

LECTURE NOTES ON MORTALITY RATES IN HETEROGENEOUS POPULATIONS, PART I: FIXED FRAILTY MODELS

DAVID STEINSALTZ

1. MORTALITY PLATEAUS

We use increasing mortality rate as a proxy for aging.

What is a hazard rate? There is an event that we are waiting for, that happens at a random time T . Conditioned on survival up to time t , the probability that it will happen in the next instant is about $h(t)$. Since there's a higher chance of T happening in a longer instant, we write

$$\mathbb{P}\{T \in (t, t + \Delta t) \mid T > t\} \approx h(t)\Delta t.$$

This means that

$$\mathbb{P}\{T > t + \Delta t \mid T > t\} \approx 1 - h(t)\Delta t \approx e^{-h(t)\Delta t}.$$

Using the multiplicative rule for probabilities, we get then the survival function

$$S(t) := \mathbb{P}\{T > t\} = e^{-\int_0^t h(s)ds}.$$

Turning this around, we get

$$(1) \quad \frac{-S'(t)}{S(t)} = \frac{h(t)e^{-\int_0^t h(s)ds}}{e^{-\int_0^t h(s)ds}} = h(t).$$

In 1825, Benjamin Gompertz [Gom25] pointed out that mortality rates seemed to increase multiplicatively with age, through the middle years of life. That is,

$$(2) \quad h(x) = Ze^{\theta(x-x_0)},$$

where x is age, and Z is the mortality rate at the initial age x_0 . This means that when mortality rate is plotted as a function of age, it looks like a straight line. Figure 1 shows how that looks for data from Canada. (Data from Statistics Canada <http://www.statcan.ca:80/english/freepub/84-537-XIE/tables.htm>.)

Note that the curve bends down at the most advanced ages. We see this more clearly when we look at the annual rate of increase of mortality rate as a function of age.

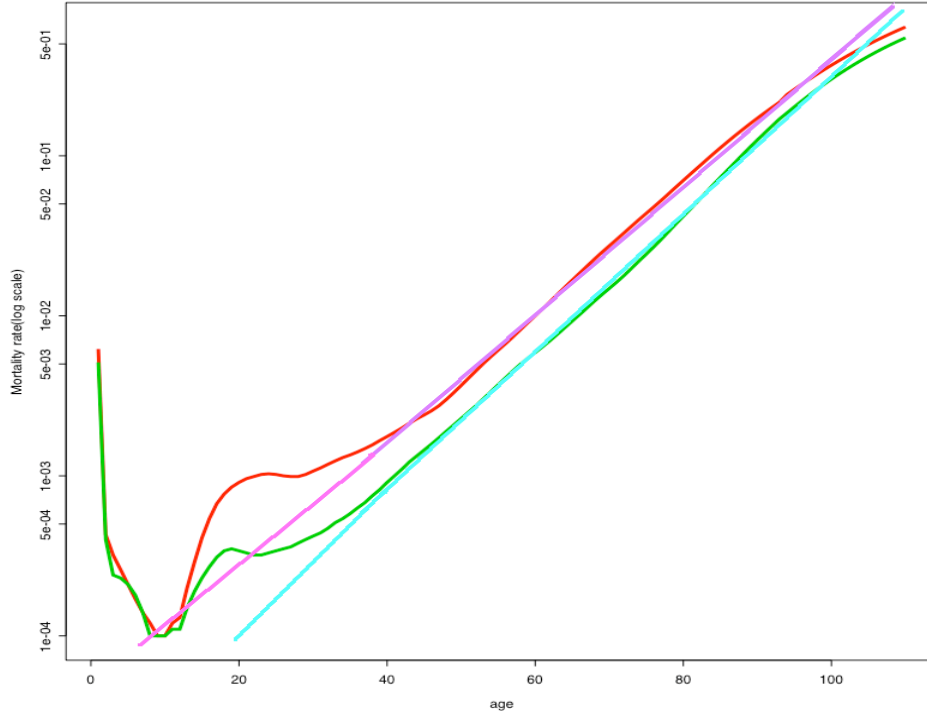


FIGURE 1. Plot of Canadian mortality (1995–7) as a function of age, on a logarithmic scale. Lines fit from age 35 to 85.

1.1. **Examples of plateaus.** One of the most sensational biodemography results was Jim Carey’s study of mortality rates in 1.2 million Mediterranean fruit flies. The results are shown in Figure 2.

2. FIXED FRAILTY MODELS

Suppose every individual has a Gompertz mortality rate, but that the parameters vary in the population. Consider a very elementary example: The mortality rate grows like

$$h(x) = Ze^{0.05 \cdot x},$$

but some individuals have blue skin, and their mortality rate starts at $Z = Z_1 = 10^{-4}$; others have red skin, and their mortality rate starts at $Z = Z_2 = 10^{-6}$. The likelihood of being born blue is p_1 , and of being born red is $p_2 = 1 - p_1$.

