

Measuring Ageing

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Abstract. This chapter is written for (health-) economists with an interest in the conceptualization and measurement of ageing in demography, biology, and gerontology. I review two alternative methods to measure ageing and a theory that explains the outcome of both of these measurements. I explain how ageing, conceptualized as increasing probability to die, can be accurately and conveniently expressed by the Gompertz-Makeham law. I discuss the stability of the estimated parameters, inferences about human lifespan, and similarities and differences of ageing across sexes and countries and over time. Alternatively, ageing can be measured as accumulation of health deficits. The chapter reviews the frailty index, designed to measure biological ageing, and demonstrates important similarities and differences between the force of mortality and the accumulation of health deficits. Regularities of health deficit accumulation across individuals, at the level of (sub-) populations, and across the world are discussed. The chapter provides also an introduction to reliability theory and shows how increasing mortality and frailty can be explained as a stochastic process of loss of built-in redundancy of organisms. The chapter concludes with some suggestions for the modeling of health and mortality in economics.

Keywords: Ageing, Mortality, Life-span, Frailty, Health Deficits, Reliability Theory.

JEL: D91, J17, J26, I12.

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1. INTRODUCTION

In chronological terms, all humans age by one year every year. In physiological terms, however, individuals age quite differently. A 70 years old person can be as healthy as a 50 years old one and vice versa. (Physiological) Ageing is defined as the intrinsic, cumulative, progressive, and deleterious loss of function that eventually culminates in death (Arking, 2006; Masoro, 2006; Lopez-Otin et al., 2013). Here we focus on ageing of organisms (mostly humans) but every car owner will recognize that the definition of ageing applies to non-living matter as well. Actually, living and inanimate systems age in a similar way, a phenomenon to which we return later.

Based on the definition of ageing, I discuss two possibilities to measure it as (i) increasing probability to die and (ii) accumulation of health deficits and functional limitations. Ageing, conceptualized as increasing probability to die and measured by the force of mortality will be discussed in Section 2 to 4. I show that ageing can be accurately and conveniently expressed by the Gompertz-Makeham law. I discuss the stability of the estimated parameters, inferences about human lifespan, and similarities and differences of ageing across sexes and countries and over time.

While the force of mortality is capable of measuring ageing in populations, an index of health deficits is furthermore capable of measuring ageing at the level of individuals. It will be discussed in Section 6 to 8. After the introduction of the frailty index as a measure biological ageing, I discuss important regularities of health deficit accumulation across individuals, at the level of (sub-) populations, and across the world and highlight similarities and differences between the force of mortality and the accumulation of health deficits. The two measurement parts are linked by Section 5, which provides an introduction to reliability theory and shows how increasing mortality and frailty can be explained as a stochastic process of loss of redundancy in organisms. The chapter concludes with some suggestions for the modeling of health and mortality in economics.

2. THE FORCE OF MORTALITY

Demographers employ several indices of mortality. For example, the probability to survive to age x , the life-expectancy at age x , or the probability of dying in the age interval $x + \Delta x$. Of these, the probability to die is the most suitable measure of ageing because it provides the *age-specific* impact on mortality independently from age-specific events at other age groups. To

see this, note that, for example, the probability of dying in the age interval $(0,1)$ clearly affects the survival probability to any age $x > 1$ as well as life expectancy at age 0, but not the other way around.

Biologists and gerontologists emphasize that individual ageing must be understood as an event-dependent not as a time-dependent process (Arking, 2006). There is no such thing as a “biological clock”; the probability of dying is thus a measure of how members of a population (a species, a population of a country) age *on average*. Another implication of this view is that the probability to die is not useful to assess or explain *individual* survival prospects.

Given a sample of a population and the observation (from a life table) that a number $S(x)$ thereof survives to age x and a number $d(x) = S(x) - S(x + \Delta x)$ dies between age x and $x + \Delta x$, the probability to die in age interval $x + \Delta x$ is given by $q(x) = d(x)/S(x)$. The discrete-time measure has the inconvenient side-effect that the probability to die depends on the length of the age-interval x . In order to get rid of this problem we take the continuous limit

$$\mu(x) = \lim_{\Delta x \rightarrow 0} \frac{S(x) - S(x + \Delta x)}{\Delta x S(x)} = -\frac{\dot{S}(x)}{S(x)}, \quad (1)$$

which provides the *force of mortality*: the conditional probability to die at age x given survival up to age x . For empirical applications and small Δx , the force of mortality can be approximated, for example, by $\mu(x) = \log [(S(x - \Delta x)/S(x + \Delta x))] / (2\Delta x)$ (Sacher, 1956). The notion of the force of mortality should be familiar not only to engineers (as the failure rate) but also to economists as the hazard rate; the hazard here is to die at age x .

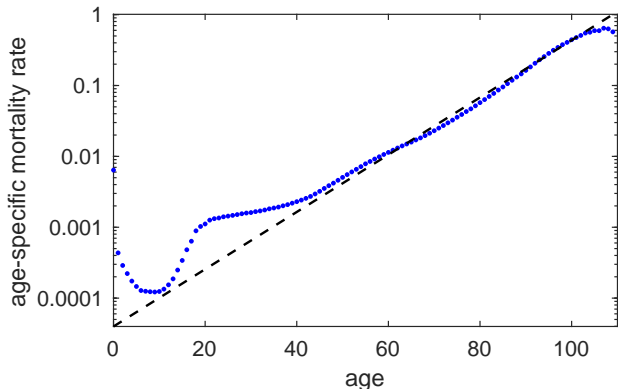
The “perpetual youth” model built on Blanchard (1985) and Yaari (1968) investigates the special case $\mu(x) = \lambda$ for all x . The assumption that the probability to die at age x is independent from x , constitutes, in fact, the definition of a non-ageing organism in biology (Arking, 2006). Thus, the most popular economic models that take probabilistic death and the finiteness of human life into account are inherently unsuitable to display and discuss aspects of human ageing. A feature, which is acknowledged by the developers of the model by coining the “perpetual youth” expression.¹

¹Of course, this criticism applies as well to the deterministic OLG model, of which the popular two-period OLG model (based on Diamond, 1965) is a special case. From an ageing perspective, it should be called the “blade runner model” (perfect health until T , then death).

