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Authors

Finch, Caleb E
Beltrán-Sánchez, Hiram
Crimmins, Eileen M

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Uneven Futures of Human Lifespans: Reckonings from Gompertz Mortality Rates, Climate Change, and Air Pollution

Caleb E. Finch[a] Hiram Beltrán-Sánchez[a, b] Eileen M. Crimmins[a]

[a]Davis School of Gerontology and Dornsife College, University of Southern California, Los Angeles, Calif., and
[b]Center for Demography of Health and Aging, University of Wisconsin-Madison, Madison, Wisc., USA

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Abstract
The past 200 years have enabled remarkable increases in human lifespans through improvements in the living environment that have nearly eliminated infections as a cause of death through improved hygiene, public health, medicine, and nutrition. We argue that the limit to lifespan may be approaching. Since 1997, no one has exceeded Jeanne Calment's record of 122.5 years, despite an exponential increase of centenarians. Moreover, the background mortality may be approaching a lower limit. We calculate from Gompertz coefficients that further increases in longevity to approach a life expectancy of 100 years in 21st century cohorts would require 50% slower mortality rate accelerations, which would be a fundamental change in the rate of human aging. Looking into the 21st century, we see further challenges to health and longevity from the continued burning of fossil fuels that contribute to air pollution as well as global warming. Besides increased heat waves to which elderly are vulnerable, global warming is anticipated to increase ozone levels and facilitate the spread of pathogens. We anticipate continuing socioeconomic disparities in life expectancy.

Since 1800, survival to older ages has increased progressively, effectively doubling life expectancy (LE), whether measured at birth [1] or at later ages [2]. This essay considers demographic evidence that human longevity is approaching a maximum (L_{max}) with current medicine, and addresses evidence from climate change that health across the lifespan could be challenged by environmental deterioration associated with global warming. As briefly noted in two 2010 reports on climate change from the US National Academies of Sciences (NAS) [3, 4], the elderly are among the disadvantaged populations with particular vulnerability.

We first considered the demographic history of mortality rates across the lifespan. Using Sweden as an example because of its unique national data since 1750, we showed that the J-shaped mortality rate profiles for cohorts have progressively dropped since 1800; the Swedish mortality profile is well matched by other industrializing countries [5, 6]. Across all postnatal ages, LE has at least doubled in the last 150–200 years due to the progressively declining mortality from infections with improved sanitation, water supply, and nutrition in the 19th century, followed by immunization and pasteurization in the early 20th century, and lastly by antibiotics after 1950 [5–7].

The J-shaped mortality curves of modern populations may be divided in 4 phases: the initially high mortality

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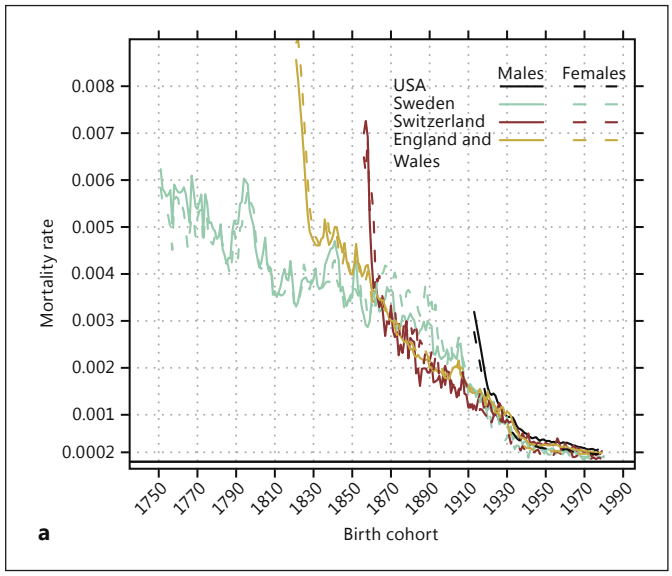
Caleb E. Finch
Davis School of Gerontology and Dornsife College
University of Southern California
Los Angeles, CA 90089-0191 (USA)
E-Mail cefinch@usc.edu



