The Transition to Ageing

by Giambattista Salinari and Gustavo De Santis

1. The general framework

In the literature on ageing reference is frequently, if implicitly, made to the existence of an alleged starting age for senescence (or ageing), that is an age when mortality risks start to increase. However, only a few studies address this topic specifically, and with profound differences both in the reasons offered as to why senescence should ever appear and in the identification of the age when it does.

Currently, the most important reference to the possible existence of a threshold age can probably be found in Vaupel's constant senescence hypothesis. Vaupel (2010) argues that at *older ages* (emphasis added) the rate of ageing may be basically the same for the whole human kind, irrespective of historical or environmental conditions, and such that the force of mortality doubles approximately every 7 years. If the constant senescence hypothesis applies only to older ages, younger ages can be structurally different, arguably with a lower rate of senescence (small increase in mortality risks by age, or even no increase at all). In the pioneering studies on mortality discussed by Olshansky and Carnes (1997), senescence was generally assumed to begin with sexual maturity, between 12 and 20 years. In the more recent demographic literature, however, this starting point has been moved forward: hunter-gatherer populations may have (had) this threshold at around 40 years (Gurven and Kaplan 2007) and the widely used Gamma-Gompertz model seems to produce accurate estimates of life expectancy only from age 50 onwards (Missov 2013) - another implicit reference to a possible structural break in the evolution of mortality risks.

The existence of a specific age at which senescence begins seems, however, hard to justify from a strictly biological point of view. Not one of the three main biological explanations of senescence – mutation accumulation, pleiotropy and disposable soma - appears to be compatible with the existence of a "triggering" age for senescence (Kirkwood and Austad 2000). According to these theories, ageing is not genetically "programmed": rather, it results from a continuous accumulation of somatic damages, which is consistent both with empirical research and with what is known on the biology of ageing at cellular level (Rattan 2008). The process of damage accumulation starts very early, possibly at the onset of sexual maturity (Hamilton 1966), if not at birth (Abrams 1991, and Milne 2006). Some scholars have tried to identify the onset of the process of damage accumulation by focusing on intrinsic mortality only, by removing "external" causes, e.g. accidents (Carnes and Olhansky 1997). This kind of approach leads Luder (1993) and Dolejs (1997) to identify the beginning of the damage accumulation process at around 20 years.

However, one of the most important, although sometimes neglected, aspect of the biological interpretation of ageing is that damage accumulation does not necessarily translate into an increase of mortality, or at least not immediately: the continuous accumulation of somatic damages may begin to affect mortality (in a significant way) only past a certain level (Kirkwood and Austad 2000:237). And the analyses carried out by Bafitis and Sargent (1977), Shock (1981) and Weale (2004) support this conjecture: they do not find any relevant decrease in vital function until at least age 30.

In this setting, it may therefore make sense to distinguish between *latent senescence*, during which damage accumulates but remains below the threshold, and consequently does not produce any sizable effect on mortality, and *observable senescence*, which is when the accumulation of damage is such that the resistance of the organism is affected, and mortality increases. This may explain why mortality starts to increase only several years after the beginning of the process of damage accumulation. Our study is entirely devoted to verify if this threshold exists, and, in this case, if it is constant over time.

Statistically speaking, we looking for is what is today known in econometrics as a point of structural break: a series of data evolves according to rule (A) up to a certain point, and to rule (B) thereafter (Bai and Perron 2003). In our case, the series is given the force of mortality by age μ_x and the break point is the moment when the relation between age and mortality changes significantly.

Unfortunately, it is not possible to consistently identify a breakpoint if one uses only one series at a time (univariate case in Bai's terminology). Bai (2010) however, proves that a breakpoint can be

consistently estimated in the context of panel data analysis if several series are analyzed simultaneously and if they share approximately the same breakpoint.
In this article we use one of the techniques developed by Bai to verify the existence of a breakpoint (transition from latent to observable senescence). Our data comes from the cohort life tables of from the Human Mortality Database (HMD, 2012): we focus on (selected) female cohorts born in 14 countries over the period between 1850 and 1937. The most surprising finding of our research is that the age at the onset of observable senescence seems to have drastically declined, from about 48 at the beginning of this period to about 32 at its end.

