New approaches to study historical evolution of mortality (with implications for forecasting)

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Наш предыдущий вклад в изучение продолжительности жизни



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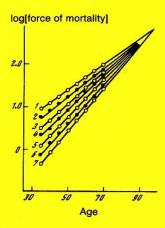
Москва, Наука, 1986

Москва, Наука, 1991

The Biology of Life Span: A Quantitative Approach

L. A. Gavrilov and N. S. Gavrilova

Edited by V. P. Skulachev



harwood academic publishers chur • london • paris • new york • melbourne

Empirical Laws of Mortality

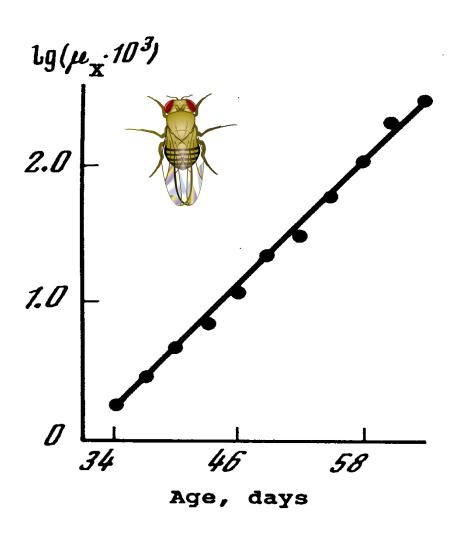
The Gompertz-Makeham Law

Death rate is a sum of age-independent component (Makeham term) and age-dependent component (Gompertz function), which increases exponentially with age.

$$\mu(x) = A + Re^{ax}$$
risk of death

A – Makeham term or background mortality $R e^{ax}$ – age-dependent mortality; x - age

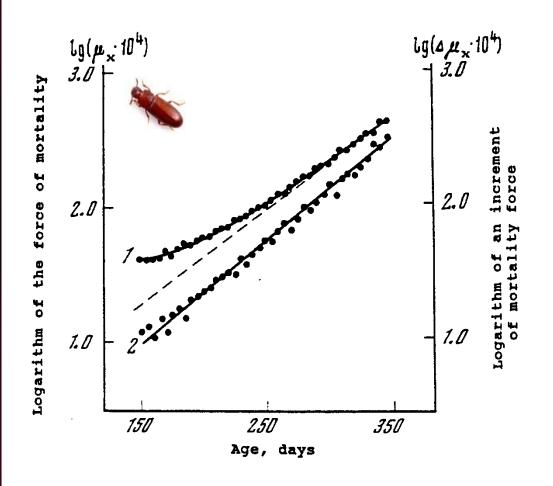
Gompertz Law of Mortality in Fruit Flies



Based on the life table for 2400 females of *Drosophila melanogaster* published by Hall (1969).

Source: Gavrilov, Gavrilova, "*The Biology of Life Spari*" 1991

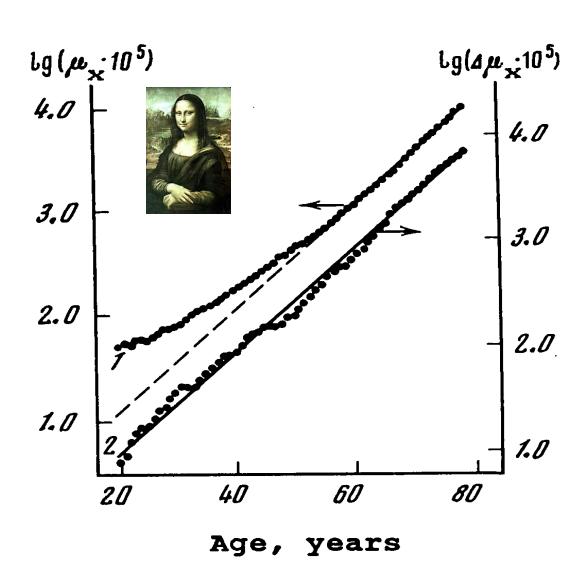
Gompertz-Makeham Law of Mortality in Flour Beetles



Based on the life table for 400 female flour beetles (*Tribolium confusum* Duval). published by Pearl and Miner (1941).

