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Earlier and more rapid ageing: Does nutrition contribute?

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Abstract: This paper estimated three parameters related to demographic ageing, i.e., the acceleration in mortality rates as people get older. These parameters are: (i) the age when the process begins (onset), (ii) the rate of ageing in a (simple) Gompertz model and (iii) the rate of ageing in a (more elaborate) Gamma-Gompertz model. These three indicators were estimated on the basis of female cohorts born in seven European countries between 1890 and 1919. Our results indicated a progressively earlier onset and a steeper rise in the rate of ageing in recent cohorts, i.e., ageing seems to have accelerated over time. The reasons for these shifts are still unknown, but due to their similarity with the results of a vast body of experiments of calorie restriction on lab animals, we suggested here that the changed dietary regime of humans since the end of the 19th century may have played a part in the evolution of their mortality schedule.

Keywords: ageing, nutrition, Gamma-Gompertz, calorie restriction, ageing onset

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1. Introduction

Modern individuals living in advanced societies are well fed and enjoy the warmth of their houses and the protection of antibiotics and vaccines. They suffer from later and slower "ageing" than their predecessors, if ageing means an increase in the risk of death connected to becoming older. The chances of survival have rapidly improved almost everywhere in the past 200 years or so. Anecdotally, one may note that in France for example, a forty-year old woman in 2005 had exactly the same life expectancy as a thirty-year old woman in 1952 (Sanderson and Scherbov, 2008; 2013). More systematic statistical information can be found almost everywhere, for instance in the HMD (Human Mortality Database), which also happens to be the source of data for our analysis. However, the connection between longevity and physiological ageing is elusive and the two concepts are not synonymous (Baudisch, 2011; Baudisch and Vaupel, 2012). Biologists and gerontologists interpret ageing (or senescence) as the process by which molecular damage increases at the cellular level (Rattan, 2006; 2008). This of course affects the probability of death but

senescence is not the only factor and it is not necessarily the most important.

In order to indirectly gauge physiological ageing, biologists, gerontologists and demographers commonly use other measures. The most frequent among these is probably the mortality rate doubling time (MRDT) or its equivalent, the rate of ageing. The general idea behind it is that the pace at which mortality increases with age reflects the pace of the underlying physiological process of molecular deterioration. Strehler and Mildvan (1960), two forerunners in this line of thinking, indicated that the MRDT was shorter where life expectancy at birth was higher or in other words, that modern populations age faster. This empirical regularity also known as the "compensation" or Strehler-Mildvan law has subsequently been confirmed by several other studies (Zheng, Yang and Land, 2011).

However, the MRDT has its drawbacks. Its estimates derive from aggregate (preferably cohort) life tables but individuals are not homogeneous and as the frailest tend to die earlier, the composition of the group under observation changes over time. At advanced ages, for example 90 years and over, this selection causes a detectable deceleration in the evolution of aggregate mortality with age (Vaupel, Manton and Stallard, 1979; Vaupel, Carey, Christensen *et al*., 1998) which biases the estimated MRDT upwards. Populations with shorter average life spans tend to display stronger mortality deceleration and therefore also higher MRDT. In other words, the "compensation law" may be nothing more than an artifact caused by selection.

To keep selection under control one needs sophisticated statistical models, a specific definition of frailty and several assumptions, both about the functional form of the individual hazard functions and on the distribution of frailty in the population. Unfortunately, most of these assumptions refer to non-observable variables and cannot be tested directly which undermines confidence in MRDT estimates.

In 2010, Gampe ventured that at very advanced ages (110+), human mortality may level off producing what is generally known as the "mortality plateau" which turns out to be consistent with only a few mortality models. It is not for instance, compatible with the accelerated-life models (Finkelstein and Esaulova, 2006) or with the assumption that frailty is log-normally distributed (Missov and Finkelstein, 2011). If a mortality plateau really exists, the only meaningful way of describing human mortality seems to be the Gamma-Gompertz model where the individual rate of ageing is constant, the hazards evolve exponentially (à la Gompertz) and frailty is Gamma distributed (Missov and Vaupel, 2015).

In 2010, Vaupel conjectured that the individual rate of ageing might be constant in all human populations but this "constant senescence hypothesis" has thus far received only partial empirical corroboration (Salinari and De Santis, 2014; Zarulli, 2013). This paper carefully studied the question of whether the rate of ageing is a constant together with a set of related questions: at what age does the force of mortality begin to increase with age? Why not earlier? Has this threshold age remained constant over time?

Our analysis encompassed seven European countries (Finland, France, Italy, the Netherlands, Norway, Sweden and Switzerland) with good cohort data in the Human Mortality Database (HMD). Salinari and De Santis (2014) had previously identified the series of Nordic countries and those of Switzerland as the best for this type of analysis because deaths were originally classified by single year of age and could be represented in parallelograms on a Lexis diagram. This paper however, also uses mortality data from France and Italy, albeit of somewhat lower quality, in order to exclude the possibility that the conclusions apply only to the specific dietary regimes of selected countries.

For each of these countries, we analyzed the evolution of female mortality in the age range of 25 to 99 years in the cohorts born between 1890 and 1919. We preferred females

over males because women were comparatively less affected by the sweeping social changes that were taking place in those years (notably in smoking and alcohol consumption) and by war. Our analyses showed that ageing started earlier and was more rapid in recent cohorts in all the seven countries. We do not yet know why this happened. However, we noted that this rather counter-intuitive result is consistent with the outcomes of about 30 years of experiments on calorie restriction (CR) imposed on animals and we argued that the changing dietary regime of humans in the past century or so may have played a part in this evolution.

2. Data and Methods

The first studies on mortality acceleration assumed that it would begin around sexual maturity, i.e., at about the age of 12 (Olshansky and Carnes, 1997), in line with the most important macro-theories of ageing which considered senescence a consequence of the progressive weakening of natural selection after puberty (Hamilton, 1966). On the other hand, empirical findings pointed in another direction. In hunter-gatherer populations for instance, the onset of mortality acceleration was estimated to occur between 40 and 50 years (Gurven and Kaplan, 2007; Gurven, Kaplan and Supa, 2007; Hill, Hurtado and Walker, 2007). Salinari and De Santis (2015) also identified a late ageing onset between 30 and 50 years for cohorts born in the nineteenth and twentieth century in fourteen different countries (earlier in more recent cohorts).

