How to model frailty?

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Abstract

The article studies a mixture model, proposed in Finkelstein and Esaulova (2006), which generalizes many popular models, most notably proportional hazards and accelerated life. In this framework we derive that a crucial feature of the frailty distribution is its regular variation at 0. Among the popular distributions to model unobserved heterogeneity, the gamma, beta, Weibull, and truncated normal densities have this property, as opposed to the inverse Gaussian and lognormal distributions.

Keywords: general mixture model, frailty distribution, functions of regular variation

1 Introduction

General mixture models, introduced in Finkelstein and Esaulova (2006) and thoroughly discussed in Finkelstein (2008), generalize many standard survival models, including the two most widely used in demography, epidemiology, medicine, biology, and engineering – the proportional hazards and the accelerated failure time models. In these settings two inverse to one another problems are addressed: (i) given a family of mixing distributions, what is the asymptotic behavior of the mixture failure rate, and (ii) given the asymptotic behavior of the mixture hazard, what is the class of underlying mixing distributions. Functions of regular variation at 0 play an important role in both cases.

Asymptotic behavior of the mixture failure rate is a key feature of mixture models. In demography, for example, the observed leveling-off of the human force of mortality raises questions regarding the underlying model and, in particular, the distribution of individual frailty, a measure of unobserved heterogeneity. The problem, restricted to proportional hazards settings, was studied in Steinsaltz and Wachter (2006). Assuming that the baseline hazard is asymptotically equivalent to a Gompertz curve and the frailty (mixing) distribution behaves in a neighborhood of zero like a power function $c\,z^{\alpha}$, where $c \equiv const$ and

$\alpha > -1$, the authors formulate and prove an Abelian theorem that the resulting mixture (population) hazard rate is asymptotically flat. Inversely, assuming that the mixture hazard rate is asymptotically flat and the underlying mortality distribution follows the Gompertz (or asymptotically Gompertz as $t \to \infty$) law, they described the set of frailty distributions that could produce this leveling-off. Thus Steinsaltz and Wachter (2006) contains also a Tauberian theorem for the proportional hazards model.

The same behavior of the mixing distribution for $z \to 0$ was assumed also in Finkelstein and Esaulova (2006), but for a more general survival model. The authors of Finkelstein and Esaulova (2006) derive independently the asymptotic result in Steinsaltz and Wachter (2006) and, moreover, prove that the mixture hazard rate for the accelerated failure time model tends to zero with time, regardless of the baseline lifetime distribution. This implies that if human mortality is asymptotically flat, then the underlying model is certainly not accelerated failure time.

In this paper we, first, generalize the Abelian theorem of Finkelstein and Esaulova (2006) for the wider class of frailty distributions with regularly varying densities. Second, given the asymptotic behavior of the mixture hazard rate, we derive simple sufficient conditions for the form of the corresponding distribution of frailty. These general results could hopefully contribute to the better understanding of oldest-old human mortality patterns like, for example, the observed special case of asymptotically flat mortality.

2 Preliminaries

Let $T \geq 0$ be a lifetime random variable characterized by a survival function $S(t)$. Suppose $S(t)$ is conditioned by a random variable $Z \geq 0$ (frailty) with a pdf $\pi(z)$:

$$S(t,z) := P(T > t \,|\, Z = z) \equiv P(T > t \,|\, z),$$

where $P(A)$ denotes the probability of event A.

Suppose the pdf $f(t,z) = -S'_t(t,z)$ exists and denote the corresponding hazard rate by $\mu(t,z)$:

$$\mu(t,z) = \frac{f(t,z)}{S(t,z)}.$$

Then the mixture survival function, density and hazard will be

$$S_m(t) = \int\limits_0^\infty S(t,z)\pi(z)dz, \;\; f_m(t) = \int\limits_0^\infty f(t,z)\pi(z)dz, \;\; \mu_m(t) = \frac{f_m(t)}{S_m(t)},$$

respectively. Assume that the mixing distribution's pdf $\pi(z), z \geq 0$, belongs to the family defined as

$$\pi(z) = z^\alpha \pi_1(z), \tag{1}$$

where $\alpha > -1$, and the function $\pi_1(z)$ is (i) bounded in $[0, +\infty)$, (ii) continuous and non-vanishing at $z = 0$. Assume, in addition, that the failure distribution is characterized by a cumulative hazard

