2223	1.4279	1.7234	2.4499	20000
Cure rate	0.2644	0.0465	0.0063	0.2360	0.2727	0.2982	20000
Intercept (β_0)	-2.9318	1.6302	0.2548	-4.4726	-3.1368	-1.5067	40000
Sex (β_1)	0.0455	0.0361	0.0016	0.0219	0.0430	0.0648	40000
Age (β_2)	0.0188	0.0331	0.0020	0.0000	0.0187	0.0381	40000
Weight (β_3)	-0.0119	0.0313	0.0015	-0.0309	-0.0105	0.0091	40000
% Doses (β_4)	-0.0672	0.0482	0.0030	-0.0930	-0.0606	-0.0346	40000
Z (RE)	3.1686	1.6284	0.2549	1.7234	3.3099	4.8038	40000
Cure rate	0.2602	0.0464	0.0043	0.2324	0.2686	0.2946	40000

* $p < 0.05$; *** $p < 0.001$

Table 9 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Weibull cure rate survival model with frailty for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda}$ = 5.7592; $\hat{\alpha}$ = 1.7089; DIC = 1696						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	1.7508	0.6108	0.1316	1.1228	1.9733	2.2596	20000
Sex (β_1)	0.0733	0.0434	0.0022	0.0434	0.0720	0.1028	20000
Age (β_2)	0.0218	0.0384	0.0026	-0.0039	0.0219	0.0469	20000
Weight (β_3)	-0.0153	0.0396	0.0022	-0.0420	-0.0161	0.0118	20000
% Doses (β_4)	-0.1021	0.0637	0.0035	-0.1400	-0.0987	-0.0592	20000
Z (RE)	-1.0719	0.6113	0.1327	-1.5873	-1.3100	-0.4183	20000
Cure rate	0.1152	0.0180	0.0011	0.1035	0.1154	0.1274	20000
Intercept (β_0)	1.8807	0.5891	0.0898	1.4290	1.9967	2.3383	40000
Sex (β_1)	0.0718	0.0434	0.0015	0.0422	0.0716	0.1012	40000
Age (β_2)	0.0206	0.0376	0.0016	-0.0053	0.0204	0.0458	40000
Weight (β_3)	-0.0163	0.0387	0.0014	-0.0420	-0.0164	0.0103	40000
% Doses (β_4)	-0.1061	0.0623	0.0024	-0.1452	-0.1039	-0.0641	40000
Z (RE)	-1.1968	0.5830	0.0895	-1.6569	-1.3204	-0.7376	40000
Cure rate	0.1145	0.0175	0.0007	0.1030	0.1149	0.1265	40000

Table 10 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Log-Logistic cure rate survival model with frailty for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda}$ = 1.0196; $\hat{\alpha}$ = 3.2342; DIC = 1578						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	-0.0194	0.3439	0.0674	-0.2527	0.0016	0.1961	20000
Sex (β_1)	0.0765	0.0643	0.0035	0.0327	0.0768	0.1199	20000
Age (β_2)	0.0763	0.0569	0.0024	0.0386	0.0736	0.1148	20000
Weight (β_3)	-0.0211	0.0569	0.0025	-0.0566	-0.0211	0.0159	20000
% Doses (β_4)	-0.1582	0.0899	0.0065	-0.2146	-0.1598	-0.1018	20000
Z (RE)	0.9087	0.3342	0.0671	0.7102	0.8860	1.1247	20000
Cure rate	0.0601	0.0160	0.0010	0.0494	0.0585	0.0697	20000
Intercept (β_0)	-0.4867	0.6711	0.1028	-0.9823	-0.3319	0.0462	40000
Sex (β_1)	0.0772	0.0640	0.0024	0.0334	0.0787	0.1203	40000
Age (β_2)	0.0761	0.0561	0.0017	0.0384	0.0753	0.1142	40000
Weight (β_3)	-0.0223	0.0567	0.0018	-0.0598	-0.0229	0.0149	40000
% Doses (β_4)	-0.1589	0.0917	0.0047	-0.2168	-0.1575	-0.0969	40000
Z (RE)	1.3767	0.6627	0.1019	0.8511	1.2125	1.8777	40000
Cure rate	0.0598	0.0157	0.0007	0.0491	0.0587	0.0696	40000

