

Mortality Plateau – the Gamma-Gompertz and Other Plausible Mixture Models

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Abstract

Statistical analysis of data on supercentenarians revealed that the human force of mortality is flat after age 110. This implies that either human mortality levels off or it abandons the observed plateau after a certain age. We consider a general model introduced by Finkelstein and Esaulova (2006) which represents a mixture of a baseline failure distribution and a mixing (frailty) distribution that accounts for unobserved heterogeneity among individuals. In this article we describe under certain assumptions a class of frailty distributions that implies the asymptotic behavior of the mixture hazard rate of this general model.

Introduction

The International Database of Longevity (IDL 2010) offers detailed information on thoroughly validated cases of supercentenarians. Gampe (2010) used these data to estimate the human force of mortality after age 110. Her analysis revealed that human mortality after age 110 levels off regardless of gender. Time trends in supercentenarian mortality between earlier and later cohorts do not play the slightest role, too. Human mortality is flat at a level corresponding to a 50% annual probability of death (Gampe 2010; Robine et al. 2005). This finding raises at least two important questions that this article addresses: i) given that human mortality becomes flat after age 110,

what is the underlying model?; ii) how sure can one be that mortality will not drop down to zero at later ages, at which there are still no officially recorded survivors, and how would this change the underlying model?

Steinsaltz and Wachter (2006) studied the inverse problem for a proportional hazards frailty model. Assuming that the baseline hazard is asymptotically equivalent to a Gompertz curve and the mixing distribution behaves like a power function z^α , $\alpha > -1$, in a neighborhood of zero, they prove an Abelian theorem that the resulting mixture hazard rate is asymptotically flat. Finkelstein and Esaulova (2006) studied a more general survival model, which has as special cases the two most widely used survival models in demography: the proportional hazards and the accelerated failure time model. Assuming the same behavior of the mixing distribution for $z \rightarrow 0+$, they derive independently the asymptotic result of Steinsaltz and Wachter (2006) and, moreover, prove that the mixture hazard rate for the accelerated life model tends to zero with time.

Steinsaltz and Wachter (2006) proved also a Tauberian theorem for the proportional hazards model, i.e. assuming that the hazard rate of the mixture is asymptotically flat and the underlying mortality distribution is undistinguishable from a Gompertz one with time, they described the set of frailty distributions that could produce this leveling-off. Thus, Steinsaltz and Wachter (2006) answer question i) in the case of proportional hazards.

If a proportional hazards model produces a mortality plateau and an accelerated failure time model results in a mortality rate that approaches zero, can we conclude that if we observe flat mortality at oldest-old ages, the model is necessarily a proportional hazards one? In general, no because Abelian theorems do not provide information on the speed of convergence of the mixture failure rate to its asymptotic value. Thus, we are not sure whether the plateau after age 110 is the eventual leveling-off of the force of mortality, or it is merely an interval of mortality constancy which could be followed, for instance, by its decrease to zero. That is why this article studies the model of Finkelstein and Esaulova (2006), which is a generalization of both proportional hazards and accelerated failure time models.

Preliminaries

Standard survival analysis models incorporate a baseline mortality law, a term that accounts for observed heterogeneity (usually a linear predictor of covariates), and a scheme by which these two are linked together. For ex-

ample, factors may affect individual hazard multiplicatively, thus producing a proportional hazards model. They may instead preserve the same mortality pattern for everyone, but assign individual-specific time scaling, thus producing an accelerated failure time model. These and other standard survival analysis models can be extended to account for unobserved heterogeneity by introducing a random variable $Z \geq 0$, called *frailty*, that captures individual-specific susceptibility to experiencing the event of interest, in demography usually death (Vaupel et al. 1979). Frailty models are by their nature proportional hazards models as frailty is assumed to act multiplicatively on individual hazard rates. This paper focuses on a wider class of models, formulated first by Finkelstein and Esaulova (2006), which includes as special cases the two most commonly used survival models in demography, epidemiology, medicine, biology, and engineering – the proportional hazards model and the accelerated failure time model.

Let $T \geq 0$ be a lifetime random variable characterized by a survival function $S(t)$ or equivalently by a cumulative hazard $H(t)$. Suppose $S(t)$ is indexed by a random variable $Z \geq 0$ 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 . Z , often called *frailty* in proportional hazards models, accounts for variability in individual predisposition to experiencing the event of interest. In proportional hazards settings Z is a multiplicative factor acting on individual hazard, which means that the bigger Z (i.e. the “frailer” an individual), the higher the corresponding hazard rate.

Suppose the pdf $f(t, z) = -S'_t(t, z)$ exists and the corresponding hazard is denoted by $\mu(t, z)$, i.e.

