

# Mortality Implications of Mortality Plateaus\*

Trifon I. Missov<sup>†</sup>  
James W. Vaupel<sup>‡</sup>

**Abstract.** This article aims to describe in a unified framework all plateau-generating random effects models in terms of (i) plausible distributions for the hazard (baseline mortality) and the random effect (unobserved heterogeneity, frailty) as well as (ii) the impact of frailty on the baseline hazard. Mortality plateaus result from multiplicative (proportional) and additive hazards, but not from accelerated failure time models. Frailty can have any distribution with regularly-varying-at-0 density and the distribution of frailty among survivors to each subsequent age converges to a gamma distribution. In a multiplicative setting the baseline cumulative hazard can be represented as the inverse of the negative logarithm of any completely monotone function. If the plateau is reached, the only meaningful solution at the plateau is provided by the gamma-Gompertz model.

**Key words.** Gompertz hazard, gamma-distributed frailty, mortality plateau, proportional hazards, additive hazards, completely monotone functions

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**I. Introduction.** George Udny Yule [1] was intrigued by the findings of “Miss Chick” [2] that bacteria subjected to the action of a toxin experienced a constant force of mortality after some length of exposure. Such a mortality plateau puzzled him. On the one hand, it seemed reasonable that death rates would rise with increasing exposure. On the other hand, it also seemed plausible that death rates should fall as the most susceptible individuals died, leaving a more robust population of survivors. That these alternative processes could exactly balance seemed impossible to Yule, so he concluded that the population of bacteria was homogeneous, each bacterium experiencing the same, constant force of mortality.

Beard [3] and Vaupel, Manton, and Stallard [4] introduced a mortality model for heterogeneous human populations that implied an asymptotic mortality plateau. If for each individual in the population the hazard of death increases exponentially according to the Gompertz formula  $Ae^{bx}$ , where  $x$  denotes age,  $b$  is the rate of aging (same for all individuals), and  $A$  is a random variable called “frailty” that follows a gamma distribution across individuals with mean  $a$  at the initial age and a squared

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<sup>†</sup>Max Planck Institute for Demographic Research, 18057 Rostock, Germany; University of Rostock, 18057 Rostock, Germany (missov@demogr.mpg.de).

<sup>‡</sup>Max Planck Institute for Demographic Research, 18057 Rostock, Germany; Max-Planck Odense Center on the Biodemography of Aging, University of Southern Denmark, Odense, Denmark; Duke University Population Research Institute, Durham, NC.

coefficient of variation  $\gamma$  at all ages, then  $\bar{\mu}(x)$ , the force of mortality for the population (i.e., on average for surviving individuals), is given by  $\bar{\mu}(x) = ae^{bx}/[1+(a\gamma/b)(e^{bx}-1)]$ . As age  $x$  increases, this force of mortality approaches a constant  $b/\gamma$ . Statistical analysis of human mortality data at ages 110+ [5] has found evidence for an actual leveling-off of the human force of mortality between ages 110 and 114 [6]. Claims of a mortality decline at advanced ages have been shown to be artifacts of inaccurate data (see [7, 8, 9]).

Mortality plateaus imply that either individual hazards in a homogeneous population decelerate and level off, or mortality selection of individuals with increasing hazards causes the hazard of a heterogeneous population to bend over and eventually flatten. Unobserved heterogeneity can have genetic, environmental, or other origins. Experiments with nonhuman species were set up to test the effects of genetically [10, 11, 12] and environmentally [13, 14] induced variation on the existence and formation of mortality plateaus. The unidentifiability of frailty models in the absence of ancillary information, though, made it impossible to differentiate between the homogeneous and the heterogeneous models. A recent article by Chen, Zajitschek, and Maklakov [15] seems to have overcome this obstacle and argues that heterogeneity explains mortality deceleration in nematodes.

There are three main questions regarding mortality-plateau modeling: (1) how does frailty affect baseline mortality, i.e., how is the mixture distribution constructed? (2) what characterizes the distributions of baseline mortality and frailty? and (3) what meaningful conjugate pairs of baseline mortality and frailty can be used in practice?