3. THE GOMPERTZ-MAKEHAM FORMULA

The force of mortality for humans increases with age in a particular way. This is shown exemplarily in Figure 1 for US American men in the period 2010-2019. A structurally similar figure can be drawn for other human subpopulations (Strulik and Vollmer, 2013). In the figure, dots represent the actual age-specific force of mortality. Human life can be roughly subdivided into two periods: an initial *phase of development* ranging from birth to puberty during which the probability to die decreases, immediately followed by the *phase of ageing* during which the probability to die increases. Remarkably, almost nowhere along the human life cycle is the probability to die constant.²

Figure 1: Age-specific Mortality Rate: U.S. American Men 2010–2019



Dots indicate data points; period data from HMD (2020). The straight line shows the Gompertz estimate, $\mu = Re^{\alpha \cdot \text{age}}$ with $R = 4 \cdot 10^{-5}$ and $\alpha = 0.093$. Semi-logarithmic scaling of axes.

The most striking feature of Figure 1 is the long period of life, ranging from about 40 to 90 years of age, for which age and the force of mortality are log-linearly related. This relationship is known as Gompertz law after actuary Benjamin Gompertz (1825) who first observed and stated it formally: $\log \mu(x) = a + \alpha x$, or equivalently,

$$\mu(x) = R \exp(\alpha x). \tag{2}$$

For humans the estimate of α is around 0.09 implying that the probability to die doubles approximately every 8 years. The Gompertz formula was further improved by William Makeham

²This rough division of human life ignores that the age at the trough of the mortality rate declined over the last century and is now reached in fully developed countries around age 10, i.e. several years before sexual maturity (Milne, 2006). Moreover, ageing understood as the increasing loss of bodily function starts at least at birth if not earlier since infants are already subject to somatic mutations and telomere shortening (Frenck et al. 1998; Kirkwood, 2005). See Dalgaard et al. (2021b) for a model of human ageing from conception to death.

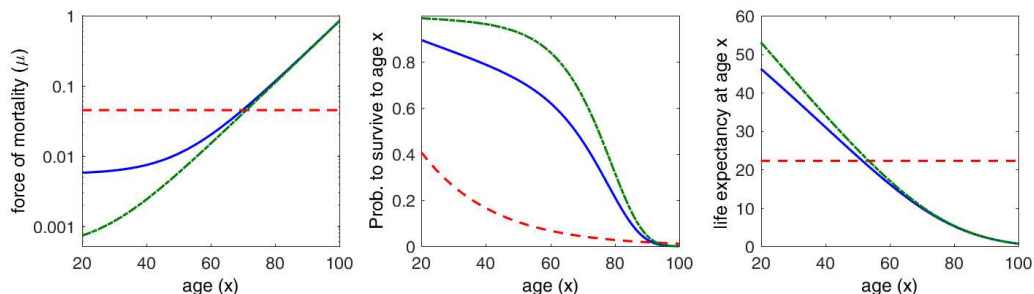
(1860) who added a constant, reflecting an age-unrelated force of mortality, to yield the famous Gompertz-Makeham formula,

$$\mu(x) = A + R \exp(\alpha x). \quad (3)$$

While the Gompertz formula approximates human mortality reasonably well for ages between 40 and 90 years, the Makeham amendment yields a good approximation also for ages between 15 and 40 years (Carnes et al., 2006). Subsequently, many researchers from various disciplines have tried to further improve the formula to little avail. Taking both simplicity and precision into account, the Gompertz-Makeham formula is to the present day the most appropriate, concise, and widely used formal description of ageing (Olshansky and Carnes, 1997). Not only for humans are its parameters estimated with great precision with a coefficient of determination above 0.9, also species as different as yeast, fruitflies, rats, and horses, have been shown to age according to the Gompertz-Makeham formula. The estimated coefficients, of course, differ greatly, reflecting the large variation in lifespan across species (Arking, 2006, Gavrilov and Gavrilova, 1991).

Notice that $\mu(x)$ is finite for finite x ; there exists no age x at which $\mu(x)$ converges towards a pole. Or more vividly put “no matter how old one is, the probability to die the next day is never unity”. With respect to economic modeling, the Gompertz-Makeham law refutes the frequently made assumption of a given “capital T ” that marks the end of life.

Figure 2: Ageing according to Gompertz-Makeham vs. Probabilistic Death



Blue (solid) lines: estimates from Swedish life tables for men born 1901-1910: $A = 0.00552$, $R = 0.000033$, $\alpha = 0.1013$ (Gavrilov and Gavriolova, 1991). Green (dash-dotted) lines: as for blue lines but $A = 0.00048$. Red (dashed) lines: hypothetical perpetual youth scenario: $\lambda = 0.025$.

Figure 2 compares mortality according to Gompertz-Makeham with mortality according to the perpetual youth assumption. Blue (solid) lines reflect estimates for Swedish men born 1901-1910. Red (dash-dotted) show perpetual youth outcomes for $\lambda = 0.025$. In the panel on the left-hand side it can be seen that the Gompertz part becomes dominating at ages around 50,

from which on the force of mortality appears to be log-linearly increasing in age. The perpetual youth model clearly overestimates mortality of young adults and underestimates it for the old. The middle panel of Figure 2 shows the probability to survive to age x . It is obtained as the solution of $\dot{S}(x) + \mu(x)S(x) = 0$ given that $S(0) = 1$, such that using (3),

$$S(x) = \exp\left(-Ax - \frac{R}{\alpha}(\exp(\alpha x) - 1)\right) \quad (4)$$

and, trivially, for the perpetually youth agent $S(x) = \exp(-\lambda x)$. According to Gompertz-Makeham, the probability to survive decreases relatively little with age at young ages and strongly at old ages. The perpetual youth model predicts just the opposite, i.e. steeply falling survival prospects at young ages.

The panel on the right hand side of Figure 2 shows life-expectancy (expected remaining years to live) at age x , $e(x) = \int_x^\infty S(a)da/S(x)$. For the perpetual-youth agent life-expectancy is independent of age (and equals $1/\lambda$) while, actually, according to Gompertz-Makeham life-expectancy is almost linearly falling with age in the range of 20 to 70 years, after which it levels off.