These findings seem to corroborate the idea that the (unobservable) physiological process of ageing does not need to translate into an immediate rise in the (observable) death rate with age because cells can absorb and partly repair molecular damage as long as it remains below a given threshold (Franceschi *et al.*, 2007; Kirkwood and Austad, 2000). Therefore, a possible way of indirectly evaluating the pace of ageing is to observe if and how its onset evolved over time, in which an earlier occurrence, i.e., an earlier arrival at the "dysfunctional threshold" may signal more rapid ageing.To estimate the onset of mortality acceleration, we employed the methodology proposed by Bai (2010) for the identification of common breaks in panel data. For the sake of simplicity, we assumed that the mortality of a group of C homogeneous cohorts (for instance the ten Swedish cohorts born between 1890 and 1899) is observed between 25 and 75 years and that ageing starts within this interval, at an unknown age k_0, which means that the force of mortality μ_x is approximately constant up to age $x \leq k_0$ and increases thereafter. We also assumed that all the individuals of a given cohort share the same age at the onset of mortality acceleration. In a more realistic but complex scenario, this acceleration is admitted to start at different ages but even in this case, the same methodology can be applied using the *mean* age at the beginning of the process (Salinari and De Santis, 2015). This can be formalized as follows:

$$\mu_{c,x} = \alpha_c + \varepsilon_{c,x} \quad x = 25, 26, \cdots, k_0 \tag{1}$$

$$\mu_{c,x} = \alpha_c e^{\beta x} + \varepsilon_{c,x} \quad x = k_0 + 1, \cdots, 75$$

where c denotes a cohort in the group, x stands for age, α_c is the mortality experienced before the onset of mortality acceleration, β is the rate of ageing and $\varepsilon_{c,x}$ is the error term. Bai's technique is insensitive to the distribution of errors, which we therefore disregarded in the following. In all cases, it is possible to show that the error terms in equations (1)–(3) are normally distributed (Brillinger, 1986; Horiuchi and Wilmoth, 1998; Salinari and De Santis, 2014; 2015).

After logarithmic transformation (Figure 1(A)) we arrived at:

$$\ln \mu_{c,x} = \ln \alpha_c + \nu_{c,x} \quad x = 25, 26, \cdots, k_0 \tag{2}$$

$$\ln \mu_{c,x} = \ln \alpha_c + \beta x + \nu_{c,x} \quad x = k_0 + 1, \cdots, 75$$

with the new error terms $\nu_{c,x}$.

Differentiating by age yields a new set of series δ_x:

$$\delta_{c,x} = \ln(\mu_{c,x+1}) - \ln(\mu_{c,x})$$

which by assumption, will oscillate around zero until age k_0 and around β after age k_0, where β is the slope of the log force of mortality:

$$\begin{aligned} \delta_{c,x} &= 0 + \omega_{c,x} \quad x = 25, 26, \cdots, k_0 . \\ \delta_{c,x} &= \beta + \omega_{c,x} \quad x = k_0 + 1, \cdots, 75 \end{aligned} \tag{3}$$

Equation (3) is a "shift model" (Figure 1(B)), where the series "jump" from zero to β at age k_0.

The break point k_0 can be estimated by trying various values for k [25≤k≤74] and selecting the one that minimizes the errors. To do so, one must first compute the mean before and after k for each cohort:

$$\bar{\delta}_{c,1} = \frac{1}{k-24} \sum_{x=25}^{k} \delta_{c,x}; \quad \bar{\delta}_{c,2} = \frac{1}{75-k} \sum_{x=k+1}^{75} \delta_{c,x}$$

Then the total sum of squares (Figure 1(C)):

$$S_c(k) = \sum_{x=25}^{k} \left(\delta_{c,x} - \bar{\delta}_{c,1}\right)^2 + \sum_{x=k+1}^{75} \left(\delta_{c,x} - \bar{\delta}_{c,2}\right)^2$$

Finally, the total sum of squares for all cohorts:

$$SSR(k) = \sum_{c=1}^{C} S_c(k)$$

The least square estimate for k_0 becomes simply (Figure 1(D)):

$$\hat{k} = \min_{25 \le k \le 74} SSR(k)$$

An important assumption of Bai's technique is that of homogeneity within groups, which means that all the series (cohorts) must share the same breakpoint. In practice, we worked under the assumption that contiguous birth cohorts were homogeneous and we formed partly overlapping groups as follows:

1890–1899, 1891–1900, …, 1910–1919... 1911–1919, 1912–1919…1916–1919.

For the sake of simplicity, we labeled these groups using the first birth cohort: 1890, 1891, etc. Note that the first groups, up to 1910–1919, include ten birth cohorts which later became fewer and fewer and down to four (1916–1919) for the final group. This is due to the fact that in the HMD the cohort life tables are generally available only up to cohorts born in 1919.

A second way of indirectly determining the average pace of physiological ageing is to look at the intensity of mortality acceleration after its onset. We are interested in the individual rate of ageing but we can only observe aggregated (e.g., cohort) ones and the two may differ because of selection. To circumvent this problem, we adopted two different approaches.

With the first and simpler approach, we estimated the parameters of the Gompertz (1825) model in an age range where selection and mortality deceleration are still weak. After some preliminary controls we selected the age interval 75–89, where Gompertz still

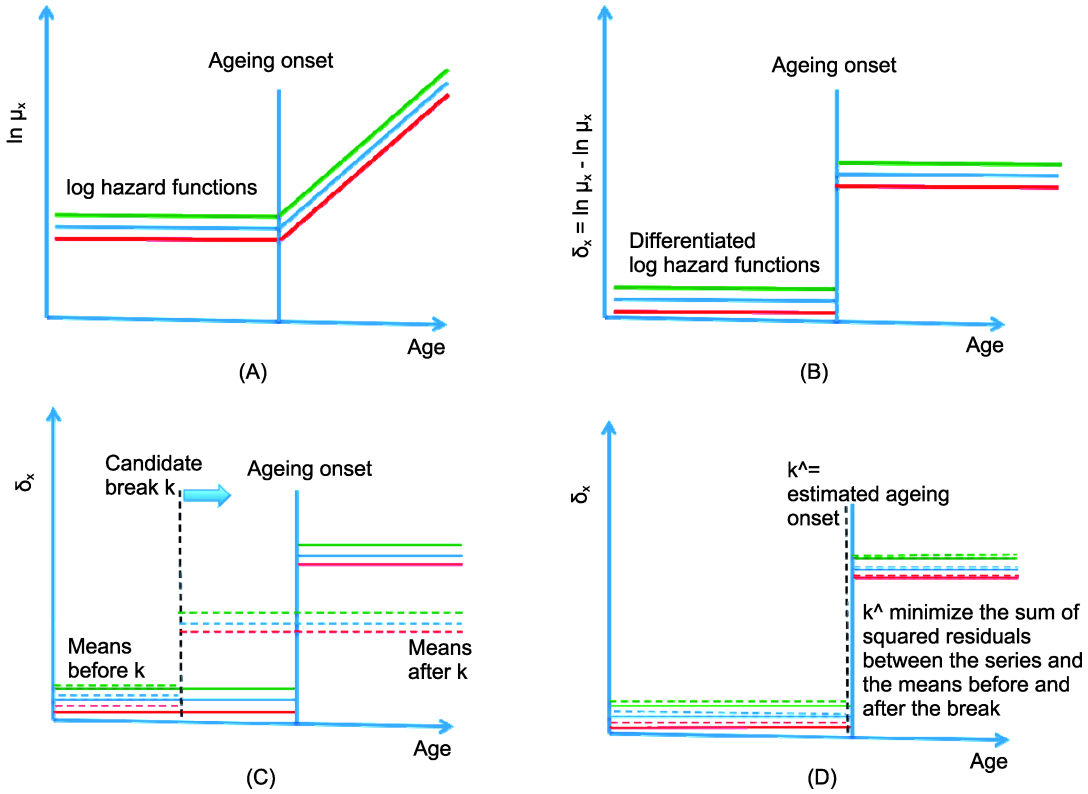

Figure 1. Identifying the onset of mortality acceleration.