**2. Modeling Mortality Plateaus.** Models in which  $b$  is constant for all individuals, but  $A$  varies from individual to individual, are known as proportional hazards (multiplicative) models. Their wide application is to a great extent due to the fact that the marginal distribution is expressed in terms of the Laplace transform of the frailty distribution. In this setting, Steinsaltz and Wachter [16] approached question (2) by applying the Abelian and Tauberian theorems (see Chapter XIII in [17]) for the Laplace transform of a frailty distribution whose density is equivalent to a gamma density in a vicinity of zero. The Tauberian theorem returned, though, a much wider class of frailty distributions, which indicated that “gamma distributions are common but not generic distributions for frailty among survivors” [16, p. 26].

Finkelstein and Esaulova [18] independently reached the same (as in [16]) conclusion about frailty. However, they considered a general framework incorporating accelerated failure time, proportional hazards, and additive hazards models. In accelerated failure time models both parameters  $A$  and  $b$  can vary from individual to individual. Finkelstein and Esaulova [18] proved that if  $b$  follows a continuous distribution over all positive or nonnegative numbers, then the population’s (marginal) force of mortality must decline to zero with age. This finding implies that mortality plateaus cannot be modeled by accelerated failure time models. That is why proportional hazards and additive hazards models are of particular importance for modeling mortality plateaus.

Missov and Finkelstein [19] extended the findings in [16] and [18] by proving that frailty at the initial age can have any distribution with density that regularly varies at zero (the distributions specified in [16] and [18] belong to this family). Conversely, Missov and Finkelstein [19] proved that if the force of mortality approaches a plateau at advanced ages, then frailty is characterized by a regularly-varying density. In addition, Abbring and van den Berg [20] proved that such distributions converge with age to a gamma distribution. That is, in proportional hazards models a wide range

of initial frailty distributions (“of regular variation”) approach a gamma distribution as  $x \rightarrow \infty$ .

There are numerous discrete-age models for stage-structured populations (e.g., [21, 22]) that lead to a plateau. In some of them the force of mortality first rises and then declines to eventually flatten out, unlike the hazard of death for humans and bacteria which continuously increases until it levels off. There is at least one continuous-time stage-based model (by Le Bras [23]) that generates the latter schedule. However, Yashin, Vaupel, and Iachine [24] proved its equivalence to the model by Vaupel, Manton, and Stallard [4].

In general, individual lifetimes are modeled by two alternative methods, either (A) by specifying a lifetime distribution accounting for unobserved heterogeneity (frailty models) or (B) by considering lifetimes as first passage points of a random deterioration process. The idea for the latter was proposed initially by [25] in terms of “vitality”: death occurs when vitality falls below a threshold, accounting for the magnitude of incoming “challenges.” Weitz and Fraser [26] use a different name (“viability”) with a death threshold at 0, while Steinsaltz and Evans [27] consider multidimensional Markov processes (i.e., multiple sources of change in vitality) with an initial quasi-stationary distribution of states. The conceptual novelty in these models is the inclusion of changing frailty (the model by Weitz and Fraser is essentially the same as the one analyzed by Anderson [28] and later extended in [29]). Steinsaltz and Evans [27] consider both changing frailty and multidimensionality of the underlying deterioration process. Wachter [30] studies a class of Markovian evolutionary demographic models for the genesis of mortality plateaus, and Demetrius [31] studies mortality plateaus in the context of populations with bounded growth whose evolutionary stable strategy aims at maximizing entropy [32]. All these models present sufficient conditions for mortality plateaus, while in this article we look for necessary conditions.

In this article we follow modeling scheme (A) for several reasons. Although in both (A) and (B) we define a mortality model for the individual, we often work with aggregate data, i.e., models for the population. For frailty models we have a simple tool (the Laplace transform) to switch from the individual (conditional on frailty) model to the one (marginal) for the population. Second, in modeling scheme (A) the fixed frailty term accounts for all the information that the deterioration process dynamics in (B) contain. The latter is more interesting to explore if one is interested in the biology of aging. In this article, though, we have a more modest goal: to clarify how we should model lifetimes based on the information that mortality rates level off. Third, in frailty models every parameter has a specific demographic meaning. Demographers, epidemiologists, and evolutionary biologists compare these parameters across different populations. This is why we try to keep the model parsimonious, so that statistical estimation of parameters is feasible. Finally, we assume frailty to be fixed for a simple reason: models are usually fitted to data starting from some later (adult) age  $x_0$ , when all effects of infant, child, adolescent, and young-adult mortality are no longer present. If frailty (at birth) changes (and it probably does) as one ages, we can assume that it changes from birth to the initial age  $x_0$  at which we start fitting. After that, we assume that it stays constant.