If we look only at blue individuals, their hazard rate at age x is

$$h_1(x) = 0.0001e^{0.05 \cdot x}.$$

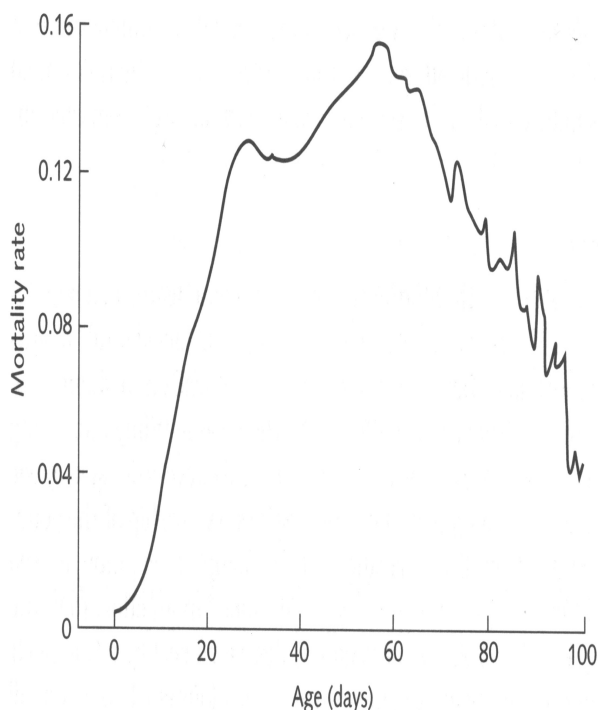


Figure 2.24 Mortality rates of a population of 1.2 million medflies maintained in cages of 7,200 animals each. Note that the age-specific mortality rates initially rose exponentially with age but then leveled off at about 20 days of age (16 percent survival), slowly increased to a peak at 58 days of age (0.2 percent survival), and declined thereafter. (Redrawn from data in Carey et al. 1992.)

FIGURE 2. Age-specific mortality rates recorded for 1.2 million Mediterranean fruit flies.

If we look only at red individuals, their hazard rate at age x is

$$h_2(x) = 0.000001e^{0.05 \cdot x}.$$

Suppose, now, we are color-blind, and see an undifferentiated population. What mortality rate will we see as a function of age?

A common mistake would be to say

$$(3) \quad p_1 h_1(x) + p_2 h_2(x).$$

In fact, it is

$$(4) \quad h(x) = -\frac{p_1 S_1'(x) + p_2 S_2'(x)}{p_1 S_1(x) + p_2 S_2(x)}.$$

What is the difference? The first expression (3) implicitly assumes an unchanging distribution in the population. In fact, though, after 180 days, only about 1 in 10 million of the blue population remains, but 85% of the reds are still alive. We may rewrite (4) as

$$(5) \quad h(x) = p_1(x)h_1(x) + p_2(x)h_2(x),$$

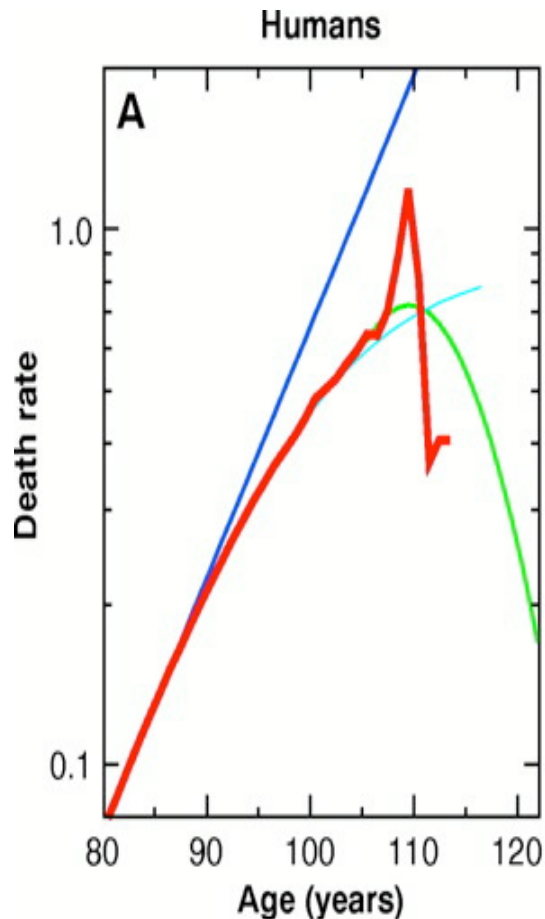


FIGURE 3. Age-specific mortality rates for human females, from age 80 to 122. Red line is aggregation of 14 countries (Japan and 13 Western European) over 1950 to 1990 (to 1997 for ages 110 and over). Best log-linear curve fit shown black; log-quadratic green; logistic exponential blue. Copied from [VCC+98].

where

$$(6) \quad p_i(x) := \frac{p_i S_i(x)}{p_1 S_1(x) + p_2 S_2(x)}$$

is the proportion of the population aged x which is from type i . The effect on the population mortality rate may be seen in Figure 2.

