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On Review of Multivariate Frailty Distributions

S.G. Parekh[1*], S.R. Patel[2]

[1*]Faculty of Business Administration, Dharmsinh Desai University, Nadiad, India
[2]Department of Statistics, Sardar Patel University, Vallabh Vidyanagar, India

Corresponding Author: sg_parekh@yahoo.com

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***Abstract*—**This paper deals with the construction of bivariate frailty models and discusses in general multivariate frailty models. Whenever the observations are unmeasurable and not observable then in that case we assume the probability model and generating simulated data analysis of these distribution known as frailty distribution is carried out and compared it with that of real data. The frailty models have been categorised in to three forms such as discrete frailty models, continuous univariate frailty model and multivariate frailty model. In discrete frailty model generally starting from Bernoulli frailty to multinomial frailty model. In continuous multivariate frailty models starting from bivariate frailty models were constructed such as bi-variate gamma frailty model, bi-variate compound Poisson frailty model, bi-variate log-normal frailty model. Further multivariate normal frailty model has been discussed for its properties.

Keywords*—*Frailty distribution, bi-variate frailty models, bi-variate gamma frailty model, bi-variate compound Poisson frailty model, bi-variate log-normal frailty model, Multivariate normal frailty model.

I. INTRODUCTION

Instead of univariate frailty models multivariate frailty models are used in many situations. The model for association in bivariate life tables and its applications in chronic diseases is studied by Clayton, D.G. [2]. The case of a bivariate lognormal frailty discussed by Xue and Brookmeyer [44] and they introduced a modified expectation- maximization algorithm for estimation. Mahe and Chevret [20] have taken the models for estimating both regression coefficients and correlations. Extensively fair literature has been given by Hougaard [11]. Nayak [27], Hougaard [10], Whitmore and Lee [39], Jaisingh, Day, and Griffith [14] have discussed many articles on shared frailty models in the reliability. Hougaard [11] has introduced multivariate frailty model for the dependence of covariates. Further Catalina Stefanescu and Bruce W. Turnbull [1] have considered correlated failure data for Bayesian methods and fitted the models to the data. For finite mixture of stable frailty distributions, Nalini Ravishanker and Dipak K. Dey [26] have used the model for dependent multivariate survival data and they have estimated the parameters of proportional hazard model using Markov chain Monte Carlo method by using kidney infection data. A multivariate frailty model is appropriate for intra cluster depending data. Sahu and Dey [36] have considered frailty models for bivariate data using bivariate exponential and Weibull distribution. They further generated data on diabetic patients for studying retinopathy and compared with the actual data. Using reversed hazard rate multivariate correlated gamma frailty model have been considered by P.G. Sankaran and V.L. Gleeja [33]. Using flexible base line hazard, Madhuja Mallick and Nalini Ravishanker [19] considered an additive stable frailty model for multivariate times to event data. Hanagal [6] has used bivariate Weibull regression frailty model which is generated by a gamma or positive stable or power variance function distribution. Hangal's assumption was that the bivariate survival distribution follows bivatiate Weibull distribution. Hanagal [7] introduced bivariate Weibull regression model with heterogeneity which is generated by Weibull distribution. Taking three base line distributions Weibull, generalized exponential and exponential power distribution Hanagal et al. [9] proposed Inverse Gaussian distribution as frailty distribution. Three different Inverse Gaussian shared frailty models proposed by using three base line distributions and they perform a simulation study and compare the true value of the parameters with the estimated value by taking real data given by McGilchrist and Aisbett [22] of kidney infection data by using MCMC method.

Sahu et.al. [35], Hanagal [8], Parekh et al. [30] have defined bivariate frailty distributions by using either probability measure or conditional distribution and some of them have used for kidney diseases or cancer diseases. Kheiri et.al. [15], Santos et.al. [37] and Parekh et al.[31] have proposed Bayesian frailty models and obtained frailty estimates.

For Bi-variate frailty Models we use the preliminaries as under.

