Methuselah Found? Why linear increases in life expectancy do not require ever faster declines in mortality rates

Richard G.A. Faragher[*], Arne Freimann[†], Tom Huber[‡],
Linda Partridge[§], Jochen Ruß[**] [corresponding author]

This version: 10th of February, 2026

Abstract

Several prominent studies suggest that further increases in human life expectancy at a pace similar to that observed over the past century would require an ever-faster decline in mortality rates – at least as long as the human aging process remains unalterable. Motivated by recent developments in the field of aging research, we investigate whether reductions in mortality would translate into increases in life expectancy in a structurally different manner if aging can be slowed. We examine several hypothetical biomedical scenarios on the future of human aging. Our findings indicate that, in those scenarios in which the aging process can be altered, a constant – or even moderately declining – rate of mortality reduction could be sufficient to sustain a linear increase in life expectancy. This suggests that, with a different "type of medical progress", a constant "speed of medical progress" would suffice to sustain a linear increase in human life expectancy.

---

[*] School of Applied Sciences, University of Brighton, Brighton, East Sussex, BN2 4GJ, UK (R.G.A.Faragher@brighton.ac.uk).

[†] Institute for Finance and Actuarial Sciences (ifa), Max-Born-Str. 12, 89081 Ulm, Germany (a.freimann@ifa-ulm.de).

[‡] Institute of Insurance Science, University of Ulm, Helmholtzstr. 20, 89069 Ulm, Germany (tom.huber@uni-ulm.de).

[§] Institute of Healthy Ageing and GEE, UCL, London, WC1E 6BT; United Kingdom. (linda.partridge@ucl.ac.uk)

[**] Institute for Finance and Actuarial Sciences (ifa), Max-Born -Str. 12, 89081 Ulm, Germany & Institute of Insurance Science, University of Ulm, Helmholtzstr. 20, 89069 Ulm, Germany (j.russ@ifa-ulm.de).

1 Introduction

Future trends in human mortality and life expectancy will not only have a significant impact on retirement and healthcare systems but will also generate broader socio-economic effects worldwide. Accordingly, estimates of these trends, and quantifying the uncertainty inherent in them, is important not only for specific sectors of the economy (e.g., pension, insurance, and healthcare) but also for the socioeconomic system more broadly. While relatively steady increases in life expectancy were seen throughout the 20th century (Oeppen and Vaupel, 2002), significant uncertainty has now emerged regarding both the direction and scale of future mortality trends[1].

One school of thought, closely associated with the seminal work of Olshansky (Olshansky *et al*., 1990; Olshansky *et al*., 2001), argues that, unless the fundamental mechanisms of human aging can be modified, future increases in life expectancy at a pace similar to those seen in the last 100+ years are implausible if not impossible. This conclusion follows from a biodemographic effect often referred to as "entropy in the life table": as life expectancy increases, mortality is postponed to later ages and is increasingly compressed, requiring progressively larger relative reductions in mortality rates to achieve further gains in life expectancy. Olshansky *et al*. (2001) illustrate the essence of life table entropy as follows: "*when life expectancy at birth is 50, it takes an estimated 4.1% reduction in total mortality at every age to raise life expectancy 1 year [...]. By contrast, raising life expectancy from 80 to 81 years requires a 9.1% reduction in total mortality at every age.*" Thus, *ceteris paribus*, a linear increase in life expectancy requires the rate of medical progress (plausibly taken as the primary driver of the rate of mortality decline) to grow ever faster. In a recent study, Olshansky *et al*. (2024) found that for a group of nine countries, the percentage reduction in death rates from all causes at all ages required to raise period life expectancy at birth by 1 year has been increasing relative to the year 1990 following a pattern predicted by their work two decades earlier. Further, they observed that increases in overall life expectancy in the eight countries with the highest life expectancy have decelerated since 1990, accompanied by a reduction in lifespan inequality and a greater compression of

---

[1] Potential causes of increasing mortality (i.e., decreasing life expectancy) include, but are not limited to, pollution (Lelieveld *et al*., 2020), the emergence of multi-drug resistant bacteria (Cassini *et al*., 2019), effects of climate change (Barrett, 2015; Dunnell *et al*., 2022; Longevity Science Panel, 2022) and lifestyle issues, such as an increasing prevalence of obesity (Peeters *et al*., 2003). Conversely, decreased mortality (i.e., increased life expectancy) may result from the adoption of healthier lifestyles (Khaw *et al*., 2008), the development of novel therapies such as stem cell research (Strauer and Kornowski, 2003) or from pharmaceutical innovation more generally (Lichtenberg, 2022).

mortality at the oldest ages.[2] Based on these findings, they infer that "*unless the processes of biological aging can be markedly slowed, radical human life extension is implausible in this century*".

These researchers have been careful to stress throughout their work that their conclusions might not hold for a future society where the modification of fundamental aging mechanisms was possible. Although such interventions seemed remote in 1990, subsequent progress in biogerontology has been rapid and some treatments based upon this improved understanding of the biology of aging (such as the use of senolytics or rapalogues) are now in early stage clinical trials (Gerdes *et al.*, 2021) but as yet have not impacted life expectancy at the population level.

A broad consensus now exists within biogerontology that some mechanisms that cause aging have been clearly identified and are druggable. A detailed discussion of this area is outside the scope of our article, but we would stress that multiple compounds that can modulate aging rates have been identified in rodent models and have entered the translational pipeline (Guarente *et al.*, 2024). There is also a plethora of data on the extension of healthy lifespan in invertebrates, often involving biological mechanisms that are also present in mammals including humans.

Although the precise times to market, access, and compliance regimes for these gero-therapeutics are unclear, attempts are being made to forecast their effects on mortality for actuarial purposes (Faragher *et al.*, 2025; Stengele *et al.*, 2024). It seems likely that the structure of changes in mortality rates (and hence human life expectancy) caused by a modification of the biology of aging will differ from previously observed alterations. In particular, the axiomatic assumption that steady increases in life expectancy require ever faster declines in mortality rates is potentially unsound if a modification of the biology of aging increases the human lifespan limit. This is of particular relevance since there are a variety of reports in the biogerontological literature of interventions that significantly extend the lifespan of animals.[3] These discoveries directly challenge the widely held modelling

---

[2] For further recent studies documenting the deceleration of life expectancy gains in the 21st century, we refer to Andrade *et al.* (2025) and Crimmins (2025).