At the upper age range, for the *oldest old*, the Gompertz-Makeham formula loses precision. In contrast to what one might have expected, at ages of above 90 the force of mortality increases *less* than log-linearly with age. Various amendments to the original formula have been suggested to take the oldest old into account (e.g. Perks, 1932). If this leveling off becomes so strong that the force of mortality stops increasing, the oldest old become indeed non-ageing. The possibility that – once a certain age has been reached – humans may turn out to be non-ageing has inspired research and debate in demography and gerontology (Wachter and Finch, 1997; Carnes and Olshansky, 2007; Barbi et al., 2018; Gavrilov and Gavrilova, 2020; Vaupel et al., 2021).

Over the last century, human life expectancy at birth has increased by more than 20 years in most of the fully developed countries (Riley, 2001). It is interesting to investigate how these huge improvements of human longevity have affected the Gompertz-Makeham law. For this purpose the notion is helpful that the Makeham-parameter A reflects the age-unrelated forces of mortality. In particular we expect prevention, eradication, or cure of age-unrelated diseases to be reflected in A . We expect progress with respect to the ageing process itself to be reflected in a change of Gompertz-parameters R and/or α .

While the Gompertz parameters R and α are relatively stable over time, the background risk parameter A steeply declined over the last century. For Sweden, for example, the parameter A fell by about one order of magnitude from 0.55 percent to 0.048 percent (Gavrilov and Gavrilova, 1991). This means that so far, advances in longevity manifested themselves mostly in reduced background risk. Human ingenuity has not yet been able to manipulate much the biological mechanism behind the ageing process, captured by the age related parameters R and α . Results for $A = 0.0048$ are shown by green (dash-dotted) lines in Figure 2. Apparently, until the 1980s, technological, economic, and cultural progress had predominantly improved the survival probabilities for young people. Life-expectancy at age 80 in the 1980s differed little from what it has been at the beginning of the 20th century.

The structural stability of the Gompertz-parameters is also helpful to explain the popular ideas of “rectangularization” and “compression of morbidity” (Fries, 1980). The middle panel of Figure 2 conveys the information that compared to the beginning of the century a higher share of Swedish men reaches an old age of, say 70 years, and expires then more quickly during their last years before death. Visually, the survival curve becomes closer to rectangular over time. On average, individuals spend more of their life in a relatively healthy condition. Across individuals, however, ageing became a more salient phenomenon: less young and intrinsically healthy people are killed from exogenous forces, implying a rising share of the population dying from age-related diseases and chronic illnesses.

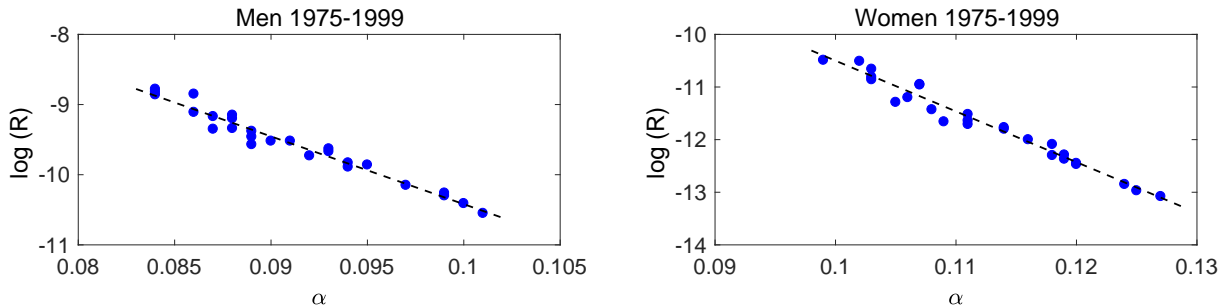
4. HUMAN LIFE SPAN AND THE STREHLER–MILDVAN CORRELATION

Whereas life expectancy is a population specific characteristic, lifespan is usually conceptualized as a species specific characteristic (*the* lifespan of humans, mice, or elephants). It has already been shown that strictly speaking such a thing as *maximum* human lifespan does not exist. Even under time-invariance of the Gompertz-Makeham parameters, the simple fact that the “sample size” of people who ever lived on earth increases continuously implies that the maximum ever-observed life-length will rise as time proceeds (Finch and Pike, 1996). Alternatively, it has been suggested to use the Gompertz parameter to infer lifespan as the age at which individuals from different populations face the same force of mortality.

Although the parameters α and R show little variation over time they differ across sexes and across countries. On average, across countries, women face a lower R and a higher α (Garilov

and Gavrilova, 1991), indicating that women have an initial advantage of lower ageing, which is with rising age eventually caught up by men. In fact, there is a strong inverse (log-linear) association between R and α known as the Strehler-Mildvan correlation or the compensation effect of mortality (Strehler and Mildvan, 1960, Gavrilov and Gavrilova, 1991). Figure 3 shows the association between these parameters for men and women from 26 developed countries over the period 1975–1999.

Figure 3: The Compensation Effect of Mortality



Data for estimates of α and R for 26 countries from Strulik and Vollmer (2013); raw data from HMD (2020). Regression lines: $\log R = -0.76 - 96.6 \cdot \alpha$ for men ($R^2 = 0.97$); $\log R = -0.86 - 96.4 \cdot \alpha$ for women ($R^2 = 0.97$).

The estimated Strehler-Mildvan correlation is given by

$$\log R_i = \log M - L \cdot \alpha_i \tag{5}$$

where for $i = 1, \dots, n$ the R_i and α_i are the country- and sex-specific realizations of the Gompertz parameters and M and L are the invariant coefficients of the Strehler-Mildvan correlation. Inserting the Strehler-Mildvan correlation into the Gompertz-Makeham law $\mu_i = A_i + R_i \exp(\alpha_i x)$ provides:

$$\mu_i - A_i = M \exp[\alpha_i(x - L)]. \tag{6}$$

The modified Gompertz-Makeham law implies a fixed point. It predicts that – controlling for country-specific background risk – men and women across countries share a common force of mortality M at age L . For humans the point estimate is close to $L = 96$ years (Gavrilov and Gavrilova, 1991; Strulik and Vollmer, 2013). The time invariance of the Gompertz law and the Strehler-Mildvan correlation suggests that, controlling for country-specific background risk, humans share a common mechanism of ageing, a common stochastic process according to which individual bodies lose function over time and bodily failures and health deficits are accumulated.

