Rethinking Mortality Deceleration

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Almost two hundred years ago, Benjamin Gompertz (1825) proposed the first analytical model for the *increase of mortality with age*: in Gompertz's model the force of mortality among adults (i.e. after childhood) was assumed to increase as an exponential function of age. Gompertz himself, however, recognized that his model could not fully capture what happened at older ages, above 75 or 80 years (Horiuchi and Wilmoth 1998), when ageing tended to slow down. Even though, very few people survived to be that old in the early nineteenth century, the biodemographic literature that flourished after Gompertz stressed the relevance of this deceleration: examples, listed by Olshansky (1998), include Makeham (1867), Brownlee (1919), Perks (1932), Greenwood (1928), and Strehler (1960).

In the 1990s, a team of researchers (Kannisto, Lundstrom, Thatcher, and Vaupel, among others) systematically collected age-specific mortality rates, from thirteen Western European countries, for those in their eighties and older. The database they built permitted them to prove that, at older ages, mortality deviates from its predicted exponential trend (Vaupel 1997; Vaupel*et al*. 1998): it increases less and less, until it reaches an "old-age mortality plateau" around age 110, which Gampe (2010) and Barbi et al. (2018) later estimated at about 0.5.

In the meantime, data on the evolution of the mortality of animals had started to be gathered in. Economos (1979) was probably the first to discover that mortality deceleration was not unique to humans, but also characterized four invertebrate species and three different types of rodents. Later on, these results were confirmed for Drosophila (Curtsinger et al. 1992), for *Caenorhabditis elegans* (Vaupel*et al*. 1994), for Mediterranean fruit flies (Carey *et al*. 1992, Carey *et al*. 1995) and for yeasts (Jazwinski *et al*. 1998; Vaupel *et al*. 1998), too.

Finally, a process of deceleration was also identified in the progressive dysregulation of several physiological indicators, such as blood pressure, body-mass index, total cholesterol etc.: these are, of course, indicators which characterize ageing phenotypes (Crimmins *et al*. 2003; Crimmins *et al*. 2006).

In short, by the end of the 1990s, the scientific community had to admit that Gompertz's model could describe the evolution of adult mortality only up to a point, and that new ideas were needed.

Today probably the most influential explanation for late-life mortality deceleration calls selection into play (Beard 1959; Vaupel*et al*. 1979; Yashin *et al*. 2002). If cohorts are heterogeneous and some individuals more resilient than others, the frailest die earlier while the strongest survive, and the composition of the cohort changes over time. This line of reasoning, which led to the formulation of frailty models (Hanagal 2011), implies that mortality deceleration does not necessarily occur with individuals: it is only observable at the aggregate (cohort) level.

A different explanation was suggested, as far back as 1939, by Greenwood and Irwin: namely, behavioral change. "Even the juvenile of 60, if ordinarily intelligent, eschews the violent exercises of the child of 40" (Greenwood and Irwin, 1939:14). The interesting point here is the assumption that individual frailty can be modified and that individuals are not passive in the face of ageing. This idea contradicts, to a certain extent, selection theory and frailty models where individual frailty is considered to be a lifelong constant. The literature on the behavioral changes that take places at older ages is large. One of its conclusions is that both attitudes to risk (Dohmen *et al*. 2005; Rolison *et al*. 2013; Dohmen 2015; Josef *et al*. 2016) and social networks (Bhattacharya *et al*. 2016) tend to decline with age. These changes have sometimes been attributed to hormonal transformation: e.g., the reduction of free testosterone (Ferrini and Barrett-Connor 1998; Harman *et al*. 2001; Yeap 2009), which regulates aggressiveness, risk-taking behavior and sociality (Herbert 2015), and the increase in cortisol (Larsson *et al*. 2009), a hormone associated with stress, fear and anxiety (Mehta and Josephs 2010). Put in the simplest possible terms, hormonal change may lead to behavioral changes that slow down mortality.

The evolution of car-passenger mortality by age seems to be consistent with the behavioral hypothesis. Figure 1, for instance, describes the situation in the US at the beginning of the 1990s. Both panels compare two different types of mortality rates: the number of deaths per 100 million miles; and the

number of deaths per 100,000 licensed drivers. Panel 1.A uses a fixed base index (16-19 years mortality = 100) while panel 1.B illustrates the percentage change in these two indexes from one age group to the next. Mortality due to car accident increases sharply after 60-64 years, probably because of ageing (delay in reaction time, partial visual impairment, partial hearing loss, higher physiological fragility, etc.). This increase, however, is steeper if it is gauged by the first index (deaths *per* million miles), which nets out the decline with age in the average number of miles driven *per* year (Figure 2.A), a typical behavioral change. This is a first indication that behavioral changes may slow mortality progression.