2.1. Carey-Vaupel medfly data. This approach has been applied to more than 2 subpopulations. For example, in an analysis of the Carey

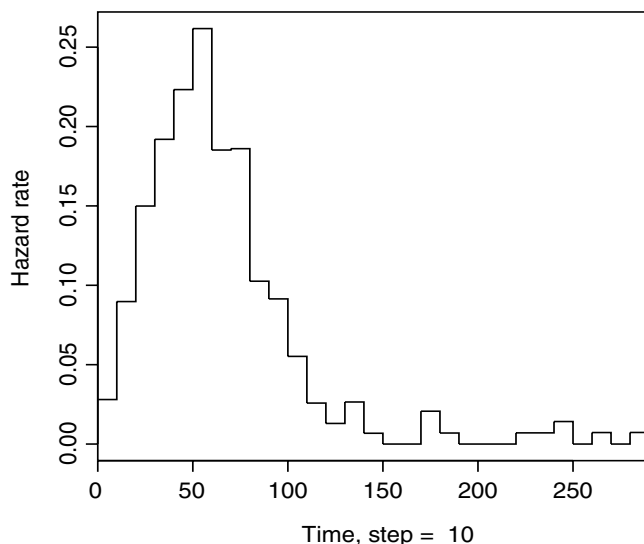


FIGURE 4. Age-specific failure rates for an experimental array of 750 miniature lightbulbs. Copied from [Fin05].

medfly data [VC93], 12 groups were used to approximate the mortality rates with the Gompertz model $h_Z(x) = Ze^{0.3x}$, and 5 groups with the Weibull model $h_Z(x) = Zx^2$. The parameters are given in Table 1. The fit mortality curves are shown in Figure 2.1.

This was presented, with considerable justification, as a kind of *reduction ad absurdum* for the heterogeneity explanation. If the subpopulations are all purely Gompertz or quadratic Weibull, the late-life mortality is determined by the emergence of a subpopulation consisting of about 130 individuals out of the initial population of 1.2 million, who were effectively invulnerable at the outset, and are the only ones still alive after 80 days or so.

In general, suppose Z is a random parameter, and individuals with that frailty $Z = z$ have survival function $S_z(x)$ and hazard rate $h_z(x) = -S'_z(x)/S_z(x)$ at age x . The proportion of individuals with frailty z is multiplied at age x by $S_z(x)/\mathbb{E}[S_Z(x)]$. In particular, if Z has a density g :

$$\mathbb{P}\{z_1 \leq Z \leq z_2\} = \int_{z_1}^{z_2} g(z)dz;$$

then the density of frailties of individuals at age x is

$$g(z; x) := \frac{g(z)S_z(x)}{\int_0^\infty S_y(x)g(y)dy}.$$

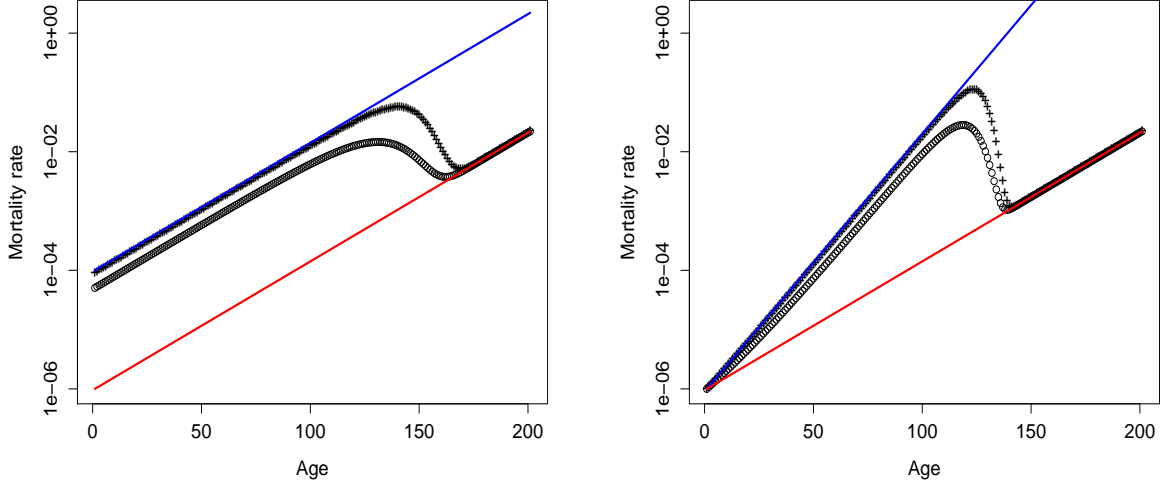


FIGURE 5. Mortality rate for populations mixed from two Gompertzian subpopulations, plotted on a logarithmic scale. The blue is the high-mortality subpopulation, the red is the low-mortality subpopulation. Circles show a mixture with initially 50% high mortality, crosses show a mixture with initially 90% high mortality. In the first plot, both subpopulations have $\alpha = .05$, but differ in initial mortality $Z = 10^{-4}$ or $Z = 10^{-6}$. In the second plot, both have $Z = 10^{-6}$, but differ between $\alpha = .05$ and $\alpha = .10$.