The hazard function of Cox- model called shared frailty model is

$h(t_1, t_2) = Z.h_0(t_1, t_2)e^{X'\beta}$

where T_1 and T_2 are time variables, h_0 is base line hazard function, $\beta' = (\beta_1, \beta_2, \dots \beta_p)$ is a vector of fixed effect

parameters, $X' = (X_1, X_2, \dots X_p)$ is vector of fixed observations and Z has frailty distribution with probability density function $f(z, \theta)$, where θ is frailty parameter. This is known as shared frailty model.
The survival function, $S(t_1, t_2)$ is

$S(t_1, t_2) = L_z\left[\{H_0(t_1) + H_0(t_2)\}e^{X'\beta}\right]$

where $H_0(t_1)$ and $H_0(t_2)$ are cumulative hazard functions of T_1 and T_2 respectively,
L_z is Laplace transformation of Z.
Conditional survival function is given by

$S(t_1, t_2 \mid Z) = S_1(t_1)^z S_2(t_2)^z$

where $S_1(t_1)$ and $S_2(t_2)$ are marginal survival functions.
We consider particular multivariate frailty models in the following section.
Section II discusses bivariate Gamma frailty model by constructing it. In section III we have obtained moment estimator and maximum likelihood estimator of bivariate log-normal frailty model. Section IV discusses the construction of bivariate compound Poisson frailty model. Multivariate normal frailty model with some very important characterizations are discussed in section V. section VI is devoted for conclusion.

II. BI-VARIATE GAMMA FRAILTY MODEL

Fisher R.A. [5] suggested that smoking and lung cancer are correlated and it causes the genetic factors. Further De Faire et al. [4], Marenberg et al. [21] have used genetic study in coronary heart disease. Yashin et al. [45, 46] presented correlated gamma frailty model and used it as life time models. The relation of correlation between frailties and lifetimes analyzed by Lindeboom and Van Den Berg [18]. Correlated gamma frailty model extended by Paik et al. [28]. Yashin and lachine [47, 48, 50, 51, 52], Yashin et al. [49], Iachine et al. [13], Petersen [32], lachine [12], Wienke et al. [42, 43] have discussed that consistency and asymptotic normality of the non-parametric maximum likelihood estimator in the multivariate correlated gamma frailty model with observed covariates.
Bi-variate gamma frailty model can be constructed as under
Let $\gamma_0, \gamma_1, \gamma_2$ be some real positive numbers. Set $p_1 = \gamma_0 + \gamma_1$ and $p_2 = \gamma_0 + \gamma_2$.
Let Y_0, Y_1, Y_2 be independently gamma distributed random variables with $Y_0 \sim G(\gamma_0, p_0), Y_1 \sim G(\gamma_1, p_1), Y_2 \sim G(\gamma_2, p_2)$. Then bivariate gamma frailty variables W_1 and W_2 are given as

$W_1 = \frac{p_0}{p_1} Y_0 + Y_1 \sim G(\gamma_0 + \gamma_1, p_1)$

$W_2 = \frac{p_0}{p_2} Y_0 + Y_2 \sim G(\gamma_0 + \gamma_2, p_2)$

and $EW_1 = EW_2 = 1, V(W_1) = \frac{1}{p_1} := {\sigma_1}^2, V(W_2) = \frac{1}{p_2} := {\sigma_2}^2$

the following results can be easily obtained

(i) $Cov(W_1, W_2) = \frac{\gamma_0}{(\gamma_0+\gamma_1)(\gamma_0+\gamma_2)}$

The correlation coefficient, ρ between W_1 and W_2 is

(ii) $\rho = \frac{\gamma_0}{\sqrt{(\gamma_0+\gamma_1)(\gamma_0+\gamma_2)}}$

Since Y_0, Y_1, Y_2 are independently distributed as Gamma variates, the range of the correlation coefficient between frailties depends on the values of σ_1 and σ_2:

(iii) $0 \leq \rho \leq min\left\{\frac{\sigma_1}{\sigma_2}, \frac{\sigma_2}{\sigma_1}\right\}$

If $\sigma_1 \neq \sigma_2$, ρ is always less than 1.