Source: Gavrilov, Gavrilova, "The Biology of Life Span" 1991

Gompertz-Makeham Law of Mortality in Italian Women



Based on the official Italian period life table for 1964-1967.

Source: Gavrilov, Gavrilova, "*The Biology of Life Span*" 1991

Using parametric models (mortality laws) for mortality projections

The Gompertz-Makeham Law

Death rate is a sum of age-independent component (Makeham term) and age-dependent component (Gompertz function), which increases exponentially with age.

$$\mu(x) = A + R e^{ax}$$

risk of death

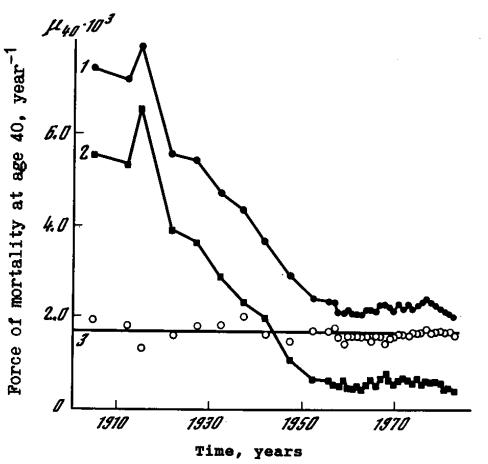
A – Makeham term or background mortality $R e^{ax}$ – age-dependent mortality; x - age

How can the Gompertz-Makeham law be used?

By studying the historical dynamics of the mortality components in this law:

Historical Stability of the Gompertz Mortality Component

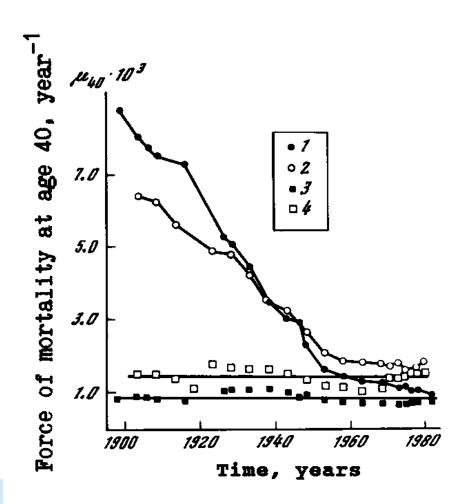
Historical Changes in Mortality for 40-year-old Swedish Males



- 1. Total mortality, μ_{40}
- 2. Background mortality (A)
- Age-dependent mortality (Re^{a40})
- Source: Gavrilov, Gavrilova,
 "The Biology of Life Spari"
 1991

Predicting Mortality Crossover

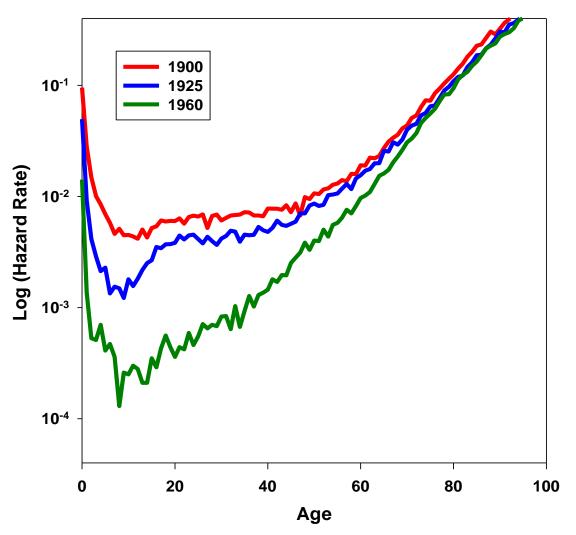
Historical Changes in Mortality for 40-year-old Women in Norway and Denmark



- 1. Norway, total mortality
- 2. Denmark, total mortality
- Norway, agedependent mortality
- Denmark, agedependent mortality

Source: Gavrilov, Gavrilova, "The Biology of Life Span" 1991

Changes in Mortality, 1900-1960



Swedish females. Data source: Human Mortality Database

In the end of the 1970s it looked like there is a limit to further increase of longevity

Debate

Gerontology 29: 176-180 (1983)