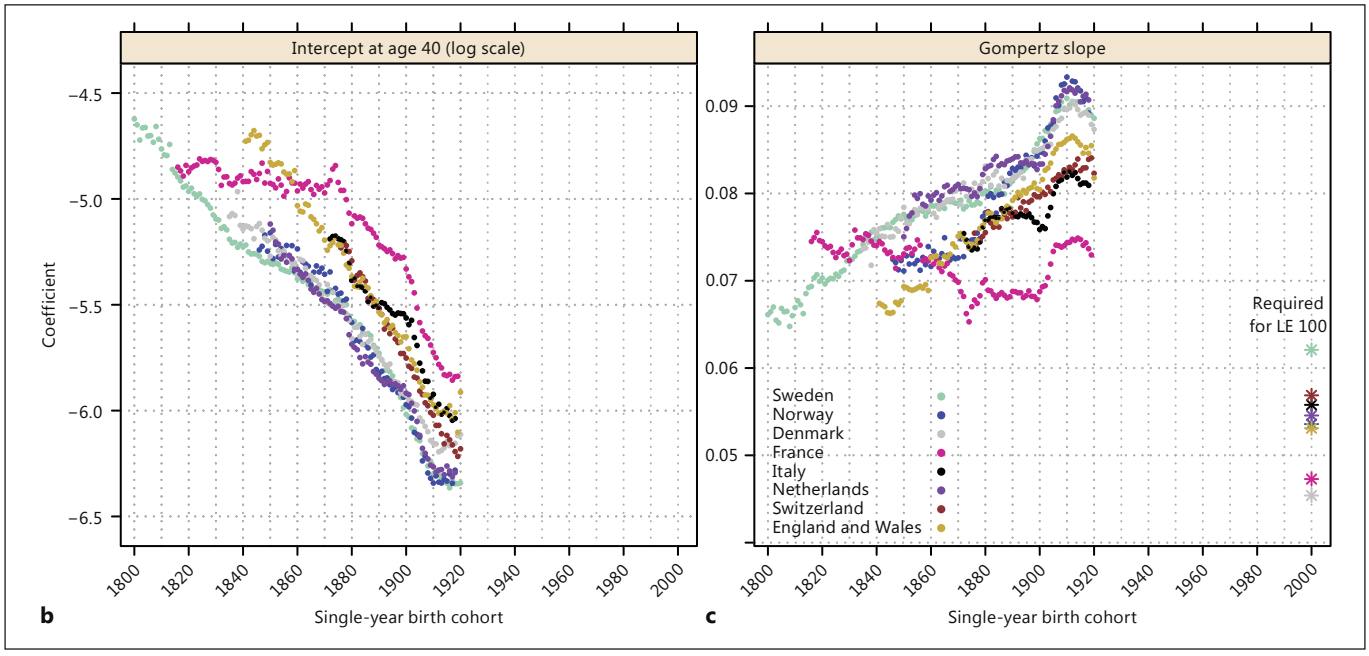


Fig. 1. Human mortality trends by age from the Human Mortality Data Base (HMDB). **a** Minimum mortality rates or lowest mortality rates in human populations for 5 countries at age 10–20 for historical cohorts from England-Wales, Sweden, Switzerland, and the USA show progressive decline with improving overall mortality as the Gompertz curves descend. The 'minimum mortality' phase may extend beyond age 30. With the virtual elimination of mortality from infections in the latter years of the 20th century, the minimum mortality is approaching a limit of about 2 deaths per 10,000 per year. Redrawn from [8]. **b**, **c** Observed Gompertz parameters from cohorts born between 1800 and 1920 for Sweden, Norway, Denmark, France, Italy, Netherlands, Switzerland, and England and Wales: m(x) = intercept [exp]slope(x), where age is x, intercept is mortality rate at age 40, and slope is calculated for ages 40–90. **b** Intercept (background mortality) at age 40 (ln scale). **c** Slopes; at far right, the calculated slopes which would be required for LE at birth of 100 years, assuming basal mortality at age 40 in the 2000 period. This calculation used the Gompertz survival equation [9] as for L_{max} values cited in the text above.

phase of infants and children declines with adolescence to a phase of lower background mortality that we describe as 'minimum mortality' after 10 year of age and lasting 10 or more years [8], which is followed by a third phase of accelerating mortality (Gompertz curve). For economically developed countries, mortality accelerations begin their exponential upsweep after 30–40 years of age, which is described by the Gompertz mortality model. A putative fourth phase of mortality plateau at advanced ages when mortality approaches or exceeds 0.5/year is discussed below.