III. BI-VARIATE LOG-NORMAL FRAILTY MODEL

The correlated log-normal frailty model was used first time by Xue and Brookmeyer [44] has applied it to mental health data to evaluate the health policy effects for inpatient psychiatric care. The correlated log-normal frailty model is used in two-state mixed renewal process for chronic disease by Cook et al. [3] Lee and Lee [16] extended the model to allow for heterogeneity in the frailty distribution. Pankratz et al. [29] perform genetic analysis on age at onset in breast cancer in a large familial cohort using correlated log-normal frailty models.
If $(U_1, U_2)'$ is distributed as bi-variate normal distribution with mean vector $(\mu, \mu)'$and variance co-variance matrix as $\begin{pmatrix} \sigma^2 & \rho\sigma^2 \\ \rho\sigma^2 & \sigma^2 \end{pmatrix}$ and if $U_j = lnW_j (j = 1,2)$
Then bivariate log normal frailty $(W_1, W_2)'$ has bivariate lognormal frailty variables with frailty parameters σ^2 and ρ which can be obtained as under

$\mathrm{E(W_j)} = \mathrm{e}^{\mu + \frac{\sigma^2}{2}}\ ;\ j = 1, 2$

$V(W_j) = e^{2\mu+\sigma^2}(e^{\sigma^2} - 1)\ ;\ j = 1, 2$

$corr(W_1, W_2) = \frac{e^{\rho\sigma^2 - 1}}{e^{\sigma^2} - 1}$

Log normal frailty model is more flexible than Gamma frailty model but Gamma frailty model is easier than log normal frailty model in getting maximum likelihood equations. However maximum likelihood equations are solved by using Markov Chain Monte Carlo (MCMC) method. Yashin et al. [46], Wienke et al. [40, 41] have obtained maximum likelihood estimators of Gamma frailty models whereas McGilchrist [23], Lillard et al. [17], Sastry [38] and Ripatti et al. [34] have obtained maximum likelihood estimators of lognormal frailty distribution.

IV. BI-VARIATE COMPOUND POISSON FRAILTY MODAL

Shared frailty model fails to explain the frailty in the situation where some individuals like cancer patients may survive from cancer. If one of the individuals of the married couple has some problem in fertility and thereby they do not conceive a child which is known as zero susceptibility, so that they may take some time to divorce, which means couples have zero susceptibility. In such situations correlated compound Poisson frailty distribution is useful.

Mogar et al. [24] and Mogar and Aalen [25] considered compound Poisson frailty models with a random scale.

Bivariate compound Poisson frailty model can be obtained as the mixture of Poisson variates and such as if k_0, k_1 and k_2 are real positive numbers and if Y_0, Y_1, Y_2 are independently distributed as compound Poisson variate as $Y_0 \sim CP(\gamma, k_0, \lambda)$, $Y_1 \sim CP(\gamma, k_1, \lambda)$ and $Y_2 \sim CP(\gamma, k_2, \lambda)$ then the bivariate compound poisson frailty variables U_1 and U_2 are

$U_1 = Y_0 + Y_1 \sim CP(\gamma, k_0 + k_1, \lambda)$

$U_2 = Y_0 + Y_2 \sim CP(\gamma, k_0 + k_2, \lambda)$

Some results about U_1 and U_2 are as under

(i) $EU_1 = EU_2 = 1,\ V(U_1) = V(U_2) = \sigma^2$

(ii) $cov(U_1, U_2) = k_0(1-\gamma)\lambda^{\gamma-2}$

The correlation coefficient, ρ between U_1 and U_2 is

(iii) $\rho = \frac{k_0}{k_0 + k_1}$

Gamma and Inverse Gaussian correlated frailty models are special cases of this compound Poisson frailty model.