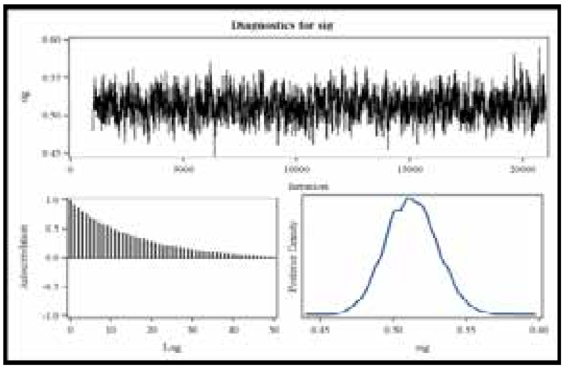
Table 11 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Gamma cure rate survival model with frailty for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda} = 0.7999$; $\hat{\alpha} = 1.4028$; DIC = 1827						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	-0.1592	0.5485	0.1161	-0.5769	-0.2707	0.3398	20000
Sex (β_1)	0.0318	0.0726	0.0038	-0.0173	0.0340	0.0802	20000
Age (β_2)	0.0230	0.0667	0.0032	-0.0207	0.0226	0.0664	20000
Weight (β_3)	0.0241	0.0634	0.0024	-0.0180	0.0228	0.0662	20000
% Doses (β_4)	0.0665	0.0808	0.0053	0.0098	0.0684	0.1211	20000
Z (RE)	0.5689	0.5369	0.1141	0.0634	0.7040	0.9693	20000
Cure rate	0.2048	0.0337	0.0022	0.1817	0.2042	0.2278	20000
Intercept (β_0)	0.1696	0.7566	0.1159	-0.4516	0.0889	0.6670	40000
Sex (β_1)	0.0315	0.0712	0.0026	-0.0167	0.0330	0.0793	40000
Age (β_2)	0.0230	0.0635	0.0021	-0.0183	0.0226	0.0649	40000
Weight (β_3)	0.0237	0.0626	0.0017	-0.0180	0.0233	0.0657	40000
% Doses (β_4)	0.0685	0.0826	0.0040	0.0109	0.0699	0.1237	40000
Z (RE)	0.2413	0.7513	0.1154	-0.2522	0.3448	0.8417	40000
Cure rate	0.2045	0.0344	0.0017	0.1813	0.2033	0.2271	40000

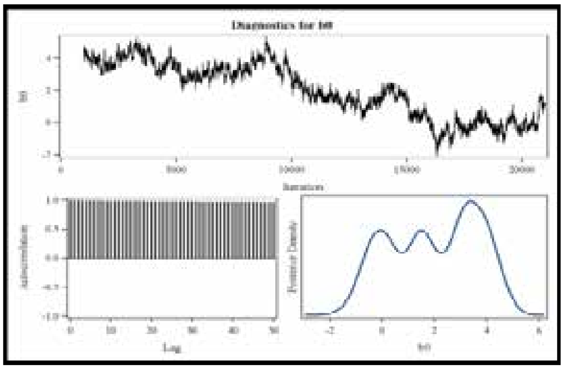
Table 12 Posterior summaries of Pulmonary Tuberculosis data under Bayesian Log-Normal cure rate survival model with frailty for n = 467, Censored % = 10 at 20000 and 40000 iterations

Parameters	$\hat{\lambda} = 0.1385$; $\hat{\alpha} = 0.5126$; DIC = **1444**						Iteration
Covariates	Mean	SD	MCSE	Percentiles			
				25%	50%	75%	
Intercept (β_0)	1.9766	1.6786	0.3615	0.4197	2.0388	3.4266	20000
Sex (β_1)	-0.1632	0.1657	0.0114	-0.2724	-0.1666	-0.0479	20000
Age (β_2)	-0.1147	0.1407	0.0091	-0.2100	-0.1134	-0.0175	20000
Weight (β_3)	0.0066	0.1356	0.0093	-0.0868	0.0070	0.0977	20000
% Doses (β_4)	0.1272	0.1845	0.0094	0.0014	0.1335	0.2575	20000
Z (RE)	-0.9363	1.6622	0.3612	-2.4123	-0.9498	0.6409	20000
Cure rate	0.1220	0.0460	0.0025	0.0882	0.1184	0.1505	20000
Intercept (β_0)	1.4383	2.8926	0.4473	-1.1908	1.5655	3.6347	40000
Sex (β_1)	-0.1635	0.1645	0.0079	-0.2735	-0.1639	-0.0508	40000
Age (β_2)	-0.1183	0.1380	0.0062	-0.2118	-0.1198	-0.0235	40000
Weight (β_3)	0.0018	0.1349	0.0051	-0.0911	-0.0013	0.0929	40000
% Doses (β_4)	0.1272	0.1856	0.0073	0.0050	0.1291	0.2514	40000
Z (RE)	-0.3941	2.8850	0.4473	-2.5881	-0.5311	2.2330	40000
Cure rate	0.1220	0.0463	0.0019	0.0887	0.1178	0.1504	40000