O 1983 S. Karger A.G. Basel 0304-324X/83/0293-0176\$2.75/0

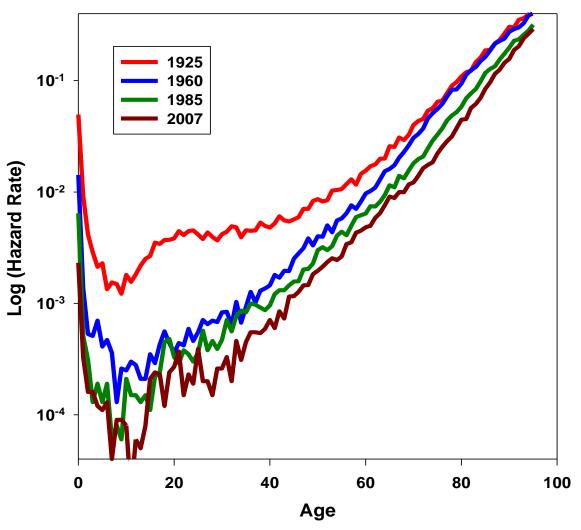
Human Life Span Stopped Increasing: Why?

Leonid A. Gavrilov, Natalia S. Gavrilova, Victor N. Nosov

A.N. Belozersky Laboratory of Molecular Biology and Bioorganic Chemistry, and Department of Biology, Moscow State University, Moscow, USSR

Increase of Longevity After the 1970s

Changes in Mortality, 1925-2007



Swedish Females. Data source: Human Mortality Database

Age-dependent mortality no longer was stable

In 2005 Bongaarts suggested estimating parameters of the logistic formula for a number of years and extrapolating the values of three parameters (background mortality and two parameters of senescent mortality) to the future.

Shifting model of mortality projection

Using data on mortality changes after the 1950s Bongaarts found that slope parameter in Kannisto-Makeham formula is stable in history. He suggested to use this property in mortality projections and called this method shifting mortality approach.

The main limitation of parametric approach to mortality projections is a dependence on the particular formula, which makes this approach too rigid for responding to possible changes in mortality trends and fluctuations.

Non-parametric approach to mortality projections

Lee-Carter method of mortality projections

The Lee-Carter method is now one of the most widely used methods of mortality projections in demography and actuarial science (Lee and Miller 2001; Lee and Carter 1992). Its success is stemmed from the shifting model of mortality decline observed for industrialized countries during the last 30-50 years.

Lee-Carter method is based on the following formula

$$\ln(\mu_{x,t}) = a(x) + b(x)k(t)$$

where a(x), b(x) and k(t) are parameters to be estimated. This model does not produce a unique solution and Lee and Carter suggested applying certain constraints $\sum k(t) = 0$; $\sum b(x) = 1$

Then empirically estimated values of k(t) are extrapolated in the future

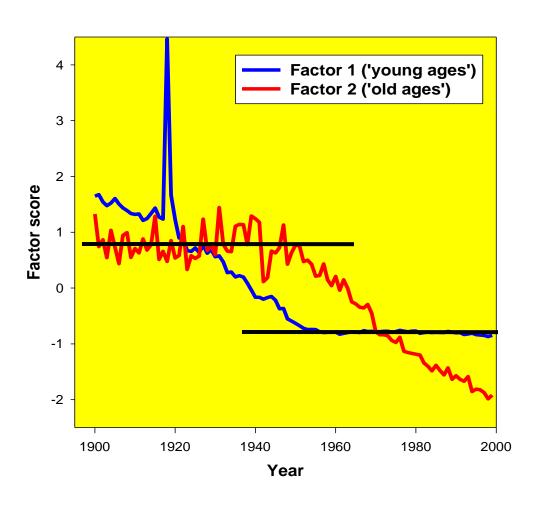
Limitations of Lee-Carter method

The Lee-Carter method relies on multiplicative model of mortality decline and may not work well under another scenario of mortality change. This method is related to the assumption that historical evolution of mortality at all age groups is driven by one factor only (parameter k).

