On the Speed of Ageing

Giambattista Salinari and Gustavo De Santis

1. Introduction

The rate of ageing is a measure of the pace at which mortality increases at adult ages and it is supposed to reflect the process of physiological deterioration undergone by of an organism as it ages. Vaupel (2010) has recently advanced the hypothesis that, in humans, the rate of ageing may be a basic biological constant. Which would be rather disappointing, incidentally: it would imply, for instance, that neither physical activity, nor a proper dietary regime, nor anything else can slow down our rate of ageing (or senescence) and improve our chances of survival.

The most important piece of evidence in favor of the constant ageing hypothesis probably comes from a recent analysis of the asymptotic characteristics of human mortality. In 2010, using the database collected by Kannisto on super-centenarians, Gampe concluded that between 110 and 120 years the yearly probability of death levels-off to a value of about 0.5, with scarcely variation across cohorts (and perhaps also genders, but the number of males of this age was extremely limited).

The theoretical importance of the mortality plateau is that it is compatible with only a few mortality models. Not, for instance, with the accelerated failure time models (Finkelstein and Esaulova 2006), and not with the proportional hazard models in which frailty is assumed to be distributed as a lognormal or as an inverse Gaussian (Missov and Finkelstein 2011). To date, only two models seem to be consistent with the existence of the mortality plateau: the Gamma-Gompertz (GG) model and the Gamma-Makeham-Gompertz (GMG) model (Missov and Vaupel 2015). Empirical verifications, however, have thus far been rather disappointing: the estimated rates of ageing vary for cohorts born in different epochs and countries (Barbi 2003; Barbi et al. 2003; Salinari and De Santis 2014), or having gone through different historical experiences (Zarulli 2013).

In this paper we submit the hypothesis that the rate of ageing may be gradually increasing over adult ages, and become constant only in old age. The rate of ageing is virtually zero (and mortality almost stationary) from 20-25 years up to an age between 30 and 50 years (Salinari and De Santis 2015). After that, the rate of ageing increases (mortality acceleration; Horiuchi and Wilmoth 1998), but, because of the "perturbations" produced by selection, it is not clear when this increase slows down and stops (Vaupel et al. 1979). However, it seems necessary to assume that this increase in the rate of ageing will sooner or later converge to its asymptotic (constant) value, otherwise there would be no mortality plateau between 110 and 120 years (Missov and Vaupel 2015).

Our model, an extension of the Gamma-Gompertz (EGG), is not far from the Gamma Log-quadratic (GLQ) model proposed by Horiuchi (2003), but we assume that the increase in the rate of ageing follows an "S" shaped function. This version captures the evolution of mortality from the age of 30 years onwards, and reproduces the main historical characteristics observed in the evolution of mortality over time. Most importantly, because it converges to a GG model at older ages, our model shows all the good asymptotic property of the GG model producing a plateau around a probability of death of 0.5. And, with this extension, the rate of ageing appears to be remarkably constant by country and year of birth, although not by sex.

2. The EGG model

The main assumption in the GG model is that the individual force of mortality follows the Gompertz model (1825)

$$\mu_{i,x} = \alpha_i e^{\beta x} \tag{1}$$

where the force of mortality μ of individual i at age x is supposed to depend on two parameters: an individual-specific parameter α which describe the initial force of mortality, and a universal parameter β which describes how mortality increases with age (the rate of ageing). Eq. (1) may be rewritten in a more convenient way as follows:

(2) $$\mu_{i,x} = z_i \alpha e^{\beta x}$$

Where this time the α parameter represents the initial force of mortality experienced by the standard individual of the cohort, and z_i is the (relative) frailty of the *i-th* individual, that is:

(3) $$z_i = \frac{\alpha_i}{\alpha}$$

where the frailty of an individual *i* is thus defined as the ratio between the initial mortality of *i* and the initial force of mortality experienced by the standard individual of the population (Vaupel et al. 1979).
Equation (2) assumes that β, the rate of ageing, is constant across individuals and at all ages. The latter characteristic, however, contradicts the observations that life tables ageing rates (LAR) of human cohorts are initially (25-45 years) close to zero and increase subsequently, before (possibly) converging their asymptotic value (Salinari and De Santis 2015; Horiuchi 1998). In order to solve this problem we modeled the evolution of the force of mortality from, let us say, 30 years onwards as follows:

(4) $$\mu_{i,x} = z_i \alpha e^{F_x \beta x}$$

Where the new term F_x – the ageing "dimmer" - represents a cumulative distribution function (CDF) whose functional form must be empirically identified. At young ages F_x is probably very close to zero, so that model (4) reduces to $\mu_{i,x} = z_i \alpha$, where mortality is constant. At older ages, however, F_x increases, causing an increase in the rate of ageing (the exponent of eq. 4). At very old ages F_x will finally converge to 1, so that model (4) overlaps with the Gompertz model described by eq. (2).
In this framework the β parameter represents the asymptotic of the rate of ageing, while the age-specific rate of ageing will be given by $F_x \beta$. In order to test Vaupel's hypothesis it is thus necessary, in the present settings, to show that at every age the rate of ageing $F_x \beta$ does not change significantly.
If frailty is Gamma distributed, it may be proved (Vaupel et al. 1979) that the aggregate (cohort) force of mortality $\bar{\mu}$ at age x is given by:

(5) $$\bar{\mu}_x = \frac{\mu_{s,x}}{1+\sigma^2 M_{s,x}}$$

where $\mu_{s,x}$ represents the force of mortality of the standard individual of the cohort, σ^2 represents the initial variance of frailty and $M_{s,x}$ is the cumulative force of mortality of the standard individual, which can be computed by a numeric integration of eq. (4). Summing up, in order to determine $\bar{\mu}_x$ in eq. (5) we need to estimate five parameters: the background mortality (α), the asymptotic rate of ageing (β), the initial variance of frailty (σ^2), and the two parameters θ_1 and θ_2 that are necessary to determine the specific functional form of the ageing dimmer (all the cumulative distribution functions here considered are characterized by two parameters).
These five parameters can be estimated from the observed force of mortality by assuming that deaths are Poisson distributed (Brillinger 1986) so that:

(6) $$D_x = Poisson(E_x \bar{\mu}_x)$$

Where D_x and E_x indicate respectively the number of deaths and the exposures at age x. In such a framework the log-likelihood corresponding to a given combination of the five parameters is given by:

(7) $$\ln L(\alpha, \beta, \sigma^2, \theta_1, \theta_2) = \sum_x (D_x \ln \bar{\mu}_x - E_x \mu_x)$$

By maximizing this quantity we eventually obtained the estimates of the five parameters of eq. (5).
The main problem with eq. (4) is how to determine the functional form of the ageing dimmer. In this paper we have compared the outcomes of seven different CDF's: beta, gamma, exponential, inverse

Gaussian, lognormal, normal and Weibull. At the end of our examination (results are given in the full paper), we selected the lognormal.
The estimation of the EGG model parameters allowed us to identify three important thresholds for adult mortality (the onset of ageing, the onset of mortality deceleration, and the end of the increase in ageing) and the asymptotic probability of death. These estimates are in line with - and, in our opinion, more reliable than - those customarily found in the specialized literature (details in the full paper).

