Bayesian Estimation of Parameters for Bivariate Gompertz Regression Model with Shared Gamma Frailty under Random Censoring

David D. Hanagal and Richa Sharma

Department of Statistics, University of Pune, Pune-411007, India.
Email: david_hanagal@yahoo.co.in; richa_stat@rediffmail.com

Abstract

In this paper, we consider shared gamma frailty model with Gompertz distribution as baseline hazard for bivariate survival times. The problem of analyzing and estimating parameters of bivariate Gompertz distribution with shared gamma frailty is of interest and the focus of this paper. We solve the inferential problem in a Bayesian framework with the help of a comprehensive simulation study. We introduce Bayesian estimation procedure using Markov Chain Monte Carlo (MCMC) technique to estimate the parameters involved in the proposed model and then compare the true values of the parameters with the estimated values for different sample sizes. A search of the literature suggests there is currently no work has been done for Bayesian estimation of parameters of bivariate Gompertz distribution with shared frailty.

Key words: Bayesian Estimation, Censored sample, Gamma frailty, Gompertz distribution, Markov Chain Monte Carlo (MCMC), Shared frailty.

1 Introduction

Gompertz distribution is used as a survival model in reliability and survival analysis. It has an increasing hazard rate for the life of the systems. The Gompertz distribution was first introduced by Gompertz (1825). This distribution does not seem to have received enough attention. Recently, many authors have contributed to the studies of statistical methodology and characterization of this distribution. Garg et al. (1970) studied the properties of the Gompertz distribution and obtained the maximum likelihood (ML) estimates for the parameters. Gordon (1990) provided the ML estimation for the mixture
of two Gompertz distributions. Applications and more recent survey of the Gompertz
distribution can be found in Ahuja and Nash (1979).

The objective of this paper is to introduce a bivariate Gompertz (BVG) distribu-
tion with shared frailty which is generated by gamma distribution. It is considered as a
distribution of the lifetimes of two components where each lifetime follows a Gompertz
distribution. The dependence in \( T_1 \) and \( T_2 \) is induced by gamma distributed frailty vari-
able. After integrating out frailty, \( T_1 \) and \( T_2 \) have a bivariate distribution. Thus, the
term bivariate Gompertz is used for the dependence generated in \( T_1 \) and \( T_2 \) after inte-
grating out frailty. We tried to get real data for the proposed model. Unfortunately, we
are not able to get proper data and so carry out the Bayesian estimation procedure from
simulated data.

The paper is organized as follows: In Section 2, we introduce the notion of shared
gamma frailty model with Laplace transformation. We introduce the BVG regression
model with shared gamma frailty with covariates in Section 3. The joint survival function
of proposed BVG distribution after integrating out frailty is also derived in this section.
Likelihood function of the failure data given the parameters is presented in Section 4.
In Section 5, joint posterior density function of the parameters given the failure times is
defined. In the same section, we also discuss how MCMC technique is used to estimate
the parameters of the proposed models. Final results of simulation study with different
sample sizes are given in Section 6. Finally, the paper ends with a discussion of our
findings in Section 7.

2 Shared Gamma Frailty Model

The shared frailty model is relevant to event time of related individuals, similar organs
and repeated measurements for example, if the timing of failure of paired organs like
kidneys, lungs, eyes, ears, dental implants etc. are considered. In this model individuals
from a group share common covariates.

The shared gamma frailty model was suggested by Clayton (1978) for the analysis
of the correlation between clustered survival times in genetic epidemiology. In a shared
frailty model, frailty is defined as a measure of the relative risk which individuals in a
group share. Thus, the frailty variable is associated with groups of individuals rather than individuals as such.

Suppose $n$ individuals are observed for the study and let a bivariate random variable $(T_{i1}, T_{i2})$ be the first and second survival times of $i^{th}$ individual ($i = 1, 2, 3, \ldots, n$). Also suppose that there are $p$ observed covariates collected in a vector $X_i = (X_{i1}, \ldots, X_{ip})'$ for $i^{th}$ individual where $X_{ik}$ ($k = 1, 2, 3, \ldots, p$) represents the value of $k^{th}$ observed covariate for $i^{th}$ individual. Here we assume that the first and second survival time $T_1$ and $T_2$ for each cluster share the same value of the covariates. Assuming that the frailties are acting multiplicatively on the baseline hazard function and both the survival times of individuals $T_1$ and $T_2$ are conditionally independent for given frailty $U_i = u_i$. The conditional hazard model for $i^{th}$ cluster at $j^{th}$, ($j = 1, 2$) survival time $t_{ij} > 0$, for given frailty $U_i = u_i$ has the form:

