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Univariate frailty distributions: A Review

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***Abstract*—**The main idea of this review article is to review different univariate frailty models discussed by various authors. Particularly Discrete, Gamma, Inverse Gaussian, Generalized exponential, Log normal, Compound Poisson and Compound Negative Binomial frailty distributions are discussed. So far we have furnished the development of different frailty distributions with some important features and we have also provided the recent developments of many frailty distributions. By generating the observations of some distributions, we have obtained maximum likelihood estimators of the parameters with their standard errors involved in these frailty distributions.

Keywords*—Frailty models, Gamma, Inverse Gaussian, Generalized exponential, Log normal, Compound Poisson, Compound Negative Binomial, distributions.*

I. INTRODUCTION

If not all the necessary covariates are included in the model, the distribution is modified making the model parameters based. i.e. it makes the assumption of homogeneity unrealistic. Therefore one needs to introduce some random variables that account for the neglected covariates. We call it hidden heterogeneity or frailty, characterizing the survival changes due to individual variation which is apparently unobservable.

A fair literature of frailty models is available. Starting from the frailty models as exponential distribution early work has been done by many authors such as Sukhatme [58], Epstein and Sobel [14], Epstein [15]. Most of them have considered life time distribution as exponential and they also have given the statistical methodology for hazard rate, cumulative hazard rate, survival time etc. Amongst many authors who have contributed in statistical methodology Mendenhall [37], Govindarajula [17] are main. The Weibull distribution is widely used as life time distribution and many authors like Weibul [61], Berretoni [7], Nelson [42], Whittemore and Altschuler [62] have studied the distribution extensively. Recently Yu [64] and Santosh et al. [52] studied shared Gamma frailty model using base line as Weibull distribution. Clayton [11] has contributed initially for the frailty distribution without the mentioning frailty word. Later on Vaupel et al. [59] has used frailty word in studying survival data. Generally frailty models were utilized for unobserved and unmeasurable data. For heterogamete data Nickell [43] used binary frailty model. Furthermore, this frailty distribution was used by Vaupel and Yashin [60]. Considering the regression model for analysing the effect of omitted variables Schumacher [55], Chamberlain [9], Hougaard et al. [25], Schmoor and Schumacher [53] have used frailty regression models. Murthy et al. [41] differentiated between proportional models and frailty models. Morley et al. [40] have used the notion of frailty in the medical data analysis. Carol and Vonta [8] have utilized frailty model for statistical inference. Jeremy et al. [28] has used the inverse Gaussian model for the improvement of cure rate model. Parekh et al. [44] have extended the idea of homogeneity and introduced the neglected covariates and used random variable for multinomial distribution as frailty distribution. Parekh and Patel [45, 46, 47] have discussed univariate Bayesian frailty models Compound Poisson as well as Compound Negative Binomial and Lognormal frailty models.

Section II deals with some univariate frailty models like, discrete frailty models, Gamma frailty model, generalized exponential frailty model, Log-normal frailty model and Inverse Gaussian frailty model. In section III we have presented some Compound frailty models like, Compound Poisson frailty model and Compound negative Binomial frailty model. In section IV we have concluded the paper theme and suggested future research.

II. SOME UNIVARIATE FRAILTY MODELS

(A) Discrete Frailty Models

Nickell [43] has studied Bernoulli frailty distribution for two types of genotype (presence or absence). Later on Vaupel et al. [60] and Schumacher et al. [54] have considered this type of frailty model. This Bernoulli frailty model has been studied in different context by Fried LP et al. [16], Clegg A et al. [12]. Also Shin SY et al. [57] described genetic influences on human blood metabolites. Krisztina Mekli, James Y. Nazroo et al. [29] and Krisztina Mekli, Alan Marshall [30] both have stated that frailty is the condition of increased stresses in older people which increases in the falling of disability and death. Macdonald [33] has considered 4 types of genotypes of blood such as O, A, B, and AB for discrete frailty model. Parekh et al. [44] obtained maximum likelihood estimator of the parameters of the generated data using multinomial distribution and compared with those of the real data.

(B) Gamma Frailty Model

Gamma distribution is widely used as mixture distribution which has been stated by Vaupel et al. [59], Congdon [13] and Hougaard [26]. Abbring and van den Berg [5] used Laplace transform in survival analysis of the Gamma distribution as frailty model. Many applications of Gamma frailty model are available in the literature such as Lancaster [31], Manton et al. [34], Aalen [1]. Jeong et al. [27] all have used Gamma frailty model for survival data of breast cancers. Parekh and Patel [47] have obtained maximum likelihood estimator of parameter of Gamma distribution by using simulated data given by McGilchrist and Aisbett [36] for kidney infection.