A general pattern emerging from the Strehler-Mildvan correlation is that economically more advanced countries are characterized by a lower R and higher α , i.e. by a lower initial mortality rate and faster speed of ageing. This implies that the mortality rate is for all ages below L lower in the economically advanced country. An important conclusion from this observation is that ageing rapidly (i.e. being endowed with a high α) is actually not a burden but an indication of superior fitness. This notion will be further substantiated in the next section on reliability. Finally, note that if R falls continuously and α rises such that lifespan L remains constant, life-expectancy improves continuously. If L is constant, however, there exists an asymptotic limit to improvements of life expectancy.

Strulik and Vollmer (2013) studied the Strehler-Mildvan correlation from 1900 to 1999 and confirmed that for the first half of the 20th century (and presumably also earlier in human history) the data supports the notion of an invariant human lifespan of about 87-89 years. Then, in the 1950-74 period, female lifespan increased about 8 years to 96 years and male lifespan followed in the 1975-99 period. Observable improvements in life-expectancy during the first half of the century originated from declining background mortality (sanitation, vaccination) and from a reduction of R in association with a movement along the mortality compensation line, indicating better (initial) physiological conditions (better nutrition, e.g. Fogel and Costa, 1997). The results suggest that humans, unlike any other species managed to increase lifespan, which increased in sync with life expectancy during the later 20th century, confirming that limits to life expectancy seem indeed to be “broken” (Oeppen and Vaupel, 2002). This “manufactured life-time” (Carnes and Olshansky, 2007) likely originated from medical technological progress, in particular the “cardiovascular revolution” (Hansen and Strulik, 2016) of the 1970s, which allowed for an extension of human life by repairing and replacing failed organs.

5. RELIABILITY THEORY

The fact that all humans appear to age according to a common formula, which we moreover share with fruitflies, rats, and other animals, motivates the search for a common process that drives ageing. The quest for such a process is challenging because, as emphasized already, there exists no biological clock. Trying to explain ageing following a line of reasoning by stating that humans age because their organs (e.g. the cardiovascular system) age, and that organs age because the tissue they are made of ages etc. will turn out to be utterly futile. At some point a

micro-level will be reached that consists of non-ageing entities, for example atoms. Eventually, we want to explain why a system ages that consists of non-ageing elements.

In explaining ageing systems, we do not have to start from scratch. We can built upon a subdiscipline in engineering, reliability theory, which has been developed to understand how complicated mechanical systems consisting of non-ageing elements (like cars) are increasingly losing function over time so that the failure rate, i.e. the probability of the expiry of the system, increases with age (Barlow and Proschan, 1975). There are several, sometimes complementing, reliability theories of human ageing available (Gavrilov and Gavrilova, 1991, Novoltsev, 2006, Finkelstein, 2008). Here, we consider the basic idea by describing two particularly straightforward models. The presentation follows Gavrilov and Gavrilova (1991, 2001), who were the first to integrate reliability research into the realm of biology.

Consider an organism constructed of n non-ageing blocks. Non-ageing means that the failure rate λ is constant over time. Given age x the probability of a block to fail is $1 - \exp(-\lambda x)$. Blocks are connected in parallel and the organism lives as long as at least one block is in order. The probability that the organism expires before age x is given by $F(x) = [1 - \exp(-\lambda x)]^n$ and the probability to survive to age x is $S(x) = 1 - F(x)$. The unconditional probability to die at age x is thus given by $dS/dx = -\lambda n \exp(-\lambda x)[1 - \exp(-\lambda x)]^{n-1}$ and the force of mortality is

$$\mu(x) = \frac{\lambda n \exp(-\lambda x)[1 - \exp(-\lambda x)]^{n-1}}{1 - [1 - \exp(-\lambda x)]^n}.$$

Taking an approximation at young ages, when $1 - \exp(-\lambda x) \approx \lambda x$, the expression simplifies to $\mu(x) \approx n\lambda^n x^{n-1}$ and, for old ages, using L'Hospital's rule, we obtain $\lim_{x \rightarrow \infty} \mu(x) = \lambda$.

The simple model is thus capable of explaining ageing: the force of mortality $\mu(x)$ increases with age x . Ageing is explained as a *loss of redundancy* over time. This notion of ageing as accelerated loss of organ reserve is in line with the mainstream view in the medical science. For example, initially, as a young adult, the functional capacity of human organs has been estimated to be tenfold higher than needed for survival (Fries, 1980). The meta study of Sehl and Yates (2001) computes for 13 human organ system a mean loss of functional capacity of 0.65 percent per year.

The model is also useful to explain mortality of the oldest-old. With increasing age the organism loses redundancy until survival depends, in the limit, just on the survival of the last functioning non-ageing block. Thus the organism converges towards the constant mortality

rate λ of its non-ageing elements. This is a general result from reliability theory: the rate of ageing, i.e. the age-dependent component of the mortality rate (the failure rate), is increasing in the complexity (redundancy) of the system. We can expect that, for example, light bulbs and bacteria, age at a much lower rate than cars or humans. Seen this way, ageing appears as a positive trait. It occurs because complex systems start out at a high level of redundancy and are thus less likely to expire at young age.

The problem with the simple model is that the derived $\mu(x)$ at young ages does not obey the Gompertz law. It follows – similar to the failure rate of mechanical systems – a Weibull distribution. In order to describe the ageing process of humans, the model has to be made “more human”. Next we consider one of several possible extensions. Suppose an organism consists of m *irreplaceable* blocks, i.e. blocks connected in series such that the organism dies if one block fails. Each block consists of n elements, connected in parallel with age-independent failure rate λ . Following the computations from above we know that the failure rate of a block is $n\lambda^n x^{n-1}$ for small x and approaches the constant λ for large x . Because blocks are connected in series (each of them being essential), the failure rate of the organism equals the sum of the failure rates of blocks i.e. $m \cdot n\lambda^n x^{n-1}$ for small x and $m\lambda$ for large x .