$$H(t, z) = \int_0^t \mu(x, z)dx = A(z\phi(t)). \tag{2}$$

where $A(\cdot)$ and $\phi(\cdot)$ are differentiable and strictly increasing, i.e. $\lim_{s\to+\infty} A(s) = +\infty$ and $\lim_{t\to+\infty} \phi(t) = +\infty$. Model (2), defined at the level of the cumulative hazard rather than the hazard rate itself, generalizes many standard models. For instance, when $A(s) \equiv s$ and $\phi(t) = H(t)$, it reduces to proportional hazards. If $A(s) = H(s)$ and $\phi(t) \equiv t$, then (2) is equivalent to accelerated failure time. Note that, (2) can be trivially adjusted by an additive term to account for additive hazards and related models (see Finkelstein (2008)).

Under weak assumptions (see Finkelstein and Esaulova (2006)) the mixture hazard $\mu_m(t)$ has the following asymptotics

$$\mu_m(t) \sim (\alpha + 1)\,\frac{\phi'(t)}{\phi(t)} \qquad t \to \infty, \tag{3}$$

where $a(t) \sim b(t)$ denotes $\lim_{t\to\infty} a(t)/b(t) = 1$. Eq. (3) means that asymptotic behavior of $\mu_m(t)$ depends only on α and the derivative of the logarithm of the scaling function $\phi(t)$. Thus, for the Gompertz proportional hazards model

$$A(s) \equiv s\,, \qquad \phi(t) = H(t) = \frac{a}{b}\,(e^{bt} - 1)\,,$$

the mixture failure rate tends to a constant:

$$\mu_m(t) \sim (\alpha + 1)b \equiv const.$$

Note that, this result is true for any mortality distribution such that (see Steinsaltz and Wachter (2006))

$$\lim_{t\to\infty} \frac{\mu(t)}{H(t)} = b.$$

We will refer further to such distributions as “Gompertz-like”.

In this paper we show, first, that the Abelian theorem proved in Finkelstein and Esaulova (2006) holds not only for frailty densities (1), but also for any pdf that is a product of z^α

and a function of regular variation with power α larger than -1. Then, we prove the inverse (Tauberian) result: given (3), we derive the corresponding class of mixing distributions. We derive a simple sufficient condition for checking whether a mixing distribution belongs to this family. Finally, we consider, as simple examples, a number of widely used frailty distributions, among which the gamma, the log-normal, and the inverse Gaussian, and check whether they are plausible in the sense of the Tauberian result.

3 Abelian Theorem for Densities of Regular Variation

We adopt the definitions in Feller (1971) for functions of slow and regular variation at 0 (see also Bingham et al. (1989)).

Definition 1: A positive function $G(t)$ defined on $(0, \infty)$ is slowly varying at 0 if

$$\lim_{t \to 0} \frac{G(kt)}{G(t)} = 1.$$

for every fixed $k > 0$.

Definition 2: A positive function $F(t)$ defined on $(0, \infty)$ is regularly varying at 0 with power $-\infty < p < \infty$, if

$$\lim_{t \to 0} \frac{F(t)}{t^p \, G(t)} = 1.$$

where $G(t)$ is a slowly varying function at 0.

As far as we know, only a few papers relate these functions to mixture models. For example, in the special case of a mixture of exponential distributions (see Abbring and van den Berg (2007)) if "proportional frailty" Z is regularly varying at 0, then the random variable Zt converges in distribution to the gamma distribution with parameters 1 and p (see also Block and Joe (1997)). We will use the idea of regular variation for $z \to 0$ to generalize the Abelian theorem in Finkelstein and Esaulova (2006).

As asymptotic relationship (3) depends on the mixing distribution just in terms of its power characteristic α in a neighborhood of zero, the definitions above suggest that (3) can be valid for a wider than (1) class of mixing distributions with a pdf

$$\pi(z) = z^{\alpha} \, G(z) \, \pi_1(z), \tag{4}$$

where $G(z)$ is a slowly varying at 0 function. In fact, instead of $G(z) \, \pi_1(z)$ we can assume, in general, any regularly varying function with power α, but in view of Definition 2 and relationship (1), we consider in this section frailty with density (4). The proof in Finkelstein and Esaulova (2006) can be generalized to account for the extra multiplicative term $G(z)$. Thus, the following extension to the Abelian theorem for the general mixture model (2) holds:

Theorem 1. *Let the cumulative hazard $H(t, z)$ of a mixture failure model be given by (2) and the pdf of frailty Z be*

$$\pi(z) = z^{\alpha}\, G(z)\, \pi_1(z),$$

where $\alpha > -1$, $G(z)$ is a slowly varying at 0 function, and $\pi_1(z)$, $\pi_1(0) \neq 0$, is a bounded in $[0, \infty)$ and continuous at $z = 0$ function.