Extension of the Gompertz-Makeham Model Through the Factor Analysis of Mortality Trends

Mortality force (age, time) =
$$a_0(age) + a_1(age) \times F_1(time) + a_2(age) \times F_2(time)$$

Factor Analysis of Mortality Swedish Females



Data source: Human Mortality Database

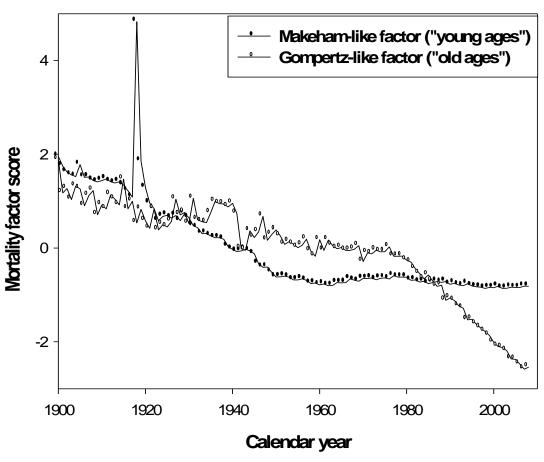
Preliminary Conclusions

- There was some evidence for 'biological' mortality limits in the past, but these 'limits' proved to be responsive to the recent technological and medical progress.
- Thus, there is no convincing evidence for absolute 'biological' mortality limits now.
- Analogy for illustration and clarification: There was a limit to the speed of airplane flight in the past ('sound' barrier), but it was overcome by further technological progress. Similar observations seems to be applicable to current human mortality decline.

Implications

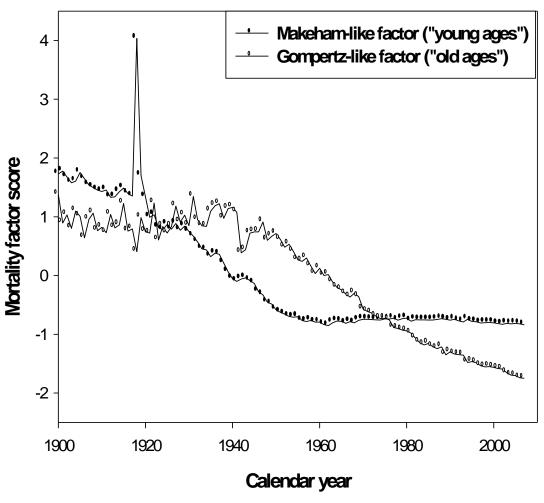
 Mortality trends before the 1950s are useless or even misleading for current forecasts because all the "rules of the game" has been changed

Factor Analysis of Mortality Recent data for Swedish males



Data source: Human Mortality Database

Factor Analysis of Mortality Recent data for Swedish females



Data source: Human Mortality Database

Advantages of factor analysis of mortality

First it is able to determine the number of factors affecting mortality changes over time.

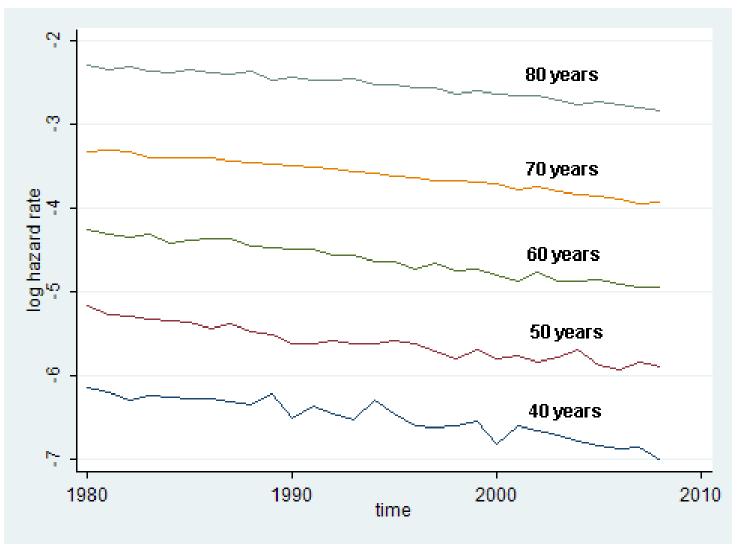
Second, this approach allows researchers to determine the time interval, in which underlying factors remain stable or undergo rapid changes.