The hazard rate at age x is then

$$(7) \quad h(x) = \mathbb{E} \left[h_Z(x) \frac{S_Z(x)}{\mathbb{E}[S_Z(x)]} \right] = \int_0^\infty h_z(x) g(z; x) db.$$

2.2. Gamma-distributed initial mortality. A favorite example, from [VMS79], takes the assumption that all individuals have mortality rates

$$(8) \quad h_Z(x) = Z z_0 e^{\alpha x},$$

where α is constant, and Z is distributed as a gamma distribution. This is a two-parameter family of distributions on positive real numbers whose densities are given by

$$(9) \quad \gamma_{r,\nu}(z) = (r^\nu / \Gamma(\nu)) z^{\nu-1} e^{-rz}$$

The parameter r is called the rate, while ν is called the shape parameter. We may assume that Z has mean 1 (since an arbitrary constant

Gompertz		Weibull	
Z	p	Z	p
1.0×10^{-2}	0.41	1.5×10^{-2}	0.47
2.25×10^{-3}	0.38	6.6×10^{-3}	0.39
5.1×10^{-4}	0.13	2.2×10^{-3}	0.14
9×10^{-5}	0.046	7.2×10^{-4}	3.9×10^{-3}
2.8×10^{-5}	0.020	4.8×10^{-5}	1.0×10^{-4}
6.0×10^{-6}	8.2×10^{-3}		
1.1×10^{-6}	1.7×10^{-3}		
2.2×10^{-7}	4.6×10^{-4}		
3.3×10^{-8}	1.3×10^{-4}		
4.2×10^{-9}	5.3×10^{-5}		
1.5×10^{-10}	1.3×10^{-5}		
2.2×10^{-12}	4.3×10^{-5}		

TABLE 1. Parameters for heterogeneous Gompertz or Weibull models, from [VC93], producing the fits shown in Figure 2.1.

may be absorbed into z_0), which implies that $r = \nu = \text{Var}(Z)$. (Some examples are shown in Figure 2.2.) Applying (7), we see that

$$\begin{aligned}
 S(x) &= \int_0^\infty \exp\left\{-\frac{z \cdot z_0}{\alpha} (e^{\alpha x} - 1)\right\} \gamma_{r,\nu}(z) dz \\
 &= \int_0^\infty e^{-r'z} \frac{r^\nu}{\Gamma(\nu)} z^{\nu-1} dz \\
 &= \left(\frac{r}{r'}\right)^\nu \int_0^\infty \gamma_{r',\nu}(z) dz \\
 &= \left(\frac{r}{r'}\right)^\nu .
 \end{aligned}$$

where

$$r' = \frac{z_0}{\alpha} (e^{\alpha x} - 1) + r.$$

Thus,

$$S(x) = \left(1 + \frac{z_0}{r\alpha} (e^{\alpha x} - 1)\right)^{-\nu}.$$

The hazard rate is

$$h(x) = -\frac{S'(x)}{S(x)} = z_0 \frac{e^{\alpha x}}{1 + z_0/r\alpha (e^{\alpha x} - 1)}.$$

This is the “logistic Gompertz” hazard rate, the form $e^{\alpha x}/(A + Be^{\alpha x})$ that is a favored alternative to Gompertz when plateaus are to be included. (See, for instance, [HW98].)

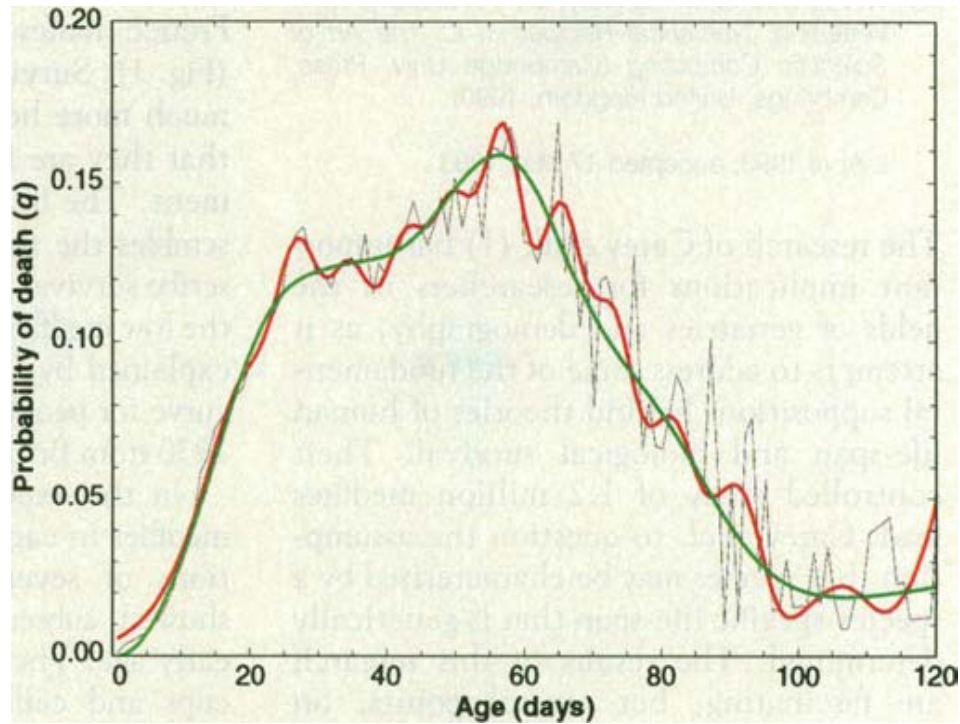


FIGURE 6. Fit of heterogeneous Gompertz (red) and Weibull (green) to age-specific mortality rates of 1.2 million medflies (black) as reported in [CLOV92].