$$h(t_{ij} | U_i, X_i) = u_i h_0(t_{ij}) \exp(x_i' \beta); \quad i = 1, 2, \ldots, n; \quad j = 1, 2$$  \hspace{3cm} (2.1)

where $U_i$ is the unobserved (random) common risk factor shared by all subjects in cluster $i$, $h_0(t_{ij})$ is the common baseline hazard function, $X_i$ is a vector of observable covariates and $\beta$ is a vector of unknown regression coefficients.

Here $\exp(x_i' \beta)$ is the factor that gives the subject specific contribution to the hazard. Model (2.1) is called the shared frailty model because subjects in the same cluster share the same frailty factor. This model induces correlation between survival times of subjects within the same cluster. The value of the frailty $U_i$ is common to the individuals in the group, and thus it is responsible for creating dependence. This dependence is always positive.

The conditional integrated hazard function for $i^{th}$ individual at $j^{th}$ survival time $t_{ij} > 0$ for given frailty $U_i = u_i$ is,

$$H(t_{ij} | U_i, X_i) = u_i H_0(t_{ij}) \exp(x_i' \beta)$$ \hspace{3cm} (2.2)

where $H_0(t_{ij})$ is integrated baseline hazard function at time $t_{ij} > 0$.

The conditional survival function for $i^{th}$ individual at $j^{th}$ survival time $t_{ij} > 0$ for
given frailty $U_i = u_i$ is,

$$S(t_{ij} \mid U_i, X_i) = \exp[-H(t_{ij} \mid U_i, X_i)]$$

$$= \exp[-u_i H_0(t_{ij}) \exp(x'_i \beta)]$$  \hspace{1cm} (2.3)

Under the assumption of independence, the conditional survival function in the bivariate case for given frailty $U_i = u_i$ at time $t_{i1} > 0$ and $t_{i2} > 0$ is,

$$S(t_{i1}, t_{i2} \mid U_i, X_i) = S(t_{i1} \mid U_i, X_i)S(t_{i2} \mid U_i, X_i)$$

$$= \exp[-u_i \{H_{01}(t_{i1}) + H_{02}(t_{i2})\} \exp(x'_i \beta)]$$  \hspace{1cm} (2.4)

where $H_{0j}(t_{ij})$ is the integrated baseline hazard of $T_{ij}$, $(i = 1, 2, ..., n; \ j = 1, 2)$. From this, we immediately derive the bivariate survival function by integrating out $U_i$ having the probability function $f(u_i)$, for $i^{th}$ individual.

$$S(t_{i1}, t_{i2} \mid X_i) = \int_{U_i} S(t_{i1}, t_{i2} \mid u_i, x_i)f(u_i)du_i$$

$$= \int_{U_i} \exp[-u_i \{H_{01}(t_{i1}) + H_{02}(t_{i2})\} \exp(x'_i \beta)]f(u_i)du_i$$

$$= E\left[\exp[-u_i \{H_{01}(t_{i1}) + H_{02}(t_{i2})\} \exp(x'_i \beta)]\right]$$

$$= L_{U_i}\left[(H_{01}(t_{i1}) + H_{02}(t_{i2})) \exp(x'_i \beta)\right]$$  \hspace{1cm} (2.5)

where $L(\cdot)$ is the Laplace transform of the distribution of $U$. Thus, the bivariate survivor function is easily expressed by means of the Laplace transform of the frailty distribution, evaluated at the total integrated conditional hazard.