Simple model of mortality projection

Taking into account the shifting model of mortality change it is reasonable to conclude that mortality after 1980 can be modeled by the following log-linear model with similar slope for all adult age groups:

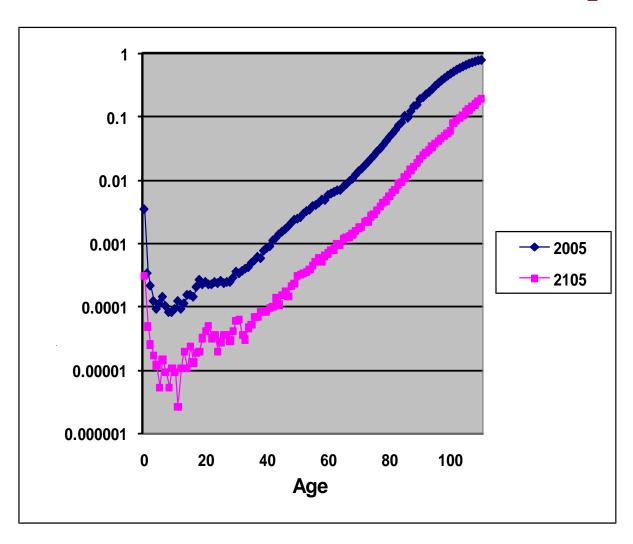
$$\ln(\mu_{x,t}) = a(x) - kt$$

Mortality modeling after 1980Data for Swedish males



Data source: Human Mortality Database

Projection in the case of continuous mortality decline

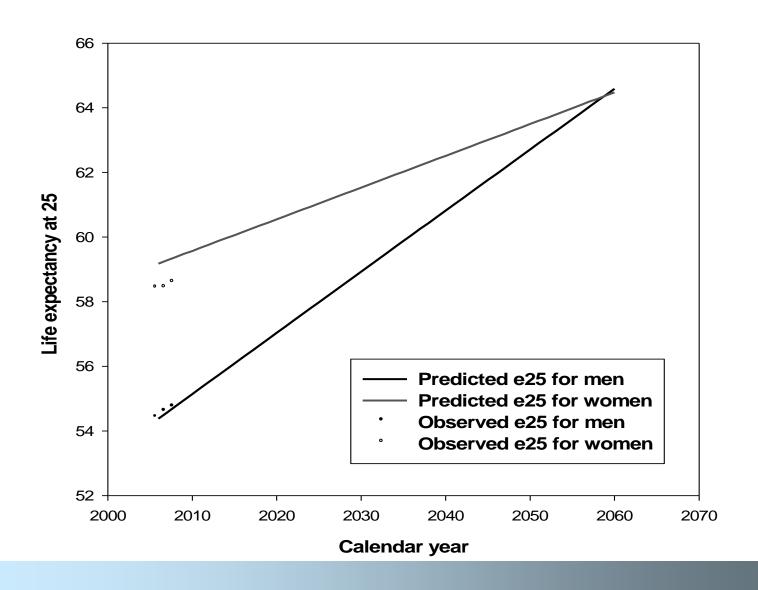


An example for Swedish females.

Median life span increases from 86 years in 2005 to 102 years in 2105

Data Source: Human mortality database

Projected trends of adult life expectancy (at 25 years) in Sweden



Conclusions

Use of factor analysis and simple assumptions about mortality changes over age and time allowed us to provide nontrivial but probably quite realistic mortality forecasts (at least for the nearest future).



How Much Would Late-Onset Interventions in Aging Affect Demographics?

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Center on Aging
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Chicago, USA

What May Happen in the Case of Radical Life Extension?

Rationale of our study

A common objection against starting a large-scale biomedical war on aging is the fear of catastrophic population consequences (overpopulation)



Rationale (continued)

This fear is only exacerbated by the fact that no detailed demographic projections for radical life extension scenario were conducted so far.

What would happen with population numbers if aging-related deaths are significantly postponed or even eliminated?

Is it possible to have a sustainable population dynamics in a future hypothetical non-aging society?

The Purpose of this Study

This study explores different demographic scenarios and population projections, in order to clarify what could be the demographic consequences of a successful biomedical war on aging.

"Worst" Case Scenario: Immortality

- Consider the "worst" case scenario (for overpopulation) -- physical immortality (no deaths at all)
- What would happen with population numbers, then?
- A common sense and intuition says that there should be a demographic catastrophe, if immortal people continue to reproduce.
- But what would the science (mathematics) say?