Currently the minimum mortality at 10–30 years of age is approaching 2 deaths/year/10,000 [8, 9] (fig. 1a). There must be some lower limit to young adult mortality because of accidents, residual birth defects, and rare dominant heritable diseases. The approaching lower limit in mortality requires that further gains in the 21st century can only come from slowing or delaying mortality acceleration in midlife. Further analysis may identify the duration of minimum mortality, which also defines the onset of the Gompertz curve. Because of demographic variabil-

ity, we use mortality rates at age 40 to approximate the foot of the Gompertz curve [9].

Using the Gompertz model for mortality rate accelerations after age 40, the foot of the acceleration curve (Gompertz intercept) shows progressive decrease of the initial mortality rate since 1800 (fig. 1b). Reciprocally, the rate of mortality acceleration with age increased progressively as overall mortality dropped up to the cohort born in 1900 (fig. 1c). This relationship was first noted by Strehler and Mildvan [10] in 1960 for cross-sectional data, which we extended to cohorts [9].

Gender differences in minimum mortality are consistent with women having lower Gompertz curves than men at age 40 in the 19th and 20th centuries, represented in the lower values at age 40, the 'Gompertz intercept', calculated elsewhere [9]. Moreover, women born in the 20th century have shown slower mortality rate accelerations than men [9]. Both parameters contribute to their greater LE and the greater L_{max} than males (discussed below).

At later ages, the mortality picture remains incomplete, despite major efforts on oldest-old demography. The 1998 analysis by Vaupel et al. [11] suggested that mortality rates decelerated towards a plateau after age 80, with a possible decline in mortality rates after 100 (the fourth phase of the mortality trajectory above). While mortality rate plateaus at later ages are well documented for lab flies and worms [11], they have not been shown for lab rodents [12, 13]. Further analysis of the increasingly authenticated centenarian databases, e.g. the International Database on Longevity (IDL), shows that mortality plateaus are not defined until after age 110 in countries with the most rigorous data, when the annual probability of death reaches >0.5, 'consistent with a plateau around ages 110–114' [14]. However, in the recent analysis by Gavrilov and Gavrilova [15] of US Social Security data by cohort, mortality rates continued to increase up to the age of 106, following the Gompertz model, with no indications of a plateau; the mortality rate acceleration at ages 88–106 was the same as calculated for 40–104. Ages after 110 are a difficult domain for demographic analysis because of health heterogeneity in the very few who reach 110, <1 per million, most of whom are women.

Despite the exponential increase of centenarians over the last 50 years [16], Jeanne Calment's world record lifespan of 122.5 years in 1997 has not been surpassed. Using Gompertz parameters estimated from 630 birth cohorts born throughout the 19th and early 20th centuries and assuming the mortality conditions that characterize the 1920 cohort who would be now approaching 95, we calculated for a world population of 10 billion that the L_{max} would be 120 years for women and 113 years for men [9]. These values closely match current records for each gender. The greater L_{max} of women is a result of their lower mortality values 40–90 and their slightly slower rates of mortality acceleration noted above. The unchallenged L_{max} with faster mortality accelerations rising from lower background mortality also support the conclusions of Fries [17] and Olshansky et al. [18] that the current biological limits cannot be exceeded without major reduction of degenerative diseases and rates of aging.

Looking to the future, Christensen et al. [19] forecast survival probabilities of at least 50% from birth to age 100 in 21st century birth cohorts for industrialized countries. This calculation assumes that mortality rates below age 50 are maintained at the 2006 year level, with a steady yearly increase of LE by 0.2 years. These LE forecasts are considerably longer than those computed for the US population [20]. Although the USA tends to have higher adult mortality rates than Europe, official Social Security projections of mortality decline estimate that less than 9% of the 2000 birth cohort will survive to age 100.