Note: The solid lines indicate the log-force of mortality (A) and the differentiated log-force of mortality (B, C and D) in the life tables of three different cohorts. The dashed lines represent the mean values of the differentiated log-force of mortality of each cohort before and after each "candidate" break point k (C). The best among these candidates, k^, minimizes the (squared sum of the) errors.

offers a good fit (Gavrilov and Gavrilova, 2011). The model:

$$\ln \bar{\mu}_x = \ln \alpha + \beta x + \varepsilon_x \qquad x \in [75,89] \tag{4}$$

where the aggregate force of mortality $\bar{\mu}_x$ of each cohort is supposed to be a function of age x, β is the rate of ageing and $\ln\alpha$ represents the log-mortality of the cohort at the start of the observation, which is at 75 years of age. The results of this approach were directly comparable with those of CR experiments also based on Gompertz, which will be discussed later.

In our second approach we used the Gamma-Gompertz model. Under the assumption that frailty is Gamma-distributed, this model estimated the rate of individual ageing net of the bias caused by selection. The model can therefore be estimated on a wider range of ages and we eventually selected 75–99 years (Not higher because of the small number of observations especially in older cohorts and various problems of data quality including open-ended age classes). The corresponding equation is:

$$\ln \bar{\mu}_x = \ln \alpha + \beta x + \gamma \ln(\bar{s}_x) + \varepsilon_x \quad x \in [75,99] \tag{5}$$

where the term $\bar{s}_x$ is the aggregate survival function at age x, which can be assumed to be proportional to the strength of selection (Vaupel, Manton and Stallard, 1979).

In both Equations 4 and 5, the estimation starts at a relatively late age, 75 years, when one can assume that mortality acceleration has already begun for every individual despite variability in its onset. Both models (Equations 4 and 5) were estimated with weighted least squares (WLS) where the weights are the number of deaths of each cohort at each age.

WLS as opposed to OLS (ordinary LS) reduces the risk of bias due to heteroscedasticity (Horiuchi and Coale, 1990; Horiuchi and Wilmoth, 1998).

3. Results

Our first major finding was a decline in the age for the onset of mortality acceleration (Salinari and De Santis, 2015). Figure 2 presented the log-probability of death for two groups of cohorts: 1895 (i.e., born in 1895–1904) and 1910 (i.e., born in 1910–1919) together with the estimates of their threshold ages. Note that in all the panels of Figure 2, two different phases in the evolution of the death probabilities emerged: (1) when they are approximately stationary, (2) when they increase exponentially (i.e., log-linearly). In other words, both conditions for the correct identification of the onset of mortality acceleration are satisfied.

The estimated age at the beginning of mortality acceleration is close to 50 years in the first cohorts, born between 1895 and 1904. It progressively declined to about 40 years in the most recent cohorts, born in 1910 or later with a large variation of about ten years

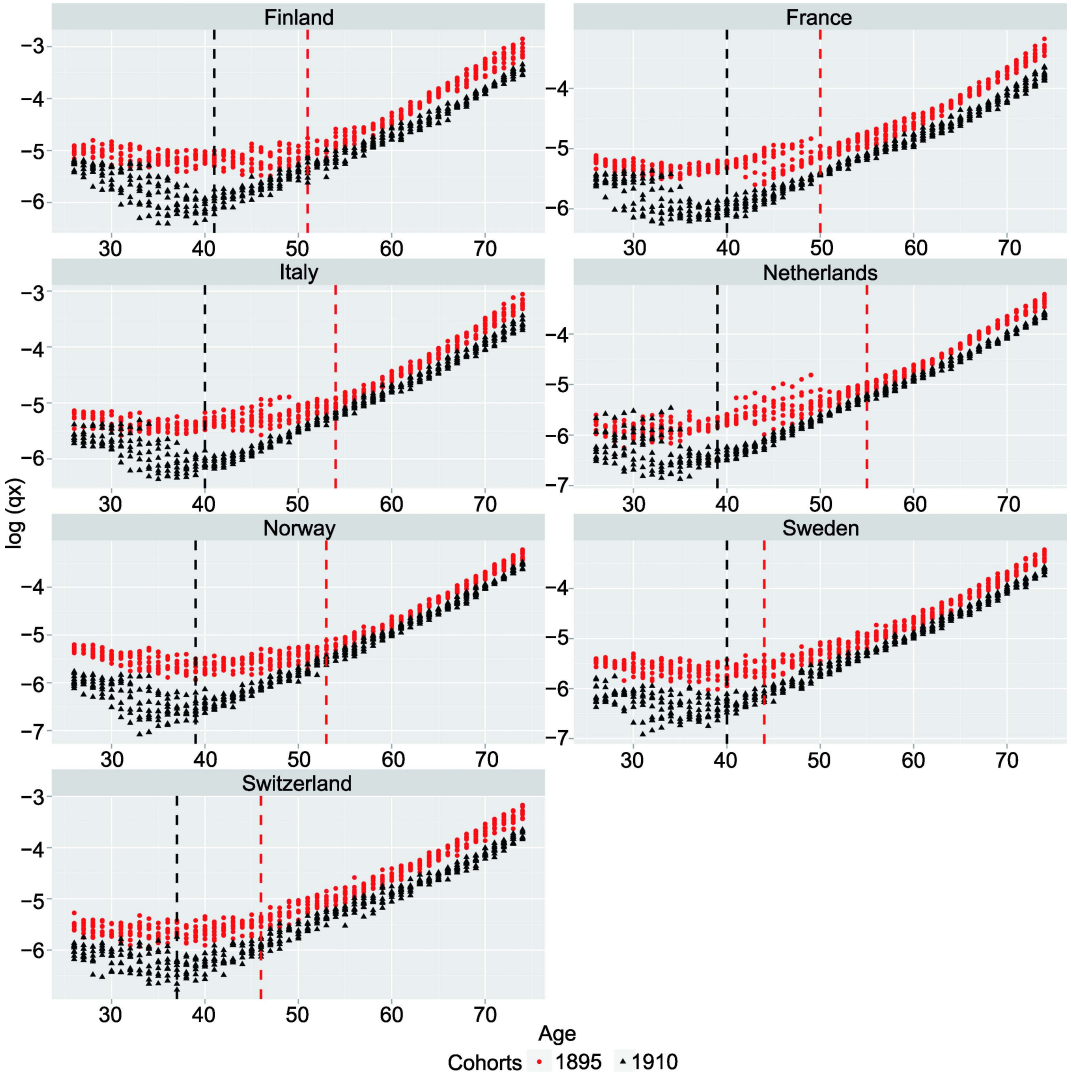

Figure 2. The onset of mortality acceleration in the cohorts born from 1895–1904 and 1910–1919.
Source: Authors' elaborations on HMD data.