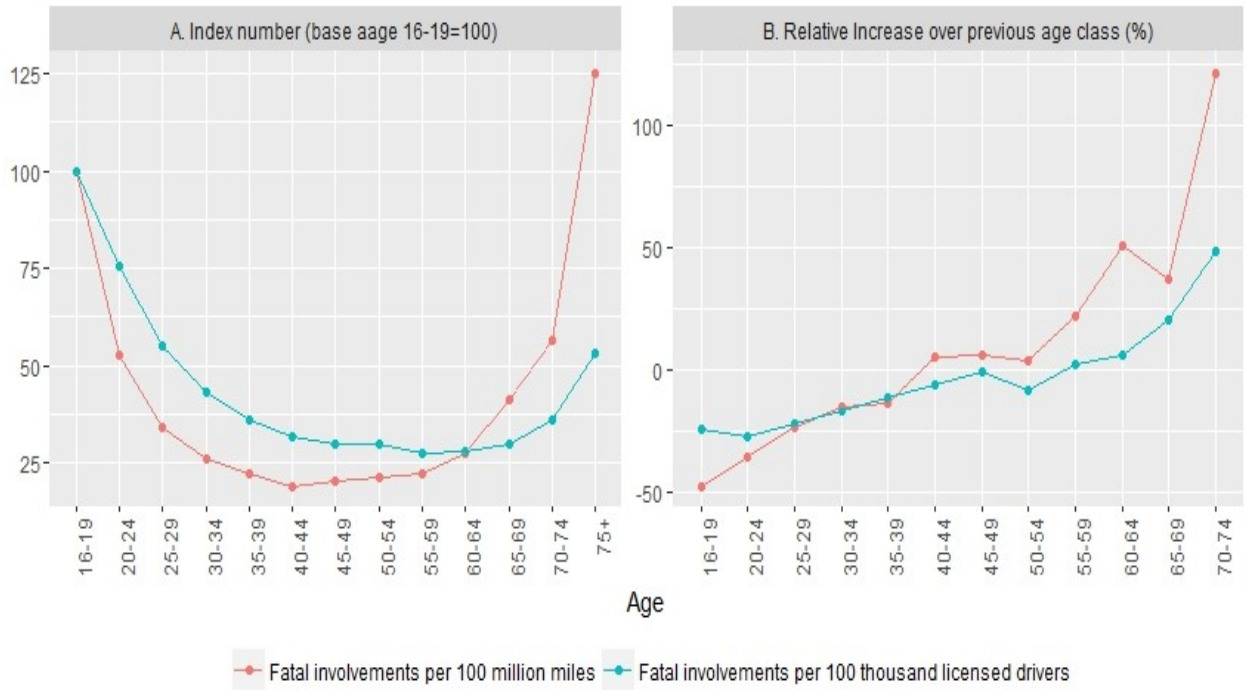
Finally, a third hypothesis (Horiuchi and Wilmoth 1998) is that mortality may actually increase more slowly, or not at all, once individuals have reached a certain age (physiological slow-down). This hypothesis derives mainly from the observation that several forms of cancer and cardiovascular diseases tend to decline (in absolute term) after 80 or 85 years (Harding *et al*. 2012; Akushevich*et al*. 2016). This is true both in terms of cohort incidence and prevalence, things which does not seem to be entirely attributable to selection (Anisimov *et al*. 2005).

These three explanations (selection, behavioral change and physiological slow-down) were considered to be of comparable importance for some time (see, e.g., Vaupel 1997). Subsequently, however, something changed. Perhaps because of the popularization of frailty models, the selection hypothesis became more and more popular (Billari 2015; Salinari and De Santis 2014; Zarulli 2016,2013) and behavioral change and physiological slow-down gradually disappeared as explanations.

To the best of my knowledge, however, no quantitative assessment of the role played by selection in the process of ageing deceleration has yet been proposed for humans[1].