2. The model and Bai's methodology

Our model and our empirical research focus on the ages 21 to 70. At younger ages, mortality is mainly characterized by a downward trend (ontogenescence), stemming from the increasing adaptation of individuals to the external environment (Siler 1979; Levitis 2010). At (very) old ages, 90+, instead, senescence (the rate of increase of mortality risks) decelerates, because of selection (Vaupel et al. 1979). The age range that we use should not be affected by these disturbing processes (or, at worst, only marginally), which permits us to better focus on the topic of this paper: the quest for the beginning of observable ageing (a breakpoint in the series).
Let $t = 20, 21, \ldots, T$ be the age of an individual, and $x=t-20$ its translated equivalent. Let us assume that the force of mortality can be represented for individual i by the following equation:

$$\mu_{i,x} = L_i + O_{i,x}D_{i,x} + \varepsilon_{i,x} \quad (1)$$

where L_i is a constant representing mortality during the period that we have labelled of *latent senescence*, $O_{i,x}$ is a strictly increasing function describing how observable senescence evolves with age and $D_{i,x}$ (=1 if $O_{i,x}>k_0$; $D_{i,x}=0$ otherwise) is an indicator variable, or switch, representing the threshold for dysfunction: it is 0 as long as senescence $O_{i,x}$ is lower than, or equal to, k_0, and it is 1 when aging passes that threshold, which is when mortality starts to increase. Note that since every individual follows a specific senescence process $O_{i,x}$, individuals may cross the threshold k_0 at different ages $x_{0,i}$ (individual heterogeneity at the beginning of senescence). Finally $\varepsilon_{i,x}$ stands for the error term[1].
Having thus advanced a possible theoretical justification for the existence of a threshold age (when mortality changes: from flat to increasing with age), let us now turn to the main purpose of this paper: the identification of this age with Bai's methodology. In order to apply it, however, let us first rewrite model in terms of log-differences $\delta_x = \log(\mu_{x+1}) - \log(\mu_x)$. In this case, under the assumption that ageing follows a Gompertz model ($O_{i,x} = \alpha_i e^{\beta x}$), calculating the increase δ_x in the force of mortality of eq. (1) leads (approximately) to:

$$\delta_{i,x} \cong \beta_L + \beta_O D_{i,x} + \varepsilon_{i,x} \quad (2)$$

which simply means that the $\delta_{i,x}$ series (log-differences of $\mu_{i,x}$, that is the slope of the regression line of log μ_x on x), has mean zero before x_0 (in eq. 2, $\beta_L=0$ is written explicitly, for the sake of clarity) and mean β_0 after x_0, while $D_{i,x}$ is our switch, whose value is 0 when age is less than, or equal to, x_0, and 1 otherwise.
Since, in the age range covered by this analysis (21-70, that is 50 years of age), the effects of heterogeneity are supposed to be weak, the aggregate series at cohort level $\bar{\delta}_x$ will closely mirror the individual series $\delta_{i,x}$. This means that we can analyze the transition from latent to observable senescence by directly computing the $\bar{\delta}_x$ series from ordinary life table, taking the logarithm of the aggregate force of mortality $\bar{\mu}_x$ and then differentiating.
The technique for the identification of the break point x_0 has been developed by Bai (2010) in the framework of panel data analysis. In the present context, this techniques works on N series

[1] Bai's techniques does not need any assumption on the distribution of the error terms. In all cases, this distribution can be proved to be approximately normal (Salinari and De Santis 2013).

simultaneously, under the assumption that the cohorts share approximately the same starting age for observable senescence. Bai's techniques proceeds to the identification of the break point by exhaustion of cases: for each candidate breakpoint *b* and for each cohorts *j*, one needs first to compute the two sub-period means $M_{j,1}$ and $M_{j,2}$