In this article we address the following question: given that mortality eventually levels off, can we describe the underlying model? In particular, if the underlying model is given in terms of proportional hazards or additive hazards, what are the distributions of baseline mortality and frailty? If (i) a population is heterogeneous, (ii) its force of mortality eventually levels off, and (iii) the underlying model is defined

in terms of proportional hazards or additive hazards, we characterize the class of baseline mortality distributions. We also show the conditions under which the model with exponentially increasing baseline and gamma-distributed frailty holds, since the gamma-Gompertz model seems to be the one of greatest practical importance.

**3. General Relationships for Heterogeneous Populations.** Let the force of mortality at age  $x$  for an individual with frailty  $Z = z$  be denoted by  $\mu(x|z)$ . Frailty  $Z$  is a random variable that measures unobserved individual susceptibility to death. The population's force of mortality  $\bar{\mu}(x)$  at age  $x$  is then the weighted average of all  $\mu(x|z)$  with respect to the frailty distribution, with density  $\pi(x, z)$ , of survivors to  $x$ :

$$\bar{\mu}(x) = \int_0^{\infty} \mu(x|z)\pi(x, z)dz.$$

Without specifying  $\pi(x, z)$  and  $\mu(x|z)$ , we can take advantage of several general results. Denote

$$\frac{\partial \mu(x|z)}{\partial x} = \dot{\mu}(x|z).$$

Then (see [33, 34])

$$(3.1) \quad \dot{\bar{\mu}}(x) = \bar{\dot{\mu}}(x) - \sigma_{\mu}^2(x),$$

where

$$\bar{\dot{\mu}}(x) = \int_0^{\infty} \dot{\mu}(x|z)\pi(x|z)dz$$

is the average change in  $\mu(x|z)$  with age  $x$  and

$$\sigma_{\mu}^2(x) = \int_0^{\infty} \mu^2(x|z)\pi(x, z)dz - \bar{\mu}^2(x)$$

measures the variance of  $\mu(x|z)$  across all subpopulations with different frailties.

Suppose the force of mortality is asymptotically flat:  $\lim_{x \rightarrow \infty} \bar{\mu}(x) = \bar{\mu}^*$ , i.e., for all  $\varepsilon > 0$  there exists age  $x_{\varepsilon}$  such that for  $x > x_{\varepsilon}$

$$(3.2) \quad |\bar{\mu}(x) - \bar{\mu}^*| < \varepsilon.$$

Suppose for simplicity that the mortality plateau is reached. This means that there exists  $x^*$  such that for  $x > x^*$ ,  $\bar{\mu}(x) = \bar{\mu}^*$  and, consequently,  $\dot{\bar{\mu}}(x) = 0$ . As a result, for  $x > x^*$  (3.1) is equivalent to

$$(3.3) \quad \bar{\dot{\mu}}(x) = \sigma_{\mu}^2(x).$$

This equation can be solved analytically only under strong assumptions about the frailty distribution or the behavior of  $\mu(x|z)$  with age. Taking advantage of the fact that plateaus cannot result from accelerated failure time models (see [18]), we will first focus on the solution of (3.3) in a proportional hazards setting. Accelerated failure time and proportional hazards provide the two most widely used frameworks for analyzing time-to-event data in demography, epidemiology, medicine, biology, and engineering. That is why the solution of (3.3) in the latter case could be useful.

**4. Mortality Plateau Inferences for Proportional Hazards.** Suppose the force of mortality  $\mu(x|z)$  at age  $x$  for an individual with frailty  $z$  is given by (see [4])

$$(4.1) \quad \mu(x|z) = z\mu(x|1).$$

Then

$$(4.2) \quad \bar{\mu}(x) = \bar{z}(x)\mu(x|1),$$

$$(4.3) \quad \bar{\dot{\mu}}(x) = \bar{z}(x)\dot{\mu}(x|1),$$

$$(4.4) \quad \sigma_{\mu}^2(x) = \mu^2(x|1)\sigma_z^2(x),$$

where

$$(4.5) \quad \bar{z}(x) = \int_0^{\infty} z\pi(x, z)dz$$

is the average frailty of survivors to age  $x$ . Dividing both sides of (3.1) by  $\bar{\mu}(x)$ , we can draw an inference about the relative change in the population's force of mortality,

$$\frac{\dot{\bar{\mu}}(x)}{\bar{\mu}(x)} = \frac{\bar{\dot{\mu}}(x)}{\bar{\mu}(x)} - \frac{\sigma_{\mu}^2(x)}{\bar{\mu}(x)}.$$