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

Then the mixture survival function and pdf, i.e. the survival and density functions of the population, will be defined as

$$S_m(t) = \int_0^\infty S(t, z)\pi(z)dz, \quad f_m(t) = \int_0^\infty f(t, z)\pi(z)dz$$

Then the mixture failure rate, i.e. the hazard rate of the population, will be given by

$$\mu_m(t) = \frac{\int_0^{\infty} f(t, z)\pi(z)dz}{\int_0^{\infty} S(t, z)\pi(z)dz}$$

Mixture failure rates behave asymptotically as a positive constant in Gompertz proportional hazards frailty models (Finkelstein and Esaulova 2006; Steinsaltz and Wachter 2006) and as a decreasing to zero function in accelerated failure time models (Finkelstein and Esaulova 2006) if the mixing distribution's probability distribution function $\pi(z)$, $z \geq 0$, is defined as (Finkelstein and Esaulova 2006)

$$\pi(z) = z^\alpha \pi_1(z), \quad (1)$$

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

$$H(t, z) = \int_0^t \mu(x, z)dx = A(z\phi(t)), \quad \frac{dA(s)}{ds} > 0, \frac{d\phi(t)}{dt} > 0 \quad (2)$$

As the cumulative hazard $H(t, z)$ is always a differentiable non-decreasing function equal to zero at $t = 0$, it is assumed that the functions $A(\cdot)$ and $\phi(\cdot)$ are differentiable, as well as $A(z\phi(0)) = 0$. Finkelstein and Esaulova (2006) introduce a slightly stronger assumption about $A(\cdot)$ and $\phi(\cdot)$ (increasing instead of merely non-decreasing), which means that $\lim_{s \rightarrow +\infty} A(s) = +\infty$ and $\lim_{t \rightarrow +\infty} \phi(t) = +\infty$. For $e^{-A(z\phi(t))}$, which is the survival function of the mixture lifetime distribution, Finkelstein and Esaulova (2006) introduce an additional assumption, namely the existence of its $(\alpha + 1)$ -st moment

$$\int_0^{\infty} e^{-A(s)} s^\alpha ds < \infty \quad (3)$$

This indicates that the mixture lifetime distribution is not “too heavy-tailed”. Thus, assuming (1), (2), and (3), (Finkelstein and Esaulova 2006) proved that

$$\mu_m(t) \sim (\alpha + 1) \frac{\varphi'(t)}{\varphi(t)} \quad t \rightarrow \infty \quad (4)$$

where $a(t) \sim b(t)$ denotes $\lim_{t \rightarrow \infty} a(t)/b(t) = 1$. Eq. (4) means that the asymptotic behavior of the mixture failure rate depends solely on the behavior of the mixing distribution in the neighborhood of zero and the derivative of the logarithm of the scaling function $\varphi(t)$. Thus for the Gompertz proportional hazards model, i.e. $A(s) \equiv s$, $\varphi(t) = H(t) = a/b(\exp(bt) - 1)$ in (2), the mixture failure rate tends to a constant: $\mu_m(t) \sim (\alpha + 1)b \equiv \text{const}$. Note that this result is true for any mortality distribution such that $\mu(t)/H(t) \rightarrow b$ as $t \rightarrow \infty$ (Steinsaltz and Wachter 2006). We will call the class of such distributions “Gompertz-like” as their relative derivative is asymptotically constant.

The Main Finding: A Tauberian Theorem for the Mixture Failure Rate

The mortality plateau observed by Gampe (2010) is independent of gender and time trends in supercentenarian mortality between earlier and later cohorts. As univariate frailty models are not identifiable in the absence of covariates (Elbers and Ridder 1982; Heckmann and Singer 1984; Hoem 1990; Yashin et al. 1994), we have to specify the underlying mortality distribution if we want to draw inference about 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 (10) is given by the following

Theorem 1. *Let the cumulative hazard rate $H(t, z)$ is given by (2). Suppose that the mixture failure rate $\mu_m(t)$ satisfies*

$$\mu_m(t) \sim c \frac{\varphi'(t)}{\varphi(t)} > 0 \quad t \rightarrow \infty$$

Assume that the mixing distribution has a probability density function $\pi(z)$ such that $\forall z \geq 0$

$$z\pi'(z) - (c-1)\pi(z) \geq 0 \quad \text{or} \quad z\pi'(z) - (c-1)\pi(z) \leq 0 \quad (5)$$

and in addition $\pi(z)$ is differentiable and non-vanishing in a neighborhood of $z = 0$. Then $\pi(z)$ is the solution to the equation

$$\lim_{z \rightarrow 0^+} [z\pi'(z) - (c-1)\pi(z)] = 0 \quad (6)$$

The proof of Theorem 1 is presented in the Appendix. Note that

$$\pi(z) \sim C z^{c-1} \quad z \rightarrow 0^+, \quad (7)$$

where $C > 0$ is a constant, is one of the solutions in (6). This is exactly the class of distributions (1) specified in the Abelian theorems of Finkelstein and Esaulova (2006) and Steinsaltz and Wachter (2006).