(3) $$M_{j,1} = \frac{1}{b+1}\sum_{x=0}^{b} \bar{\delta}_{j,x} \qquad \text{and} \qquad M_{j,2} = \frac{1}{50-(b+1)}\sum_{t=b+1}^{50} \bar{\delta}_{j,x}$$

Then, for each series ($\bar{\delta}_{j,x}$), the sum $S_j(b)$ of the squared residuals with respect to $M_{j,1}$ and $M_{j,2}$ is calculated

(4) $$S_j(b) = \sum_{x=0}^{b}\left(\bar{\delta}_{j,x} - M_{j,1}\right)^2 + \sum_{x=b+1}^{50}\left(\bar{\delta}_{j,x} - M_{j,2}\right)^2$$

while the sum of squared residuals (SSR) for all N series is

(5) $$SSR(b) = \sum_{j=1}^{N} S_j(b)$$

The least squares estimator for the break point will then be:

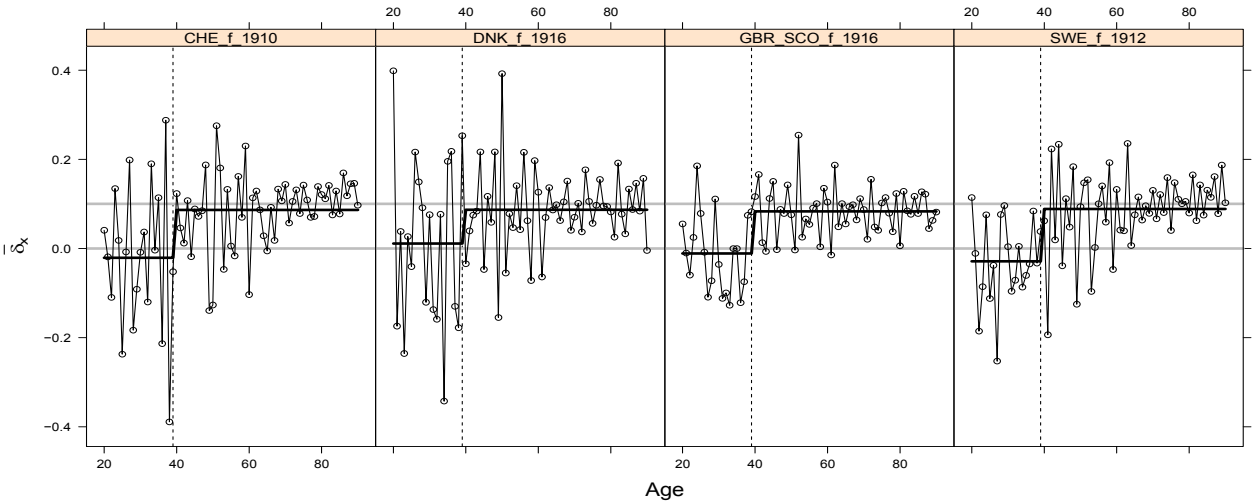
(6) $$\hat{x}_0 = \min_b SSR(b)$$

Bai (2010) proves that this estimator is consistent, gives a simple procedure for the computation of confidence intervals, and indicates how to extend the methodology to the case of multiple breaks and regimes.

3. Findings

The data on which we run our analysis comes from the HMD and covers the female cohorts born in 14 countries (Australia, Belgium, Canada, Switzerland, Denmark, Spain, Finland, France, UK, Italy, Netherlands, Norway Sweden, US) during three distinct periods: 1920-1937, 1902-1919, 1850-1869.

Figure 1. *Log-differences in mortality between age (x+1) and x for selected female cohorts*



Note: CHE=Switzerland; DNK=Denmark; GBR_SCO=Scotland; SWE=Sweden.