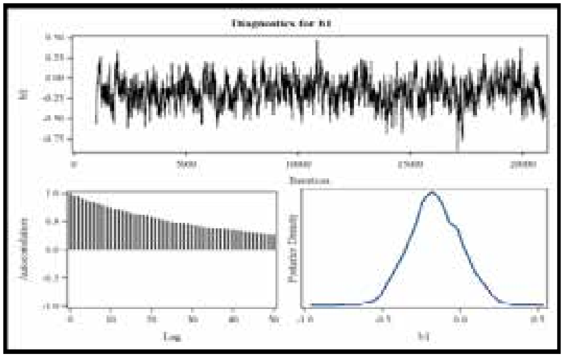
* $p < 0.05$



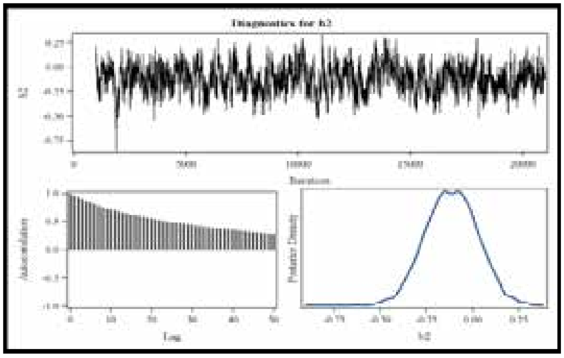
15 Sig-Shape



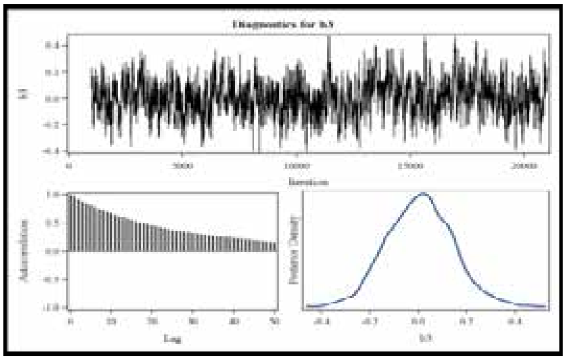
16 b0-Intercept



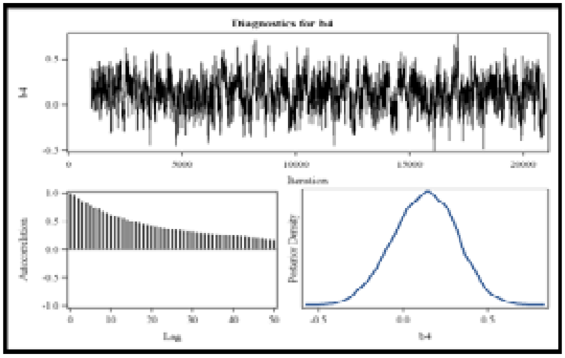
17 b1-Sex



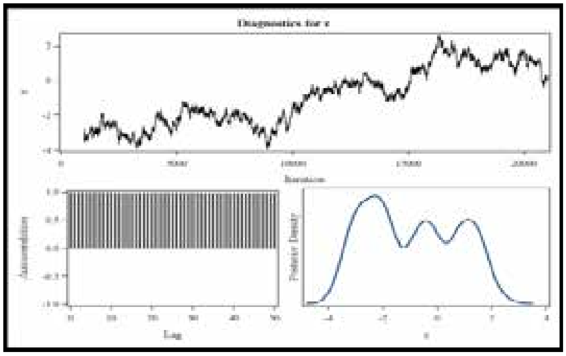
18 b2- Age



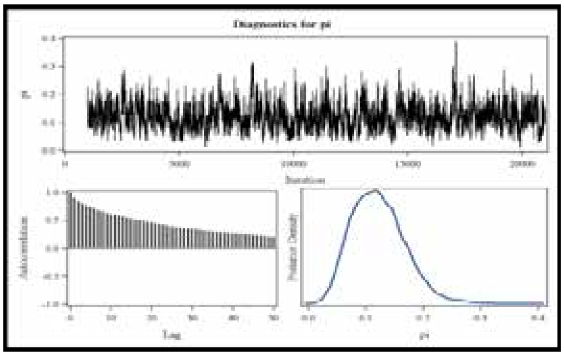
19 b3- Weight



20 b4- % Doses