(somewhat less in Sweden), that takes place over a shorter lapse of time (twenty birth cohorts or so) in all of the countries and almost all of the cohorts considered with minor exceptions (Figure 3). For the earliest cohorts, born in the years beginning 1890 to 1894, this threshold age could not always be identified and only two series out of seven were complete. These older cohorts entered our observation window 25 years later, at the eve of the Spanish flu pandemics of 1918–1919, in the age group that was hit particularly hard by this disease (Almond and Mazumder, 2005) and would most likely be the cause of the poor performance of the method in these cases.

Further indirect evidence supporting the hypothesis of acceleration in physiological ageing over time came from an analysis of the rate of ageing. Figure 4 showed that there is a good agreement between the estimates of the rate of ageing produced with the Gompertz model (on the age range of 75–89) and those produced with the Gamma-Gompertz model (on the age range of 75–99). In all the seven countries of our analysis, the rate of ageing first increased and then more or less stabilized. The estimates for β passed from about 0.100 for the initial cohorts (1890) to about 0.115 for the final ones (1919). The online material gave more details on the estimates of the three indicators and their confidence intervals.

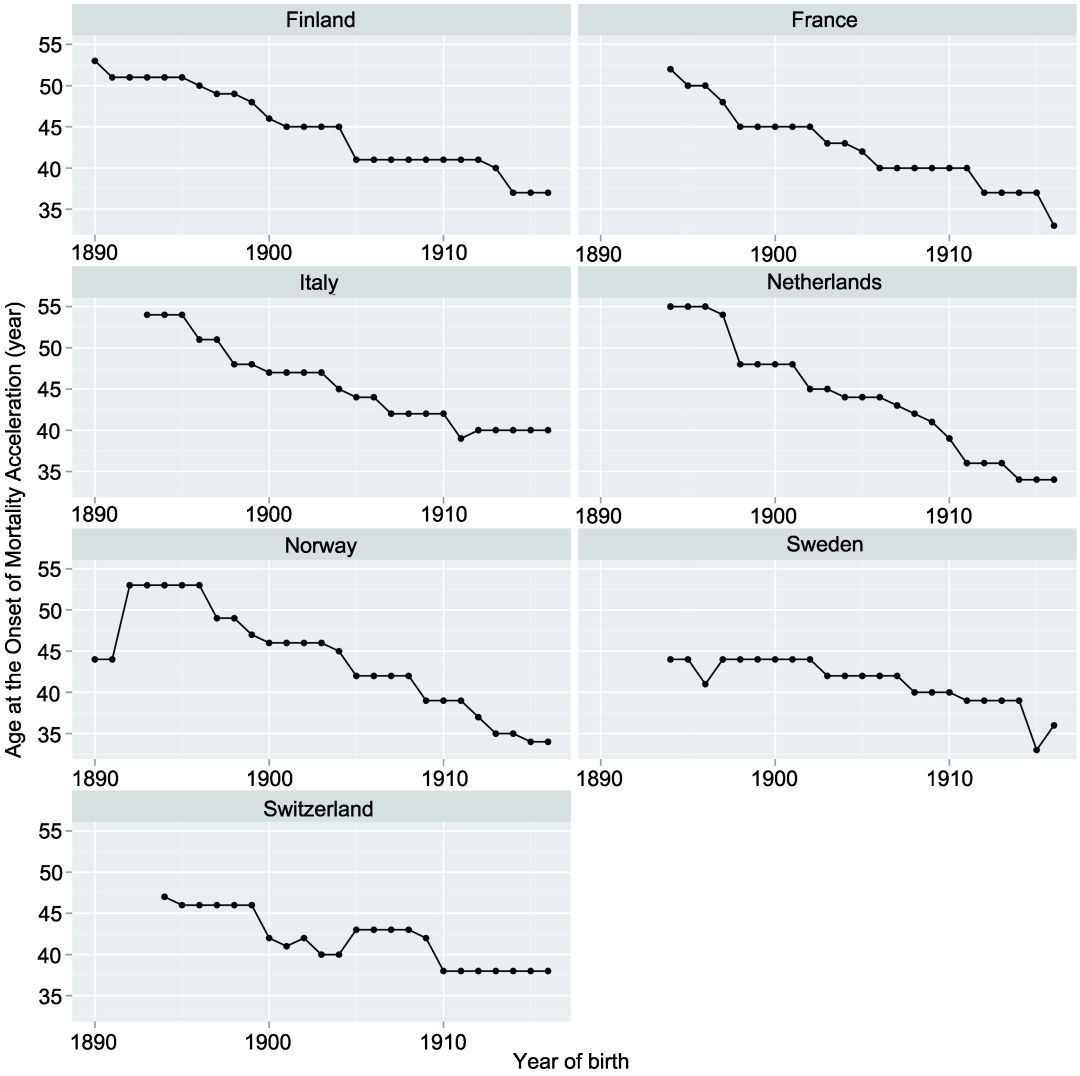

Figure 3. Evolution of the mean age at the onset of mortality acceleration by birth cohort in seven European countries.
Source: Authors' elaborations on HMD data.