Figure 1 gives an example of what we find. It represents the $\bar{\delta}_{j,x}$ series of a few randomly selected female cohorts born between 1902 and 1919. The vertical dotted line in the figure indicates the break point that we identify with Bai's technique: age 40 in all the cases presented. In Figure 1 the grey horizontal lines represents the two "theoretical" extremes of the rate of ageing (0.0 and 0.1), the former derives from our conjecture that ageing produces no effect before the breakpoint, and the latter derives

from Vaupel's hupothesis that β_O=0.1 from the breakpoint on. The black horizontal lines represent the actual mean calculated before and after the breakpoint. As it turns out, between age 20 and 39 the mean rate of ageing is indeed close to 0, while at later ages the rate of senescence approximates the 0.1 figure predicted by Vaupel.

The same type of analysis can be conducted separately by birth cohort, and country. Two main results emerge from our analysis: a) the age at the onset of observable senescence declines markedly in our sample: from 48 years in the cohorts born in 1850-1869 to 32 years for the cohorts born between 1920 and 1937; b) the rate of senescence during the phase of latent senescence passes from a weak positive value (β_L=0.01) for cohorts born in 1850-1869 to a weak negative value (β_L=-0.03) for those born in 1920-37. In the full paper we show that this phenomenon cannot be easily explained: for instance, Luder's (1993) hypothesis - according to which higher levels of extrinsic mortality may delay the onset of senescence by obscuring intrinsic mortality - does not apply to our case. We also show that the reduction observed in the rate of ageing during the phase of latent senescence cannot be attributed to period effects.

References

Abrams P.A. (1991), The fitness costs of senescence: the evolutionary importance of events in early adult life, *Evol. Ecol.* 5:343-360.

Bai J. (2010), Common breaks in means and variances for panel data. *Journal of Econometrics* 157:78-92.

Bai J., Perron P. (2003), Computation and analysis of multiple structural change. *Journal of Applied Econometrics* 18:1-22.

Bafitis H., Sargent F. (1977), Human phisiological adaptability through the life sequence. *Journal of Gerontology* 32(4):402-410.

Carnes B.A., Olshansky S.J (1997), A biological motivated partitioning of mortality. *Experimental Gerontology* 32(6):615-613.

Dolejs J. (1997), The extension of Gompertz law's validity. *Mechanisms of Ageing and Developments* 99:233-244.

Gurven M., Kaplan H. (2007). Longevity among hunter-gatherers. A cross-cultural examination. *Population and Development Review* 33(2):321-366.

Hamilton W.D: (1966). The moulding of senescence by natural selection. *Journal of Theoretical Biology* 12:12-45.

Kirkwood T.B.L, Austad S.N. (200). Why do we age? *Nature* 409:233-238.

Levitis D.A. (2010), Before senescence: the evolutionary demography of ontogenesis. *Proceedings of the Royal Society*, doi:10.1098/rspb.2010.2190.

Luder H.U. (1993), Onset of human aging estimated from hazard functions associated with various causes of death. *Mechanisms of Ageing and Development* 67:247-259.

Milne E.M.G. (2006), When does human ageing begin? *Mechanisms of Ageing and Development* 127:290-297.

Missov T.I. (2013). Gamma-Gompertz life expectancy at birth. *Demographic Research* 28:9, 259-270.

Olshansky S.J., Carnes B.A. (1997). Ever since Gompertz. *Demography* 34(1):1-15.

Rattan S.I.S. (2008), Increased molecular damage and heterogeneity as the basis of aging, *Biol. Chem.* 389:267-272.

Shock N.W. (1981), Indices of functional age, in Danon D., Shock N.W., Marois M. (eds.), *Aging: A challenge to Science and Society*. Oxford, Oxfrod University Press, pp. 302-319.

Siler W. (1979), A competing-risk model for animal mortality. *Ecology* 60(4):750-757.

Vaupel J. (2010). Biodemography of human ageing. *Nature* 464(7288):536-542.

Vaupel, J., Manton, K. and Stallard, E. (1979), The impact of heterogeneity in individual frailty on the dynamics of mortality. *Demography* 16(3):439-454.

Weale R.A. (2004), Biorepair mechanisms and longevity. *Journal of Gerontology* 59A:449-454.