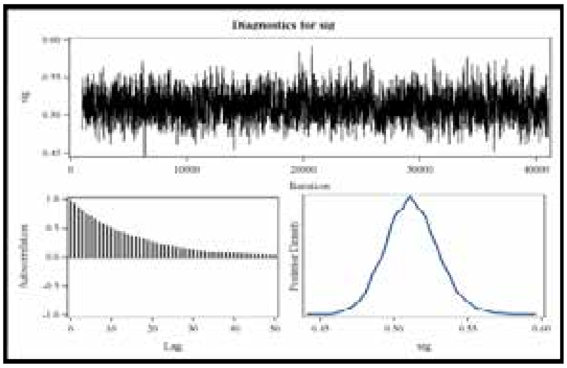


21 Z – Random effect (RE)

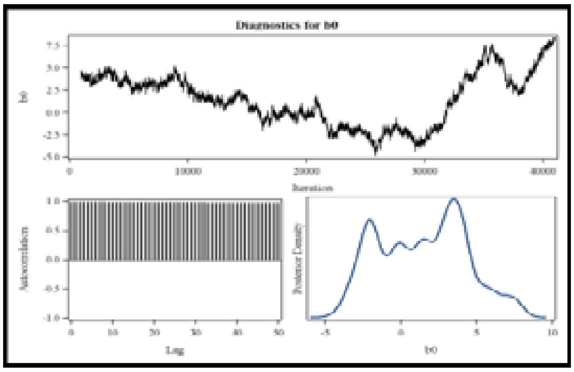


22 pi – Cure rate

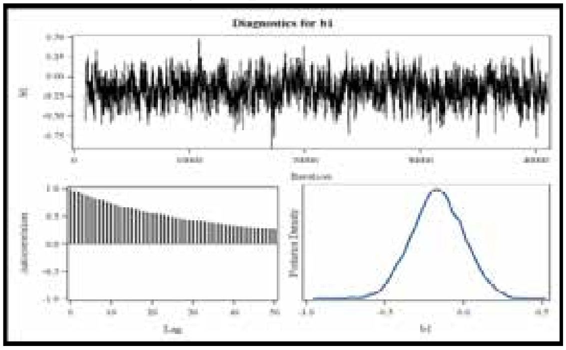
Figure 15-22 Trace plots, Autocorrelations and Marginal posterior densities of coefficients using Bayesian Log-Normal cure rate survival model with frailty after 20000 iterations for Pulmonary Tuberculosis data