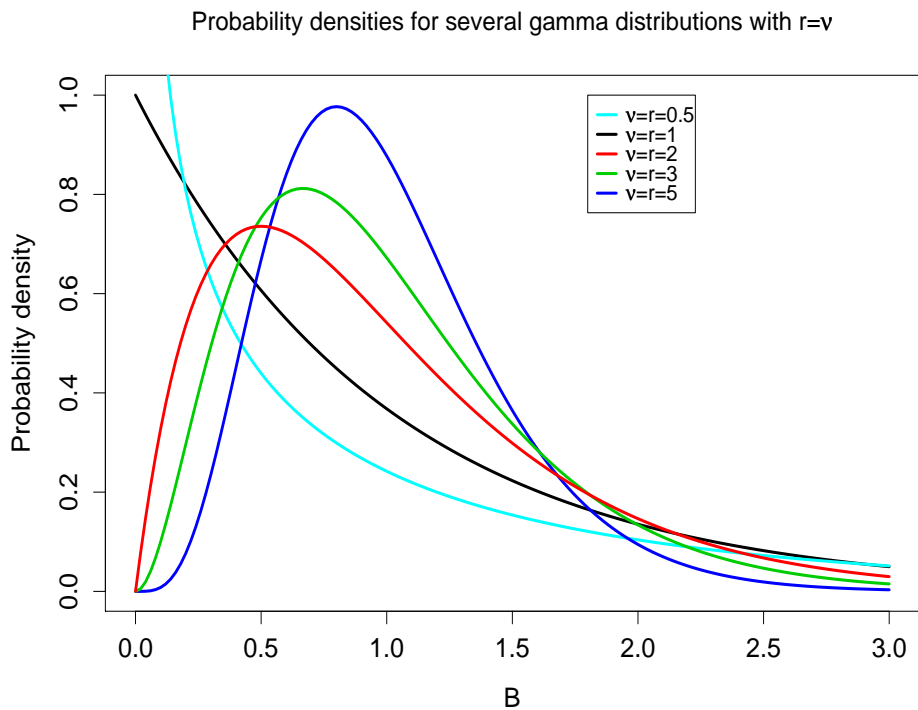


FIGURE 7. Examples of probability densities of gamma distributions with expectation 1.

3. USING LAPLACE TRANSFORMS FOR PROPORTIONAL HAZARDS

Given any population distribution of mortality rates, we can compute the population mortality rate from equation (7). Is that the last word?

The following approach is from [SW06]: If Z is a positive real-valued random variable, its Laplace transform is defined to be the function

$$(10) \quad \lambda(s) = \mathbb{E}[e^{-sZ}].$$

Some properties of the Laplace transform are obvious — for instance, $\lambda(s)$ must be decreasing — many others are not. (Accounts of Laplace transforms may be found in most standard probability textbooks, such as [Fel68]. The most thorough account of properties of the subject is [Doe50], but it is in German.)

Suppose we have a proportional-hazards model, such as the Gamma model of section 2.2. That is, each individual i has a random frailty multiplier Z_i , and the hazard rate at age x is $h_i(x) = Z_i h_0(x)$. We assume that the mean of Z is 1.

Let

$$M(x) = \int_0^x h_0(y) dy.$$

Then

$$\mathbb{P}\{i \text{ survives until age } x \mid Z_i = z\} = e^{-zM(x)}.$$

Consequently, if i is a random individual,

$$\mathbb{P}\{i \text{ survives until age } x\} = \mathbb{E}e^{-ZM(x)} = \lambda(M(x)).$$

This yields

$$(11) \quad h(x) = h_0(x) \frac{-\lambda'(M(x))}{\lambda(M(x))}.$$

Other important quantities may be computed as follows: The Life Expectancy (LE) is just $\int_0^\infty P\{\text{survive to age } x\} dx$, so

$$\text{LE} = \int_0^\infty \lambda(M(x)) dx = \int_0^\infty \frac{\lambda(s)}{h_0(M^{-1}(s))} ds.$$

The rate of change of the logarithm of the aggregate hazard rate has been called the “Lifetable Aging Rate” (LAR) by [HC90, HW97]. The LAR is constant under Gompertz mortality, and variations in the LAR show deviations from the Gompertz pattern. Also $\log(2)/LAR$ may be thought of as the instantaneous mortality rate doubling time. It is given by

$$\text{LAR}(t) = \frac{h_0'(t)}{h_0(t)} + \frac{h_0(t)}{\lambda(M(t))\lambda'(M(t))} [\lambda''(M(t))\lambda(M(t)) - (\lambda'(M(t)))^2].$$

3.1. Asymptotics. How does the mortality rate behave for extreme ages? By (11), it depends on the behavior of the Laplace transform for extreme values of $M(x)$, hence of x . Intuitively, if s is very large, $\lambda(s)$ will be affected only by values of Z on the order of $1/s$. That is, the behavior of $\lambda(s)$ for large s is tied to the distribution of Z close to 0. That makes sense: At extreme ages, we are left with the population of only very robust individuals.