A special case of Theorem 1 is the Tauberian theorem of Steinsaltz and Wachter (2006). The proof of the latter is based, though, on the asymptotic properties of the Laplace transform, which plays an important role in proportional hazards models: $\mu_m(t)$ is the Laplace transform of the mixing distribution, calculated for the baseline hazard $H(t)$ (Hougaard 1986). In (2), however, the mixture failure rate $\mu_m(t)$ cannot be expressed, in general, in terms of the Laplace transform. That is why the proof of Theorem 1 is based solely on the properties of limits and integrals.

Theorem 1 is an inverse (Tauberian) theorem to the Abelian theorem by Finkelstein and Esaulova (2006). As Tauberian theorems are by default weaker than their Abelian counterparts, Theorem 1 imposes an extra condition (5). It postulates that the density of the mixing distribution $\pi(z)$ should be such that $z\pi'(z) - (c-1)\pi(z)$ has a non-alternating sign. We will explore in the following section how restrictive this assumption can be by looking at several popular mixing distributions: the Gamma distribution (Vaupel et al. 1979), the log-normal distribution (McGilchrist and Aisbett 1991), the compound Poisson distribution (Aalen 1992), and the inverse Gaussian distribution.

Examples of Mixing Distributions

The Gamma distribution with unit mean and variance $\sigma^2 = 1/k > 0$ was introduced by Vaupel et al. (1979) for studying univariate frailty models. Its density

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

satisfies the second inequality in (5) if

$$c \geq k$$

This is consistent with (7), as for $f_{\Gamma}(z; k)$ we have $c = k$. As a result, the Gamma distribution is a plausible mixing distribution for the general model (2). If we assume that the mixture failure rate $\mu_m(t)$ is asymptotically constant, i.e. that $\varphi'(t)/\varphi(t) \sim b \equiv \text{const}$, then this plateau results from a Gamma-Gompertz or a Gamma-“Gompertz-like” mixture model.

The log-normal distribution with a location parameter $m \in \mathbb{R}$ and a squared scale parameter $\sigma^2 > 0$ was used in survival models by McGilchrist and Aisbett (1991). If we substitute its density

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

in the right-hand side of (5), then we will get values of opposite signs before and after $z = \exp\{m - \sigma^2 c\}$. As a result (5) is not fulfilled for the log-normal distribution. Thus the latter cannot be picked up as a mixing distribution in (2).

The compound Poisson distribution, introduced by Aalen (1992), is generated by Gamma variables, i.e. a compound Poisson random variable Z is defined as

$$Z = \begin{cases} 0 & N = 0 \\ \sum_{i=1}^N Z_i & N > 0 \end{cases}, \quad (8)$$

where N is a Poisson random variable and Z_1, \dots, Z_N are mutually independent Gamma random variables that are also independent of N . This model is constructed in such a way that its Laplace transform could be easily calculated. It provides a generalization of the three-parameter model in Hougaard (1986). The density of the Gamma-generated compound Poisson distribution can be explicitly given by

$$f_{\text{CPois}}(z; \lambda, \alpha, \delta, \gamma) = f_{\text{Pois}}(0; \lambda) \cdot \exp \left\{ -\frac{\alpha}{\delta(\alpha - 1)} \right\} + (1 - f_{\text{Pois}}(0; \lambda)) \cdot \exp \left\{ -\frac{\alpha}{\delta} \left(\frac{z}{\gamma} + \frac{1}{\alpha - 1} \right) \right\} \cdot \frac{1}{z} \sum_{k=1}^{\infty} \frac{(\alpha/\delta)^{k\alpha} (z/\gamma)^{k(\alpha-1)}}{k! \Gamma(k(\alpha - 1)) (\alpha - 1)^k}$$