Assume that

$$\int_0^{\infty} e^{-A(s)} s^{\alpha}\, ds < \infty, \tag{5}$$

and, in addition

$$\lim_{s\to\infty} A(s) = \infty \qquad \text{and} \qquad \lim_{t\to\infty} \phi(t) = \infty.$$

Then

$$\mu_m(t) \sim (\alpha + 1)\, \frac{\phi'(t)}{\phi(t)}.$$

The gamma distribution satisfies (4), whereas (4) does not hold for the inverse Gaussian and the log-normal.

4 Tauberian Results for the Mixture Failure Rate

Mixture models are not identifiable in the absence of covariates (see Elbers and Ridder (1982)). Knowing the mixture distribution, we have to specify first, implicitly or explicitly, the underlying failure distribution in order to describe the mixing distribution. We will assume that the cumulative hazard rate for individuals with frailty $Z = z$ is given by (2). Then a class of frailty distributions that produce a mixture hazard rate with asymptotics (3) is given by the following

Theorem 2. *Let the cumulative hazard rate* $H(t,z)$ *be given by (2) and* $\lim_{t\to\infty}\phi(t) = \infty$, $\lim_{s\to\infty} A(s) = \infty$. *Suppose that the mixture failure rate* $\mu_m(t)$ *satisfies*

$$\mu_m(t) \sim c\,\frac{\phi'(t)}{\phi(t)} > 0 \qquad t\to\infty,$$

where $c > 0$.

Then the pdf $\pi(z)$ *of the mixing (frailty) distribution satisfies for* $z \to 0$

$$\frac{\int\limits_0^\infty e^{-A(z\,\phi(t))}\, z\,\pi'(z)\,dz}{\int\limits_0^\infty e^{-A(z\,\phi(t))}\,\pi(z)\,dz} \sim c-1. \tag{6}$$

Condition (6) is given in asymptotic terms. As a result, it is difficult to describe explicitly the class of admissible frailty distributions within the framework of model (2). Nevertheless, it can be shown that certain functions of regular variation belong to this class. We will prove first the following

Theorem 3. *Suppose the assumptions of Theorem 2 hold and, in addition, the pdf* $\pi(z)$ *satisfies*

$$\lim_{z\to 0}\frac{z\,\pi'(z)}{\pi(z)} = c-1 \tag{7}$$

Then relationship (6) holds.

Assumption (7) provides a convenient criterion for checking the admissibility of $\pi(z)$. The following theorem simplifies this procedure even more.

Theorem 4. *Let*

1. $\pi(z)$ *be a regularly varying at* 0 *function defined as*

$$\pi(z) = z^{c-1}\,G(z)\,, \tag{8}$$

where $c > 0$.

2. $\pi'(z)$ be asymptotically monotone as $z \to 0$.

Then relationship (7) holds.

The proofs of Theorems 1, 2, 3, and 4 can be found in Missov and Finkelstein (2011).

5 Examples of Mixing Distributions

In this section, for simple illustration, we will examine several popular mixing distributions for modelling frailty – the gamma Vaupel et al. (1979), the log-normal McGilchrist and Aisbett (1991), the inverse Gaussian Hougaard (1984), as well as the beta and the Weibull distributions that are less commonly used. For each of them we will check whether its density satisfies the sufficient condition (7) of Theorem 3. Thus, we can classify the distributions mentioned above into two groups: "admissible" and "non-admissible" within the general framework (2).

5.1 "Admissible" Frailty Distributions

The Gamma Distribution

The density of the gamma distribution

$$f_\Gamma(z;\lambda,k) = \frac{\lambda^k}{\Gamma(k)}\, z^{k-1}\, e^{-\lambda z}$$

satisfies (7) for $k = c$. Indeed,

$$z\,\pi'(z) = \pi(z)\,(k-1-\lambda z)$$

and that is why

$$\lim_{z\to 0} \frac{z\,\pi'(z)}{\pi(z)} = k-1.$$

We can prove this also by checking the necessary conditions of Theorem 4: the gamma density satisfies (8) with $k = c$, the function $G(z) = \lambda^k\, e^{-\lambda z}/\Gamma(k)$ is slowly varying at 0, and its derivative is asymptotically ($z \to 0$) monotone.