As another approach to estimating recent cohort survival to later ages, we fitted a Gompertz mortality model for ages 40–90 in 8 European countries for cohorts born between 1800 and 1920 (fig. 1b, c). Assuming mortality rates at age 40 remain at the 2000 period level, we asked what Gompertz slope would be required for those born in 2000 to match the forecast of Christensen et al. [19] of an LE of 100. Figure 1c for 2000 shows that the Gompertz slopes required are 50% below those historically experienced. Such a large downshift of the Gompertz slope would require a fundamental slowing in the rate of aging. Another demographic model for an LE of 100 would be to delay the onset of the mortality acceleration curve, which is not evident in current trends.

Looking closer at these cohort data since 1900, we note a possible reversal or inflection of the Gompertz slope trend in 5 of 8 countries (fig. 1c) despite continued lowering of background mortality in these same cohorts (fig. 1b). This apparent deviation from long-term historical trends in the Strehler-Mildvan relationship will be discussed in a separate report.

Our reservations concerning the forecasted major increases for LE in the 21st century are shared by the recent analysis of Goldman et al. [21] that potential gains from a delayed aging scenario with reduced heart disease and cancer would only modestly increase LE at age 51. If cancer and vascular conditions and the underlying aging processes become minimized by step-by-step engineering of neg-

ligible senescence, as proposed by de Grey [22], then LE could be extended beyond its apparent L_{max} [9]. Although we remain reserved about forecasts that centenarian lifespans would be achieved by 50% of births [19], animal models show these possibilities. In mouse mutants, the Gompertz mortality acceleration was slowed and its onset delayed by genetic manipulations of growth hormone [23] and mitochondrial catalase [24, 25]. A human counterpart may be the lower incidence of cancer in Ecuadorian carriers of the Laron dwarf mutation, as in dwarf mice [26].

Another concern about forecasted major increases of LE is the emerging heterogeneity of survival at later ages, e.g. as described in the 2011 NAS report 'Explaining divergent levels of longevity in high-income countries' [27]. As one example of heterogeneity, US white females with <12 years of education have lost 5 years of LE from 1990 to 2008 [28]. The well-named 'obesity epidemic' continues to expand globally and is expected to offset some advances in medicine and technology. In addition to this well-recognized concern, we also believe the worsening climate will also have a negative impact.

Climate changes are upon us, with major implications for LE as well as health throughout life [3, 4]. The 2013 Federal Advisory Committee's Draft Climate Assessment Report [29] summarizes evidence that demonstrates a progressive increase of extreme weather events, including heat waves and heavy downpours, since 1960. Concurrent rises in sea levels increase brackish pools conducive for mosquitos and other insects, which probably increase insect-borne diseases [3, 4, 30]. Warming alone also increases ground-level ozone [3, 4], e.g. Southern California is expected to incur 6–30 more days per year of hazardous ozone by 2050 [31]. Besides the long-term trends for temperature, global air quality is worsening from increasing fossil fuel consumption. These and other factors threaten to diminish, or even reverse, the environmental and medical advances that enabled the increase in LE since 1800.

One obvious concern to the elderly is heat waves, which are predicted to become increasingly frequent and intense [3, 4, 32, 33]. The elderly are among the disadvantaged populations with particular vulnerability to the effects of climate change. In the killer summers of 1995 (USA) and 2003 (Europe) [32, 33], elderly men were particularly vulnerable. Elders with diabetes and congestive heart failure had an approximately threefold increase in mortality per 1 °C increase in summer temperature (Medicare data, 135 US cities) [34]. The majority of elderly reside in cities which are warmer by 1–4°C than the countryside ('urban heat islands') [4]. Many elderly cannot afford air conditioning, which is a major protective factor in heat vulnerability [35]. Although the threshold temperature for excess mortality differs between cities [34], there is consensus that increased mortality is highly likely because of the continuing increase in the number of days with extreme temperatures [4, 29]. Moreover, ozone and other air pollutants further increase mortality during heat waves [36].