[3] There is now evidence that deletion of senescent cells in experimental animals in middle and late life improves health and extends median lifespan with modest effects on maximum lifespan (cf. e.g., Yousefzadeh *et al.*, 2018; Wang *et al.*, 2024; Kowald and Kirkwood, 2021). We also refer to the observation that single gene mutations produce significant extensions of maximum lifespan in mammals (e.g., the Ames dwarf mice- first reported ~1995) some of which may be relevant to humans; to the observation that genetic variations (e.g., foxo3a rs2802292) within human populations confer extended health and thus longevity (first report 2008); and to the discovery that complex non-aging metazoans (e.g., the Quahog) exist - see Treaster *et al.* (2014). Perhaps the most important work in this regard is the observation by Gkioni *et al.* (2025) of significantly increased maximum lifespan in mice treated with a combination of rapamycin & trametinib.

assumption that a fixed species-specific lifespan limit is an intrinsically non-modifiable feature of living organisms.

Accordingly, this paper reports a re-analysis of Olshansky *et al*. (2001) in which their assumptions are relaxed, and their results extended to determine whether reductions in mortality rates translate into an increase in life expectancy in a structurally different way once aging can be slowed. Crucially, and contrary to Olshansky *et al*. (2001), we have therefore also allowed for hypothetical biomedical scenarios in which mortality improvements also affect very high ages and/or extend lifespan limit – conditions that may plausibly arise in a world where aging can be slowed. Although motivated by recent advances in geroscience, our scenarios are purely hypothetical. They are deliberately not intended to reflect historical mortality trends but rather intended to serve as a starting point for "what-if-analyses". Importantly, we do not claim that their future realization is likely or even guaranteed, nor do we assign any probability to their occurrence. Rather, we argue that further advances in geroscience could produce a type of medical progress that might fundamentally alter the structural relationship between mortality improvements and life expectancy. The sheer possibility of such advances justifies an analysis of "what-if-scenarios" to better understand how this structural relationship could change. We find that, in these hypothetical scenarios, a constant or even moderately decreasing rate of mortality reduction (i.e., intuitively speaking, a constant or moderately decreasing "speed of medical progress") can be sufficient to sustain a linear increase in human life expectancy.

The structural link between changes in mortality and the resulting impact on life expectancy has been examined in earlier demographic research, well before Olshansky *et al.* (2001). Keyfitz (1977) considered a proportional change δ in hazard rates at all ages and showed that the resulting change in life expectancy can be approximated by $-H\delta$, where H denotes the entropy of the life table capturing the elasticity of life expectancy with respect to proportional mortality shifts. This classical demographic setup has been taken up by several authors, including Goldman and Lord (1986) and Vaupel (1986), and later extended by Goldstein and Cassidy (2012), who also analysed how varying the pace of senescence, i.e., the rate of ageing, affects life expectancy. They find that the impact of changes in the rate of ageing is the complement of that of changes in mortality levels, and that the impact of slowing down aging on life expectancy becomes larger the smaller life table entropy is.

Our analysis differs from and complements these earlier contributions in several important respects. First, while Goldstein and Cassidy (2012) focus on the (static) relationship between changes in mortality levels (or the rate of ageing) and life expectancy, we take a dynamic approach and examine how this relationship evolves over time across a range of hypothetical future biomedical scenarios. Second, and more importantly, this dynamic perspective enables us to disentangle the implications of the two key assumptions made by Olshansky *et al.* (2001), namely that mortality cannot substantially be reduced at the highest ages and that there exists a fixed, non-extendable upper limit to human lifespan. Given that future breakthroughs in slowing down the human ageing process could render one or both of these assumptions invalid, such a differentiated analysis is both particularly relevant and timely.

2 Results: the relation between mortality improvements and life expectancy if aging can be slowed

Olshansky *et al*. (2001) calculate the percentage rate by which mortality rates for all ages need to be reduced to increase period life expectancy by one further year. As mentioned above, they find that this rate increases ever faster in the prevailing life expectancy. Intuitively speaking, a progressively increasing "speed of medical progress" is required to generate a linear increase in life expectancy (cf., Web fig. 4 in Olshansky *et al*., 2001)[4]. However, they assume that only mortality rates up to age 100 can be (medically) reduced, and that mortality rates for ages above 100 cannot be affected. This inevitably leads to a compression of mortality at the highest ages, to a rectangularization of the survival curve, and, implicitly carries the critical assumption that there is a fixed limit to human lifespan that cannot be extended.[5] The explicit assumption that medical knowledge will never reach the point at which it can impact mortality rates above the age of 100 seems questionable even under a "medicine as usual"-scenario and is definitely inconsistent with situations in which human aging mechanisms can be directly targeted. Given the current state of the art it also seems plausible to assume that maximum human lifespan would extend in a scenario in which interventions targeting human aging mechanisms exists. This would be consistent with either the hypothesis of a limit with respect to biological (as opposed to chronological) age, or with the hypothesis that there is no limit at all for maximum human lifespan that could not in principle be overcome with sufficient knowledge of the fundamental biology of aging.

Accordingly, we now analyse how the structure of the results in Olshansky *et al*. (2001) change, when either the first or both assumptions are relaxed, i.e., when mortality improvements at the highest ages are considered possible with or without the assumption of a fixed limit to human lifespan, respectively.

---

[4] The figure is available at https://www.science.org/doi/suppl/10.1126/science.291.5508.1491/suppl_file/1058601s4_med.gif

[5] The authors state in their paper that they also perform the analyses under the assumption that mortality rates for all ages above 50 (i.e., also beyond 100 but not below 50) are being reduced (again without an increase of maximum lifespan). However, corresponding results are not displayed.