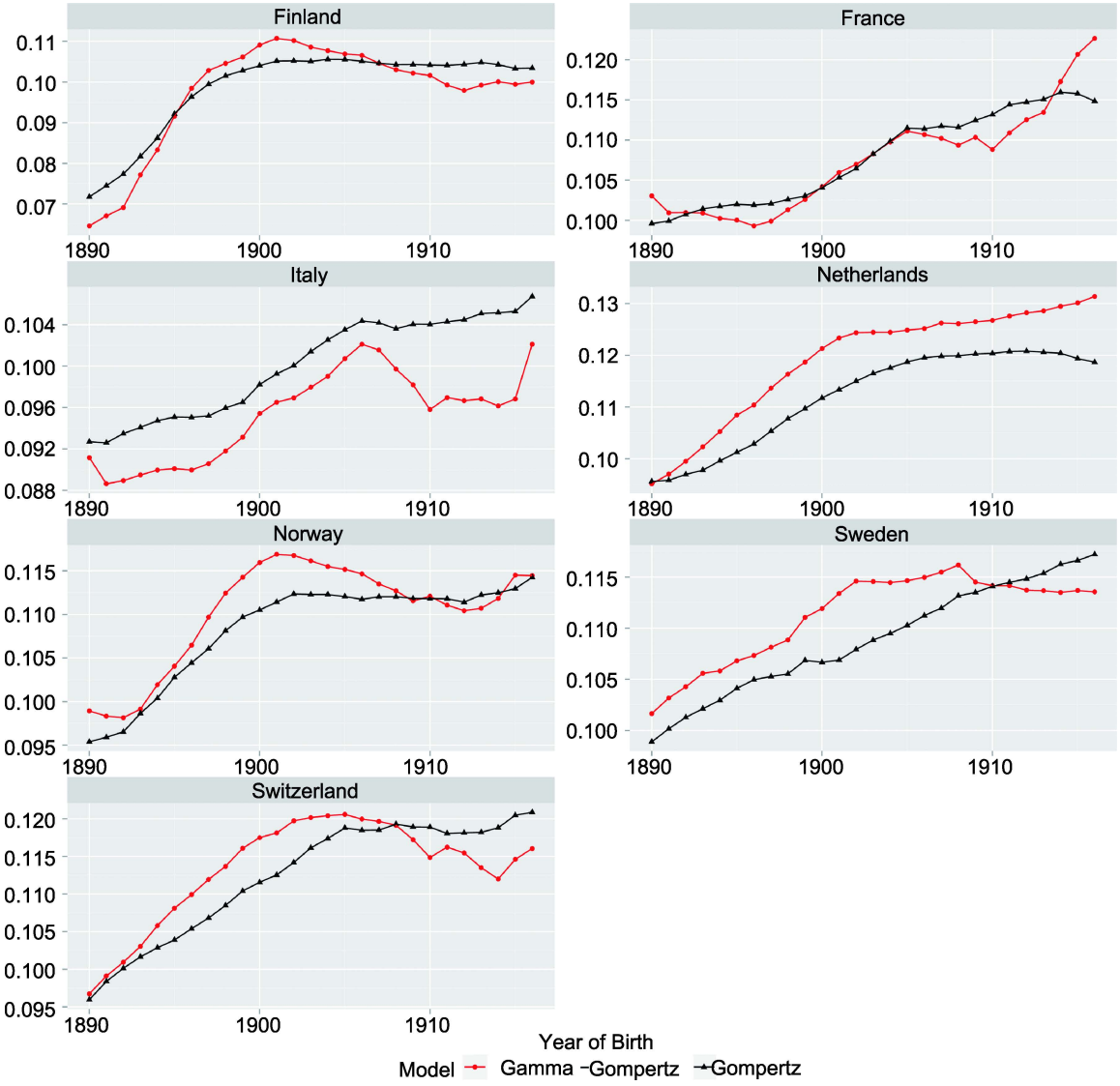

Figure 4. Evolution of the rate of ageing (b) estimated with Gompertz and Gamma-Gompertz.
Source: Authors' elaborations on HMD data.

Because cohort data on survival extends over several years, period effects may bias the results. However, the cohorts born between 1890 and 1919 entered our observation 75 years later, in an epoch characterized by rapid improvements in survival mostly due to medical progress. This should have resulted in a reduction, i.e., an underestimation, in the cohort rate of ageing (Salinari and De Santis, 2014) but it was the opposite of what we found.

The rate of ageing β (higher in recent cohorts) and its onset (earlier in recent cohorts) were not independent of each other. Indeed, they proved strongly and negatively correlated in both models (Gompertz and Gamma-Gompertz) with and without controls for possible disturbing factors (Table 1).

This evolution of ageing however should not make us lose sight of the fact that mortality declined consistently and considerably at all ages in all countries (Figure 2). The higher life expectancy of the most recent cohorts was not in doubt but the processes behind this outcome are not yet clear.

Table 1. Regressing the onset of ageing on the rate of ageing.

	Gompertz		Gamma-Gompertz	
	Without controls	Controlling for cohort and country	Without controls	Controlling for cohort and country
Intercept	66***	61***	76***	66***
Rate of ageing	–193***	–166**	–294***	–224***
R^2	0.28	0.83	0.38	0.83

** p < 0.01, *** p < 0.001,
Source: Authors' computation on HMD Data.

3.1 Comparing Our Results with the Outcomes of the Calorie Restriction Experiments

If an acceleration of physiological ageing did indeed occur over time, it seems natural to wonder why. We do not know the answer, but we submit that the changed nutritional habits may have possibly played a major part in all this.

The relationship between nutrition and mortality has always interested demographers since the times of Malthus (1798). In the last two to three decades, calorie restriction experiments on animals have improved our knowledge because when the external (disturbing) factors are kept under control or altogether eliminated, the role of nutrition can be better understood. What holds for animals may hold for humans too or at least give some insights into the process.

The first experiment of calorie restriction (CR) on rats dating back to the 1930s by McCay *et al*. (Masoro, 2005), led to the counter-intuitive conclusion that a restriction in food intake resulted in an extension of the rats' lives. However, these results did not attract much attention until the 1980s when they were confirmed by other similar experiments. CR experiments have been carried out on yeast (Jiang, Jaruga and Repnevskaya, 2000), fruit flies (Bross, Rogina and Helfand, 2005; Mair, Goymer, Pletcher *et al*., 2003), nematodes (Houthoofd, Braeckman, Lenaerts *et al*., 2002; Lenaerts, van Eygen and van Fleteren, 2007; Yen and Mobbs, 2008), crustaceans (Ingle, Wood and Banta, 1937), spiders (Austad, 1989), rodents (Masoro, 2005; 2009), dogs (Kealy, Lawler, Ballam *et al*., 2002), cattle (Pinney, Stephens and Pope, 1972), primates (Bodkin, Alexander, Ortmeyer *et al*., 2003; Colman, Anderson, Johnson *et al*., 2009; Colman, Beasley, Kemnitz *et al*., 2014; Mattison, Roth, Beasley *et al*., 2012), and occasionally even on humans (Bartke, 2012; Holloszy and Fontana, 2007; Longo and Fontana, 2009; Roth and Polotsky, 2012).

The outcomes of these experiments were summarized in Figure 5 (redrawn from Fontana, Partridge and Longo, 2010) which showed three different conditions of food intake: starvation, calorie restriction and normality. The normal condition was defined as a situation of *ad libitum* feeding, starvation meant that caloric intake was very low (below 50–

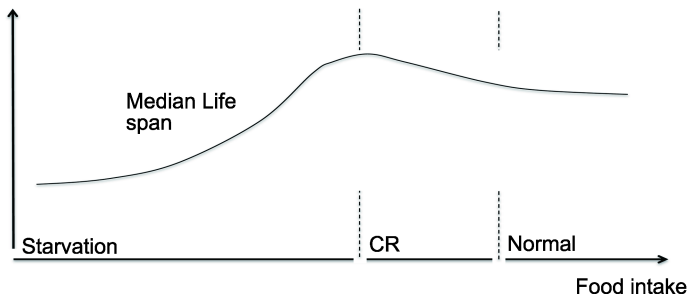

Figure 5. Relationship between food intake and median life span.
Source: Redrawn from Fontana (2010).