Next suppose that many elements are initially defect and that the probability of an initially functioning element is given by q . The failure rate of a block with i initially functioning elements is thus $\mu_B(i) = i\lambda^i x^{i-1}$ for small x and $\mu_B(i) = \lambda$ for large x . Blocks, ordered according to their number of initially functioning elements, are binomially distributed. We approximate the binomial with a Poisson distribution:

$$P(i) = c \cdot \exp(-k) \frac{k^i}{i!},$$

where $k \equiv nq$ is the mean number of initially functioning elements and c is a normalizing constant ensuring that the sum of probabilities equals one. The failure rate of the system, computed as the sum of the failure rate of blocks, is then obtained as

$$\mu(x) = \sum_{i=1}^n mP(i)\mu_B(i) = mc \cdot \exp(-k) \sum_{i=1}^n \frac{k^i}{i!} \mu_B(i).$$

Now consider a complex, redundant organism with a large number of elements. In the limit, for $n \rightarrow \infty$, it can be shown that $\mu(x)$ can be approximated by

$$\mu(x) \approx \begin{cases} Re^{\alpha x} & \text{for small } x \\ c \cdot m \cdot \lambda & \text{for large } x. \end{cases} \quad (7)$$

with $\alpha = k\lambda$ and $R \equiv mc\lambda k \exp(-k)$ (Gavrilov and Gavrilova, 1991). The organism ages according to Gompertz law. For large ages (the oldest old) the force of mortality converges to a high plateau. Taking log's of R we get $\log R = \log(cm\lambda k) - k$ and inserting $\alpha = k\lambda$ we arrive at $\log R = \log M - \alpha L$ with $M = \alpha mc$ and $L = 1/\lambda$, which is the Strehler-Mildvan correlation. The reliability model is capable to generate the most important regularities of human ageing.

For an interpretation of parameters, first note that L is uniquely pinned down by λ , the age-independent failure rate of an element. If λ is a species-specific constant, then the model predicts a unique focal point (lifespan) L for the species. Across species, L depends inversely on the robustness of its non-ageing elements. If we reasonably assume that m , the number of irreplaceable blocks, is also a species dependent constant, then all variation within a species results from variation of a k , the mean number of initially functioning elements.

The parameter k is a compound parameter $k = nq$. Consider first variation in n , the number of elements per block. For humans these differences could exist across countries, because their citizens are on average of different size. This could in principle come through country-specific diet and/or Darwinian selection because optimal body-size depends on ambient temperature (Bergmann, 1847; Dalgaard and Strulik, 2015). The model thus predicts in line with the evidence a positive association between lean body size (height) and life-expectancy (Waller, 1984; Peck and Vagero, 1989; Koch, 2011). It rationalizes why health and life expectancy improve as individuals, on average, grow taller, a phenomenon associated with economic development during the 20th century (Dalgaard and Strulik, 2016, Dalgaard et al., 2021a). The explanation offered by reliability theory is increasing redundancy. Larger humans have a larger organ reserve to live off.

Next, hold n constant and consider variation of q , the probability for an element to be initially functioning. The idea here is that available nutrition (for mother and child) and disease exposure early in life have shaped q . Taking the historic improvement in nutrition and health into account, the model predicts that individuals age faster today than hundred years ago because they start

out better at young age, endowed with more functioning organ reserve. Consequently, survival prospects and life-expectancy have improved at any age. The model predicts “fetal origins” (Barker, 1995; Almond and Currie, 2011; Dalgaard et al., 2021b), i.e. lasting consequences of early events in life on late-life mortality and morbidity. Since individuals are also predicted to be taller because of the generally improved conditions (Fogel, 1994) and because of less exposure to inflammation and infections (Crimmins and Finch, 2006), mortality improves because of the simultaneous and amplifying effect of increasing n and q on $k = nq$.

While the model does a fairly good job in explaining basic mechanisms of human ageing, a better approximation of the actual ageing process can be achieved by adding more details. Extensions of the basic model include cascading effects, i.e. the phenomenon that failure of one element of the system entails failure of other elements (Gavrilov and Gavrilova, 1991), mechanisms of imperfect (cell-) maintenance and repair (Finkelstein, 2008), and mechanism for redundancy expansion in early life (Milne, 2008). Allowing more complex interaction between elements leads to network theories of ageing at the molecular level (based on Kowald and Kirkwood, 1996) and at the level of functional limitations and frailties (Rutenberg et al., 2018).

A common characteristic of all reliability-based models is that organisms are conceptualized as complex systems consisting of essential parts (e.g. organs, tissue) connected in series, which are in turn built of smaller entities (such as cells and molecules) connected in parallel. Parallel connectivity means that every reliability theory is built upon the idea of redundancy. Another common theme is a stochastic failure rate for the basic entities. The notion of ageing as driven by a “natural” stochastic process helps to explain the “unfair” nature of human fate, i.e. why we actually observe large differences of ageing on the individual level. Reliability theory can explain why individuals raised under equal conditions and/or built from the same genes (monozygotic twins) can age and eventually die in very different ways. At the same time the models provide a toehold to explain how genetic endowments, population- (e.g. country-) specific characteristics, and the environment early in life have bearing on aggregate ageing behavior of populations. In short, it integrates “good luck” as a major third important driver of longevity besides “good genes” and “good behavior”. The view that ageing and death are best conceptualized as accidental stochastic shocks at the molecular level is firmly established in the natural sciences and has entered biology textbooks (Arking, 2006).

6. THE FRAILTY INDEX

Although age is a powerful predictor of mortality at the aggregate level, it is a relatively poor predictor at the individual level and biologists are tirelessly emphasizing that ageing should not be conceptualized as time-dependent but as an event-dependent process. We thus turn next to the measurement of ageing as it is expressed in individuals and the question of how it is related to chronological age. Physiological ageing is complex and several proposals of complex measurements of the state of health have been made, including, for example, healthy (disability-free) life expectancy (Jagger and Robine, 2011), activities of daily living (Katz, 1983), the healthy ageing index (Sanders et al., 2014; O’Connell et al., 2019), the healthy ageing score, or allostatic load scores of biomarkers (Seaman et al., 2001), see Michel et al., (2019) for an overview. Here, we focus on a particularly straightforward and useful methodology, the so called frailty index.