### 2.1 Gamma Frailty

The most popular distribution used for the frailty is the gamma distribution (Vaupel et al., 1979; Oakes, 1982). This model was suggested by Clayton (1978) and Oakes (1982) and hence the model is known as Clayton model or Clayton-Oakes model. As the gamma variates are positive, it fits the non-negative criterion of frailties with no transformation. The gamma distribution (we use notation $\text{Gamma}(\alpha, \kappa)$ for the two parameter distribution with shape parameter $\alpha$ and scale parameter $\kappa$) is one of the
most commonly used distributions to model variables that are necessarily positive. The popularity of the model is due to the fact that the model functions are very easy to derive because of the simplicity of the derivatives of the Laplace transform. Later dependence can be estimated from the early observed values using the gamma frailty assumption. The probability density function (PDF) of gamma distribution is

$$f_U(u) = \frac{\kappa^\alpha u^{\alpha-1} \exp(-\kappa u)}{\Gamma(\alpha)}$$

(2.6)

The Laplace transform of gamma-distributed random variable $U \sim \text{Gamma}(\alpha, \kappa)$ is of a very simple form as:

$$L(s) = E(e^{-us}) = (1 + \frac{s}{\kappa})^{-\alpha}$$

(2.7)

To make the model identifiable, although we consider two parameter gamma distribution, we restrict that expectation of the frailty equals 1, variance be finite and scale parameter = shape parameter, so that only one parameter needs to be estimated.

Thus the mathematical convenient choice for the distribution of the frailty $U$ is the one parameter ($\kappa = \alpha = \theta^{-1}$) gamma distribution i.e.

$$U \sim \text{Gamma}(\theta^{-1}, \theta^{-1})$$

(2.8)

with the corresponding density function

$$f_U(u) = \frac{u^{\theta-1} \exp(-u/\theta)}{\theta^{1/\theta} \Gamma(1/\theta)}$$

(2.9)

The Laplace transform of gamma distribution and unconditional bivariate survivor function are respectively as follows.

$$L_U(s) = (1 + s\theta)^{-1/\theta}$$

(2.10)

and

$$S_\theta(t_{i1}, t_{i2}) = L_U\left[\left\{H_{01}(t_{i1}) + H_{02}(t_{i2})\right\} \exp(x_i'\beta)\right]^{-1/\theta}$$

(2.11)

Since the baseline hazard $h_0(t)$ is the same for all subjects, the hazard function differences between subjects are due to either the frailty term (the cluster they belong to) or the fixed effects.
3  Bivariate Gompertz Regression Model With Gamma Frailty

In parametric proportional hazards model we assume a particular parametric function for the baseline hazard \( h_0(t) \). One of the parametric choice for \( h_0(t) \) leads to lifetimes with a Gompertz distribution as the baseline hazard rate. A vast literature on human mortality suggests the use of the Gompertz baseline hazard rate to describe the mortality and also to model the risk of disease.

The Gompertz baseline hazard rate corresponds to

\[
    h_0(t) = \lambda \exp(\gamma t) \tag{3.1}
\]

with \( \lambda > 0, \gamma \in \mathbb{R} \). For \( \gamma = 0 \) the baseline hazard (3.1) reduces to the exponential hazard.

The corresponding survival function is

\[
    S_0(t) = \exp[-\lambda \gamma^{-1}(\exp(\gamma t) - 1)] \tag{3.2}
\]

We note that for \( \gamma > 0 \), \( S_0(t) \) goes to zero for \( t \to \infty \). With \( \gamma < 0 \), \( S_0(t) \) goes to \( 0 < \exp(\lambda \gamma^{-1}) < 1 \) for \( t \to \infty \). Therefore the event never occurs for a proportion \( \exp(\lambda \gamma^{-1}) \) of the population. We therefore consider the case \( \gamma > 0 \).

In this paper, the two-parameter Gompertz distribution is considered. Let us assume that the two random variables \( T_1 \) and \( T_2 \) have Gompertz distribution with parameters \( \lambda_1, \gamma_1 \) and \( \lambda_2, \gamma_2 \) respectively. In short we say \( Gomp(\lambda_j, \gamma_j), (j = 1, 2) \).

Using (2.1) the resulting regression model

\[
    h(t_{ij}|U_i, X_i) = u_i \lambda_j \exp(\gamma_j t_{ij}) \exp(x_i^j \beta), \quad (j = 1, 2; \; i = 1, \ldots, n) \tag{3.3}
\]

is indeed an extended proportional hazards model conditional on frailty and fixed factors with conditional survival function of the \( j^{th} \) individual in the \( i^{th} \) pair given as

\[
    S(t_{ij}|U_i, X_i) = \exp[-u_i \lambda_j \gamma_j^{-1} \exp(x_i^j \beta) (\exp(\gamma_j t_{ij}) - 1)], \quad t_{ij} \geq 0, \lambda_j > 0, \gamma_j > 0 \tag{3.4}
\]

Thus, the conditional probability density function of the random lifetime \( T_{ij}, (j = 1, 2) \) of the \( i^{th} \) pair, \( (i = 1, 2, \ldots, n) \), takes the following form

\[
    f(t_{ij}|U_i, X_i) = u_i \lambda_j \exp(\gamma_j t_{ij}) \exp(x_i^j \beta) S(t_{ij}|U_i, X_i), \quad t_{ij} \geq 0, \lambda_j > 0, \gamma_j > 0 \tag{3.5}
\]
where \( S(t_{ij}|U_i, X_i) \) is the conditional survival function of \( T_{ij} \) in \( i^{th} \) pair, which is given in (3.4).