60% of the *ad libitum* condition) and calorie restriction was somewhere in between. Figure 5 showed that the relationship between caloric intake and survival was not linear. In starvation, an increase in nutrition enhances the likelihood of survival, which is also true in humans (Woodward, 1998). What was probably surprising was that survival peaked under severe caloric restriction, at about 50% of the *ad libitum* intake and started to decline beyond this threshold.

Upon closer inspection of the settings and results of the CR experiments, focusing only on rodents, the following points deserved attention:

1. Experiments on rodents are generally carried out in a pathogen-free environment. The presence of pathogens may alter the connection between nutrition and survival.
2. A long-term 30-60% reduction in calorie intake below *ad libitum* feeding causes an increase in maximum life ranging between 30-60% if calorie restriction starts just after weaning and 10-20% if CR starts in adulthood instead (Omodei and Fontana, 2011).
3. Much of the improvements registered in the mean and maximum life span derived from a retardation in the age-dependent increase in mortality (Weindruch and Walford, 1982; Harper, Leathers and Austad 2006) and from a lower rate of ageing usually measured by OLS estimates of a Gompertz model (Masoro, 2005).
4. In CR rodents, several age-related diseases appear later in life and are less lethal. This holds true for cancer, cardiovascular diseases, stroke, kidney failure, diabetes, Alzheimer, Parkinson and Huntington's disease (Omodei and Fontana, 2011).
5. CR rodents show lower levels of a few well-known biomarkers of ageing among which are reactive oxygen species (ROS) and pro-inflammatory cytokines (Omodei and Fontana, 2011).

Two main conclusions emerged. First, CR has long lasting effects (point 2). Secondly, most of the evidence on the effects of caloric restriction points to ageing rates (the β parameter) rather than to the initial level of mortality (the α parameter), points 3–5.

These CR experiments seem to contradict a large body of evidence from historical demography (Bengtsson, 2004), epidemiology (Waaler, 1984), economic history (Fogel & Costa, 1997; Fogel, 2004) and biology (Bateson *et al*., 2004), which suggested that better nutrition is associated with higher survival in humans. The central point is probably represented by the fact that CR experiments are carried out in a pathogen-free setting (point 1) which is clearly not the case for historic populations. A relatively recent line of research has investigated the characteristics of the immune system of CR rodents and its capacity to respond to infectious pathogens. The results have been mixed. On one hand, CR apparently attenuates age-related decline in the immune system of rodents (delayed immune-senescence) (Kristan, 2008; Pahlavani, 2004). On the other, studies using bacteria (Sun, Muthukumar, Lawrence *et al*., 2001), viruses (Gardner, 2005; Ritz and Gardner, 2006; Ritz, Aktan, Nogusa *et al*., 2008) and parasites (Kristan 2007) showed a significantly reduced capacity of long-term CR rodents to respond to and to survive such infections despite their better immune system. This happened because the response of the immune system to an infectious pathogen is very expensive in terms of energy and the body of CR rodents may fail to mobilize the energy needed (Ritz and Gardner, 2006).

In Figure 6 we summed things up. In a pathogen-free environment, a reduced caloric intake apparently retards ageing and slows it down (Figure 6(A)). However, with pathogens, a reduced caloric intake produces an upward shift of the mortality hazard function as a consequence of the difficulties of the immune system in mobilizing the energies the body needs to fight infections and heal wounds (Figure 6(B)).

Results presented in Figures 2 to 4 were essentially consistent with the outcomes of the

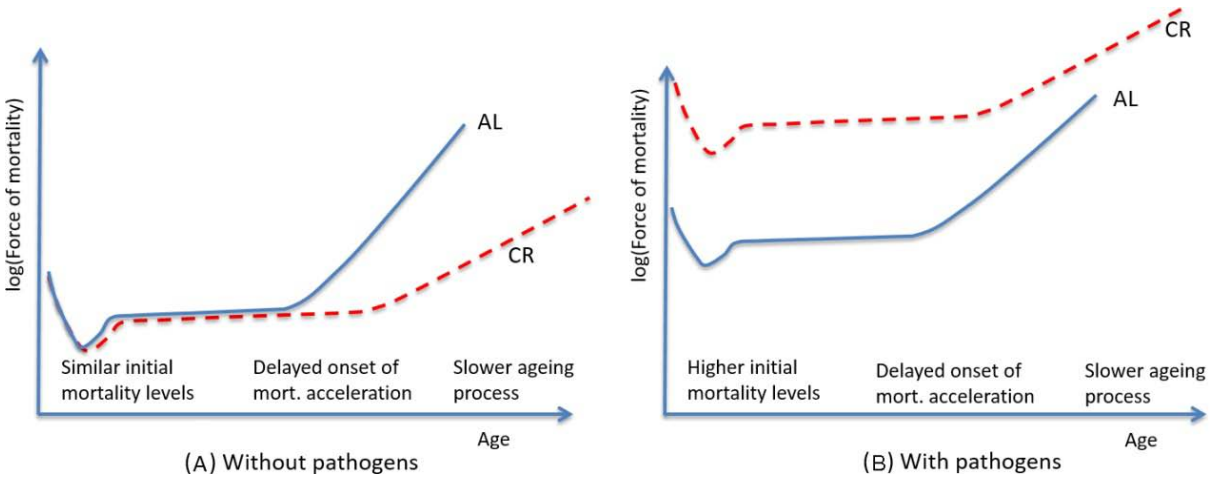

Figure 6. A hypothesis about the effects of CR on the hazard mortality function.
Note: The two diagrams displayed the hypothesized (stylized) effect of calorie restriction on the hazard mortality function (a) without pathogens and (b) with pathogens. AL and CR stand respectively for animals fed *ad libitum* or subject to caloric restriction.

CR experiments synthetized in Figure 6(B) with pathogens. Older cohorts are similar to the "treated" CR group in the CR experiments with higher mortality, a delayed onset of mortality acceleration and a slower rate of ageing. By contrast, younger cohorts displayed the same characteristics of the control group (AL): a more favorable mortality regime but an anticipated onset in, and a faster rate of ageing.

The cohorts born between 1890 and 1919 did in fact experience a gradual increase in their daily caloric intake and the heights of conscripts (for the five countries of our seven for which it is known: France, Italy, the Netherlands, Norway and Sweden) increased by about 2 cm for the cohorts born between 1890 and 1919 (Hatton and Bray, 2010).

In Figures 7 and 8 we plotted the two indicators of the previous section, onset and rate of ageing against the height of conscripts. The plot of the regression where the dependent variable is the rate of aging according to the Gompertz model is virtually identical to that of Figure 7 and it was not reported here. Admittedly, this analysis is very rudimentary and the number of observations limited. However, the results consistently showed that an increase in stature is associated with an anticipation in the onset of mortality acceleration and an increase in the rate of ageing.