V. MULTIVARIATE NORMAL FRAILTY MODEL

Let $\underline{X} = (X_1, X_2, \dots, X_p)'$ have multivariate normal distribution with mean vector $\underline{\mu} = (\mu_1, \mu_2, \dots, \mu_p)'$ and variance-covariance $(p \times p)$ matrix, Σ

$$\Sigma = \begin{pmatrix} \sigma_{11} & \sigma_{12} \dots\dots\dots & \sigma_{1p} \\ \sigma_{21} & \sigma_{22} \dots\dots\dots & \sigma_{2p} \\ \vdots & \vdots & \vdots \\ \sigma_{p1} & \sigma_{p2} & \sigma_{pp} \end{pmatrix},$$

that is $\underline{X} \sim N_p(\underline{\mu}, \Sigma)$.

Then some of the important results of this frailty distribution are as under

(i) $E(\overline{\underline{X}}) = \underline{\mu}$

(ii) $E\left(\frac{S}{N}\right) = \Sigma$

Where S is variance-covariance matrix of sample $\underline{X}_1$, $\underline{X}_2, \dots, \underline{X}_N$ having $\underline{X}_i \sim N(\underline{\mu}, \Sigma)$, $(i = 1, 2, \dots, N)$ distribution and $\overline{\underline{X}} = \left(\overline{\underline{X}}_1, \overline{\underline{X}}_2, \dots, \overline{\underline{X}}_N\right)'$.

(iii) The maximum likelihood estimator of μ and Σ are $\overline{\underline{X}}$ and $\frac{S}{N}$ respectively.

(iv) If $\underline{X} = \begin{pmatrix} \underline{X}_{(1)} \\ \underline{X}_{(2)} \end{pmatrix}_{p-r}^{r}$, $\underline{\mu} = \begin{pmatrix} \underline{\mu}_{(1)} \\ \underline{\mu}_{(2)} \end{pmatrix}_{p-r}^{r}$, $\Sigma = \begin{pmatrix} \Sigma_{11} & \Sigma_{12} \\ \Sigma_{21} & \Sigma_{22} \end{pmatrix}$

where Σ_{11} is $r \times r$ matrix, $r < p$, Σ_{12} is $r \times p$ matrix, Σ_{21} is $p \times r$ matrix, Σ_{22} is $p \times p$ matrix then the conditional distribution of $\underline{X}_{(1)}$ given $\underline{X}_{(2)}$ is r-variate normal such as

$\underline{X}_{(1)} | \underline{X}_{(2)} \sim N_r\left(\underline{\mu}_{(1)} - \Sigma_{12}\Sigma_{22}^{-1}(\underline{X}_{(2)} - \underline{\mu}_{(2)}),\ \Sigma_{11.2}\right)$,

were $\Sigma_{11.2} = \Sigma_{11} - \Sigma_{12}\Sigma_{22}^{-1}\Sigma_{21}$.

(v) $\underline{\mu}_{(1)} - \Sigma_{12}\Sigma_{22}^{-1}(\underline{X}_{(2)} - \underline{\mu}_{(2)})$ is the regression of $\underline{X}_{(1)}$ on $\underline{X}_{(2)}$ which also gives regression coefficients

(vi) The variance-covariance matrix $\Sigma_{11.2}$ give rise to partial and multiple correlation coefficients.

VI. CONCLUSION

We have discussed various frailty models in this paper. When the covariates are not observable or not measurable then the model is assumed which is called frailty model. We have discussed discrete and continuous multivariate frailty models such as Bi-variate gamma frailty model, Bi-variate compound Poisson frailty model, Bi-variate log-normal frailty model, Multivariate normal frailty model. In many of them we have constructed the bivariate frailty models and obtained the hazard function, cumulative hazard function and survival function of the frailty model. One may investigate these multivariate frailty models for simulated data and utilize modern techniques in them for future inference.

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