Taking into account (4.2)–(4.4), we get

$$\frac{\dot{\bar{\mu}}(x)}{\bar{\mu}(x)} = \frac{\dot{\mu}(x|1)}{\mu(x|1)} - \frac{\sigma_z^2(x)}{\bar{z}(x)}\mu(x|1).$$

Denoting  $\hat{\mu}(x) = \dot{\mu}(x)/\mu(x)$  and using the fact that  $CV_z^2(x) := \sigma_z^2(x)/\bar{z}^2(x)$  is the squared coefficient of variation of the frailty distribution at age  $x$ , we finally find

$$(4.6) \quad \dot{\bar{\mu}}(x) = \hat{\mu}(x|1) - \bar{\mu}(x)CV_z^2(x).$$

Thus, the relative change  $\dot{\bar{\mu}}(x)$  in the marginal (population's) force of mortality  $\bar{\mu}(x)$  is equal to the difference between the relative change in the baseline force of mortality  $\mu(x|1)$  and  $\bar{\mu}(x)$  itself, modulated by the squared coefficient of variation  $CV_z^2(x)$  of the frailty distribution  $\pi(x, z)$  among survivors to age  $x$ .

Suppose  $\mu(x|1)$  follows a Gompertz curve,

$$\mu(x|1) = ae^{bx}.$$

Then, if the distribution of frailty at age 0 is gamma  $\Gamma(k, \lambda)$ , i.e., its density  $\pi(0, z)$  is given by

$$\pi(0, z) = \frac{\lambda^k}{\Gamma(k)} z^{k-1} e^{-\lambda z}, \quad k, \lambda > 0,$$

the population's force of mortality has a logistic shape and levels off with age  $x$  (see [3, 4]), i.e.,

$$\lim_{x \rightarrow \infty} \bar{\mu}(x) = \bar{\mu}^* \equiv \text{const}.$$

As a result, the assumptions about Gompertz baseline mortality and gamma frailty distribution at age 0 is a sufficient condition for an eventual mortality plateau.

Formulating necessary conditions for mortality plateaus requires the solution of equations which are valid only asymptotically. Steinsaltz and Wachter [16] as well as Missov and Finkelstein [19] derived such conditions, i.e., proved the respective Tauberian theorems for the multiplicative model and a general model (with the multiplicative as a special case), respectively. In this article we avoid asymptotic equations by assuming that the marginal hazard actually reaches the plateau.

Suppose the force of mortality is asymptotically flat and the plateau is reached for  $x > x^*$ . Then  $\dot{\mu}(x) = 0$  and, for  $x > x^*$ , (4.6) is equivalent to

$$(4.7) \quad \dot{\mu}(x | 1) = \bar{\mu}^* CV_z^2(x).$$

When the solution of (4.7) is degenerate, i.e.,  $\dot{\mu}(x | 1) = CV_z^2(x) = 0$ , then the population is homogeneous and the baseline hazard is flat. Another interesting special case is when (4.7) has a trivial solution

$$(4.8) \quad \dot{\mu}(x | 1) = b \equiv \text{const}, \quad CV_z^2(x) = \frac{b}{\bar{\mu}^*} \equiv \text{const}.$$

The first relationship in (4.8) implies that for  $x > x^*$  the relative derivative of  $\mu(x | 1)$  is constant, which means that  $\mu(x | 1)$  follows a Gompertz curve. The second relationship in (4.8) implies that the frailty distribution at age 0 should be such that the resulting frailty distribution among survivors to age  $x$ ,  $x > x^*$ , has a constant coefficient of variation.