The Weibull Distribution

Although not frequently used as a frailty (but rather as a baseline failure) distribution, the Weibull distribution with parameters $a > 0$ and $b > 0$ is also admissible in terms of (7). Its density

$$\pi(z) = f_{\text{Weibull}}(z; a, b) = \frac{a}{b} \left(\frac{z}{b}\right)^{a-1} e^{-\left(\frac{z}{b}\right)^a} \tag{9}$$

implies that

$$z\,\pi'(z) = \pi(z) \left(a - 1 - \frac{a}{b^a}\, z^a\right)$$

and, as a result,

$$\lim_{z \to 0} \frac{z\,\pi'(z)}{\pi(z)} = a - 1$$

The Beta Distribution

The beta density is given by

$$\pi(z) = f_{\text{Beta}}(z; a, b) = \frac{z^{a-1}(1-z)^{b-1}}{B(a,b)}, \tag{10}$$

where $B(a,b) = \int\limits_0^1 x^{a-1}\,(1-x)^{b-1}\,dx$ is the beta function. Taking advantage of

$$z\,\pi'(z) = \pi(z) \left(a - 1 - \frac{b-1}{1-z}\, z^a\right),$$

we can see that (7) is fulfilled for $a = c$. Alternatively, we can prove that the beta distribution is admissible by applying Theorem 4.

The Truncated Normal Distribution

The truncated normal density is given by

$$\pi(z) = f_{\mathrm{tN}}(z;\mu,\sigma^2,a,b) = e^{-\frac{z^2}{2}} \frac{1}{\sigma\sqrt{2\pi}\left(\Phi(\frac{b-\mu}{\sigma} - \frac{a-\mu}{\sigma})\right)}, \tag{11}$$

where $\Phi(x)$ is the cumulative distribution function of the standard normal distribution. Taking advantage of

$$z\,\pi'(z) = -z^2\,\pi(z),$$

we can see that (7) is fulfilled for $a = 1$.

5.2 "Non-Admissible" Frailty Distributions

The Log-Normal Distribution

The log-normal distribution with a location parameter $m \in \mathbb{R}$ and a squared scale parameter $\sigma^2 > 0$, used in survival models among others in McGilchrist and Aisbett (1991), has a density

$$\pi(z) = f_{\mathrm{logN}}(z;m,\sigma^2) = \frac{1}{z\sigma\sqrt{2\pi}} \exp\left\{-\frac{(\ln z - m)^2}{2\sigma^2}\right\},$$

which implies

$$z\,\pi'(z) = \pi(z)\left(-1 - \frac{\ln z - m}{\sigma^2}\right).$$

In this case (7) does not hold as $\lim_{z\to 0} \ln z = -\infty$. As a result, the log-normal distribution cannot be picked up as a mixing distribution in the framework of (2).

The Inverse Gaussian Distribution

The inverse Gaussian distribution with parameters $\mu, \lambda > 0$ has a pdf

$$\pi(z) = f_{\mathrm{InvGauss}}(z;\mu,\lambda) = \sqrt{\frac{\lambda}{2\pi z^3}} \exp\left\{-\frac{\lambda(z-\lambda)^2}{2\mu^2 z}\right\},$$

which yields

$$z\,\pi'(z) = \pi(z)\left(-\frac{3}{2} - \frac{\lambda}{2\mu}\,z + \frac{\lambda^3}{2\mu z}\right).$$

Due to the last term in the parentheses, which tends to infinity as $z \to 0$, (7) does not hold. Therefore, the inverse Gaussian distribution is also excluded from the class of plausible distributions for the general model (2).

6 Conclusion

This paper aims at answering the question what distributions we may use for frailty if mortality has certain asymptotic behavior (see Missov and Finkelstein (2011)). We study a general mixture model, proposed by Finkelstein and Esaulova (2006), which includes as special cases the proportional hazards and the accelerated failure time models. The latter cannot produce a plateau as its mixture hazard rate tends to zero. In the case of proportional hazards, the mortality distribution is "Gompertz-like" and the frailty distribution is given either as in Steinsaltz and Wachter (2006), or by (6). If the model is not proportional hazards, then we can still classify the plausible mixing distributions by (6) or (7). Theorem 4 offers a suitable sufficient condition for checking whether a distribution belongs to a subset of the "plausible" class. Among the popular distributions used to describe frailty, the ones that satisfy (6) are the gamma, beta, and Weibull distribution.

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