The frailty index, developed by Mitnitski and Rockwood and several coauthors in a series of articles (based on Mitnitski et al., 2001), simply records the fraction of a large list of ageing-related health conditions that is present in an individual. The list of potential deficits ranges from mild ones to near lethal ones and it has been shown that it does not matter which particular health deficits are included in the unweighted index as long as there are sufficiently many. The intuition for this remarkable feature is that health deficits are connected to other health deficits. For example, hypertension is associated with the risk of stroke, heart diseases, kidney diseases, dementia, and problems of walking fast and sleeping well. This means that if a particular health deficit is missing from the list, its effect (on, for example, probability of death) is taken up by a combination of other health deficits. The health deficit index has a microfoundation in reliability theory and in a network theory of human ageing (Rutenberg et al., 2018). As the index rises towards one, the individual is viewed as increasingly frail, and in this sense physiologically older. The gradual loss of functional capacity of human organs is expressed as a gradual increase of the frailty index. The index thus captures in one number the state of health and the biological ageing process defined as the intrinsic, cumulative, progressive, and deleterious loss of function.

The literature has outlined 5 criteria for health deficits to be included in the frailty index (Searle et al., 2008): (i) A deficit’s prevalence must generally increase with age, although some clearly age-related adverse conditions can decrease in prevalence at very advanced ages due to survivor effects. (ii) The deficits need to be associated with health status. Graying hair, for example, would be inadmissible although it is obviously age related. (iii) The chosen deficits

must not saturate too early. For example, as humans age, it becomes harder to focus on close objects (presbyopia); by around age 55 the disease is nearly universal and thus less than ideal to include. (iv) The deficits that make up a frailty index must cover a range of systems. If the index becomes too narrowly focused, say on cognitive deficits, it potentially no longer captures overall ageing but simply cognitive ageing. (v) To ensure that the index is independent from the specific deficits taken into account, a sufficiently large number of deficits – 30 to 40 – needs to be included.

The quality of the frailty index has been demonstrated by its predictive power for death at the individual level and for mortality at the group level, as well as for other adverse health outcomes such as the risk of institutionalization in nursing homes and becoming a disability insurance recipient (Rockwood and Mitnitski, 2007; Hosseini et al., 2021). Another reason for the popularity of the frailty index is that it can be easily compared across samples, datasets, and populations (Searle et al., 2008).

On average, individuals accumulate health deficits exponentially with age. The frailty index increases by about 2 to 5 percent from one birthday to the next. This regularity, akin to the Gompertz law, has been shown first for Canadians (Mitnitski et al., 2002; 2016) and replicated for populations from Europe, the U.S., and across the world (Harttgen et al., 2013; Abeliansky and Strulik, 2018a; Abeliansky et al., 2020; Dalgaard et al., 2021c). The exponential accumulation of health deficits suggests that biological ageing is a self-productive process (Dragone and Vanin, 2021), in which the presence of many health deficits is conducive to the faster development of new deficits.

On average, women, at given age, display more health deficits than men and men develop new health deficits faster than women (Mitnitski et al., 2002, 2005, 2016; Yang, 2010; Gordon et al., 2017; Abeliansky and Strulik 2018a). Since mortality is usually lower for women than for men and since the frailty index has been shown to be highly predictive of mortality, these observations contribute to the morbidity-mortality paradox. Apparently, a given score of the frailty index exerts a stronger effect on mortality for men. (Mitnitski et al., 2002; Gu et al., 2009, Romero et al., 2012; Mitnitski et al., 2016). Potential explanations of the paradox within the frailty-index literature include the features that women suffer more often from non-lethal health deficits and that women visit doctors more often and report more diagnoses of deficits. These explanations have also been discussed in the rich literature on the morbidity-mortality

paradox outside the frailty-index paradigm, which also discusses genetic gender differences, immune system responses, hormones, disease patterns, and gender differences in health behavior as potential explanations (e.g. Bird and Rieker, 1999; Case and Paxson, 2005; Oksuzyan et al., 2008, Schuenemann et al., 2017).

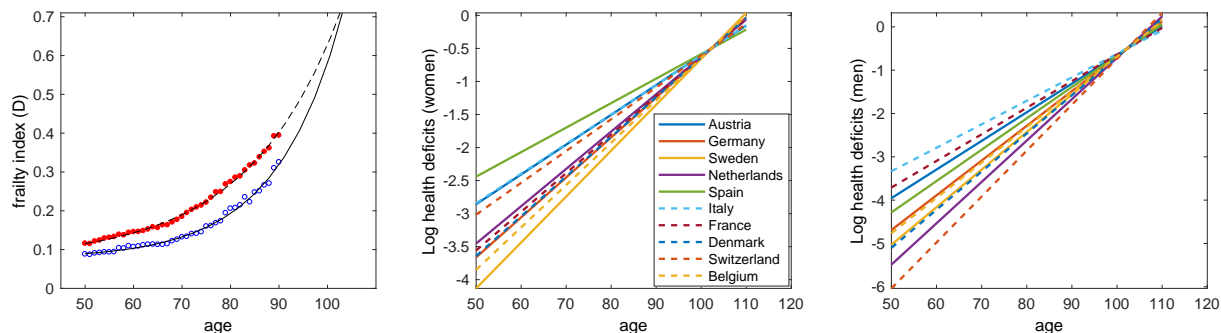
As an example, we next have a closer look at some of these regularities within Europe. Abeliansky and Strulik (2018a) used the Survey of Health, Ageing and Retirement in Europe (SHARE dataset release 5.0.0, Börsch-Supan et al., 2013) and considered four waves with health-related information, which took place between 2004 and 2013. The study computed a frailty index consisting of 38 symptoms, signs, and disease classifications for individuals aged 50 to 90 from the 10 countries that participated in all 4 waves: Austria, Belgium, Denmark, France, Germany, Italy, Netherlands, Sweden and Switzerland. In log-linear regressions, akin to the Gompertz law, and controlling for individual fixed effects, the point estimate of the age coefficient was 0.023 for women and 0.026 for men. Inspired by the Gompertz-Makeham law of mortality and its adaption to frailty analysis by Mitnitski et al. (2002), non-linear regression was used to estimate

$$D_{ag} = A_g + R_g \cdot \exp(\alpha_g \cdot age_{ag}) + \epsilon_{ag}. \quad (8)$$

In order to get reliable estimates, individuals were binned in one-year age groups. The index a refers to age group and g refers to the gender (male, female). Results using data pooled over all waves and countries are shown in the panel on the left-hand side of Figure 4. Women are represented by red (filled) circles and men by blue (empty) circles. The predictions from the regression are shown by solid and dashed lines. The quasi-exponential growth equation fits the data well ($R^2 = 0.99$). It shows that men start out healthier and then accumulate health deficits more quickly. At about age 103 the regression lines intersect.