To this end, we perform similar calculations as in Olshansky *et al*. (2001) using mortality data from the Human Mortality Database.[6] We conduct our analyses on mortality data for the total populations of Japan, Sweden, West Germany, the U.S.A. and the U.K. (separated by sex). For all countries, we consider data from three different periods: year 2015, year 2019, and for the 5-year interval 2015–2019. Since the results are structurally the same across all considered data sets, we only show the results for U.S.A. for the period 2015–2019.

Using different hypothetical biomedical scenarios, we examine how mortality rates can structurally decrease when life expectancy increases. While the first scenario follows the methodology from Olshansky *et al*. (2001), the remaining scenarios are designed to be consistent with the assumption that the human aging process can be slowed down. Under each scenario, we repeatedly determine the required reduction in mortality to increase period[7] life expectancy by one additional year.[8] More specifically, if current life expectancy amounts to T years, we denote by c_T the relative reduction in mortality rates that is required to increase life expectancy to $T + 1$ years.[9]

Biomedical Scenario 1: Human fundamental aging mechanisms are unalterable. Following Olshansky *et al*. (2001), we start with mortality rates that imply a limit to human lifespan. Specifically, we impose a maximum attainable age of 110 years by setting the mortality rate at age 110 equal to one. To achieve an increase in life expectancy, we then apply a relative reduction in age-specific death rates for all ages below 100. Mortality rates beyond age 100 and hence also the lifespan limit of 110 is assumed to remain unchanged. As mentioned above, this scenario was intended by its authors to model a situation where the aging process cannot be modified.

Biomedical Scenario 2: Modulation of human aging process is possible but there is a fixed limit for human lifespan: We argue that in a scenario in which the human aging process can be markedly modified, mortality rates will decrease also in (very) high ages.

---

[6] Data assessed on July 22nd, 2024, from www.mortality.org. For consistency with Olshansky *et al*. (2001), we also assume that the mortality probability at age zero cannot fall below a level of 0.5%.

[7] We focus on period (rather than cohort) life expectancy to maintain comparability with Olshansky *et al.* (2001). In a shift-based model, where the mortality experienced by a given cohort can be expressed by period mortality with adjusted ages (cf. Goldstein and Cassidy, 2012) our main structural results would straightforwardly apply to cohort life expectancy as well.

[8] We use this measure (and the linear increase in life expectancy implied by it) solely for comparability with Olshansky *et al*. (2001). We do not claim that a linear increase or any other future trajectory of life expectancy would be particularly desirable.

[9] Note that we do not specify the time over which the respective mortality reductions occur, as this only affects the slope of future increases in life expectancy, not the linearity itself.

Therefore, in this scenario a relative reduction in age-specific death rates from the life table is applied for all ages. The lifespan limit of 110 is, however, assumed to remain unchanged, i.e., only the first of the above mentioned two assumptions is dropped.

Biomedical Scenario 3a: Modification of human aging process is possible and there is no intrinsic limit to human lifespan (life table model): In order to additionally allow for an extension of lifespan limit, we extend Scenario 2 by the assumption that the lifespan limit in the underlying life table is dynamically increased by one year for every additional year of life expectancy gained. More Details are given in Appendix A.I.

Biomedical Scenario 3b: Modification of human aging process is possible and there is no limit for human lifespan (Gompertz model): For the scenario with modification of aging and extension of lifespan limit, we also consider an alternative modelling approach based on the well-established Gompertz law of mortality, which has no explicit upper limit to age and lifespan. However, when the Gompertz model is fitted to real data, there is some kind of "implicit lifespan limit", beyond which survival is very unlikely. In our approach, we first fit the Gompertz model to the survival rates of the given life table from Scenario 1 and then modify the Gompertz parameters to incrementally increase life expectancy by one further year. If mortality is reduced in this manner, the "implicit lifespan limit" in the sense described above also increases.[10] Since the resulting relative reduction in mortality rates is age-dependent, we here derive c_T as the average of the age-dependent reduction rates (weighted by the survival rates).

The Gompertz model has two parameters: α representing the baseline level of mortality, and β denoting the rate at which the force of mortality increases exponentially with age. As described in detail in Appendix A.II.a, a reduction in either parameter between two points in time can be interpreted as an intervention to the human aging process: a reduction of α would appropriately model the effect of an intervention that delays the human aging process by the same amount of time for all ages (delay of ageing), while a reduction of β would appropriately model the effect of an intervention that slows down the human aging process by the same relative rate for every age (deceleration of ageing). Historical mortality patterns have generally been consistent with a reduction in α over time (cf. Vaupel, 2010) whilst a systematic reduction in β has not been observed in human populations to date. Nevertheless, one might argue that a modification of the fundamental biology of ageing might lead to this (previously unobserved) effect on mortality patterns.

---

[10] This means that for any small number ϵ, the highest age beyond which survival is possible with a probability of ϵ increases when the parameters of the Gompertz model are modified as described below to increase life expectancy.

Of course, it cannot yet be known which interventions to human aging will become available and how they will structurally affect mortality. A successful intervention, which could significantly extend lifespan limit, would probably lead to a reduction in both parameters of the Gompertz-model.[11] As a starting point, we consider two stylized boundary scenarios, where the increase in life expectancy is caused solely by a reduction of either α or β, respectively. We argue that a realistic scenario would therefore likely lie somewhere between these boundary scenarios.

- **Version 3b-$\boldsymbol{\alpha}$:** Here, we modify the Gompertz parameter α to incrementally increase life expectancy by one year while maintaining the parameter β fixed. As explained above, this is consistent with a scenario in which biological age is reduced by the same amount of time for all ages.
- **Version 3b-$\boldsymbol{\beta}$:** Here, we modify the Gompertz parameter β to incrementally increase life expectancy by one further year, while maintaining the parameter α fixed. As explained above, this is consistent with a scenario in which biological age is reduced by the same relative rate for every age.

---

[11] Note that studies where life expectancy in mice can be extended with little or no increase in maximum lifespan often find a decrease in α in combination with an increase in β, cf. e.g. Kowald and Kirkwood (2021) and references therein. Also note that historical mortality developments over the past 10 to 15 years are typically consistent with a decline in α and an increase in β, reflecting the compensation effect of mortality, cf. Gavrilova and Gavrilov (2024). In contrast, we also consider a hypothetical scenario, in which a slowdown of aging leads to a decrease in β.