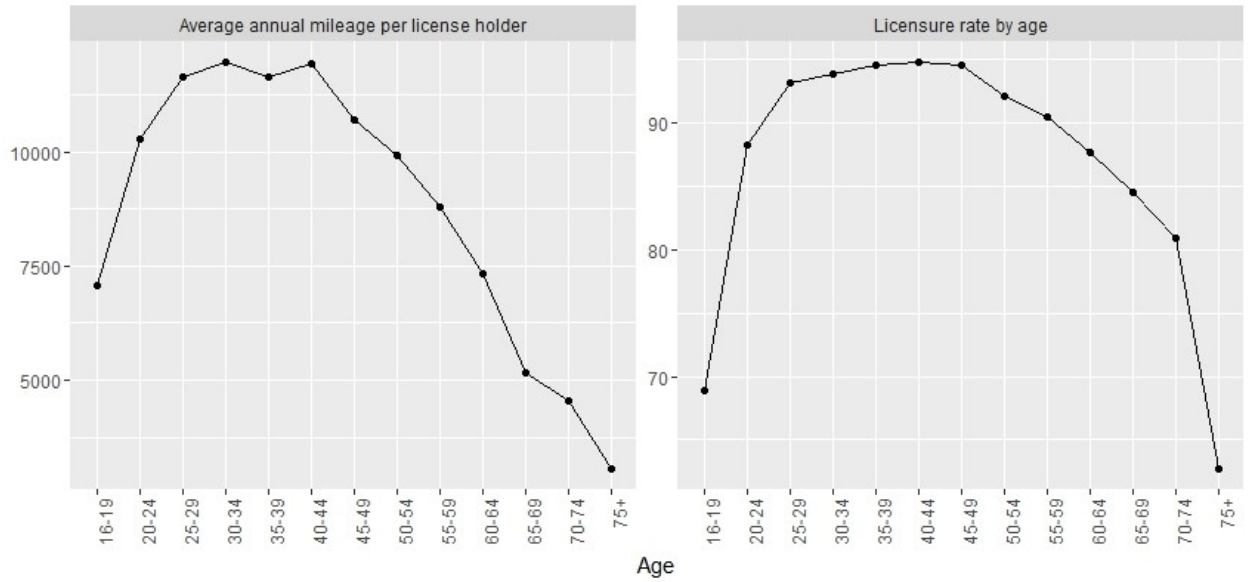
[1] Things are different for non-human species. Curtsinger (2016), for instance, makes a similar argument to the one here presented about human mortality for fruit flies.

Figure 1. Fatal Involvement Mortality by Age



Source: Massie and Campbell (1993)

Figure 2. Average Miles Driven and Licensure Rate by Age



Source: Massie and Campbell (1993)

Therefore, in the rest of this note I run a simple test to verify whether selection can be regarded as being uniquely responsible for the mortality deceleration process in old age.

The test

To test whether mortality deceleration exists at the individual level it is necessary to acquire information on the shape of the individual hazard function. This may be done in different ways according to the different hypotheses introduced. We can, for instance, assume that all individuals in a cohort share the same hazard function (the homogeneity assumption). In these settings, we can easily estimate the individual survival function by resorting to the Kaplan-Meier estimator or other similar techniques. The problem with this kind of approach is, of course, that the homogeneity assumption is too strong a hypothesis, because individuals differ in their individual death risks. A different approach might then be represented by employing a Cox regression and by considering the baseline hazard function estimated through this model as an approximation of the individual hazard function. This approach is, however, justified only if the individuals who present a given combination of covariates also share the same hazard function (Hanagal 2011). In other words, to use the Cox regression to produce a reliable estimate of the individual hazard function we must include all relevant risk factors in the model. Unfortunately, no empirical analysis appears able to do this. Usually Cox regressions can explain only a limited part of the overall variability in the age at death, because individuals who shares the same covariates may, in any case, differ in many other unobserved respects (unobserved heterogeneity). The problem of unobserved heterogeneity led Vaupel et al. (1979) to introduce the concept of frailty.

In selection theory frailty denotes an unobserved random factor defined as the ratio between the hazard function of a given individual and that of the standard individual of the cohort. Individual frailty is supposed to remain constant through life and to affect the baseline hazard function multiplicatively. Frailty is usually assumed to be gamma-distributed in human populations. This hypothesis was

probably originally introduced (Beard 1959; Vaupel *et al*. 1979) for mathematical convenience. However, some recent theoretical and empirical results, appear to support this hypothesis. From a theoretical point of view, Abbring and van den Berg (2007) were able to prove that proportional hazard models, if frailty distribution is characterized by a regular-varying density, spontaneously converge on a gamma distribution. Later, Missov and Finkelstein (2011) proved that if mortality levels off at older ages (the mortality plateau), then frailty is characterized by a regular-varying density. The recent discovery (Gampe 2010; Barbi et al. 2018) of the old age mortality plateau, thus, provides important empirical support in favour of the gamma hypothesis (Missov and Vaupel 2015).

In this paper it is assumed that frailty in a cohort is gamma-distributed. This will allow for the estimation of the slope of the individual log-hazard function across four age intervals (80-84, 85-89, 90-94, 95-99). The comparison of these four slopes will eventually allow for a test on the existence of an individual level process of mortality deceleration.