We next consider results from regressions of (8) for each country separately. Interestingly, the country-specific parameters of R and α , denoted by R_c and α_c , are negatively associated, akin to the Strehler-Mildvan correlation. Regressing, $\log(R_c) = \beta + F\alpha_c$, provides the estimate $F = -103.2 (\pm 2.6)$, suggesting a common age of about 103 years at which European men and women display, on average, the same frailty index. The estimation results are visualized in the center and right panels of Figure 4. For better visibility, deficits are displayed in logs and results are shown for men and women separately. We observe a compensation effect of morbidity: in countries where individuals are healthier at initial age 50, they experience subsequently faster

Figure 4: Ageing within and across 10 European Countries



Left panel: frailty index by age for European women (red filled circles) and men (blue empty circles) and prediction from non-linear regression (solid and dashed lines). Center and right panel: Health deficit accumulation across countries, $D_c = \exp(\beta) \exp(\alpha_c(\text{age} + F))$, in which α_c stems from estimating (8) by country and β and F stem for the compensation law regression $\log(R_c) = \beta + F\alpha_c$, logarithmic scale of D_c .

ageing, confirming the prediction from reliability theory that initially more robust systems age faster. The intersection is about at $D = 0.7$, a value, which has been suggested as the maximum observable frailty index (Rockwood and Mitnitski, 2006).

The frailty index has been developed to measure visible health deficits in elderly persons. Basic principles of reliability theory suggest that damage of body cells occurs at any age (Kirkwood, 2005) albeit at young ages these micro damages are mostly not yet visible in form of diagnosed health deficits and functional limitations.³ In order to assess ageing in young adults, Belsky et al. (2015) used biomarkers to measure physiological deterioration of multiple organ systems (pulmonary, periodontal, cardiovascular, renal, hepatic, and immune function). They collected 18 biomarkers for a cohort of New Zealanders of which only 1% had been diagnosed with an age-related chronic disease. Biological age at chronological age 38 was computed from biomarker function and found to be normally distributed ranging from age 28 to 61. Since biomarkers were also collected at age 26 and 32, age-patterns of biomarker could be obtained and it was found that biologically older individuals aged at a faster rate. On average, each year increase of biological age was associated with a 5 percent faster deterioration of biomarkers, implying that deficits in organ systems grow similar to health deficits in elderly persons. Levine (2012) discusses the use of biomarkers for the computation of biological age as a predictor of mortality. Blodgett et al. (2017) computed a frailty index from abnormal laboratory test results and showed that it correlates with and displays similar characteristics as the conventional frailty

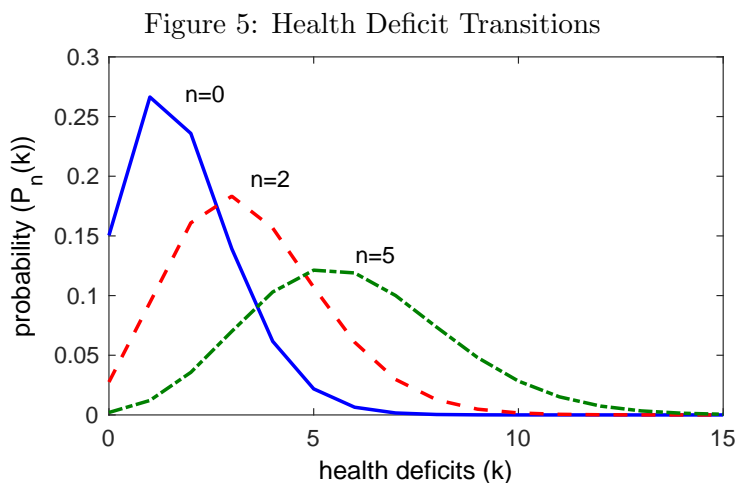
³It is possible, however, to explore the influence of early-life and in utero circumstances on old-age frailty. Abelian-sky and Strulik (2018b) show that individuals exposed to hunger in childhood develop health deficits faster in old age and Abelian-sky and Strulik (2020) show how the season of birth is related to late-life health deficit accumulation.

index. The lab-based index is higher at young ages and increases less steeply with age than the conventional index, indicating that deficits arise first at the cellular level before they become visible as accumulated damage at the organ and tissue level.

7. INDIVIDUAL AGEING

Whereas health deficits appear to increase monotonically with age at the population level, there is scope for repair and recovery at the individual level. Moreover, individual health trajectories are highly idiosyncratic reflecting individual-specific exposure to stressors and individual specific recovery time. The self-productive feature of health deficit accumulation, however, is also visible at the individual level. Specifically, it has been shown that health deficits are approximately Poisson distributed whereby the probability of an individual with n deficits to display k deficits next period is given by $P_n(k) = A_n(\rho_n)^k/k!$ (Mitnitski and Rockwood, 2006), in which ρ_n is the mean and the variance. Introducing death as an absorbing state assumed with probability $P_n(d)$ and requiring that probabilities add up to one, the normalizing constant can be eliminated and the transition probability can be written as

$$P_n(k) = e^{-\rho_n}(1 - P_n(d)) \frac{(\rho_n)^k}{k!}. \quad (9)$$



Probability distribution of health deficits (k) for individuals with n health deficits two years ago. Estimation for Canadians aged 65+ (estimates from Mitnitski and Rockwood, 2006).

Mitnitski and Rockwood (2006) show that a simple linear approximation, $\rho_n = a_1 + b_1n$ and $P_n(d) = a_2 + b_2n$ fits the observed health transition of Canadians aged 65+ quite well ($R^2 = 0.98$). Stochastic changes in individual health status are thus described by an age-independent Markov

chain such that the mean and variance of health deficits next period increases with the number of currently present health deficits. These results are illustrated in Figure 5. While it is always possible to transit back to a state with fewer health deficits, the general trend goes towards the accumulation of more deficits capturing ageing as the cumulative, progressive, and deleterious loss of function that eventually culminates in death. Hosseini et al. (2021) provide a refinement of the stochastic process for frailty dynamics with age-dependent variance. Grossmann and Strulik (2019) discuss implications for health inequality and public policy.