Here frailty, \( U \) is common to both components in a group. When there is no variability in the distribution of \( U \), that is, when \( U \) has a degenerate distribution then there is no dependency. When the distribution is not degenerate, the dependence is positive. The value of \( U \) can be considered as generated from unknown values of some explanatory variables. Conditional on \( U = u \), the bivariate survival function is

\[
S(t_{i1}, t_{i2}|U_i, X_i) = S(t_{i1}|U_i, X_i)S(t_{i2}|U_i, X_i)
= \exp[-u_i \exp(x_i' \beta)\{\lambda_1 \gamma_1^{-1}(\exp(\gamma_1 t_{i1}) - 1) + \lambda_2 \gamma_2^{-1}(\exp(\gamma_2 t_{i2}) - 1)\}]
\]

(3.6)

where \( U \) follows gamma distribution given in (2.9).

Integrating over \( U \), we get unconditional joint survival function and is given by

\[
S_\theta(t_{i1}, t_{i2}|X_i) = [1 + \theta \exp(x'_i \beta)\{\lambda_1 \gamma_1^{-1}(\exp(\gamma_1 t_{i1}) - 1) + \lambda_2 \gamma_2^{-1}(\exp(\gamma_2 t_{i2}) - 1)\}]^{-1/\theta}
\]

(3.7)

Once we have unconditional survival function of bivariate random variable \((T_{i1}, T_{i2})\) we can obtain likelihood function and estimate the parameters of the model. For simplicity of expressions, now we will use \( t_{ij} \) as \( t_j \); \( x_i \) as \( x \) and \( S_\theta(\ldots|X_i) \) as \( S_\theta(\ldots) \) for notations in this section.

Now \( S_\theta(t_1, t_2) \) be the bivariate joint unconditional survival function that is absolutely continuous with margins \( S_\theta(t_1, 0) \) and \( S_\theta(0, t_2) \). Consequently, the conditional survival function of \( T_2 \) given \( T_1 = t_1 \) is

\[
S_\theta(T_2|T_1 = t_1) = \frac{\partial S_\theta(t_1, t_2)}{\partial t_1} \left| \frac{\partial S_\theta(t_1, 0)}{\partial t_1} \right|
\]

(3.8)

where

\[
S_\theta(t_1, 0) = [1 + \theta \exp(x' \beta)\lambda_1 \gamma_1^{-1}(\exp(\gamma_1 t_{11}) - 1)]^{-1/\theta}
\]

(3.9)

and

\[
\frac{\partial S_\theta(t_1, 0)}{\partial t_1} = -\exp(x' \beta)\lambda_1 \exp(\gamma_1 t_1)[1 + \theta \exp(x' \beta)\lambda_1 \gamma_1^{-1}(\exp(\gamma_1 t_1) - 1)]^{-(1+\theta)/\theta}
\]

(3.10)
Thus (3.8) becomes

\[ S_\theta(T_2 | T_1 = t_1) = \left[ \frac{1 + \theta \exp(x' \beta) \{ \lambda_1 \gamma_1^{-1} (\exp(\gamma_1 t_1) - 1) + \lambda_2 \gamma_2^{-1} (\exp(\gamma_2 t_2) - 1) \}}{1 + \theta \exp(x' \beta) \lambda_1 \gamma_1^{-1} (\exp(\gamma_1 t_1) - 1)} \right]^{-(1+\theta)/\theta} \]

\[ = \left[ 1 + \frac{\theta \exp(x' \beta) \lambda_2 \gamma_2^{-1} (\exp(\gamma_2 t_2) - 1)}{1 + \theta \exp(x' \beta) \lambda_1 \gamma_1^{-1} (\exp(\gamma_1 t_1) - 1)} \right]^{-(1+\theta)/\theta} \]