By assuming that frailty is gamma-distributed it can be shown analytically (Vaupel*et al*. 1979; Vaupel and Missov 2014) that the aggregate (cohort) force of mortality $\overline{\mu}(x)$ at age x is given by:

$$\overline{\mu}(x) = \mu(x)[\overline{s}(x)]^{\gamma} \quad (1)$$

Where $\mu(x)$ represents the baseline individual hazard function, $\overline{s}(x)$ is the aggregate (cohort) survival function and γ indicates the initial variance of frailty. Taking the logarithm of eq. (1) we get:

$$\ln \overline{\mu}(x) = \ln \mu(x) + \gamma[\ln \overline{s}(x)] \quad (2)$$

In human populations (Jones *et al*. 2014) the individual hazard function $\mu(x)$ is generally assumed to be, at adult age, a monotonically increasing function of age, so its log must also increase monotonically. Notice, however, that in eq. (2) the term $\gamma[\ln \overline{s}(x)]$, which captures the process of mortality deceleration, is non-positive (because $\ln \overline{s}(x) \leq 0$ and $\gamma \geq 0$). This implies that, at cohort level, the log force of mortality increases more slowly than at the individual level.

By differentiating eq. (2) with respect to age we get:

$$\overline{b}(x) = b(x) - \gamma\overline{\mu}(x) \quad (3)$$

The quantity $\overline{b}(x)$ is generally known as life-table ageing rates (LAR; Horiuchi and Wilmoth 1998), while $b(x)$, the *rate of ageing*, represents the relative derivative of the baseline hazard function. The value of $\overline{b}(x)$ at age x can be estimated from ordinary lifetables by differentiating the annual mortality rates: $\overline{b}_x = \ln m_x - \ln m_{x-1}$. The value of $\overline{\mu}(x)$ can, instead, be estimated as the geometric mean of two adjacent annual mortality rates: $\overline{\mu}_x = \sqrt{m_x m_{x-1}}$. Note, that in the previous formulas suffix notation is adopted for $\overline{b}_x, \overline{\mu}_x$, because they denote the estimates of $\overline{b}(x)$ and $\overline{\mu}(x)$ derived from a life table. Ordinary regression analysis can now be used to get some insights into the shape of the baseline hazard function:

$$\overline{b}_x = b_0 + \sum_{k=1}^{K} \xi_{x,k}\beta_k - \gamma\bar{\mu}_x + \varepsilon_x \quad (4)$$

where each $\xi_{x,k}$ indicates a dummy variable, whose value is one when *x* belongs to a given age interval (for instance, ages 85-89) and otherwise 0. In practice, by means of the $\xi_{x,k}$s, the age interval on which the analysis extends has been "segmented" in *K+1* segments, each characterized by its specific rate of ageing. In the present analysis four segments are used, for the ages 80 to 99,[2] each of five years. In this framework, b_0 represents the mean value of the rate of aging in the first segment of the hazard function (80-84), whereas the β_k (k=1, …, K) coefficients gauge the variation in the rate of aging in the following K segments (85-89, 90-94, 95-99). The mean rate of ageing b_k experienced by the cohort during the k-th segment (85-89) can be calculated as $b_k = b_0 + \beta_k$. In the following I will refer to the b_k coefficients as the *age-specific rate of ageing*.

For the empirical estimation of eq. (4), I resorted to the yearly life tables of the female cohorts born between 1878 and 1915 in nine countries (Denmark, England and Wales, Finland, France, Italy, the

[2] A different possibility would have been to estimate the individual rate of ageing by means of a P-spline smoothing technique, as in Barbi and Camarda (2011a, 2011b), but this would be at the cost of a more complex formal development.

Netherlands, Norway, Sweden, and Switzerland), for ages 80-99. The data come from the last release of the Human Mortality Database (HMD).

The analysis takes only female cohorts to protect results from the smoking pandemic, which affected male cohorts more heavily than female cohorts (Pampel 2010). The analysis stops at age 99 because the raw data employed by the HMD for building cohort lifetables frequently present an open-ended class (100+).