8. AGEING OF POPULATIONS

Finally, we extend the methodology, which was until recently applied exclusively to individuals, to the use of macro data by computing the frailty index of populations, following Dalgaard et al. (2021c). Consider the definition of the frailty index of individual i from country c ,

$$D_{ic} = \frac{1}{N} \sum_{d=1}^N \mathbf{1}_{ic}(d), \quad (10)$$

where $\mathbf{1}_{ic}(d)$ is an indicator function that takes on the value 1 if individual i suffers from deficit d and N is the number of potential deficits. The average frailty index in country c , D_c , is computed as $D_c = (1/P_c) \sum_i^{P_c} D_{ic}$, where P_c is the size of the population in country c . Using equation (10), a simple rearrangement of the sum allows us to write the average frailty index as:

$$D_c = \frac{1}{N} \sum_{d=1}^N \frac{P_{dc}}{P_c}, \quad (11)$$

where P_{dc} is the number of people in country c that suffer from deficit d . The aggregate frailty index is then simply computed as the average of N prevalence rates, P_{dc}/P_c , in each country. Analogously, the frailty index for an age group a in country c is computed as $D_{ac} = (1/N) \sum_{d=1}^N (P_{dac}/P_{ac})$, where P_{dac}/P_{ac} is the prevalence rate of d within age group a in country c . Frailty indices for men and women were constructed analogously.

Dalgaard et al. (2021c) obtained data on prevalence rates for men and women aged 20 to 94 for five year age groups from the Global Burden of Disease Study (GBD) for the period 1990 to 2019 (Vos et al., 2020). Applying the methodology of selecting items for the index as explained above, they constructed a frailty index consisting of 32 health conditions for 201 countries. Controlling for country and year fixed effects, Dalgaard et al. (2021c) found that the average women in the world accumulates 2.7 percent more health deficits from one birthday to

the next. The rate is 2.8 for men, who start out healthier and display less deficits until about age 80. These growth rates turned out to be astonishingly stable; varying between 2.6 and 2.9 percent when different subdivisions of the world were considered.

Next, Dalgaard et al. (2021c) explored the mortality-morbidity nexus at the population level, for a selected group of countries for which age-specific mortality rates were available from HMD (2020). In log-log regressions they found an elasticity of mortality rate with respect to frailty of 3.0 for men and 2.8 for women. These numbers turned out to be very robust to the inclusion of country and year fixed effects. Combined with the previous results, they confirm the morbidity-mortality paradox at the population level. Women display, on average, greater frailty but are less likely to die at the same level of the frailty index. The numbers are also intuitive. Recalling Gompertz law of mortality $\log \mu = \alpha^M \text{age}$, with $\alpha^M \approx 0.09$ and inserting health deficit accumulation $\log(D) = \alpha^D \text{age}$ with $\alpha^D \approx 0.03$, suggests a mortality elasticity of $\alpha^M / \alpha^D = 3$.

9. DISCUSSION AND CONCLUSION

This chapter has introduced two measures of human ageing, the force of mortality and the frailty index. It has been shown that both measures grow about exponentially in chronological age. Chronological age, however, is not causing physiological ageing. Instead, ageing can be understood as the deterioration of a complex and highly redundant system experiencing stochastic damage at the subcellular level. This view, formalized in reliability theory, is capable of explaining the exponential increase of health deficits and mortality, the compensation laws of mortality and morbidity, and other regularities of human ageing.

The frailty index has been introduced in health economics by the health deficit model (Dalgaard and Strulik, 2014). The health deficit model computes the derivative of the frailty index (equation 8) with respect to age, $\dot{D} = \alpha D - A$ and it takes it into account as a state equation in economic life-cycle modeling. In the deterministic version of the model, death occurs when an upper limit of health deficits has been accumulated. In the stochastic version, survival probability is a negative function of the frailty index. The parameter A is conceptualized as the main gateway through which health behavior (such as, for example, smoking or exercising) affects ageing: it lets health deficit grow (somewhat) faster or slower than exponentially. The model predicts that health expenditure increases with age but it is also consistent with the observation that age per se does not much affect health expenditure once time to death is controlled for

(Zweifel et al., 1999; Schuenemann et al., 2020). Current and future medical progress promises to reduce the natural force of ageing α , perhaps eventually to a level at which health investments in prevention and repair allow humans to become non-ageing (De Grey, 2013; Lopez-Otin et al., 2013; Sinclair and LaPlante, 2019). For a first discussion of these ideas in an economic life cycle model, see Dragone and Strulik (2020).

The main feature of the health deficit model is that it implements the self-productive nature of health deficits: the presence of many health deficits is conducive to the faster development of new deficits. Considering two individuals of the same age, the one in worse health is predicted to develop more health deficits in the next period. The feature of self-productivity captures human ageing as intrinsic, cumulative, progressive, and deleterious loss of function that eventually culminates in death and it explains the exponential (or, more generally, convex) association of morbidity and mortality with chronological age.

Against this background, it is remarkable that the health capital model (based on Grossman, 1972), which for a long time served as the main paradigm in life-cycle health economics, assumes just the opposite. There, it is assumed that the state of health is represented by health capital H , whereby more health capital identifies a healthier person, and that health capital depreciates at some positive rate δ , such that the loss of health is $\dot{H} = -\delta H$. The process of health capital depreciation is self-depleting (Dragone and Vanin, 2021): the presence of much health capital is conducive to larger losses of health capital. Considering two individuals of the same age, the healthier one (endowed with more health capital) is predicted to lose more health capital (faster decline of health) in the next period. Notice that introducing an age-dependent depreciation rate cannot “repair” the prediction of faster physiological ageing of physiologically younger individuals. This counterfactual feature can be regarded as the origin of the many shortcomings and limitations of the health capital model highlighted in the literature (e.g. Wagstaff, 1986, Zweifel and Breyer, 1997, Case and Deaton, 2005; Almond and Currie, 2011; Strulik, 2015; and Dalgaard et al., 2021b).

From the empirical side, the greatest limitation of the health capital model is perhaps the feature that its main object of investigation, health capital, is unobservable and alien to medical scientists. Health capital may be constructed from the absence of health deficits or approximated by self-assessed health status, which likely depends on the presence of health deficits. The frailty

index, in contrast, provides an opportunity to formulate, calibrate, and test health economic life-cycle models with a straightforward metric that measures health deficits directly. The measure has an established methodology in gerontology where it has been applied by now in hundreds of studies. It allows economists and medical scientists to discuss human ageing using a common language and methodology.

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