In general, if no degenerate or trivial solutions are considered, (4.7) implies that for  $x > x^*$  the relative change in the baseline force of mortality  $\dot{\mu}(x | 1)$  should equal the adjusted (by a factor  $\bar{\mu}^*$ ) squared coefficient of variation of the frailty distribution among survivors to age  $x$ . Suppose for simplicity  $\bar{\mu}(x) = \mu^*$  for  $x > 0$ . Then marginal survivorship can be expressed as

$$(4.9) \quad \bar{s}(x) = \mathcal{L}_{\pi(0,z)}(H(x | 1)) = e^{-\mu^* x},$$

where  $\mathcal{L}_{\pi(0,z)}(H(x | 1))$  is the Laplace transform of the frailty distribution  $\pi(0, z)$  calculated for the baseline cumulative hazard  $H(x | 1) = \int_0^x \mu(t | 1) dt$ . Reorganizing (4.9), we get<sup>1</sup>

$$(4.10) \quad x = -\frac{1}{\mu^*} \ln \mathcal{L}_{\pi(0,z)}(y), \quad y = H(x | 1).$$

Applying Bernstein's theorem [35], which characterizes Laplace transforms of positive Borel measures on  $[0, \infty)$ , we get that  $\mathcal{L}_{\pi(0,z)}(\cdot)$  is the class of completely monotone functions with supremum equal to 1 (recognizing that  $\pi(0, z)$  is a pdf). As a result,  $H(x | 1)$  can be any function that is inverse to the adjusted (by  $1/\mu^*$ ) negative logarithm of a completely monotone function. How restrictive is this condition?

As the cumulant generating function  $\psi(H)$  of  $H(x | 1) =: H$  is given by the left-hand side of (4.10), we find

$$(4.11) \quad x = \psi(H) = \kappa_1 H - \frac{\kappa_2}{2} H^2 + \frac{\kappa_3}{6} H^3 + \dots,$$

<sup>1</sup>This idea and most derivations given to the end of this section are from Kenneth W. Wachter (personal communication).

where  $\kappa_i$ ,  $i = 1, 2, \dots$ , are the cumulants of the frailty distribution at the starting age. By series reversion we can express the baseline cumulative hazard  $H$  as

$$(4.12) \quad H = \frac{1}{\kappa_1}x + \frac{\kappa_2}{2\kappa_1^3}x^2 + \frac{3\kappa_2^2 - \kappa_1\kappa_3}{6\kappa_1^5}x^3 + \dots$$

and the baseline hazard  $\mu(x|1)$  itself (multiplied by  $\kappa_1$ ) as

$$(4.13) \quad \kappa_1 \mu(x|1) = 1 + \frac{\kappa_2}{\kappa_1^2}x + \frac{3\kappa_2^2 - \kappa_1\kappa_3}{2\kappa_1^4}x^2 + \dots$$

or, on a log-scale, as

$$(4.14) \quad \ln\{\kappa_1 \mu(x|1)\} = \frac{\kappa_2}{\kappa_1^2}x + \frac{2\kappa_2^2 - \kappa_1\kappa_3}{2\kappa_1^4}x^2 + \dots$$

As a result, the baseline hazard can have various shapes, including the Gompertz shape, that are conjugate to gamma-distributed frailty. The existence of an infinite number of conjugate pairs producing the same mortality plateau was recognized by Vaupel and Carey [36]. These shapes, however, are ad hoc and may not be biologically plausible.

**5. The Gamma-Distributed Frailty at the Plateau.** Vaupel, Manton, and Stalard [4] introduced  $\Gamma(k, \lambda)$  as a frailty distribution at age 0 and showed that the distribution of frailty among survivors to any subsequent age  $x$  is also gamma with the same shape parameter  $k$  and a different scale parameter  $\lambda(x) = \lambda + H(x|1)$ , accounting for the cumulative risk of dying according to the baseline mortality schedule  $\mu(x|1)$ . The mean frailty of individuals at age 0 is  $k/\lambda$ , whereas the mean frailty among survivors to age  $x$  is given by  $k/[\lambda + H(x|1)]$ . The variance of frailty at age 0 is  $k/\lambda^2$ , and the variance of frailty at age  $x$  is  $k/[\lambda + H(x|1)]^2$ . Thus, for all  $x$ , the frailty distribution among survivors to age  $x$  has a constant squared coefficient of variation  $CV_z^2(x)$  equal to  $1/k$ . As a result, the gamma distribution satisfies the second relationship in (4.8) for all  $x$  (not just  $x > x^*$ ).