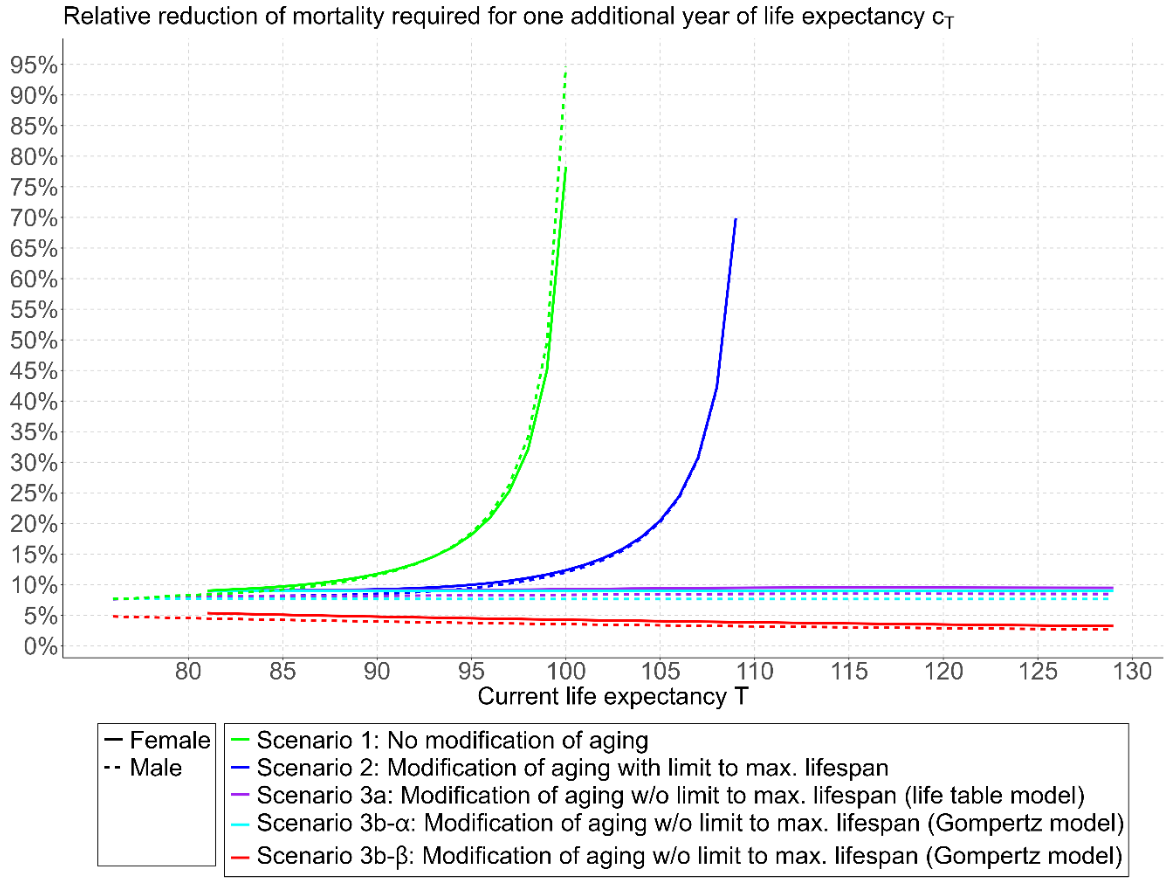

Figure 1 Reduction in death probabilities required to increase life expectancy by one additional year in the considered scenarios.

Our main results are shown in Figure 1. The charts start at the initial life expectancy implied by our data set which is around 75 (males) and slightly above 80 (females). First, we note that the structure of the results for females (sold lines) and males (dashed lines) is very similar in all considered scenarios. The results of Stylized Scenario 1 (no modification of human aging process) resemble those of Olshansky *et al*. (2001) which was to be expected since it is based on their assumptions: A linear increase in life expectancy requires an ever-faster pace of medical progress, i.e., with each additional year of life expectancy gained, an ever-stronger reduction in mortality is required to gain an additional year of life expectancy. In particular, the required percentage reduction increases dramatically when life expectancy approaches 100, the age beyond which no mortality improvements are assumed.

Under the assumption that mortality improvements are possible for all ages but still assuming a fixed lifespan limit of 110 (Stylized Scenario 2), the required rate of reduction remains rather stable as long as life expectancy is below 95. However, once life expectancy passes 95, the curve again increases dramatically as it approaches the lifespan limit of 110. Hence,