3. Results

The estimates presented in this section have been produced using the cohort life tables of four Nordic countries and the Netherland. The series have different time extension in the different countries: for Sweden, the country with the longest series, we considered the cohort born from 1820 to 1899; for Finland, the country with the shortest series we considered only the cohorts born between 1880 and 1899. Most of the series considered start around mid-19th century.
In order to produce our estimates we worked on groups of non-overlapping cohorts, rather than on single cohorts, so as to obtain more robust estimates. The groups of cohorts that we formed are born in the following years: [1820-29], [1830-39],…, [1890-1899].
The estimates were obtained on the age span 30-109. We selected 30 years (and not earlier) as the starting age in order to protect the analysis from the phenomenon of the youth mortality hump (Goldstein 2011). The age of 109 is, instead, the highest age covered by the HMD.
Figure 1 presents a few selected examples of the results that we obtained with our best model. The data (the black points) represent the evolution of the force of mortality from age 5 to a maximum age of 109 in the female Swedish cohorts born between 1820 and 1889. The red lines represents the EGG model estimates (on the ages 30-109). The two vertical lines in each panel of Figure 1 represent the estimates of the onset of demographic ageing and mortality deceleration.
From age 30 onwards the fit is always very good in all the groups of cohorts considered. In some cases, especially for the earliest cohorts, the fit is very close also at younger ages, starting from 15 or 20 years, which my depend on the progressive anticipation of the youth mortality hump (Goldstein 2011).
In Figure 2 we present the age-specific rates of ageing computed at age 60, 70,.., 100 for each of the 52 groups of cohorts that were formed for the present analysis. The data presented in Figure 2 allow to compare the age-specific rate of ageing by period of birth, country and sex, which all appear to be remarkably stationary.
In order to statistically ascertain the constancy of the rate of ageing over time we regressed the series of age-specific rate of ageing (separately for each age shown in Figure 2 and for both genders) against the year of birth of the cohorts. For all the ages covered in Figure 2 and for both genders the slope of the regression line was not significantly different from zero (p.value >0.1), except for the rate of ageing at 100 years in males, where a slight but significant downward trend emerged from our analysis.
The only systematic difference among the age-specific rates of ageing seems to emerge between males and females. The mean rate of ageing at age 60 for males is higher (32 per cent) than that for females, but this difference reduces subsequently.
The cohorts born in the five countries analyzed in this paper over the period 1820-1899 show a continuous improvement in life expectancy at birth. The EGG model describes this process in terms of a downward translation of the individual hazard (i.e., a reduction in background mortality α), without any significant change in the age-specific rates of ageing ($F_x\beta$). This result is consistent with the existence of a mortality plateau and, with a few adjustments, is in line with Vaupel's conjecture of a constant beta.

References

Barbi, E. (2003). Assessing the Rate of Ageing of the Human Population. MPIDR Working Paper WP 2003-008.
Barbi, E., Caselli, G., Vallin J. (2003). Trajectories of Extreme Survival in Heterogeneous Populations. Population 58(1):43-65 .

Brillinger, D.R. (1986). The natural variability of vital rates and associated statistics. Biometrics 42:693-734.
Finkelstein, M., Esaulova, V. (2006). Asymptotic behavior of a general class of mixture failure rates. Advances in Applied Probability 38: 242–262.
Gampe, J. (2010). Human mortality beyond age 110, in: Maier, Heiner, Jutta Gampe, Bernard Jeune, Jean-Marie Robine, James W. Vaupel (Eds.), *Supercentenarians. Demographic Research Monographs*, No. 7. Springer, Heidelberg (et al.), pp. 219–230.
Horiuchi, Shiro and John R. Wilmoth. (1998). Deceleration in the age pattern of mortality at older ages, *Demography* 35(4):391-412.
Horiuchi, S. (2003). Interspecies Differences in the Life Span Distribution: Humans versus Invertebrates, *Population and Development Review* 29:127-151.
Missov, T.I., Finkelstein, M. (2011). Admissible mixing distributions for a general class of mixture survival models with known asymptotics. Theoretical Population Biology 80(1): 64-70.
Missov, T.I., Vaupel, J.W. (2015). Mortality Implications of Mortality Plateaus. SIAM Review 57(1): 61-70.
Salinari, G., De Santis, G. (2014). Comparing the rate of individual senescence across time and space. Population-E, 69(2):165-190.
Salinari, G., De Santis, G. (2015). On the Beginning of Mortality Acceleration, *Demography* 52(1):39-60.
Vaupel, James W., Kenneth G. Manton and Eric Stallard (1979). "The impact of heterogeneity in individual frailty on the dynamics of mortality," *Demography* 16(3):439-454.
Vaupel, J. W. (2010). Biodemography of human ageing. *Nature*, 464 (7288), 536-542.
Zarulli, V. (2013). "The effect of mortality shocks on the age-pattern of adult mortality," *Population-E,* 68(2), pp. 265-292.