let \( S_\theta(t_1, 0) = 1 - y_1 \) then \( t_1 \) is given by the expression

\[ t_1 = \gamma_1^{-1} \log[\lambda_1^{-1} \gamma_1 \theta^{-1} \exp(-x' \beta) \{ (1 - y_1)^{-\theta} - 1 \} + 1] \]

let \( S_\theta(T_2 | T_1 = t_1) = 1 - y_2 \) then \( t_2 \) is given by the expression

\[ t_2 = \gamma_2^{-1} \log[\lambda_2^{-1} \gamma_2 \theta^{-1} \exp(-x' \beta) \{ (1 - y_2)^{-\theta/(1+\theta)} - 1 \} (1 - y_1)^{-\theta} + 1] \]

where \( Y_1 \) and \( Y_2 \) follows uniform distribution, \( U[0, 1] \).

4 Likelihood Specification

Some of the lifetimes are censored because it is not possible to wait until failure of all individuals in the sample. Here the censoring of lifetimes of two implants is due to withdrawals or death of a patient or termination of the study. For the bivariate life time distribution, we consider univariate censoring scheme given by Hanagal (1992a, 1992b) because the individuals do not enter at the same time and withdrawal or death of an individual will censor both lifetimes of the components. Also, we assume independence between the censoring time and the lifetimes of both components. This assumption is sufficient for the distribution of the event times to be identifiable in inference from the censored data (Fleming and Harrington, 1991).

We consider censoring time \( (W) \) is univariate random right censoring type for both failure times \( T_1 \) and \( T_2 \). Suppose that there are \( n \) independent pairs of components, for example, paired kidneys, lungs, eyes, ears in an individual under study and \( i^{th} \) pair of the components have lifetimes \( (t_{i1}, t_{i2}) \) and a censoring time \( (w_i) \). One of the following censoring situations can happen for each data point \( (t_{i1}, t_{i2}) \).

\[
(T_{i1}, T_{i2}) = \begin{cases} 
(t_{i1}, t_{i2}), & \text{if } \max(t_{i1}, t_{i2}) < w_i \\
(t_{i1}, w_i), & \text{if } t_{i1} < w_i < t_{i2} \\
(w_i, t_{i2}), & \text{if } t_{i2} < w_i < t_{i1} \\
(w_i, w_i), & \text{if } w_i < \min(t_{i1}, t_{i2}) 
\end{cases}
\]

(4.1)
Let \( n_1, n_2, n_3 \) and \( n_4 \) denote the random number of observations observed to fall in the range \( t_{i1} \leq w_i, t_{i2} \leq w_i; \ t_{i1} \leq w_i, t_{i2} > w_i; \ t_{i1} > w_i, t_{i2} \leq w_i \) and \( t_{i1} > w_i, t_{i2} > w_i \) respectively. Discarding factors which do not contain any of the parameters, we want to estimate the parameters in the proposed model. Now the contribution of the \( j^{th} \) individual in the \( i^{th} \) pair of the conditional likelihood of data given the parameters, based on the survival function (3.7) is given by

\[
L(t_1, t_2 | \zeta) = \left( \prod_{i \in n_1} f_{i1} \right) \left( \prod_{i \in n_2} f_{i2} \right) \left( \prod_{i \in n_3} f_{i3} \right) \left( \prod_{i \in n_4} F_i \right)
\]

where \( \zeta \) is the vector of baseline parameters, frailty parameter and regression coefficients

\[
f_{i1} = (1 + \theta) \lambda_1 \lambda_2 \exp(2x_i' \beta) \exp(\gamma_1 t_{i1} + \gamma_2 t_{i2}) S_{\theta}^{(1+2\theta)}(t_{i1}, t_{i2} | X_i), \quad \text{max}(t_{i1}, t_{i2}) < w_i
\]

\[
f_{i2} = \lambda_1 \exp(x_i' \beta) \exp(\gamma_1 t_{i1}) S_{\theta}^{(1+\theta)}(t_{i1}, w_i | X_i), \quad t_{i1} < w_i < t_{i2}
\]

\[
f_{i3} = \lambda_2 \exp(x_i' \beta) \exp(\gamma_2 t_{i2}) S_{\theta}^{(1+\theta)}(w_i, t_{i2} | X_i), \quad t_{i2} < w_i < t_{i1}
\]

\[
F_i = P[T_{i1} > w_i, T_{i2} > w_i] = S_{\theta}(w_i, w_i | X_i), \quad w_i < \text{min}(t_{i1}, t_{i2})
\]

and \( S_{\theta}(..,.) \) is given by equation (3.7).