Eq. (4) was estimated from these data for one cohort at a time. In this way I got an overall number of estimates of (1915-1878+1)×9 = 342. Eq. (4) was estimated through ordinary least squares (OLS), because, in the present context, this method seems preferable to other concurrent methods such as weighted least squares (WLS). Actually, according to Brillinger (1986) the sample variance of the log mortality rates is given by the inverse of the absolute number of deaths, $1/\mathrm{D}_x$, which entails that the sample variance of $\overline{b}_x$ can be approximated (assuming independence) by $\frac{2}{D_x}$. This means that at older ages, when the absolute number of deaths is smaller (because most of the cohort is already extinct) the sample variance of $\overline{b}_x$ grows. This does not pose a real problem, in the present settings, because the OLS estimates of the coefficients of eq. (4) remain consistent even with heteroscedasticity[3]. If WLS is used instead of OLS, there are two possibilities. Either the weights to be used in the estimation procedure are correctly specified, and thus the coefficients estimates must coincide with those estimated through OLS; or, alternatively, the weights are mis-specified, entailing a bias in the estimate of the coefficients of the model. In neither case does using WLS help, as the goal is to estimate the coefficients of eq. (4).

To test if the process of mortality deceleration can be entirely attributed to selection, I simply regressed on k (a linear transformation of age), the estimated age-specific rate of ageing $\hat{b}_{k,c}$ ($\mathrm{c} = 1, \ldots, \mathrm{n}$) in the *n = 342* cohorts under scrutiny:

[3]This is not true, of course, for the standard error of the model, which may be biased by the presence of heteroscedasticity, but which are not of great interest in this part of the analysis.

$$\hat{b}_{k,c} = \delta_0 + \delta_1 k + \varepsilon_{k,c} \quad (5)$$

If the slope (δ_1) of this simple linear regression model proves to be significantly negative, then we can conclude that a process of mortality deceleration is taking place at the individual level, as well as at the cohort level as implied by selection theory. This time, however, it is important to control for the potential bias produced by heteroscedasticity on the standard errors of the model coefficients. Indeed, the focus is now on performing a test based on the magnitude of the standard errors. To protect this part of the analysis from heteroscedasticity and to get unbiased standard errors, the heteroscedasticity-corrected (HC) sandwich estimator was employed (Cribari-Neto 2004).

Results

The frequency distribution of the estimated age-specific rates of ageing ($\hat{b}_k$) for the female cohorts under scrutiny are shown in Figure 3. By looking at this Figure it becomes apparent that these estimates present much variability, and that this variability increases by age. This phenomenon is mainly a consequence of working on the 80-99 age range, during which the absolute number of deaths follows a decreasing trend. Since the sample variance of log mortality rates depends on the inverse of the absolute number of deaths (Brillinger 1986; Horiuchi and Wilmoth 1998), the estimates become increasingly uncertain as we reach older and older age classes. What is more, the procedure of differentiation introduced to get eq. (3), further amplify this uncertainty (see on this the previous section).

The mean values of the age-specific rate of ageing are shown in Figure 4. This Figure identifies a general declining trend in the age-specific rate of ageing. These estimates decline from a mean value of 0.1 in the first age class (80-84) to a mean value of 0.08 in the last age class (95-99). As shown in Table 1 the observed decline in the age-specific rate of ageing proves to be statistically significant, though not strongly so.