In fact, we can be more specific than this. Suppose Z has a density $f(z)$. For $\rho > -1$, we say that f behaves asymptotically like z^ρ near 0 if $\lim_{z \rightarrow 0} f(z)z^{-\rho} = a$ exists and is nonzero. There are ‘‘Abelian’’ and ‘‘Tauberian’’ theorems, such as the following:

Theorem 3.1. *Suppose Z has a density $f(z)$ which behaves asymptotically like z^ρ near 0. Then*

$$(12) \quad \lambda(s) \sim a\Gamma(\rho + 1)s^{-\rho-1} \text{ for } s \rightarrow \infty.$$

A basic consequence of this is

$$\frac{-\lambda'(s)}{\lambda(s)} \sim (\rho + 1)s^{-1} \text{ for } s \rightarrow \infty.$$

By setting $s = M(x)$, we get

$$h(x) \sim (\rho + 1)\frac{h_0(x)}{M(x)}.$$

Proposition 3.2. *Suppose Z has a density $f(z)$ which behaves asymptotically like z^ρ near 0, and that there is a constant α such that the baseline hazard satisfies*

$$(13) \quad \lim_{t \rightarrow \infty} \frac{h_0(x)}{M(x)} = \alpha.$$

Then the population hazard $h(x)$ has a plateau, and

$$\lim_{x \rightarrow \infty} h(x) = \alpha(\rho + 1).$$

The condition (13) is satisfied, in particular, for Gompertz hazards.

4. GENERAL ASYMPTOTIC RESULTS

The mathematical results have been placed in a far more general context by [FE06]. Consider a class of models defined by hazard rates $h_z(x)$, and integrated hazards $M_z(x) = \int_0^x h_z(u)du$. Suppose there are functions A , ψ , and ϕ , with A and ϕ increasing, such that

$$(14) \quad M_z(x) = A(z\phi(x)) + \psi(x).$$

This includes a number of standard models:

Proportional Hazards: Let

$$A(u) = u, \quad \phi(x) = h_0(x), \quad \psi(x) = 0.$$

Then

$$h_z(x) = zh_0(x), \quad M_z(x) = zM(x).$$

Accelerated Lifetime Model: Let

$$A(x) = M(x), \quad \phi(x) = x, \quad \psi(x) = 0.$$

Then

$$h_z(x) = zh_0(zx), \quad M_z(x) = M(zx).$$

Additive Hazards Model: Let

$$A(x) = x, \quad \phi(x) = x, \quad \psi(x) \text{ increasing with } \psi(0) = 0.$$

Then

$$h_z(x) = zh_0(zx), \quad M_z(x) = M(zx).$$

Theorem 4.1. *Suppose Z has a density which behaves as z^ρ near 0. Assume, as well, that $\lim_{x \rightarrow \infty} \phi(x) = \infty$ and*

$$(15) \quad \int_0^\infty e^{-A(s)} s^\rho ds < \infty.$$

Then

$$h(x) \sim (\rho + 1) \frac{\phi'(x)}{\phi(x)} + \psi'(x) \text{ as } x \rightarrow \infty.$$

Proof. Let $\tilde{f}(x) = x^{-\rho} f(x)$, so $\tilde{f}(x)$ is continuous and bounded.

The survival function is

$$S_z(x) = e^{-A(z\phi(x)) - \psi(x)}.$$

The population survival function is

$$\begin{aligned} S(x) &= \int_0^\infty S_z(x) f(x) dx = \int_0^\infty e^{-A(z\phi(x)) - \psi(x)} z^\rho \tilde{f}(z) dz \\ &= e^{-\psi(x)} \int_0^\infty e^{-A(u)} \left(\frac{u}{\phi(x)} \right)^\rho \tilde{f}(u/\phi(x)) \frac{du}{\phi(x)} \quad (\text{change of variables}) \\ &= e^{-\psi(x)} \phi(x)^{-\rho-1} \left(\int_0^{\epsilon\phi(x)} + \int_{\epsilon\phi(x)}^\infty \right) e^{-A(u)} u^\rho \tilde{f}(u/\phi(x)) \end{aligned} \quad \sim$$

The probability density is the negative derivative:

$$\begin{aligned} f(x) &= \int_0^\infty e^{-A(z\phi(x))-\psi(x)} (A'(z\phi(x))z\phi'(x) + \psi'(x)) z^\rho \tilde{f}(z) dz \\ &= e^{-\psi(x)} \phi'(x) \int_0^\infty e^{-A(u)} u A'(u) \left(\frac{u}{\phi(x)} \right)^\rho \tilde{f}(u/\phi(x)) \frac{du}{\phi(x)} + \psi'(x) S(x) \\ &\sim e^{-\psi(x)} \phi'(x) \tilde{f}(0) \phi(x)^{-\rho-2} \int_0^\infty A'(u) e^{-A(u)} u^{\rho+1} du + \psi'(x) S(x). \end{aligned}$$

Now, integrating by parts,

$$\begin{aligned} \int_0^\infty A'(u) e^{-A(u)} u^{\rho+1} du &= (\rho+1) \int_0^\infty e^{-A(u)} u^\rho du + \lim_{z \rightarrow \infty} e^{-A(z)} z^{\rho+1} \\ &= (\rho+1) \int_0^\infty e^{-A(u)} u^\rho du \text{ by (15)}. \end{aligned}$$

Thus,

$$\begin{aligned} \frac{f(x)}{S(x)} &\sim \frac{e^{-\psi(x)} \phi'(x) \tilde{f}(0) \phi(x)^{-\rho-2} \int_0^\infty e^{-A(u)} u^\rho du}{e^{-\psi(x)} \tilde{f}(0) \phi(x)^{-\rho-1} \int_0^\infty e^{-A(u)} u^\rho du} + \psi'(x) \\ &\sim (\rho+1) \frac{\phi'(x)}{\phi(x)} + \psi'(x). \end{aligned}$$

□

4.1. Frailties bounded away from 0. What happens when the frailty distribution doesn't go all the way down to 0. What happens otherwise? It makes sense to suppose that the strongest subpopulation will dominate.