If X has frailty distribution as $G(\lambda,k)$ where the p.d.f. of $G(\lambda,k)$ is

$G(x;\lambda,k)=\frac{\lambda^k}{\Gamma k}t^{k-1}e^{-\lambda t}, x>0,\ \lambda>0,\ k>0$

its Laplace transform is

$L(s)=\left(1+\frac{s}{\lambda}\right)^{-k}.$

Using $L(s)$ one gets survival time $S(x)$, as

$S(x)\ =\ L\big(H_0(x)\big)=(1+\sigma^2H_0(x))^{-\frac{1}{\sigma^2}}$

and $h(x)=\frac{h_0(x)}{1+\sigma^2H_0(x)}$

where $h_0(x)$ is the initial hazard rate and $H_0(x)$ is the cumulative initial hazard rate.

So for maximum likelihood estimator taking the simulated observations $x_1,x,\dots,x_{5000}$ of gamma distribution Likelihood being

$L=\left(\frac{1}{\Gamma\alpha}\right)^n\prod_{i=1}^n({x_i}^{\alpha-1})\,e^{-\sum x_i}$

Likelihood equation will be

$g(\alpha)=log\tilde{x}-\psi(\alpha)$. Where $\tilde{x}$ is geometric mean and $(\alpha)=\frac{\partial log\Gamma\alpha}{\partial\alpha}$, digamma function. Parekh and Patel [47] have obtained maximum likelihood estimator with its standard error for simulated observations.

(C) Generalized Exponential Frailty Model

Instead of gamma and Weibull distribution a strong distribution, generalized exponential distribution has been suggested by Gupta and Kundu [20]. A particular case of generalized exponential distribution with location parameter zero is studied by Gupta and Kundu [19] and they obtained the hazard function, $h_0(t)$, survival function, $S_0(t)$ and cumulative hazard function, $H_0(t)$ for its, p.d.f., $f(t)$

$$f(t)=\alpha\lambda(1-e^{-\lambda t})^{\alpha-1}e^{-\lambda t},\quad t>0,\alpha>0,\lambda>0$$

$$S_0(t)=\begin{cases}1-(1-e^{-\lambda t})^{\alpha} & : t>0,\alpha>0,\lambda>0\\ 1 & : \quad o.w.\end{cases}$$

$$h_0(t)=\begin{cases}\frac{\alpha\lambda(1-e^{-\lambda t})^{\alpha-1}e^{-\lambda t}}{1-(1-e^{-\lambda t})^{\alpha}} & : t>0,\alpha>0,\lambda>0\\ 0 & : \quad o.w.\end{cases}$$

$$H_0(t)=\begin{cases}-ln[1-\left(1-e^{-\lambda t}\right)^{\alpha}] & : t>0,\alpha>0,\lambda>0\\ 0 & : \quad o.w.\end{cases}$$

In place of exponential distribution generalized exponential distribution is used as frailty model.

Parekh and Patel [47] have generated simulated data and found maximum likelihood estimator of the parameters of the frailty generalized exponential distribution for different sample sizes.

(D) Log-Normal Frailty Model

McGilchrist and Aisbett [36], Lillard et al. [32], Xue and Brookmeyer [63], Gustafson [18], Ripatti and Palmgren [50]; Ripatti et al. [51] have studied log-normal distribution as a frailty model which can be used in modelling dependence structures.

A normally distributed random variable X is used to generate frailty log-normal model by taking $Y=e^x$.

The mean and variance of the log-normal distribution with p.d.f.

$f(t;\ \mu,\sigma^2)=\frac{1}{\sqrt{2\pi}\,\sigma t}e^{-\frac{1}{2\sigma^2}(\log t-\mu)^2}, t>0,\mu\geq0,\sigma>0$

And mean $(t)=e^{\mu+\frac{\sigma^2}{2}}$, $var(t)=e^{2\mu+\sigma^2}\left(e^{\sigma^2}-1\right)$

The moment estimators are

$$\hat{\sigma}^2=log\left(\frac{m_2}{{m_1}'^2}+1\right),\quad \hat{\mu}=log{m_1}'-\frac{\hat{\sigma}^2}{2}$$

where ${m_1}'$ is sample mean and m_2 is sample variance

If $t_1,t_2,\dots,t_n$ is the random sample from the log-normal distribution with above p.d.f. then the maximum likelihood estimator $\tilde{\mu}$ and $\tilde{\sigma}^2$ of μ and σ^2 respectively are

$\tilde{\mu}=\frac{1}{n}\sum logt_i=\overline{y}$

where $y_i=logt_i, i=\ 1,2,\dots,n,\quad \tilde{\sigma}^2=\frac{1}{n}\sum(y_i-\overline{y})^2$

Parekh and Patel [47] obtained simulated data of 500 observations and obtained maximum likelihood estimator of μ and σ with their standard errors.