The inverse statement holds as well. Suppose a survival model is defined by (4.1) and  $CV_z^2(x)$  is constant. Then we can rewrite the second equation in (4.8) by taking advantage of the  $CV_z^2(x)$  representation via the Laplace transform  $\mathcal{L}_{\pi(0,z)}$  of the frailty distribution  $\pi(0, z)$  calculated for the baseline cumulative hazard  $H(x|1)$ :

$$(5.1) \quad CV_z^2(x) = \frac{\mathcal{L}_{\pi(0,z)}(s)\ddot{\mathcal{L}}_{\pi(0,z)}(s)}{\dot{\mathcal{L}}_{\pi(0,z)}^2(s)} \Bigg|_{s=H(x|1)} - 1.$$

If  $CV_z^2(x) = c - 1 \equiv const$  for all  $x$ , then the following differential equation holds:

$$(5.2) \quad y\ddot{y} = cy^2,$$

where  $y = y(s) = \mathcal{L}_{\pi(0,z)}(s)$ . Its solution is given by

$$(5.3) \quad y(s) = \left(1 + \frac{s}{c_1}\right)^{c_2},$$

where  $c_1$  and  $c_2$  are constants resulting from indefinite integration. This is the Laplace transform of the gamma distribution. As every distribution  $\pi(0, z)$  is defined uniquely

by its moment-generating function  $MG_{\pi(0,z)}(t)$ , which is simply  $\mathcal{L}_{\pi(0,z)}(s)$  for  $s = -t$ , the gamma frailty distribution at  $x = 0$  is the only one for which the frailty's coefficient of variation at any subsequent age  $x$  is constant.

The trivial solution of (4.7) suggests that if the coefficient of variation of the frailty distribution for all  $x$  is constant, then the frailty distribution is gamma and, consequently, the baseline mortality is Gompertz. This follows directly from the first equation in (4.8) by solving the respective differential equation.

**6. Discussion.** When studying human mortality, the Gompertz assumption below age 30 fails to capture either the observed high level of infant mortality or the peak at young adult ages. The latter is mostly due to accident-related mortality resulting from risky behavior. On the other hand, the popularity of the gamma distribution for modeling frailty is mainly associated with computational convenience. Moreover, the gamma-Gompertz model can be reparametrized in such a way that the resulting mixture of distributions does not change [24]. It is a general result that univariate frailty models are unidentifiable unless one of the underlying distributions is specified [37]. This means that the gamma-Gompertz model is not the only one that captures the logistic shape of the force of mortality. A wide class of plausible models is described in [16, 18, 19]. However, when it comes to modeling (in a proportional hazards setting), the simplest and perhaps the only meaningful pair is the gamma-Gompertz, which, as we have illustrated in the previous section, arises from the trivial solution (4.8).

The Gompertz distribution results from truncation at zero of a type I generalized extreme value (the Gumbel) distribution. That is why, along with the Weibull (type III generalized extreme value) distribution, it is the most widely used parametric model to capture aging processes. From a biological perspective, the death of an organism occurs when the first regulatory system fails. If the failure times of these systems are identically distributed (no matter whether correlated or not) random variables, then the limiting distribution of minimal failure times will be a generalized extreme value distribution. If the baseline is Weibull, then the marginal hazard eventually drops down to zero. As a result, the Gompertz distribution is the only meaningful candidate from the generalized extreme value distribution family that generates mortality plateaus.

$\Gamma(k, \lambda)$  provides one of the possible frailty distributions at age 0 that yields a mortality plateau. In general, in a proportional hazards setting the eventual leveling-off of the marginal force of mortality can result from any frailty distribution with a density  $\pi(0, z)$  such that  $\pi(0, z) = z^\alpha G(z)$ , where  $G(z)$  is a function of regular variation at 0 with power  $\alpha > -1$  (see [19]). Regularly varying (with  $\alpha > -1$ ) densities  $\pi(0, z)$  converge in distribution to a gamma for  $x \rightarrow \infty$  (see [20]), which means that the resulting frailty distribution  $\pi(x, z)$  among survivors to age  $x$  has a constant coefficient of variation. Thus, regularly varying densities  $\pi(0, z)$  do generate mortality plateaus in a proportional hazards setting.