(Aalen 1992), where $\alpha, \delta \geq 0$, $\lambda, \gamma > 0$, and $f_{\text{Pois}}(\cdot; \lambda)$ is the density of the Poisson distribution. However, it is more convenient in this case to work with the Laplace transform of $f_{\text{CPois}}(z; \lambda, \alpha, \delta, \gamma)$. We will check (5) by applying the Hausdorff-Bernstein-Widder theorem (Widder 1946), which states that a function is non-negative if and only if its Laplace transform is monotone. The Laplace transform \mathcal{L} of $f_{\text{CPois}}(z; \lambda, \alpha, \delta, \gamma)$ is

$$\mathcal{L} [f_{\text{CPois}}] (s) = \exp \left\{ \frac{\alpha}{\delta(1 - \alpha)} \left[1 - \left(1 + \frac{\delta\gamma}{\alpha} s \right)^{1-\alpha} \right] \right\}$$

and the Laplace transform of $zf'_{\text{CPois}}(z; \lambda, \alpha, \delta, \gamma)$ is

$$\mathcal{L} [zf'_{\text{CPois}}] (s) = -\mathcal{L} [f_{\text{CPois}}] (s) - s\mathcal{L}' [f_{\text{CPois}}] (s)$$

Differentiating $\mathcal{L} [zf'_{\text{CPois}}] (s) - (c - 1)\mathcal{L} [f_{\text{CPois}}] (s)$ with respect to s , we get that this function is monotone if and only if

$$c \leq \delta\gamma - 1 \tag{9}$$

This is the necessary and sufficient condition for a distribution from the Gamma-generated compound Poisson family to be a suitable distribution for model (2). Note that the gamma distribution, which is a special case of (8) when $N = 1$, satisfies (9).

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

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

which satisfies (5) for all values of $\mu, \lambda, c > 0$.

Conclusion

This paper aims at answering two questions: i) if mortality levels off, what frailty distributions imply this result; and ii) if mortality does not eventually level off, what can we say in this case about the underlying frailty distribution. 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. As a result, if mortality gets flat at oldest-old ages, the underlying model can be proportional hazards or some other, excluding the accelerated failure time model. 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). Among the popular distributions used to describe frailty, the ones that satisfy (6) are the Gamma, the compound Poisson distribution with parameters in accordance with (9), and the inverse Gaussian distribution.

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Appendix: Proof of Theorem 1

The mixture failure rate $\mu_m(t)$ can be expressed as a ratio of two integrals:

$$\mu_m(t) = -\frac{\int_0^{\infty} S'(t, z) \pi(z) dz}{\int_0^{\infty} S(t, z) \pi(z) dz} = -\frac{\varphi'(t) \int_0^{\infty} e^{-A(z\varphi(t))} A'(z\varphi(t)) z \pi(z) dz}{\int_0^{\infty} e^{-A(z\varphi(t))} \pi(z) dz} \quad (10)$$

The integral in the numerator of (10) reduces to

$$\begin{aligned} & - \int_0^{\infty} e^{-A(z\varphi(t))} A'(z\varphi(t)) z \pi(z) dz = -\frac{1}{\varphi^2(t)} \int_0^{\infty} e^{-A(s)} A'(s) s \pi\left(\frac{s}{\varphi(t)}\right) ds = \\ & = \frac{1}{\varphi^2(t)} \left(\int_0^{\infty} e^{-A(s)} \pi\left(\frac{s}{\varphi(t)}\right) ds + \frac{1}{\varphi(t)} \int_0^{\infty} e^{-A(s)} s \pi'\left(\frac{s}{\varphi(t)}\right) ds \right) \end{aligned}$$

and the integral in the denominator of (10) can be expressed as

$$\int_0^{\infty} e^{-A(z\varphi(t))} \pi(z) dz = \frac{1}{\varphi(t)} \int_0^{\infty} e^{-A(s)} \pi\left(\frac{s}{\varphi(t)}\right) ds$$

The asymptotic result for $\mu_m(t)$

$$\mu_m(t) \sim c \frac{\varphi'(t)}{\varphi(t)}$$

can be rewritten as

$$\frac{\frac{1}{\varphi(t)} \int_0^{\infty} e^{-A(s)} s \pi'\left(\frac{s}{\varphi(t)}\right) ds}{\int_0^{\infty} e^{-A(s)} \pi\left(\frac{s}{\varphi(t)}\right) ds} \sim c - 1$$

which is equivalent to

$$\int_0^{\infty} e^{-A(s)} \left[\frac{s}{\varphi(t)} \pi' \left(\frac{s}{\varphi(t)} \right) - (c-1) \pi \left(\frac{s}{\varphi(t)} \right) \right] ds \sim 0 \quad (11)$$

As the integrand is either a non-positive or a non-negative function for all s , (11) implies that

$$\lim_{t \rightarrow \infty} \left[\frac{s}{\varphi(t)} \pi' \left(\frac{s}{\varphi(t)} \right) - (c-1) \pi \left(\frac{s}{\varphi(t)} \right) \right] = 0$$

Substituting back $z := s/\varphi(t)$ and solving the resulting differential equation completes the proof of the theorem. Q.E.D. \square