In Table 2 we presented the results of a regression analysis where the values of the three indicators were regressed on the conscripts' average height (a proxy for nutrition) and on the probability of death between 0 and 10 years (a proxy for the disease load experienced in infancy by each cohort):

$$\text{Ageing}_{t,c} = \beta_0 + \beta_1 \text{height}_{t,c} + \beta_2 q_{0\text{-}10,t,c} + \varepsilon_{t,c}$$

The association between the evolution of heights and the three indicators turned out to be significant and to have the expected sign both without controls for the year and country of birth (not shown here) and with the relevant controls (Table 2).

4. Discussion and Conclusions

Our analysis suggested that the ageing process of the cohorts born in the last part of the nineteenth century and at the beginning of the twentieth century may have changed over time in at least two senses: ageing has appeared earlier (from about 50 years to about 40 years) and its speed has accelerated (greater slope of the Gompertz or Gamma-Gompertz curve). Can these results be a "statistical artifact"? Let us consider each of them in turn.

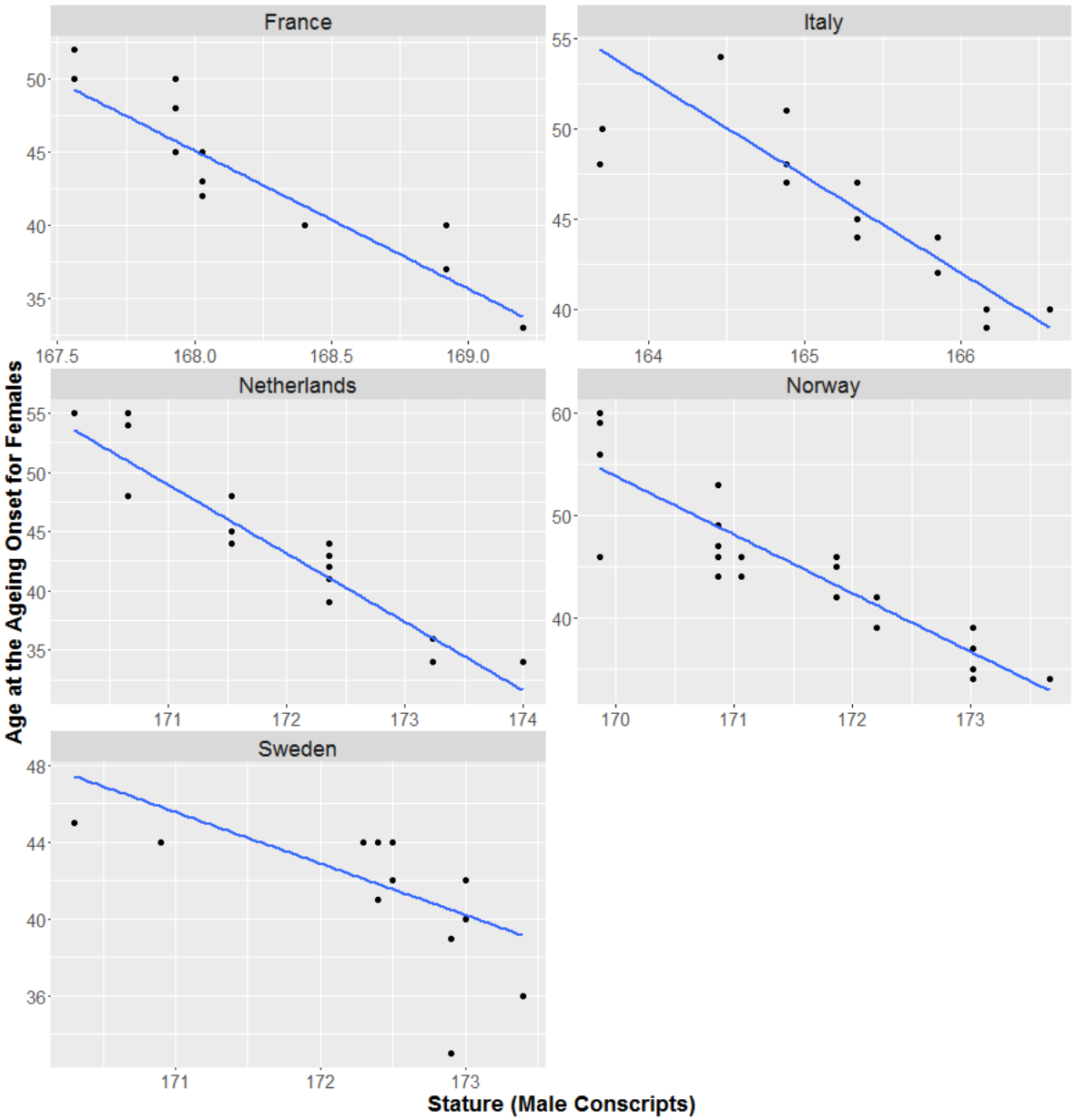

Figure 7. Relationship between stature and the onset of ageing.
Note: The data on the onset of ageing were given in Figure 3 and refer to female cohorts. The data on statures come from Hatton and Bray (2010) and refer to male conscripts (by cohort).

The onset of ageing: A change in the variability of the observed force of mortality may produce the illusion of a delayed onset of ageing in older cohorts. But this happens only when older cohorts suffer from a higher variability in the δ_x series. In our case, the opposite is true both theoretically (because of the small number of deaths among younger adults) and empirically (Salinari and De Santis, 2015).

Mortality crises too, for example wars and epidemics, could in principle, bias the results. Most of the cohorts considered in our analysis were observed only after WWI and the Spanish pandemics, the two major mortality crises of the twentieth century. Moreover, two of the countries that we analyzed, Sweden and Switzerland, did not take part in any wars and in all cases we focused on women who were much less exposed than men to the risks of war.