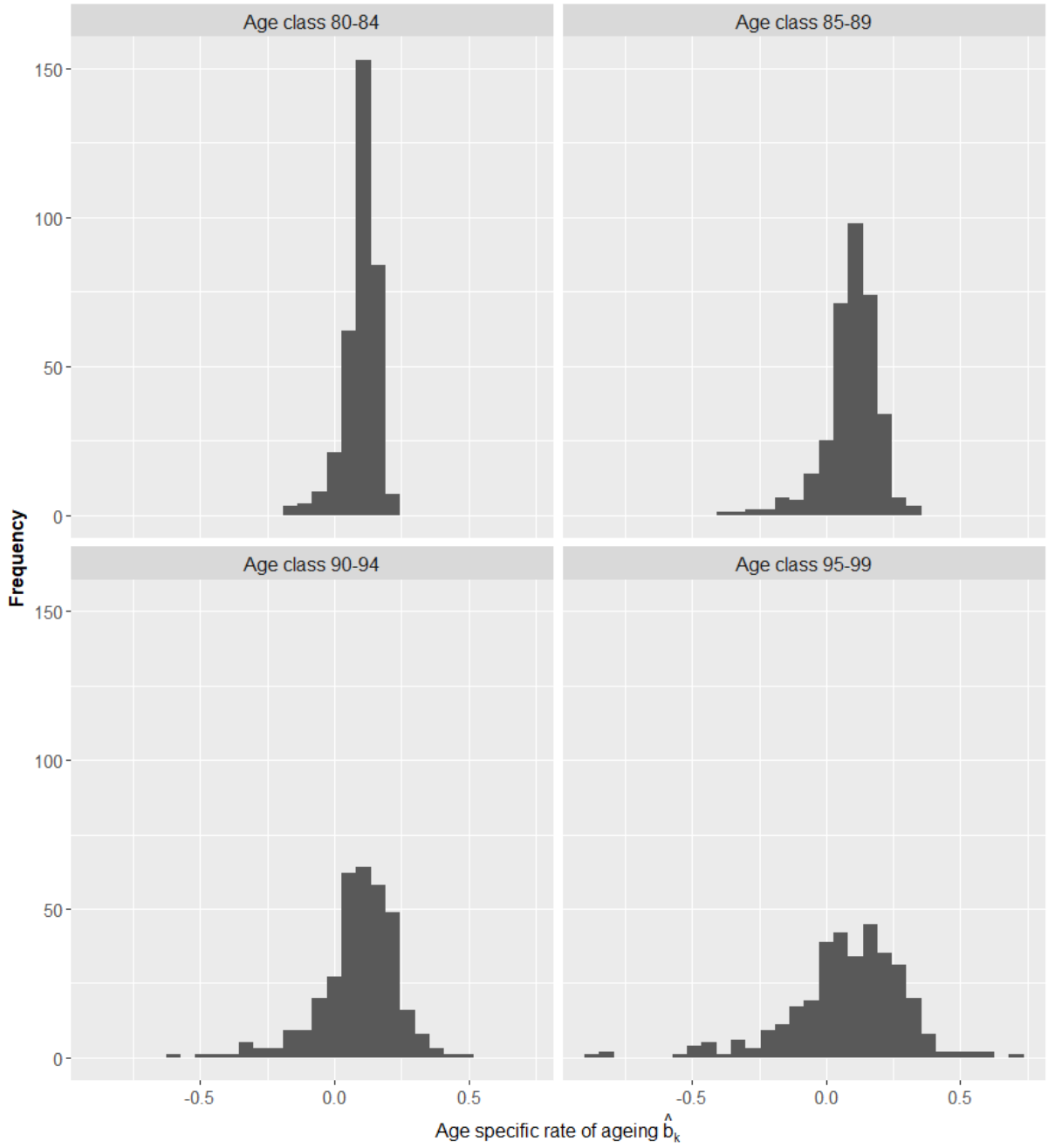
This result applies, however, on average. To verify whether most, if not all, of the individual hazard functions analyzed present a deceleration pattern, the first differences of the age-specific rates of ageing were calculated for each cohort c: $\Delta\hat{b}_{1,c} = \hat{b}_{2,c} - \hat{b}_{1,c}$, $\Delta\hat{b}_{2,c} = \hat{b}_{3,c} - \hat{b}_{2,c}$ and $\Delta\hat{b}_{3,c} = \hat{b}_{4,c} - \hat{b}_{3,c}$. If all these three quantities turn out to be negative, this will imply that the individual hazard function of cohort c undergoes a continuous process of deceleration from age 80 to age 99. Figure 5 presents the frequency distribution of the cohorts according to the number of deceleration phases identified in it. This analysis shows that 52% of the cohorts present at least two phases (out of three) of individual-level deceleration, while 67% of cohorts present at least one phase of deceleration. The surprising result of this analysis, however, is that about one third of all cohorts present a protracted acceleration process in the three phases here considered.

These results seem also to be confirmed by the analysis of the γ parameter of eq. 4 for which Table 2 presents some descriptive statistics. The mean value of this parameter across the 342 cohorts analyzed is 0.217 that confirms that most cohorts are experiencing a process of mortality deceleration. Furthermore, γ shows a significant positive time trend (results not shown). Younger cohorts generally present a larger initial variance of frailty than older cohorts. The standard deviation associated with this parameter is, however, quite large, 0.608, so that the first quartile of the distribution turns out to be a negative number, -0.263. This seems to confirm that, for a small but not negligible number of cohorts, a process of mortality deceleration cannot be identified.

Overall these results apparently lend credit to the hypothesis that selection is not the only phenomenon involved in mortality deceleration: there must be something else, which leaves room for behavioral adjustment and, possibly, for slower ageing at very old ages at the individual level. This may happen because people do not accept ageing passively and so they try to counter it in a variety of ways: by giving up smoking; by reducing alcohol consumption; by going to the gym; by eating better; by avoiding risks like those connected with driving or other dangerous activities...