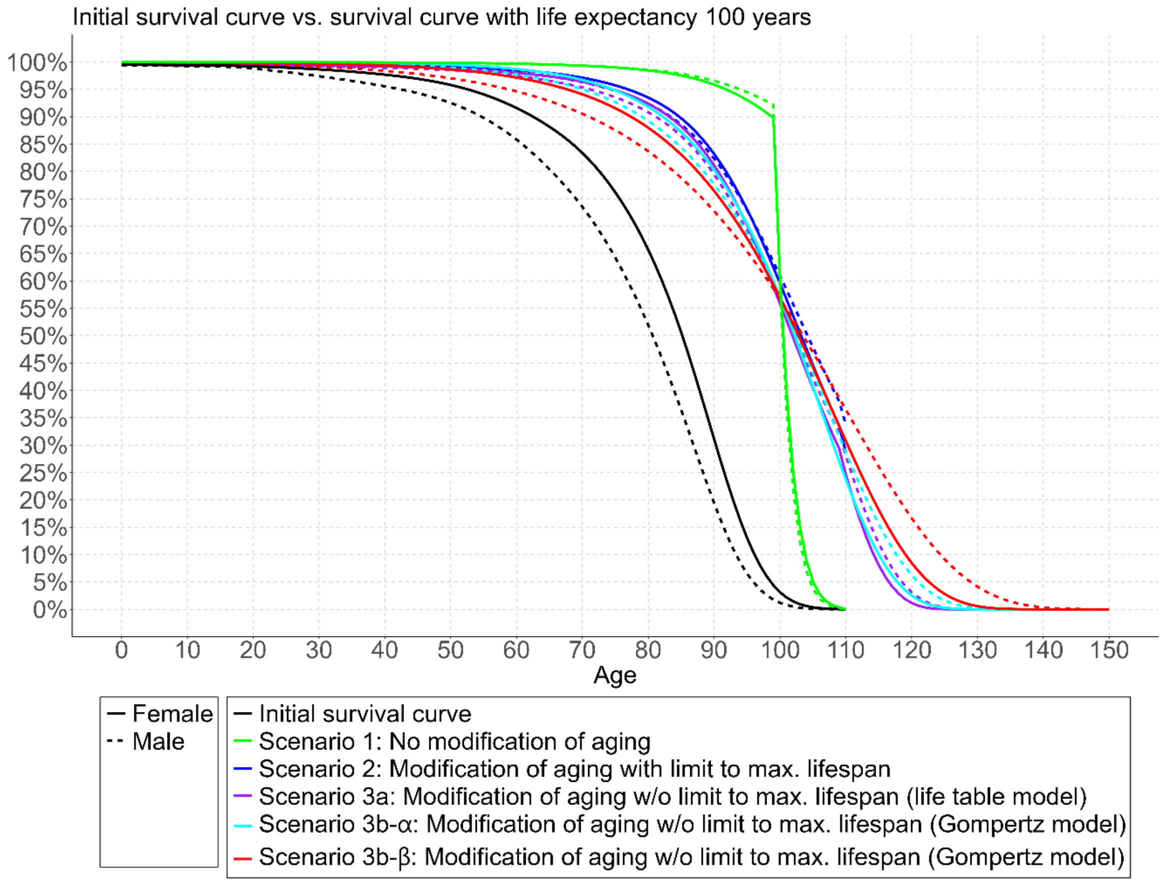

Figure 2 Resulting survival curves in the considered scenarios when life expectancy has reached 100.

the relationship between mortality improvements and life expectancy is structurally similar to Scenario 1, the only difference being that the drastic increase starts a few years later.

Interestingly, all remaining scenarios (3a, 3b-α, and 3b-β), which allow for an extension of the lifespan limit, show a structurally completely different picture: the percentage reduction required to increase life expectancy by one additional year no longer increases as life expectancy rises. Rather, in Scenarios 3a and 3b-α roughly a constant reduction factor of approximately 10% is sufficient to gain one further year of life expectancy, regardless of the level already achieved. The results for Scenario 3b-α are particularly noteworthy, as they show that even with unchanged slope of the mortality curve (i.e., with constant β in the Gompertz model), a constant rate of mortality reduction can sustain a linear increase in life expectancy. Notably, in Scenario 3b-β, the reduction in mortality required to reach one additional year of life expectancy is lower and even slightly declining.

These results strongly suggest that the relationship between mortality improvements and life expectancy would be structurally different in scenarios in which an extension of the lifespan limit is possible, which would particularly be plausible as a consequence of a potential breakthrough in the field of anti-aging research. Our results suggest that in such a scenario a constant relative reduction of mortality would be sufficient to sustain a long-term linear increase in life expectancy. This holds for all our scenarios without a limit to human life expectancy and would hence also be the case in any realistic scenario that lies between our Stylized Scenarios 3b-α, and 3b-β. We particularly note that the structural change of mortality is fundamentally different from our Stylized Scenario 1 that structurally coincides with the results in Olshansky *et al*. (2001). We would like to stress, however, that this does not contradict (but rather complement) their results (or the results from Olshansky *et al*., 2024) since the authors clearly state that their results would no longer hold if biological aging can be slowed.

Finally, we would like to point out an important issue that arises when a fixed lifespan limit is assumed. Exemplarily, Figure 2 shows the resulting survival curves in the considered scenarios when life expectancy has reached age 100. Obviously, the scenarios based on the assumption of an upper limit to human lifespan inevitably lead to a massive compression of mortality at the highest ages and to a corresponding rectangularization of the survival curve. This eventually leads to implausible survival curves. This is the underlying mechanism why – under the assumption of a fixed upper limit to human lifespan – increases in life expectancy are ever harder to achieve as life expectancy approaches this upper limit. This issue disappears if an extension of the (chronological) lifespan limit is considered possible (which is also consistent with the assumption of the existence of a maximum biological lifespan in combination with a slowdown of aging). Here, plausible shapes of survival curves are possible also for higher life expectancies.

3 Discussion

What is often referred to as “the first longevity revolution” led to an unprecedented improvement in human life expectancy in the 20th century, providing mankind with an average of 2-3 extra years of life expectancy per decade (cf. Olshansky *et al*., 2024). This remarkable success was primarily driven by advances in public health and medicine, particularly by progress in the prevention and cure of infectious diseases through improved sanitation, vaccination, and antibiotics in the first half of the 20th century, and by medical advances in cardiovascular care (the so-called cardiovascular revolution) in the second half of the century. While the initial increase in life expectancy was mainly due to an improvement in mortality at younger ages, further improvements in the second phase resulted from a decline in mortality at middle to older ages. The impact of this type of medical progress on life expectancy tends to be greater the higher the general level of mortality is at younger and middle ages. The impact on life expectancy is therefore bound to diminish as life expectancy increases. Therefore, the first longevity revolution inevitably has to come to an end, as has been observed in recent decades (cf. Olshansky *et al*., 2024).

With rapid advances in geroscience, a second longevity revolution is now on the horizon, offering the potential to slow the human aging process and, in turn, postpone the onset of several, ideally all, age-related diseases simultaneously. In spite of the overwhelming evidence that it is in principle possible to alter the biological rate of human aging, it is impossible to precisely predict if, when, and through which type of drugs or treatments this next longevity revolution will be triggered. It can, however, be argued that the impact of an alteration of the rate of human aging on human life expectancy will be structurally very different from the impact during the first longevity revolution as described above. Since a slowdown of the rate of aging could potentially delay the onset of many age-related diseases, its impact would not necessarily diminish as life expectancy increases.