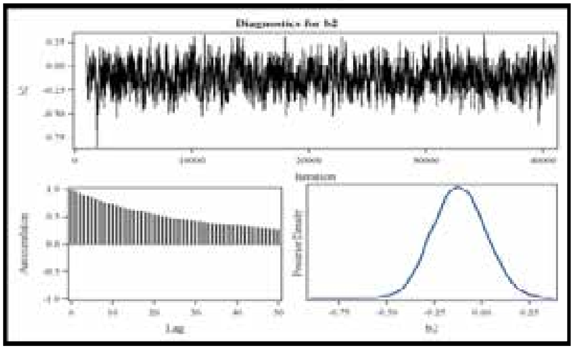
23.Sig-Shape



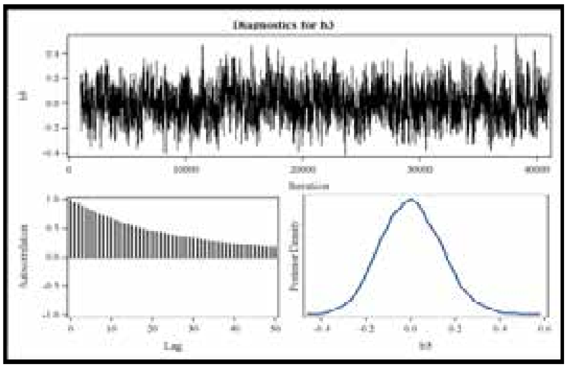
24.b0-Intercep



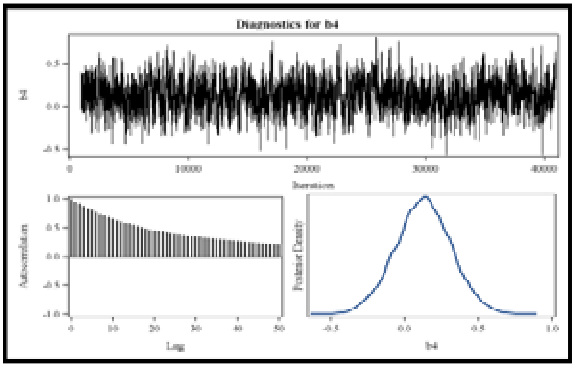
25.b1-Sex



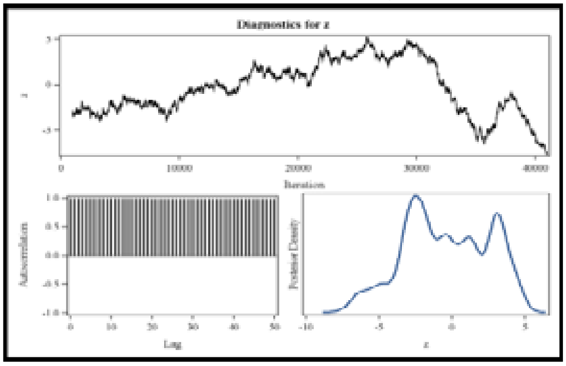
26.b2- Age



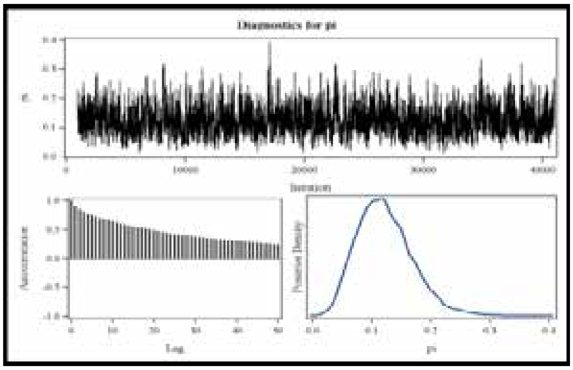
21.b3- Weight



28.b4- % Doses



29.Z – Random effect (RE)



30.pi – Cure rate

Figure 23-30 Trace plots, Autocorrelations and Marginal posterior densities of coefficients using Bayesian Log-Normal cure rate survival model with frailty after 40000 iterations for Pulmonary Tuberculosis data

6. Summary and Conclusions

The parametric Bayesian cure rate survival model with and without frailty for life time censored pulmonary tuberculosis data have been fitted in this research article. The parameters have been estimated (unknown shape, scale, Posterior Summaries of regression coefficients and random effects) using MCMC techniques with the help of SAS.

We observed from Tables 1 - 6 in section 5.1 reveal that the Bayesian *LN* cure rate survival model has smaller DIC at 20000 and 40000 iterations which is considered to be better fit compared to other models. The trace plots of Bayesian *LN* cure rate survival model in Figures 1 - 14 indicate that MC samples are mixing well at 40000 iterations. The cure rate of Bayesian *EE* cure rate survival model is higher than the other models

We found that from Tables 7 - 12 in section 5.2 the Bayesian *LN* cure rate survival model with frailty has the smaller DIC at 20000 and 40000 iterations compared to other models. The cure rate of Bayesian *EE* cure survival model with frailty is higher than the other models. We observed from Figures 15 - 30 the plots indicate that the MC samples are mixing well at 40000 iterations compared to 20000 iterations for Bayesian *LN* cure rate survival model with frailty. The performance of Bayesian *LN* cure rate survival model with frailty is better fit than the other models.

We observed from sections 5.1 and 5.2, that the Bayesian *LN* cure rate and Bayesian *LN* cure rate with frailty survival model using MCMC techniques seems to be more appropriate for the study of the right censored pulmonary tuberculosis data compared to other models based on DIC value for 20000 and 40000 iterations.

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