(E) Inverse Gaussian Frailty Model

Schrodinger first time obtained the use of Inverse Gaussian distribution. Chhikara and Folks [10], Seshadri [56] have studied Inverse Gaussian distribution extensively. Benerjee and Bhattacharyya [6] have applied Inverse Gaussian distribution for market research. Hanagal D.D. and Alok D.D. [22] have used the Inverse Gaussian Frailty Model for Bivariate Survival Data. Hougaard [23] introduced Inverse Gaussian distribution as a frailty distribution and later on used by Manton et.al. [35] and Price and Manatunga [48]. Gamma and Inverse Gaussian distribution studied by P. Ecomomou and C. Caroni [49] for unconditional survival function under baseline distribution as Weibull.

III. COMPOUND FRAILTY MODELS

(A) Compound Poisson Frailty Model

Manton et.al, [35], Vaupel and Yashin [60], Hougaard [24] have been discussed compound Poisson distribution to understand and interpret result of survival analysis. Compound Poisson distribution was introduced by Aalen [2] as a frailty distribution. This distribution has been applied to diabetic patients by Hougaard [23]. The distribution was also applied in testicular cancer by Aalen and Tretli [3]. Compound Poisson frailty distribution has been considered by Moger and Aalen [38], Aalen et al. [4], Hanagal [21]. Using the sum of Poisson distributed number of independent and identical gamma distributed random variables, the Compound Poisson distribution can be constructed. A new Compound Poisson frailty distribution was obtained by Moger T. A. et.al. [39].

The Compound Poisson frailty distribution can be constructed as under

$$Z = \begin{cases} X_1 + X_2 + \cdots + X_N & : if\ N > 0 \\ 0 & : if\ N = 0 \end{cases}$$

where N has Poisson distribution with parameter μ where μ is expected value of N and $X_1, X_2, \ldots$ are independently distributed as gamma with $X_i \sim G(m, \alpha)$.

Using the laplace transform of gamma distribution, $L_x(t)$ and that of Poisson distribution $L_N(t)$ are

$$L_x(t) = \left(1 + \frac{t}{\alpha}\right)^{-m},$$

$$L_N(t) = e^{-\mu + \mu e^{-t}}$$

The Laplace transform of Z, $L(t)$ can be obtained as

$$L(t) = e^{-\mu + \mu\left(1 + \frac{t}{\alpha}\right)^{-m}}.$$

Using $L(t)$, the survival function, $S(t)$ will be

$S(t) = L\big(H_0(t)\big)$, $H_0(t)$ is cumulative hazard function

$= m h_0(t)\big(\alpha + H_0(t)\big)^{-(m+1)}$, $h_0(t)$ is hazard function.

Parekh and Patel [47] have obtained normal equations by using maximum likelihood method for compound Poisson distribution. The normal equations are intrinsic in nature.

(B) Compound Negative Binomial Frailty Model

By inverse Binomial sampling if the items are inspected one by one till getting specified defective items which follows negative binomial distribution. If the inspection is carried out until getting one defective item then it is called geometric distribution which is a special case of Negative Binomial distribution. Compound Negative Binomial Frailty model has been used by Aalen and Tretli [3] and analysed it for cancer data.

Compound Negative Binomial frailty distribution can be constructed as

$$Z = X_1 + X_2 + \cdots + X_N$$

where N follows Negative Binomial distribution while $X_1, X_2, \ldots$, are independently distributed as gamma, with $X_i \sim G(m, \alpha)$.

Parekh and Patel [45] have obtained normal equations by using maximum likelihood method for Compound Negative Binomial distribution and normal equations obtained are intrinsic.

IV. CONCLUSION

In this article we have given mostly all univariate frailty models up till utilized. Many authors have contributed the researches on different frailty models such as, Discrete, Gamma, Inverse Gaussian, Generalized exponential, Log normal, Compound Poisson and Compound Negative Binomial frailty distributions. Recently we have also generated observations and simulated some of the frailty distributions and obtained maximum likelihood estimators of the parameters and their standard errors. In some cases we have compared these estimators with those of real data. However it can be tested the appropriateness of the frailty models by some standard methods so one should investigate whether estimators meet the desirable properties.

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