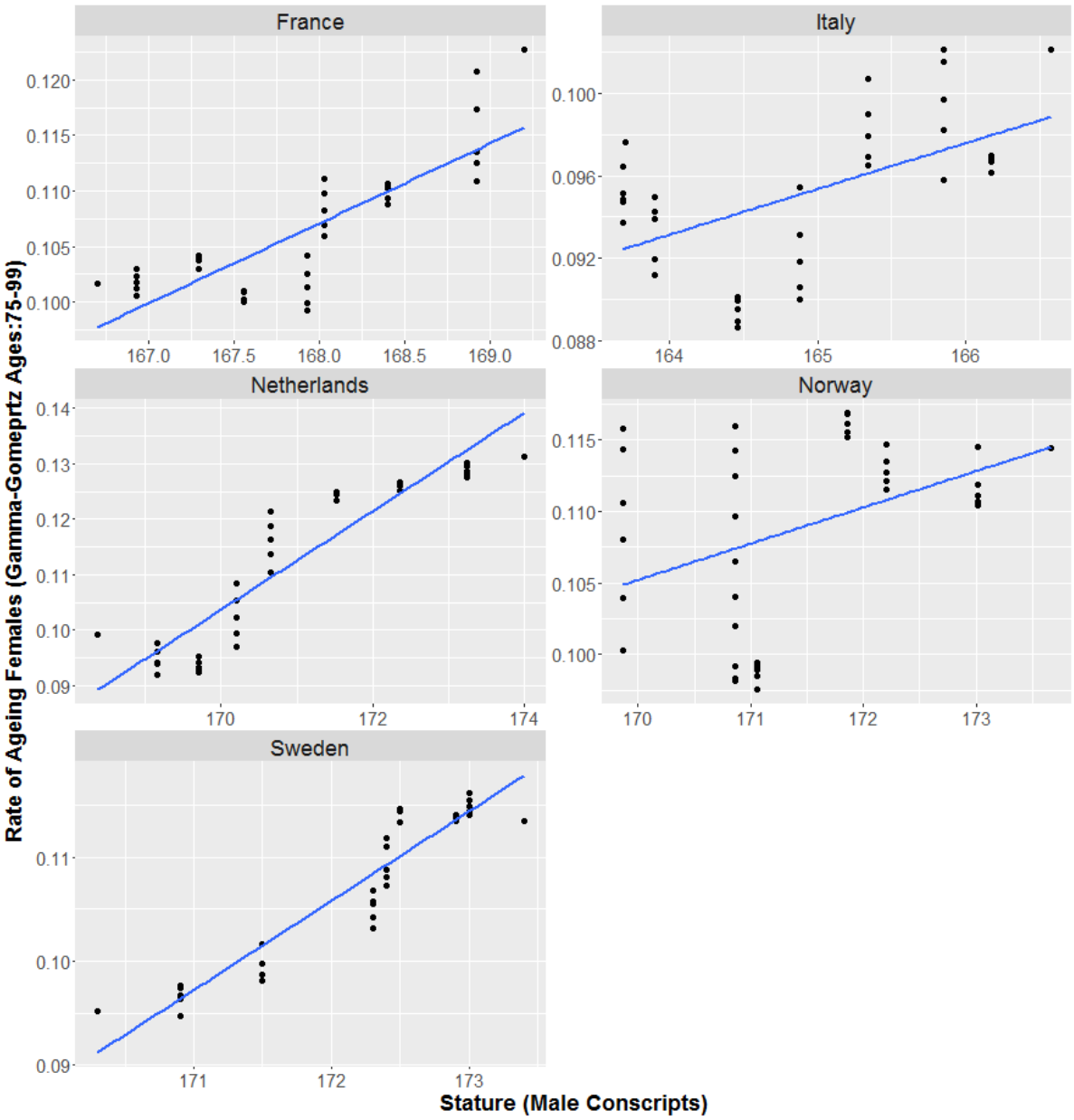

Figure 8. Relationship between stature and the rate of ageing (Gamma-Gompertz model).
Note: The data on the rate of ageing in Figure 4 refer to female cohorts. The data on statures come from Hatton and Bray (2010) and refer to male conscripts (by cohort).

Table 2. Regression analysis of the three indicators of the pace of ageing on the level of net nutrition (statures) and of diseases load (q_{0-10})

	Ageing onset	**Rate of ageing Gompertz**	**Rate of ageing G-Gompertz**
	Controlling for cohort and country	Controlling for cohort and country	Controlling for cohort and country
Intercept	564**	–0.725***	–1.328***
Height	–2.9**	0.005***	0.008***
q_{0-10}	–91.2**	0.045 .	0.017
R^2	0.87	0.75	0.75

. p < 0.1, ** p < 0.01, *** p < 0.001.

Note: G-Gompertz = Gamma-Gompertz. The data on ageing (onset and rate) given in Figure 3 and 4 refer to female cohorts. The data on statures come from Hatton and Bray (2010)and refer to male conscripts (by cohort).

A third form of distortion can be generated by a change in the frailty of the cohorts under scrutiny (Salinari and De Santis, 2015). The progressive reduction in infant, child and juvenile mortality may have weakened the selection process that takes place at very young ages. If frailer individuals are systematically associated with an earlier onset of ageing, their increased proportions among the adults observed in this study (aged 25 years and over) may be responsible for the earlier onset of ageing that has been observed. However, the few estimates produced on this issue demonstrated that the variance of frailty declined instead of increasing in more recent cohorts (Salinari and De Santis, 2014).

In a Gompertz-Makeham framework, the anticipation of the ageing onset may be explained by a reduction in "background mortality". The Gompertz-Makeham model (Makeham, 1860) stems from the Gompertz model where senescent (or age-dependent) mortality is accompanied by an age-independent (or background) component of mortality (Bongaarts, 2005). In this setting, a decrease in background mortality may seem to trigger an earlier onset of ageing because senescent mortality becomes stronger than the background mortality at an earlier age. But the apparently intuitive notion of an age-independent component of mortality has thus far not been supported by the empirical analysis of the causes of death (Carnes, Holden, Olshansky *et al*., 2006). Finally, Figure 2 which is a plain description of what can be observed, with no statistics involved, strongly suggested that the anticipation of ageing is not a statistical artifact.

Rate of ageing: Several empirical studies showed that in a Gompertzian framework, the rate of ageing is higher in recent than in older cohorts (Finch, Beltrán-Sánchez and Crimmins, 2014). But these results may be partly biased by selection: the more rapid elimination of the frailest causes cohort mortality to decelerate at older ages (Vaupel, Manton and Stallard, 1979), an effect that is arguably stronger when mortality is high that is, in older cohorts.

In order to remove this spurious negative correlation between (initial) mortality and the rate of ageing we adopted two strategies. First, we estimated the parameters of the Gompertz model in an age range between 75 and 89 years when selection is still weak. This method, rudimentary as it may be, has a great advantage over all available alternatives as it does not require any assumptions on the initial distribution of frailty. The second strategy was by using the Gamma-Gompertz model, where selection is kept under control - under the hypothesis that frailty is Gamma distributed.

In both cases we obtained similar results, the rate of ageing is higher in recent cohorts. If we had controlled for period effects as in Salinari and De Santis (2014) for instance, our conclusions would have been reinforced because of the strong decline in mortality in the past decades, thanks to medical innovations.

In short, both results (anticipation and acceleration of ageing) did not seem to depend on the tools used for the analysis. To the best of our knowledge, the most convincing attempt at an explanation that can be advanced at the moment relates to nutrition – ageing may be triggered or at least stimulated by an abundance of food as the lab experiments on animals suggest.

Our results are admittedly preliminary as none of the indicators used in this paper to measure ageing and its speed is perfect and the association between ageing and nutrition is only indirectly suggested and were not proven. We offered both conjectures (ageing is accelerating and this acceleration is at least partly due to nutrition) to researchers to carry out more stringent tests.

Conflict of Interest and Funding

The authors declare that there are no conflicts of interest.

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Ethics Statement

The analyses described in this paper were performed using secondary data obtained from publicly available sources as outlined in the Data and Methods section.

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