While the limits to future increases in human life expectancy (and the reasons for these limits) that exist in a world without the second longevity revolution are now well understood, we still lack a sufficient understanding of how declines in mortality rates caused by a potential second longevity revolution would translate into increases in life expectancy. As a starting point to this question, we have studied several stylized hypothetical biomedical scenarios that were designed to be consistent with a world in which the biological process of aging can be slowed (with or without an increase in lifespan limit). We have demonstrated that a constant or even decreasing relative reduction in mortality across all ages could be sufficient to sustain a linear increase in life expectancy. Intuitively speaking, the considered biomedical scenarios illustrate that the relationship between the "speed of medical progress" and the "speed of increase in life expectancy" will likely be structurally different during the next wave of the longevity revolution.[12]

Of course, our study is limited to structural insights gained from a set of stylized and hypothetical "what-if-scenarios". To achieve more reliable quantitative (as opposed to structural) insights, further interdisciplinary efforts are required to gain a deeper understanding of the timing, the likelihood of success, and the impact on mortality as well as morbidity of specific drugs or treatments.

We argue that such a multidisciplinary approach has now become especially timely. Multiple ageing mechanisms, sometimes known as the "hallmarks of ageing" (López-Otín *et al.* 2013, 2023) have now been discovered in multiple species (including nematodes, insects and mammals). Important milestones in uncovering these mechanisms include the demonstration that the deletion of senescent cells in transgenic mouse models produce improved health and thus lifespan (Baker *et al.* 2011; Baker *et al.* 2016) and the observation that low-dose rapamycin reproducibly extends both health and lifespan in outbred rodents (Miller *et al.*

---

[12] This assumes that corresponding treatments become widely available to the general population. We refrain from a discussion of potentially arising inequality issues if only certain subpopulations would benefit or from a discussion of other e.g. ethical or environmental issues that might result if aging can be modified.

2014; Warner, 2015). These data are consistent with the hypothesis that the accumulation of senescent cells and the dysregulation of nutrient signalling pathways are important causes of ageing in this species. A plethora of evidence also exist that these mechanisms are shared with humans. Examples include, but are not limited to, the demonstration that Werner's syndrome (a human genetic disease which is considered the closest clinical match to normal human ageing) results from the selective acceleration of cellular senescence in some, but not all tissues, (Kipling *et al.* 2004) and the observation that humans carrying rare genetic variants in the fox3a pathway (a component of the same nutrient sensing network targeted by rapamycin) show extended healthspan and reduced frailty (Willcox *et al.* 2008; Flachsbart *et al.* 2009). Perhaps most compellingly, a recent paper (Fraser *et al.* 2022) analysed co-mentions of ageing hallmarks and human age-related disease in 917,645 scientific literature abstracts and verified the differential associations between ageing hallmark and disease that emerged using manual curation. It was possible to identify distinct groups of human age related diseases specifically associated with each of the hallmarks identified from cross-species studies.

There is increasing evidence that these hallmark mechanisms are interdependent rather than independent (cf. Gerdes *et al*. 2021) and whilst the translational pipeline from rodent models into humans for late life chronic disease is often problematic for reasons discussed e.g. in Faragher and Hartley (2024) an increasing number of human clinical trials explicitly based on hallmark mechanisms now in progress (Gerdes *et al*. 2021). These include the application of senolytic cocktails based on fisetin, dasatinib, and quercetin, as well as the use of mTOR inhibitors (Mannick and Lamming, 2023). Importantly, these trials are not based on the use of new chemical entities (for which the overall trial failure rate is at lest 90% as a rule of thumb) but are based upon the use of licensed drugs which are being repurposed. In such scenarios the trial success rate is much higher (~60% success to apply a similar rule of thumb) and indeed low dose mTOR inhibitor use has been shown to dramatically enhance response rates of older people to vaccines and to reduce their overall infection rates for at least a year (Mannick *et al*. 2014, Mannick *et al.* 2018).

However, most provocative of all are important new data from Gkioni *et al*. (2025) (cf. also Footnote 3) which show that a combination treatment repurposing rapamycin & trametinib increased median mouse lifespan by 35% in females and 27% in males, critically with maximum lifespan increased between 26% (males) and 32% (females). This is clear evidence for significant extension of maximum mammalian lifespan rather than compression of late-life mortality which has been argued to be a primary effect of senolytics in rodent models (Kowald and Kirkwood, 2021).

Overall, there is overwhelming evidence that it is at least plausible (if not likely) that a modification of the fundamental biology of ageing can be achieved. This justifies what-if-analyses (as performed in this paper) in order to analyse potential consequences. While our analyses are intended as a first step in this direction, insights gained from the results of the above mentioned (and other) trials and animal studies may allow the production of more specific scenarios that can then be used to analyse the potential impact of the next wave of the longevity revolution on the demography of populations. Our findings are therefore highly relevant for anyone dealing with uncertainty in best estimate mortality projections, particularly social security institutions as well as financial entities such as pension plans and life insurers.

Appendix

A Methodology

A.I Dynamic extension of the mortality table in Stylized Scenario 3a

Our approach to dynamically extend the mortality table used in Stylized Scenario 3a is based on a simple idea: When we reduce all one-year death probabilities $q(x)$ by a certain percentage to increase the corresponding life expectancy by one year, we also reduce the last mortality probability (that has previously been 1) by the same percentage and extend the limiting age of the mortality table (and hence the lifespan limit) by 1 year. For example, assume that the current life expectancy is $T = 75$ years corresponding to a mortality table with limiting age of $\omega = 110$ years. We now reduce all one-year death probabilities to increase the life expectancy to $T + 1 = 76$ years by multiplying them with a scaling coefficient $c_T \in (0,1)$. The reduced one-year death probabilities are given by $\widetilde{q(x)} = q(x) \cdot (1 - c_T)$ for all ages $x \leq \omega$. Prior to the reduction we had $q(110) = 1$ (i.e., the probability of dying before reaching age 111 is 100%) which corresponds to a lifespan limit of 110 years. We then set $q\widetilde{(110)} = (1 - c_T) < 1$ resulting in a positive probability to reach age 111 and set $\widetilde{\omega} = 111$ and $q\widetilde{(111)} = 1$.