Theorem 4.2 (Finkelstein-Esauova). *Suppose Z has a bounded density on $[a, \infty)$, continuous and nonzero at a , that $\lim_{x \rightarrow \infty} A''(x)/(A'(x))^2 = 0$, $\lim_{x \rightarrow \infty} xA'(x) = \infty$, and for all positive $b < c$, $A'(bx)/A'(cx)$ is bounded in x .*

Then

$$(16) \quad \lim_{x \rightarrow \infty} h(x) - \psi'(x) \sim h_a(x) = a\phi'(x)A'(a\phi(x)).$$

5. IMPLICATIONS

The advantage of this approach is that it does not assume any parametric form for the frailty distribution. With gamma frailties, for example, the mortality plateau level is connected not just to the frailty distribution near 0, but implies the entire form of the mortality distribution.

The following discussion is abbreviated from [SW06]: Let us assume a proportional hazards effect of individual frailty, with the underlying mortality rate having a Gompertz-Makeham form:

$$h_0(x) = c + z_0 e^{\alpha x}.$$

The quotient $\mu(t)/M(t)$ tends to the Gompertz slope parameter α independent of the additive Makeham term c . We take $\alpha = 0.08$ and the limit of $h(x)$ equal to 0.600, drawing on a human example described below. Theorem 4.1 tells us that the lower tail of any frailty distribution generating such values should have exponent $1 + \rho = \lim h/\alpha = 0.600/0.08 = 7.5$.

To interpret such an estimate for $1 + \rho$, suppose that the tail behavior of the frailty distribution sets in at least below $Z = 1/2$. Proportional changes in hazard rates due to observed heterogeneity on the order of $1/2$ are commonplace among subgroups in human populations, so $Z = 1/2$ seems a reasonable benchmark for comparisons. The cumulative proportion of individuals with frailties less than some smaller Z , as a fraction of the proportion with frailties less than $1/2$ is given by $(2Z)^{1+\rho}$. Then one in ten-thousand of these robust individuals would have Z values less than $\hat{Z} = (1/2)10^{-4/(1+\rho)} = 0.146$ and one in a million would have values less than $\hat{Z} = (1/2)10^{-6/(1+\rho)} = 0.079$.

How extreme are such frailty values? With a Gompertz baseline hazard rate governing adult ages, a frailty Z corresponds to a shift in the modal age of death of $(1/\alpha) \log(1/Z)$, and this formula remains a good approximation with a Gompertz-Makeham baseline with parameters in the general range under consideration here. In our example, an individual with frailty $Z = 0.146$ would have a modal age at death $(1/0.08) \log(1/0.146) = 24$ years later than the individual with average frailty.

In a cohort where members with average robustness typically live to around 73, these specially robust individuals would typically need to be living to 97 if the model is to hold good. For a strictly Gompertz baseline, in which a change in frailty corresponds to a shift in the whole hazard function, this comparison would apply at other ages as well. An 80 year old with $Z = .146$ would have to resemble a typical 56 year old with regard to risk of death. The one-in-a-million specially robust individual would experience a $(1/0.08) \log(1/0.079) = 32$ year advantage across life.

Where do the parameter estimates come from? The value $\beta = .08$ in Table 2 is chosen to agree with the maximum of the Lifetable Aging Rates in Horiuchi's Figure 2A. The figure is predicated on the cohort lifetable for Swedish men born from 1880 to 1885 available on the

Human Mortality Database [HMD04]. The three columns differ in the choice of asymptote. The asymptote for the first column is chosen to accord with estimated hazard rates over 105 estimated by Robine and Saito for recent Japanese females [RS03]. The asymptotes for the second and third columns represent the lowest and highest of a set of extrapolations obtained by Wilmoth and Robine [WR03, p. 251] from fitting logistic models to two super-centenarian databases. The middle case, A2, roughly matches Horiuchi's own extrapolation. Reliance on the logistic model introduces some degree of circularity from the point of view of the comparisons undertaken here, and the asymptotes in the second and third columns may be on the high side. They exceed the values empirically observed among the supercentenarians in the data bases. The higher asymptotes do imply thinner lower tails for frailty distributions. The one-in-ten-thousand comparisons among individuals with frailties less than $Z = 1/2$, computed as above, give increments to modal ages at death in the range of 16 to 18 years, still high but easier to imagine than 24 years.