Increasing fossil fuel consumption, besides contributing to global warming as a greenhouse gas, also produces airborne particulate material (PM). Particles with a diameter smaller than 2.5 μm (PM2.5) from combustion engines are strongly associated with increased chronic diseases, including cancer and vascular disease. For example, in the Los Angeles basin, subclinical atherosclerosis (carotid intima media thickening) was increased by 5.9% per 10 $\mu g/m^3$ PM2.5 (geocoded PM2.5 data) [37]. Moreover, transients in air pollution (1–7 days) were associated with increased myocardial infarctions by 2.5% per 100 $\mu g/m^3$ PM2.5, and with smaller effects of NOx, SO_2, and ozone (meta-analysis of 34 studies) [38, 39]. An extreme example just reported from a regional analysis of China shows that household coal burning caused LE to decrease by 5.5 years, equivalent to loss of 2.5 billion life-years, alternatively calculated in terms of a 3-year loss of LE at birth per 100 $\mu g/m^3$ total PM [40]. These findings are based on the epidemiology of cardiorespiratory mortality in North versus South China, geographically defined by the East-West course of the Huai River. Households in North China have been given free coal since 1950 by the central government, with unintended dire consequences.

Globally, fossil fuel consumption is anticipated to increase by 50% up through 2040, approximately 2–3%/year [41]. Thus, the recent improvements of LE in developing countries may be eroded in conjunction with further economic growth. Besides demands for vehicular transportation and manufacturing, increased air conditioning also contributes to increased power needs. As a result, it will be very hard to diminish airborne PM in the developing world. Nonetheless, many countries, including China, have recognized the health burden of fossil fuels and are developing alternate energy sources. The next several decades may realize reduced global air pollution, with benefits to public health, as well as greenhouse gas emissions; however, we do not expect a quick fix. For example, China recently announced a policy to replace coal-powered electrical generation with natural gas in select zones [42]. Despite diminished airborne particulates, natural gas combustion still produces appreciable CO_2 without additional scrubbing.

The effects of air pollution also extend to the brain across the lifespan. Across the USA, 10 ppb higher average ozone was associated with cognitive deficits during middle-age, equivalent to accelerating 'normative cognitive aging' by 4 years [43]. These trends are likely to increase because of warming-related atmospheric ozone, as noted above. The Finch lab is studying interactions of urban nano-sized PM <0.25 μm (nPM) in rodent models. Exposure to 150 h of nPM inhalation over 10 weeks induced brain glial inflammatory reactions and selective effects on glutamate receptor function [44]. In vitro, nPM rapidly induced the free radical NO with ensuing nitrosylation of glutamate receptors [45]. Moreover, gestational exposure of rats to nPM impaired postnatal neuronal differentiation and increased adult depressive behaviors [46]. Although our exposure model did not alter rodent birth weight, the International Collaboration of Air Pollution and Pregnancy Outcomes (ICAPPO) observed associations of PM10 with lower birth weight (–8.9 g per 10 μg/m^3 of PM10) [47]. These early indications for a gestational impact of air pollution warrant further study for synergies with the many recognized developmental life influences on adult health and aging.

Increased infections are another concern of global climate change because warming alone enhances the growth of insect populations [2–4, 30, 48–50]. An example explored with detailed modeling is the tenfold increase of dengue fever, a mosquito-borne infection, in Singapore coinciding with a progressive increase in temperature over 15 years, i.e. 1989–2005 [48]. Extreme weather events with flooding and enlarged coastal brackish pools from rising sea levels are favorable breeding grounds for salinity-tolerant mosquitos and other insect vectors [30, 50]. Emerging shortages of water in many regions also challenge hygiene and public health, with consequences for the very young as well as elderly. Thus, greater exposure to pathogens coupled with the adaptive immune responses of most elderly could increase their burden of infections. The very young are also at risk for mortality from rising levels of infections. These and other aspects of climate change warrant detailed study of their impact on the globally expanding elderly populations.

The socioeconomic polarization of LE [27] seems likely to persist globally despite remarkable recent gains in many developing countries [51]. A privileged few could experience minimal challenges from climate and environmental deterioration. The top socioeconomic strata already live in protected environments at work and home. The emerging marvels of regenerative medicine for organ replacement will likely be extremely expensive. We anticipate new drugs and other treatments to slow or even prevent atherosclerosis, Alzheimer's disease, and cancer, which might extend LE and current L_{max} [9, 12]. However, such rejuvenating marvels may only be available to 'health elites' who can afford both protected environments and state-of-the-art medicine. Thus, we expect continuing socioeconomic disparities in adult health and longevity.

While this report was under review, Carnes et al. [52] published their perspective on climate change and elder health, reaching similar conclusions on several issues addressed herein.

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