A.II The Gompertz law of mortality

A.II.a Interpretation of the Gompertz parameters in the context of slowing aging

The Gompertz law of mortality (cf., Gompertz, 1825) is widely used in demography, aging research, and actuarial science to describe the distribution of lifespans. It expresses the force of mortality at age x as

$$\mu(x) = \alpha e^{\beta x},$$

where α represents the baseline mortality level (at age zero), and β reflects the exponential rate at which mortality increases with age.[13]

If one of these parameters is reduced, the Gompertz curve changes such that mortality probabilities are reduced, and life expectancy is increased. However, a reduction of α leads

---

[13] There are several alternative, equivalent representations of this model. For instance, the Gompertz law is frequently expressed in terms of a "scaling parameter" b and the modal age at death m, cf. Missov *et al.* (2015). Setting $b = \frac{1}{\beta}$ and $m = \frac{1}{\beta}\ln\left(\frac{\beta}{\alpha}\right)$, this variant can be derived from the representation used herein.

to a structurally different change of the mortality curve than a reduction of β. It can easily be seen that after a reduction of α, the mortality of an x-year old person coincides with the mortality of a person aged $x - \kappa$ before the reduction of α for some constant κ (that depends only on the reduction of α but not on age). Hence, a reduction of α would appropriately model the effect of an intervention to human aging that delays the human aging process by the same amount of time for all ages. It can also easily be seen that after a reduction of β, the mortality of an x-year old person coincides with the mortality of a person aged $\kappa \cdot x$ before the reduction of β for some constant κ (that depends only on the reduction of β but not on age). Thus, a reduction of β would appropriately model the effect of an intervention to human aging that delays the human aging process by the same relative rate for every age.

A.II.b Intuitive idea of the Stylised Scenarios 3b- α and 3b- β

As a starting point, we first fit the parameters of the Gompertz model to the given life table from Stylized Scenario 1. Afterwards, we modify either α or β (while maintaining the other parameter fixed) to incrementally increase life expectancy by one further year. The one-year death probabilities can then be derived from the resulting Gompertz curves. The reduction of death probabilities that corresponds to a one-year increase in life expectancy is then calculated as follows: Assume we have a set of Gompertz parameters that corresponds to a life expectancy of, e.g., 75 years, and a different set of parameters corresponding to a life expectancy of 76 years. For both parameterizations, we calculate the resulting one-year death probabilities based on the corresponding Gompertz curves. We then calculate the relative reduction in mortality probabilities for each age. The overall reduction of death probabilities is then derived as the weighted average of the reductions for the different ages (weighted with the survival probability of each age year before reduction).

A.II.c Calibration methods for the Stylized Scenarios 3b- α and 3b- β

In the Gompertz-model, the probability that the lifetime of a newborn is larger than t is expressed by the survival function

$$S_{\alpha,\beta}(t) = e^{-\frac{\alpha}{\beta}(e^{\beta t}-1)}.$$

The corresponding life expectancy is given by the integral over the survival curve, and the one-year death probability for age x (the probability of dying before reaching age $x + 1$ conditional on having reached age x) is given by

$$q_{\alpha,\beta}(x) = \frac{S_{\alpha,\beta}(x)-S_{\alpha,\beta}(x+1)}{S_{\alpha,\beta}(x)}.$$

In an initial calibration step, we the parameters $\tilde{\alpha}$ and $\tilde{\beta}$ that best fit the survival curve from the given life table used in the Stylized Scenario 1 by means of the least squares method.

To find a Gompertz curve which has a target life expectancy of T years in Stylized Scenario 3b-α, we keep the initial parameter $\tilde{\beta}$ constant and determine the value for the parameter α_T which yields $E_{\alpha_T,\tilde{\beta}} = T$.[14]

For each age, we calculate the reduction in mortality probabilities $c_T(x)$ that results from an increase in life expectancy from T years to $T + 1$ years as

$$c_T(x) = 1 - \frac{q_{\alpha_{T+1},\tilde{\beta}}(x)}{q_{\alpha_T,\tilde{\beta}}(x)}.$$

The (weighted) average reduction in mortality used in Stylized Scenario 3b-α is then calculated as

$$C_T = \frac{\sum_{x=1}^{\infty} c_T(x) S_{\alpha_T,\tilde{\beta}}(x)}{\sum_{x=1}^{\infty} S_{\alpha_T,\tilde{\beta}}(x)}.$$

---

[14] In Stylized Scenario 3b-β, we analogously keep $\tilde{\alpha}$ fix and solve for β. All formulae in this case are otherwise identical and therefore omitted for the sake of brevity.

References

Andrade, J., Camarda, C. G., et al. (2025). Cohort mortality forecasts indicate signs of deceleration in life expectancy gains. *Proceedings of the National Academy of Sciences*, 122(35), e2519179122.

Baker, D. J., Wijshake, T., et al. (2011). Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. *Nature*, 479(7372), 232–236.

Baker, D. J., Childs, B. G., et al. (2016). Naturally occurring p16Ink4a-positive cells shorten healthy lifespan. *Nature*, 530(7589), 184–189.

Barrett, B., Charles, J. W., and Temte, J. L. (2015). Climate change, human health, and epidemiological transition. *Preventive medicine*, 70, 69–75.

Cassini, A., Högberg, L. D., et al. (2019). Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. *The Lancet infectious diseases*, 19(1), 56–66.

Crimmins, E. M. (2025). Life Expectancy and Health Expectancy in the Twenty-first Century: The Unthinkable, the Inconceivable, and the Unknowable. *Demography*, 62(4), 1217–1236.

Faragher, R. G. A., Freimann, A., and Ruß, J. (2025). Scanning the horizon: integrating expert knowledge into the calibration of stochastic mortality models. *Working paper*.