We have considered multiplicative models for two reasons. First, Finkelstein and Esaulova [18] proved that the population's force of mortality in accelerated failure time models always tends to zero and, thus, never levels off at a positive constant level. Second, apart from proportional hazards and accelerated failure time, there are hardly any other mixture survival models that offer a reasonable interpretation of the underlying aging and selection processes. One of the possible plateau-generating mechanisms outside the proportional hazards framework is given by an additive hazards model

$$(6.1) \quad \mu(x|z) = zae^{bx} + c(x),$$



where  $c(x) \geq 0$ ,  $\lim_{x \rightarrow \infty} c(x) = c \equiv \text{const}$ , and frailty is “regularly varying” in the sense described in the previous paragraph. When  $c(x) = c$ , this is the standard gamma-Gompertz–Makeham model. It is easy to see that (6.1) satisfies (4.6) if  $\bar{\mu}(x)$  levels off. Moreover, the baseline force of mortality is asymptotically equivalent to the Gompertz curve  $ae^{bx} + c(x) \sim ae^{bx}$  for  $x \rightarrow \infty$ . Note that this is the only plateau-generating additive hazards model, which follows directly from Theorem 1 in [18].

**7. Conclusion.** The observed leveling-off of human mortality rates at ages 110+ has four major implications for the generating mechanism. First, plateaus can be modeled in the framework of multiplicative (proportional) or additive hazards, but not by accelerated failure time models. Second, the distribution of unobserved heterogeneity has a regularly-varying-at-zero density at the starting age and converges subsequently to the gamma distribution. Third, in a proportional hazards setting the baseline cumulative hazard is the inverse of the negative logarithm of any completely positive function, and the well-known gamma-Gompertz pair can be derived as a special meaningful case. Fourth, in an additive hazards setting plateaus are generated by taking the latter proportional hazards pattern and adding a frailty-independent term that levels off with age. Many conjugate pairs, i.e., pairs of baseline mortality and frailty distributions, can produce the same mortality pattern. The only demographically meaningful multiplicative model that holds at the plateau is the gamma-Gompertz.

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## REFERENCES

- [1] G. U. YULE, *On the distribution of deaths with age when the causes of death act cumulatively, and similar frequency distributions*, J. Roy. Statist. Soc., 73 (1910), pp. 26–38.
- [2] H. CHICK, *An investigation of the laws of disinfection*, J. Hygiene, 8 (1908), p. 92.
- [3] R. BEARD, *Note on some mathematical mortality models*, in *The Lifespan of Animals*, G. E. W. Woolstenholme and M. O’Connor, eds., Little, Brown and Company, Boston, MA, 1959, pp. 302–311.
- [4] J. W. VAUPEL, K. MANTON, AND E. STALLARD, *The impact of heterogeneity in individual frailty on the dynamics of mortality*, Demography, 16 (1979), pp. 439–454.
- [5] IDL, *The International Database on Longevity*, <http://www.supercentenarians.org/>, 2012.
- [6] J. GAMPE, *Human mortality beyond age 110*, in *Supercentenarians*, H. Maier, J. Gampe, B. Jeune, J.-M. Robine, and J. Vaupel, eds., Demographic Research Monographs 7, Springer, Heidelberg, 2010, Chap. 3, pp. 219–230.
- [7] B. KESTENBAUM, *A description of the extreme aged population based on improved Medicare enrollment data*, Demography, 29 (1992), pp. 565–580.
- [8] J. W. VAUPEL AND B. JEUNE, EDS., *Exceptional Longevity: From Prehistory to the Present*, Odense University Press, Odense, Denmark, 1995.
- [9] J. W. VAUPEL AND B. JEUNE, EDS., *Validation of Exceptional Longevity*, Odense University Press, Odense, Denmark, 1999.
- [10] J. W. CURTSINGER, H. H. FUKUI, D. R. TOWNSEND, AND J. W. VAUPEL, *Demography of genotypes: Failure of the limited life-span paradigm in Drosophila melanogaster*, Science, 258 (1992), pp. 461–463.
- [11] H. H. FUKUI, L. XIU, AND J. W. CURTSINGER, *Slowing of age-specific mortality rates in Drosophila melanogaster*, Experimental Gerontology, 28 (1993), pp. 585–599.
- [12] H. H. FUKUI, L. ACKERT, AND J. W. CURTSINGER, *Deceleration of age-specific mortality rates in chromosomal homozygotes and heterozygotes of Drosophila melanogaster*, Experimental Gerontology, 36 (1993), pp. 517–531.
- [13] J. R. CAREY, P. LIEDO, AND J. W. VAUPEL, *Mortality dynamics of density in the Mediterranean fruit fly*, Experimental Gerontology, 30 (1995), pp. 605–629.
- [14] A. A. KHAZAEI, S. D. PLETCHER, AND J. W. CURTSINGER, *The fractionation experiment: Reducing heterogeneity to investigate age-specific mortality in Drosophila*, Mechanisms of Aging and Development, 105 (1998), pp. 301–317.