\( f_{i1} \) is the pdf with respect to Lebesgue measure in \( R^2 \) and \( f_{i2} \) and \( f_{i3} \) are the pdf with respect to Lebesgue measure in \( R^1 \) in their respective regions.

## 5 Bayesian Estimation Strategies

In the Bayesian framework, the parameters of the model are viewed as random variables with some distribution known as prior distribution. To apply MCMC methods, we assume that, conditional on explanatory variables and on the entire set of parameters, observations are independent and prior distributions for all parameters are mutually independent. The distribution of a parameter can be updated by combining its prior distribution and the likelihood function, called as posterior density of a parameter. In our case the joint posterior density function of parameters for given failure times is given by,

\[
\pi(\lambda_1, \lambda_2, \gamma_1, \gamma_2, \theta, \beta | t_1, t_2) \propto L(t_1, t_2 | \lambda_1, \lambda_2, \gamma_1, \gamma_2, \theta, \beta) g_1(\lambda_1) g_2(\lambda_2) g_3(\gamma_1) g_4(\gamma_2) g_5(\theta) \prod_{k=0}^{p} p_k(\beta_k)
\]
where $\beta = (\beta_0, \beta_1, \beta_2, \ldots, \beta_p)'$, $g_i(.)$ $(i = 1, 2, \cdots, 5)$ indicates the prior density function which is gamma distribution with known hyper parameters of corresponding argument for baseline parameters and frailty variance; $p_k(.)$ is prior density function for regression coefficient $\beta_k$ which is normal with known hyper parameters and likelihood function $L(.)$ is given by equation (4.3). Given the distribution (4.3) and the priors, all full conditional distributions of the parameters can be calculated. These full conditional distributions are used in a Gibbs sampling procedure. We assume that all the parameters are independently distributed.

Here we use Metropolis-Hastings algorithm within Gibbs sampler to estimate the parameters of the model. Algorithm consists in successively obtaining a sample from the conditional distribution of each of the parameter given all other parameters of the model. These distributions are known as full conditional distributions. The process eventually provides samples from joint posterior distribution of the unknown parameters. In our case full conditional distributions are not easy to integrate out. So full conditional distributions are obtained by considering that they are proportional to the joint distribution of the parameters of the model.

Gelman-Rubin convergence statistic is based on a comparison of within and between chain variance for each variable. When values of this diagnostic are approximately equal to one then sample can be considered to have arisen from the stationary distribution. In this case descriptive statistics or posterior summary can be seen as valid estimates of unknown parameters. Geweke (1992) suggested a test for examining the convergence of a Markov chain in which two sub parts of markov chain (at the end and at the beginning of the convergence period) are compared. The large standardized difference between ergodic averages at the beginning and at the end of the convergence period indicates non convergence. Sample autocorrelation plots can be used to decide autocorrelation lag.

6 Simulation Study

To evaluate the performance of the Bayesian estimation procedure we carried out a simulation study. For the simulation purpose we have considered only one covariate $X = X_1$ which we assume to follow binomial distribution. With one covariate, the shared gamma
frailty model given in (3.7) has six parameters. The frailty variable $U$ is assumed to have gamma distribution with variance $\theta = 3.6$. Lifetimes $(T_{1i}, T_{2i})$ for $i^{th}$ individual are conditionally independent for given frailty $U_i = u_i$. We assume that $T_{ij}$ $(i, \ldots, n; j = 1, 2)$ follows the Gompertz baseline distribution. As the Bayesian methods are time consuming, we generate only fifty, seventy-five and one hundred pairs of lifetimes using inverse transform technique. Equation (3.12) and (3.13) are generators to generate lifetimes for model (3.7). Here we have generated different random samples of size $n = 50, 75$ and 100 for lifetimes $T_{1i}$ and $T_{2i}$ using (3.12) and (3.13). But we are giving procedure for sample generation of only one sample size, say, $n = 50$. Samples are generated using following procedure:

1. Generate 50 covariate values for $X$ from binomial distribution.

2. Compute $\exp(X_i\beta)$ with regression coefficient $\beta = 2$.

3. Generate 50 pairs of lifetimes $(t_{1i}, t_{2i})$ for given covariate $(x_i)$ using following generators,

$$t_{1i} = \gamma_{1}^{-1}\log[\lambda_{1}^{-1}\gamma_{1}\theta^{-1}\exp(-x_{i}'\beta)(1 - y_{1i})^{-\theta} - 1] + 1 \quad (6.1)$$

$$t_{2i} = \gamma_{2}^{-1}\log[\lambda_{2}^{-1}\gamma_{2}\theta^{-1}\exp(-x_{i}'\beta)(1 - y_{2i})^{-\theta/(1+\theta)} - 1(1 - y_{1i})^{-\theta} + 1] \quad (6.2)$$

for (3.7) model, where $y_1$, and $y_2$ are random variables having $U(0, 1)$ distribution and $\gamma_1$, $\lambda_1$ are respectively shape and scale parameters of marginal baseline distribution of first survival time and $\gamma_2$, $\lambda_2$ are that of second survival time.

4. Generate censoring time $w_i$ from exponential distribution with failure rate 0.9.

5. Observe $j^{th}$ survival time $t_{ij} = min(t_{ij}, w_i)$ and censoring indicator $\delta_{ij}$ for $i^{th}$ individual $(i = 1, 2, \ldots, 50$ and $j = 1, 2)$, where

$$\delta_{ij} = \begin{cases} 1, & t_{ij} \leq w_i \\ 0, & t_{ij} > w_i \end{cases}$$

Thus we have data consists of 50 pairs of survival times $(t_{i1}^{*}, t_{i2}^{*})$ and censoring indicators $\delta_{ij}$. 
We run two parallel chains for the proposed model with the different starting points using Metropolis-Hastings algorithm within Gibbs sampler based on normal transition kernels. We iterate both the chains for 95,000 times. Prior distributions that we have assumed for the parameters are respectively, $G(0.0001, 0.0001)$ for baseline parameters $\lambda_1$, $\gamma_1$ and $\gamma_2$ and $G(0.01, 0.01)$ for $\lambda_2$; $G(0.0001, 0.0001)$ for frailty parameter $\theta$ and $N(0, 1000)$ for regression parameter $\beta$. Here $G(a, b)$ is gamma distribution with shape parameter $a$ and scale parameter $b$ and $N(\mu, \sigma^2)$ represents normal distribution with mean $\mu$ and variance $\sigma^2$. For both the chains the results were somewhat similar so we present here the analysis for only one chain (i.e. chain 1) for the resulting model. Also due to lack of space we are not providing graphs.

For the proposed model, Table 1 gives Gelman-Rubin convergence statistic values and in Table 2 Geweke test values with corresponding p-values are given. From the Tables 1 and 2 we can observe that, Gelman-Rubin convergence statistic values are nearly equal to one, also Geweke test values are quite small and corresponding p-values are large enough. So we can say that the chain attains stationary distribution. Simulated values of parameters have autocorrelation of lag $k$ (values given in Table 3), so every $k^{th}$ iteration is selected as a sample from posterior distribution. The posterior mean and standard error with 95% credible intervals are reported in Table 3. From the Table 3, it can be observed that estimated values of parameters reach quite close to true values of the parameters with decreasing standard errors as the sample size goes on increasing. We have used R statistical software to perform this simulation study.

7 Conclusions

The present study focuses on parametric models, which implies parametric specification of the baseline hazard and the distribution of the frailty. We have considered two failure times by allowing for potential dependence in the random quantities corresponding to each failure time which is induced by frailty. Here we have considered the BVG distribution for modeling these two random quantities and frailties are assumed to follow a gamma distribution. In this study, the model is specified in a Bayesian framework and estimated with MCMC algorithms. We have discussed the Bayesian estimation procedure including
Gibbs sampling for computing the estimation of the unknown parameters by simulating samples of different sizes $n = 50, 75,$ and 100. We have clearly written the steps involved in the iteration procedure. As expected, the estimations for the larger sample size are far more accurate. As Bayesian methods proved to be very time-consuming, we have not generated large sample sizes, say, more than 100 for the simulation study.