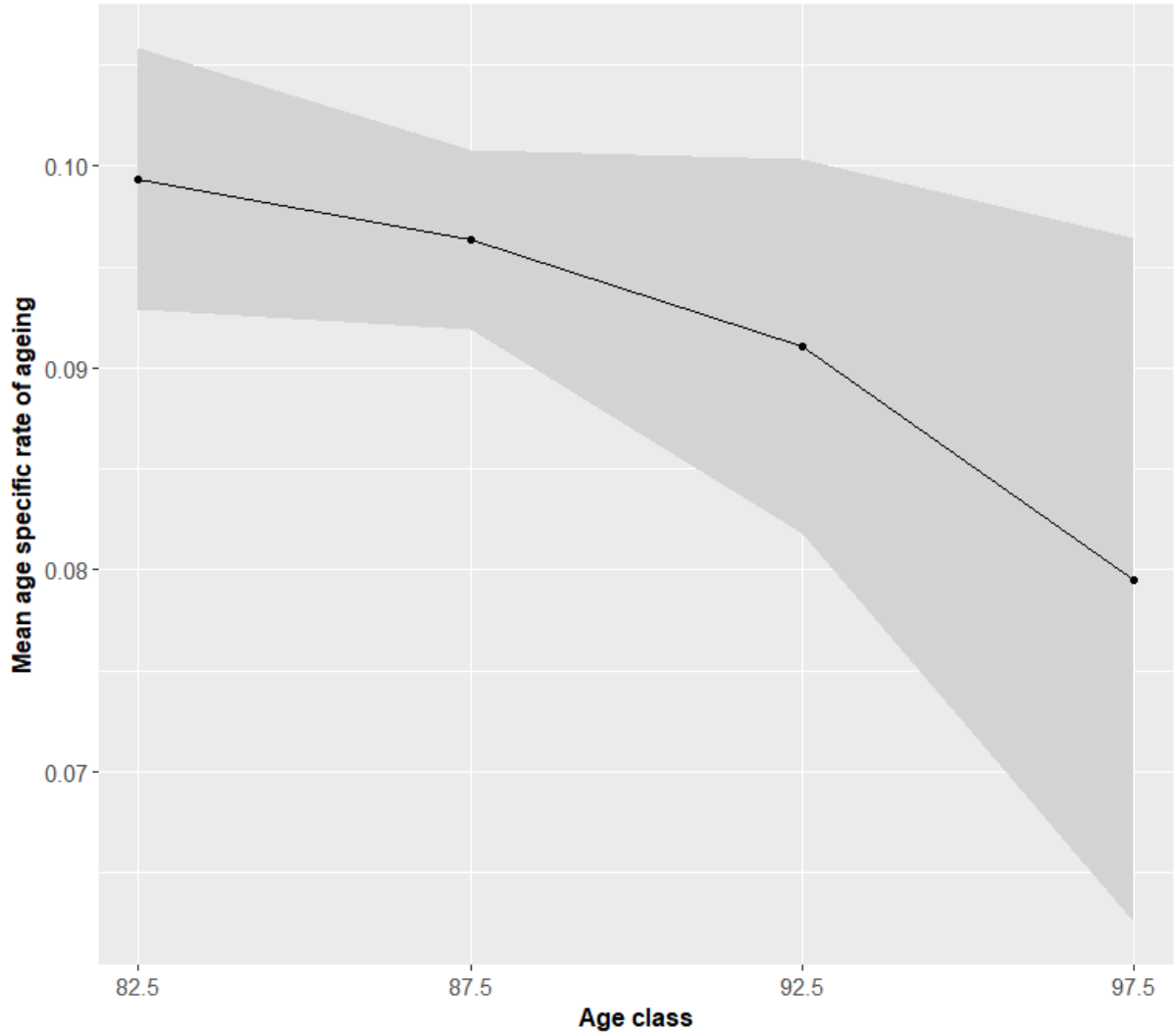
It is worth remembering, however, that the estimates for the age-specific rates of ageing have been produced here under the general assumption of a gamma-distributed frailty. As we have seen this hypothesis has recently found support with the discovery of the mortality plateau. This notwithstanding, it cannot be definitely excluded that the observed processes of deceleration/acceleration in the individual hazard function might also depend on the fact that frailty does not always conform to a gamma distribution.

Figure 3.Distribution of the estimated age-specific rate of ageing ($\hat{b}_k$) by age class in female cohorts



Source: Author's elaboration of HMD data.

Figure 4. Mean age specific rate of ageing by age class in female cohorts



Source: Author's elaboration of HMD data.

Note: On the horizontal axis the number 82.5, 87.5, …,97.5 refers respectively to the mid points of the age-class 80-84, 85-89, …, 95-99. Each point represents the mean value of the age specific rate of ageing estimated in a given age class. The grey area indicates the 95% confidence band.