- [15] H.-Y. CHEN, F. ZAJITSCHKEK, AND A. A. MAKLAKOV, *Why ageing stops: Heterogeneity explains late-life mortality deceleration*, *Biology Lett.*, 9 (2013), 20130217.
- [16] D. STEINSALTZ AND K. WACHTER, *Understanding mortality rate deceleration and heterogeneity*, *Math. Population Stud.*, 13 (2006), pp. 19–37.
- [17] W. FELLER, *An Introduction to Probability Theory and Its Applications. Vol. II*, 2nd ed., John Wiley & Sons, New York, 1971.
- [18] M. FINKELSTEIN AND V. ESAULOVA, *Asymptotic behavior of a general class of mixture failure rates*, *Adv. in Appl. Probab.*, 38 (2006), pp. 242–262.
- [19] T. I. MISSOV AND M. FINKELSTEIN, *Admissible mixing distributions for a general class of mixture survival models with known asymptotics*, *Theoret. Population Biology*, 80 (2011), pp. 64–70.
- [20] J. ABBRING AND G. VAN DEN BERG, *The unobserved heterogeneity distribution in duration analysis*, *Biometrika*, 94 (2007), pp. 87–99.
- [21] M. COCHRAN AND S. ELLNER, *Simple methods for calculating age-based life history parameters for stage-structured populations*, *Ecological Monographs*, 62 (1992), pp. 345–364.
- [22] C. HORVITZ AND S. TULJAPURKAR, *Stage dynamics, period survival, and mortality plateaus*, *The American Naturalist*, 172 (2008), pp. 203–215.
- [23] H. LE BRAS, *Lois de mortalité et âge limite*, *Population*, 31 (1976), pp. 655–692.
- [24] A. I. YASHIN, J. W. VAUPEL, AND I. A. IACHINE, *A duality in aging: The equivalence of mortality models based on radically different concepts*, *Mechanisms of Aging and Development*, 74 (1994), pp. 1–14.
- [25] B. L. STREHLER AND A. S. MILDVAN, *General theory of mortality and aging*, *Science*, 132 (1960), pp. 14–21.
- [26] J. S. WEITZ AND H. B. FRASER, *Explaining mortality plateaus*, *Proc. Natl. Acad. Soc. USA*, 98 (2001), pp. 15383–15386.
- [27] D. STEINSALTZ AND S. N. EVANS, *Markov mortality models: Implications of quasistationarity and varying initial distributions*, *Theoret. Population Biology*, 65 (2004), pp. 319–337.
- [28] J. J. ANDERSON, *A vitality-based model relating stressors and environmental properties to organism survival*, *Ecological Monographs*, 70 (2000), pp. 445–470.
- [29] T. LI AND J. J. ANDERSON, *The vitality model: A way to understand population survival and demographic heterogeneity*, *Theoret. Population Biology*, 76 (2009), pp. 118–131.
- [30] K. W. WACHTER, *Evolutionary demographic models for mortality plateaus*, *Proc. Natl. Acad. Sci. USA*, 96 (1999), pp. 10544–10547.
- [31] L. DEMETRIUS, *Mortality plateaus and directionality theory*, *Proc. R. Soc. Lond. Ser. B*, 268 (2001), pp. 2029–2037.
- [32] L. DEMETRIUS, *Demographic parameters and natural selection*, *Proc. Natl. Acad. Sci. USA*, 71 (1974), pp. 4645–4647.
- [33] J. W. VAUPEL AND T. I. MISSOV, *Unobserved population heterogeneity: A review of formal relationships*, *Demographic Res.*, 31 (2014), pp. 659–686.
- [34] J. W. VAUPEL AND Z. ZHANG, *Attrition in heterogeneous cohorts*, *Demographic Res.*, 23 (2010), pp. 737–748.
- [35] S. N. BERNSTEIN, *Sur les fonctions absolument monotones*, *Acta Math.*, 52 (1928), pp. 1–66.
- [36] J. W. VAUPEL AND J. R. CAREY, *Compositional interpretations of medfly mortality*, *Science*, 260 (1993), pp. 1666–1667.
- [37] C. ELBERS AND G. RIDDER, *True and spurious duration dependence: The identifiability of the proportional hazard model*, *Rev. Econom. Stud.*, 49 (1982), pp. 403–409.