Two different chains were run for the proposed model from different starting points using Metropolis-Hastings algorithm within Gibbs sampler. We have provided 95,000 iterations to perform simulation study. Estimations were calculated after discarding a “burn-in” interval for each chain. Trace plots for all the parameters shows zigzag pattern which indicates that parameters move more freely. The quality of convergence was checked by Gelman-Rubin statistics (see Brooks and Gelman, 1998). The values of the Gelman-Rubin statistics in this case are quite close to one and also the Geweke test values are small with large p-values. Thus the sample can be considered to have arisen from stationary distribution and descriptive statistics can be seen as valid estimates of unknown parameters. The simulation results indicate that the performance of Bayesian estimation method is quite satisfactory.

References


Appendix A: Summary of Tables

Table 1: Gelman-Rubin Convergence Statistic Values for Simulation

<table>
<thead>
<tr>
<th>Parameters</th>
<th>$\lambda_1$</th>
<th>$\lambda_2$</th>
<th>$\gamma_1$</th>
<th>$\gamma_2$</th>
<th>$\theta$</th>
<th>$\beta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>True values</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>3.6</td>
<td>2</td>
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<tr>
<td>n = 50</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>stat. value</td>
<td>1.010111</td>
<td>1.003496</td>
<td>1.002179</td>
<td>1.000078</td>
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<td>n = 75</td>
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<tr>
<td>stat. value</td>
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<td>n = 100</td>
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<td></td>
</tr>
<tr>
<td>stat. value</td>
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<td>1.000023</td>
<td>1.001366</td>
<td>1.000979</td>
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Table 2: Geweke Test Values and Corresponding p-values for Simulation

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<th>$\gamma_1$</th>
<th>$\gamma_2$</th>
<th>$\theta$</th>
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<tr>
<td>n = 50</td>
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<td></td>
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</tr>
<tr>
<td>test value</td>
<td>-0.001291892</td>
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<td>0.01427394</td>
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<tr>
<td>p-value</td>
<td>0.4994846</td>
<td>0.4971959</td>
<td>0.4970568</td>
<td>0.4994912</td>
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<tr>
<td>test value</td>
<td>-0.00153297</td>
<td>0.01471079</td>
<td>0.004627048</td>
<td>0.002096632</td>
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<tr>
<td>p-value</td>
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<td>n = 100</td>
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<tr>
<td>test value</td>
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<tr>
<td>p-value</td>
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<td>0.5072124</td>
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<td>0.4983871</td>
<td>0.4987355</td>
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Table 3: Parameters Estimates for a Shared Gamma Frailty Model with Gompertz Baseline Hazards

<table>
<thead>
<tr>
<th>Parameters</th>
<th>$\lambda_1$</th>
<th>$\lambda_2$</th>
<th>$\gamma_1$</th>
<th>$\gamma_2$</th>
<th>$\theta$</th>
<th>$\beta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>True values</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>3.6</td>
<td>2</td>
</tr>
</tbody>
</table>

$n = 50$

| Estimates  | 3.339832    | 3.58423    | 0.8029933  | 1.898675   | 3.728842 | 1.784984 |
| S.E.       | 0.5166535   | 0.5047603  | 0.2513277  | 0.2350126  | 0.3168721| 0.2564108|
| LowerLt.   | 2.17248     | 2.030812   | 0.51023    | 1.603307   | 3.039895 | 1.519136 |
| UpperLt.   | 3.935928    | 3.862703   | 1.464501   | 2.375263   | 4.159701 | 2.412618 |

$n = 75$

| Estimates  | 3.275938    | 3.352028   | 0.9781125  | 1.990647   | 3.670445 | 1.807583 |
| S.E.       | 0.4715845   | 0.4150472  | 0.2474298  | 0.1986308  | 0.2753138| 0.2123236|
| LowerLt.   | 2.235856    | 2.462795   | 0.550843   | 1.609894   | 3.114257 | 1.521822 |
| UpperLt.   | 3.927783    | 3.967307   | 1.498642   | 2.360427   | 4.147788 | 2.286009 |

$n = 100$

| Estimates  | 2.818765    | 2.805313   | 1.019907   | 1.997276   | 3.601107 | 1.829282 |
| S.E.       | 0.4173838   | 0.3207179  | 0.2032705  | 0.1980163  | 0.2688608| 0.2091362|
| LowerLt.   | 2.283129    | 2.876453   | 0.5884597  | 1.621737   | 3.180849 | 1.516968 |
| UpperLt.   | 3.783039    | 3.992017   | 1.409367   | 2.37215    | 4.156142 | 2.259177 |