Faragher, R. G. A., and Hartley, R. C. (2024). Drug discovery for ageing: SIMPs, NEDs and screening challenges. *Nature Reviews Drug Discovery*, *23*(10), 725-726.

Flachsbart, F., Caliebe, A., et al. (2009). Association of FOXO3A variation with human longevity confirmed in German centenarians. *Proceedings of the National Academy of Sciences*, 106(8), 2700–2705.

Fraser, H. C., Kuan, V., et al. (2022). Biological mechanisms of aging predict age-related disease co-occurrence in patients. *Aging Cell*, 21(4), e13524.

Gavrilova, N. S., and Gavrilov, L. A. (2024). Compensation effect of mortality is a challenge to substantial lifespan extension of humans. *Biogerontology*, 25(5), 851–857.

Gerdes, E. O. W., Misra, A., Netto, J. M. E., Tchkonia, T., and Kirkland, J. L. (2021). Strategies for late phase preclinical and early clinical trials of senolytics. *Mechanisms of ageing and development*, *200*, 111591.

Gkioni, L., Nespital, T., et al. (2025). The geroprotectors trametinib and rapamycin combine additively to extend mouse healthspan and lifespan. *Nature Aging*, https://doi.org/10.1038/s43587-025-00876-4.

Goldman, N. and Lord, G.. (1986). A new look at entropy and the life table, *Demography* 23(2): 275–282.

Goldstein, J. R., and Cassidy, T. (2012). How slowing senescence translates into longer life expectancy. *Population studies*, 66(1), 29–37.

Gompertz, B. (1825). On the nature of the function expressive of the law of human mortality, and on a new mode of determining the value of life contingencies. *Philosophical Transactions of the Royal Society of London*, 115, 513–583.

Guarente, L., Sinclair, D. A., and Kroemer, G. (2024). Human trials exploring anti-aging medicines. *Cell Metabolism*, 36(2), 354–376.

Khaw, K. T., Wareham, N., et al. (2008). Combined impact of health behaviours and mortality in men and women: the EPIC-Norfolk prospective population study. *PLoS medicine*, 5(1), e12.

Kipling, D., Davis, T., et al. (2004). What can progeroid syndromes tell us about human aging?. *Science*, 305(5689), 1426–1431.

Kowald, A., & Kirkwood, T. B. (2021). Senolytics and the compression of late-life mortality. *Experimental Gerontology*, 155, 111588.

Lelieveld, J., Pozzer, A., et al. (2020). Loss of life expectancy from air pollution compared to other risk factors: a worldwide perspective. *Cardiovascular Research*, 116(11), 1910–1917.

Lichtenberg, F. R. (2022). The effect of pharmaceutical innovation on longevity: evidence from the US and 26 high-income countries. *Economics & Human Biology*, 46, 101124.

Longevity Science Panel (2022). *The Effects of Climate Change on Health in the UK*. https://www.longevitypanel.co.uk/landg-assets/longevity-panel/climate-change-and-health.pdf

López-Otín, C., Blasco, M. A., Partridge, L., et al. (2013). The hallmarks of aging. *Cell*, 153(6): 1194–1217.

López-Otín, C., Blasco, M. A., et al. (2023). Hallmarks of aging: An expanding universe. *Cell*, 186(2), 243–278.

Mannick, J. B., and Lamming, D. W. (2023). Targeting the biology of aging with mTOR inhibitors. *Nature Aging*, *3*(6), 642-660.

Miller, R. A., Harrison, D. E., et al. (2014). Rapamycin-mediated lifespan increase in mice is dose and sex dependent and metabolically distinct from dietary restriction. *Aging cell*, 13(3), 468–477.

Missov, T. I., Lenart, A., Nemeth, L., Canudas-Romo, V., & Vaupel, J. W. (2015). The Gompertz force of mortality in terms of the modal age at death. *Demographic Research*, *32*, 1031–1048.

Oeppen, J. and Vaupel, J. (2002). Broken Limits to Life Expectancy. *Science*, 296(5570), 1029–1031.

Olshansky, S. J., Carnes B. A., and Cassel, C. (1990). In search of Methuselah: estimating the upper limits to human longevity, *Science* 250(4981), 634–640.

Olshansky, S. J., Carnes, B. A., and Désesquelles, A. (2001). Prospects for human longevity, *Science*, 291(5508), 1491–1492.

Olshansky, S. J., Willcox, B. J., Demetrius, L., & Beltrán-Sánchez, H. (2024). Implausibility of radical life extension in humans in the twenty-first century. *Nature Aging*, 4(11), 1635–1642.

Peeters, A., Barendregt, J. J., et al. (2003). Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Annals of internal medicine*, 138(1), 24–32.

Stengele, U., Slater, F., et al. (2024). *Geroscience Focus*, Issue 11, Crystallise Ltd, November 2024, https://www.crystallise.com/wp-content/uploads/2024/11/GeroscienceFocusIssue1_241107.pdf

Strauer, B. E., and Kornowski, R. (2003). Stem cell therapy in perspective. Circulation, 107(7), 929–934.

Treaster, S. B., Ridgway, I. D., et al. (2014). Superior proteome stability in the longest lived animal. *Age*, 36, 1009–1017.

Vaupel, J. W. (2010). Biodemography of human ageing. *Nature*, 464(7288), 536–542.

Vaupel, J. W. (1986). How change in age-specific mortality affects life expectancy, *Population Studies* 40(1): 147–157.

Wang, B., Wang, L., et al. (2024). Intermittent clearance of p21-highly-expressing cells extends lifespan and confers sustained benefits to health and physical function. *Cell metabolism*, 36(8), 1795-1805.

Warner, H. R. (2015). NIA's intervention testing program at 10 years of age. *Age*, 37(2), 22.

Willcox, B. J., Donlon, T. A., et al. (2008). FOXO3A genotype is strongly associated with human longevity. *Proceedings of the National Academy of Sciences*, 105(37), 13987–13992.

Yousefzadeh, M. J., Zhu, Y. I., et al. (2018). Fisetin is a senotherapeutic that extends health and lifespan. *EBioMedicine*, 36, 18–28.