TABLE 2. Asymptotes and Frailty Estimates for Humans

Species Case	Humans		
	A1	A2	A3
β per year	.08	.08	.08
Asymptote h	.600	1.000	1.250
Estimated $1 + \rho$	7.50	12.50	15.63
$(1 + \rho)^{-1/2}$.365	.283	.253
\hat{Z} (per 10^4)	.146	.239	.277
Increment in years	24	18	16

The estimates for invertebrates in Table 3 show that the inclusion of extremely robust individuals with exceptionally low frailties would be required to generate the observed asymptotes in hazard rates by selective culling alone. For medflies, with their noticeable drops in aggregate hazard functions, it has been obvious that heterogeneity in frailty alone cannot reconcile Gompertz baseline hazards with observed population curves. For the other invertebrates the increments in modal lifespans given in the table are vastly larger than the modal lifespans themselves. These increments would be experienced by one in ten-thousand of the individuals who already had frailties less than half the

TABLE 3. Asymptotes and Frailty Estimates for Invertebrates

Species Case	Medflies B	Nematodes C	Wasps D	Drosophila mel. E
β per day	.04	.06	.02	.08
Asymptote μ^*	.050	.010	.001	.010
Estimated $1 + \rho$	1.25	1.667	.500	1.250
$(1 + \rho)^{-1/2}$.894	.775	1.414	.894
\hat{Z} (per 10^4)	$3 * 10^{-4}$	$2 * 10^{-3}$	$5 * 10^{-9}$	$3 * 10^{-4}$
Increment in days	202	104	956	101
Modal lifespan	20	15	6	45

average. Heterogeneity on such a scale seems highly unlikely and simple culling does not seem to be a plausible explanation for the observed asymptotes. This conclusion agrees with Horiuchi's findings, but it relies on much weaker parametric assumptions than his approach.

Implicit in the human estimates in Table 2 is the use of Gompertz-Makeham hazards, including a constant along with an exponentially increasing term. Since the asymptotics of Theorem 1 are the same with a Gompertz-Makeham baseline as with an ordinary Gompertz baseline, the distinction does not affect the tabulated values here. But it does affect the goodness of fit to human cohort lifetables that can be achieved with frailty models over the middle age range. Not only the Swedish male cohort of 1880-85, but other recently completed cohorts from developed nations including France and Japan represented in the Human Mortality Database show steepening in the graph of log hazard rates before the onset of the flattening that is our chief concern.

REFERENCES

- [CLOV92] James R. Carey, Pablo Liedo, Dina Orozco, and James W. Vaupel. Slowing of mortality rates at older ages in large medfly cohorts. *Science*, 258(5081):457-61, October 16 1992.
- [Doe50] Gustav Doetsch. *Handbuch der Laplace-Transformation*, volume 1. Verlag Birhäuser, Basel, 1950.
- [FE06] Maxim Finkelstein and Veronica Esaulova. Asymptotic behavior of a general class of mixture failure rates. *Advances in Applied Probability*, 38(1):244-62, 2006.
- [Fel68] William Feller. *An Introduction to Probability and its Applications*, volume 1. John Wiley & Sons, New York, 3rd edition, 1968.
- [Fin05] Maxim Finkelstein. On some reliability approaches to human aging. *International Journal of Reliability, Quality and Safety Engineering*, 12(4):337-46, 2005.

- [Gom25] Benjamin Gompertz. On the nature of the function expressive of the law of human mortality and on a new mode of determining life contingencies. *Philosophical transactions of the Royal Society of London*, 115:513–85, 1825.
- [HC90] Shiro Horiuchi and Ansley Coale. Age patterns of mortality for older women: An analysis using the age-specific rate of mortality change with age. *Mathematical Population Studies*, 2:245–267, 1990.
- [HMD04] Human Mortality Database. Available at www.mortality.org. University of California, Berkeley, USA, and Max Planck Institut für Demografische Forschung, Rostock, Germany, January 2004.
- [HW97] Shiro Horiuchi and John R. Wilmoth. Age patterns of the lifetable aging rate for major causes of death in japan, 1951-1990. *Journal of Gerontology: Biological Sciences*, 52(1):B67–B77, 1997.
- [HW98] Shiro Horiuchi and John R. Wilmoth. Deceleration in the age pattern of mortality at older ages. *Demography*, 35(4):391–412, November 1998.
- [RS03] Jean-Marie Robine and Yasuhiko Saito. Survival beyond age 100: The case of japan. In James R. Carey and Shripad Tuljapurkar, editors, *Life Span: Evolutionary, Ecological, and demographic perspectives*, volume 29 (Supplement) of *Population and Development Review*, pages 208–228. The Population Council, New York, 2003.
- [SW06] David Steinsaltz and Kenneth W. Wachter. Understanding mortality rate deceleration and heterogeneity. *Mathematical Population Studies*, 2006. Accepted for *Mathematical Population Studies*, Sept. 2005.
- [VC93] James W. Vaupel and James R. Carey. Compositional interpretations of medfly mortality. *Science*, 260(5114):1666–7, June 11 1993.
- [VCC⁺98] James W. Vaupel, James R. Carey, Kaare Christensen, Thomas E. Johnson, Anatoli I. Yashin, Niels V. Holm, Ivan A. Iachine, Väinö Kannisto, Aziz A. Khazaeli, Pablo Liedo, Valter D. Longo, Yi Zeng, Kenneth G. Manton, and James W. Curtsinger. Biodemographic trajectories of longevity. *Science*, 280(5365):855–60, May 1998.
- [VMS79] James W. Vaupel, Kenneth G. Manton, and Eric Stallard. The impact of heterogeneity in individual frailty on the dynamics of mortality. *Demography*, 16(3):439–54, 1979.
- [WR03] John R. Wilmoth and Jean-Marie Robine. The world trend in maximum lifespan. In James R. Carey and Shripad Tuljapurkar, editors, *Life Span: Evolutionary, Ecological, and demographic perspectives*, volume 29 (Supplement) of *Population and Development Review*, pages 239–257. The Population Council, New York, 2003.