Figure 1. *Fitting the force of mortality of Swedish females cohorts with the EGG model*

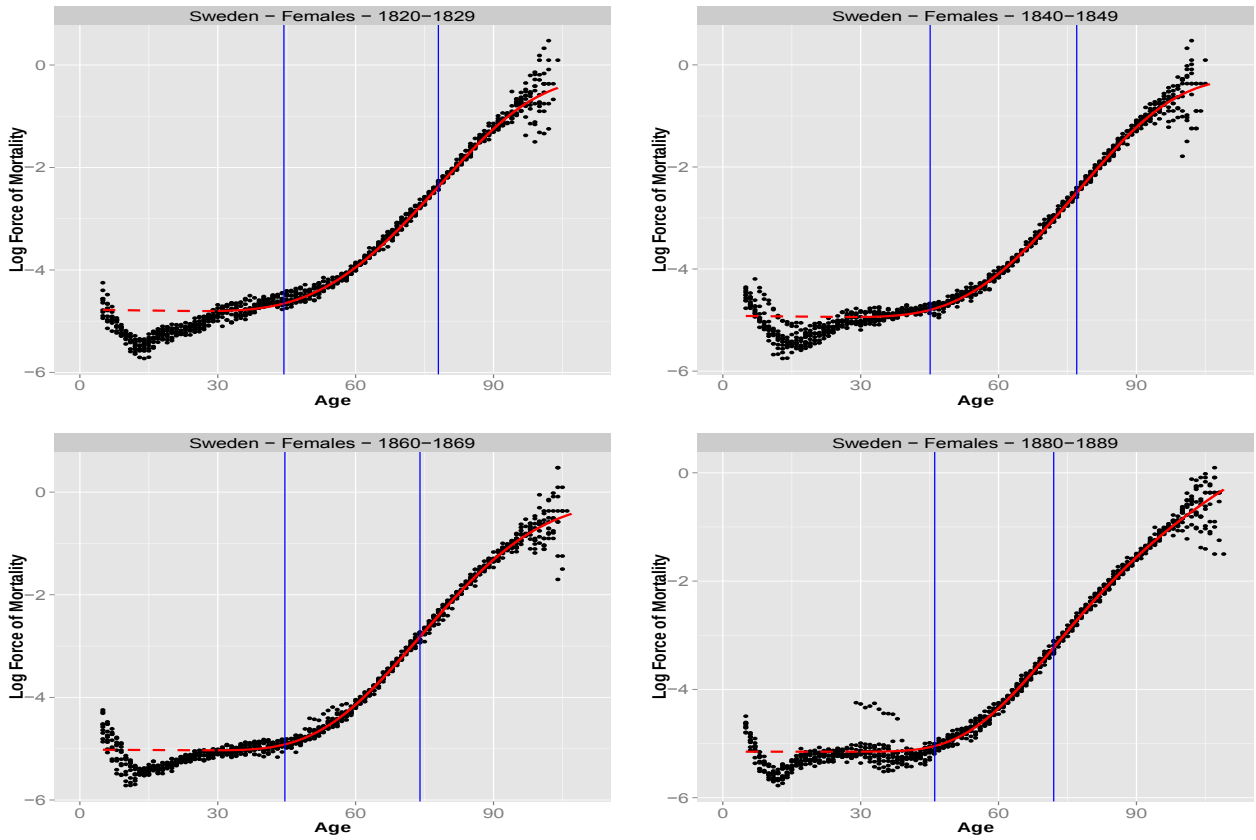

Figure 2. *Age-specific rate of ageing computed through the EGG model, by country, year of birth and sex*