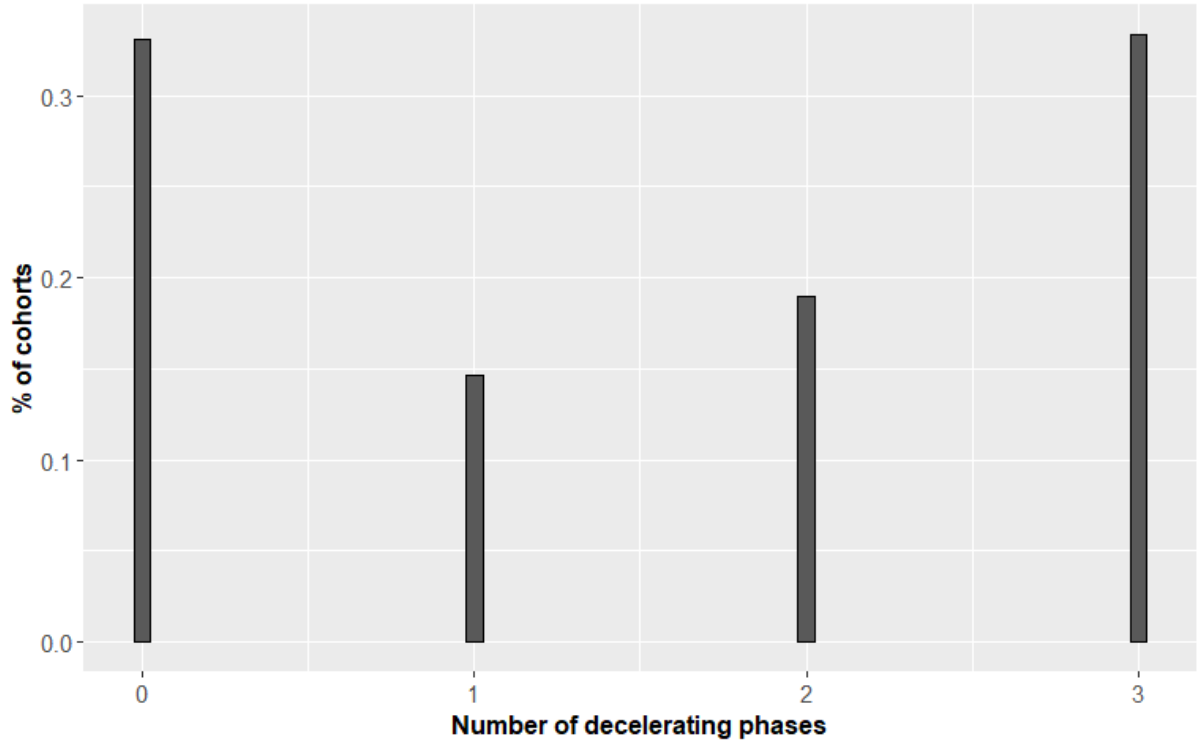
Table 1. Regression analysis of the age-specific rates of ageing (see eq. 5)

	Estimate	**SE**	**t value**	**P value**
Intercept	0.101	0.0040	25.42	0.000***
Slope	-0.006	0.0037	-1.72	0.043*

Source: Author's elaboration on HMD data.

Note: The table presents the estimate of the coefficients of eq. 5. The standard errors have been computed by the heteroscedasticity-corrected (HC) sandwich estimator (Cribari-Neto F. 2004). The p value of the slope refers to a one-tail t test (H_0: $slope \geq 0$;H_1: $slope < 0$).

Figure 5. Frequency distribution of cohorts according to the number of decelerating phases.



Source: Author's elaboration of HMD data.

Note: To identify the phases of mortality deceleration in a given hazard function c, the first differences of the age-specific rates of ageing were calculated: $\Delta\hat{\mathrm{b}}_{1,c} = \hat{\mathrm{b}}_{2,c} - \hat{\mathrm{b}}_{1,c}$, $\Delta\hat{\mathrm{b}}_{2,c} = \hat{\mathrm{b}}_{3,c} - \hat{\mathrm{b}}_{2,c}$ and $\Delta\hat{\mathrm{b}}_{3,c} = \hat{\mathrm{b}}_{4,c} - \hat{\mathrm{b}}_{3,c}$. The number of decelerating phases emerges as the number of differences $\Delta\hat{\mathrm{b}}_{h,c}$ which presents a negative value.

Table 2. Summary statistics for the distribution of the γ parameter of eq. 4

	Mean	SD	Q1	Q2	Q3
γ	0.217	0.608	-0.263	0.054	0.428

Source: Author's elaboration of HMD data.

Note: Summary statistics of the estimates of the γ parameter of eq. 4 in the 342 cohorts analyzed. SD indicates the standard deviation while Q1-Q3 are the quartiles of the distribution.

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