The case of immortal population

Suppose that parents produce less than two children on average, so that each next generation is smaller:

$$\frac{\text{Generation } (n+1)}{\text{Generation } n} = r < 1$$

Then even if everybody is immortal, the final size of the population will not be infinite, but just

$$1/(1 - r)$$

larger than the initial population.

The case of immortal population

For example one-child practice (r = 0.5) will only double the total immortal population:

$$1/(1 - r) = 1/0.5 = 2$$

Proof:

Infinite geometric series converge if the absolute value of the common ratio (r) is less than one:

$$1 + r + r^2 + r^3 + ... + r^n + ... = 1/(1-r)$$

Lesson to be Learned

Fears of overpopulation based on lay common sense and uneducated intuition could be exaggerated.

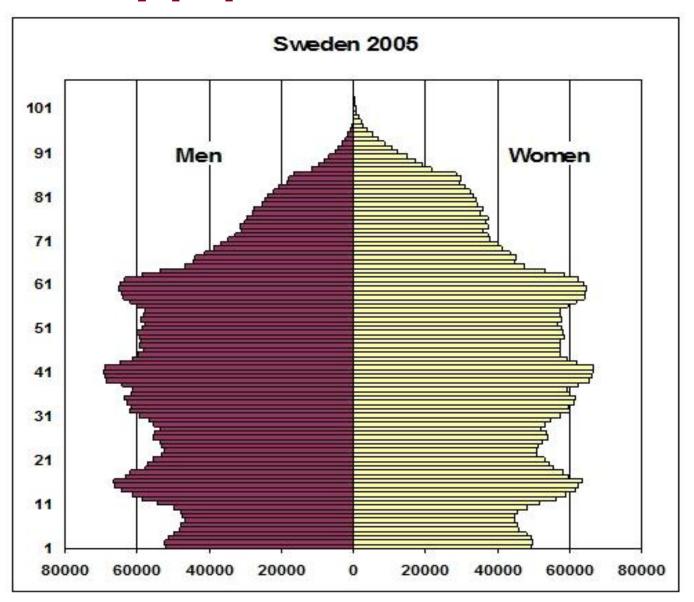
Immortality, the joy of parenting, and sustainable population size, are not mutually exclusive.

This is because a population of immortal reproducing organisms will grow indefinitely in time, but not necessarily indefinitely in size (asymptotic growth is possible).

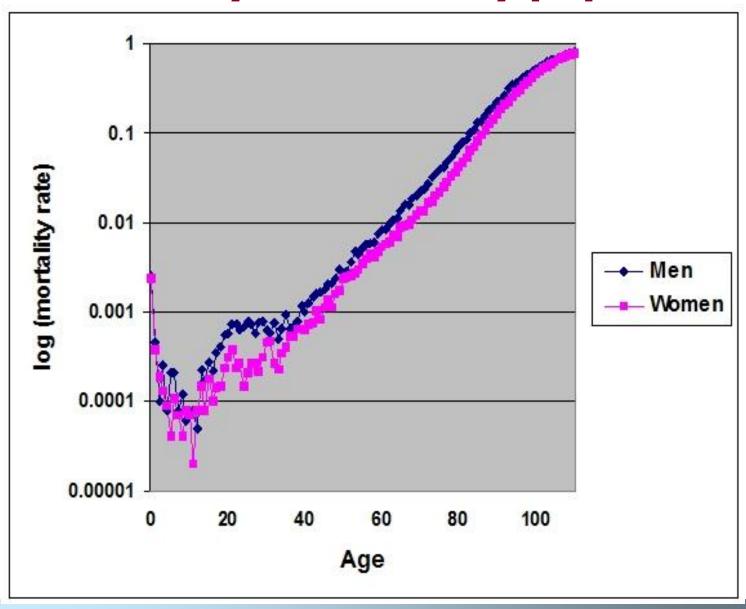
Method of population projection

- •Cohort-component method of population projection (standard demographic approach)
- •Age-specific fertility is assumed to remain unchanged over time, to study mortality effects only
- •No migration assumed, because of the focus on natural increase or decline of the population
- •New population projection software is developed using Microsoft Excel macros

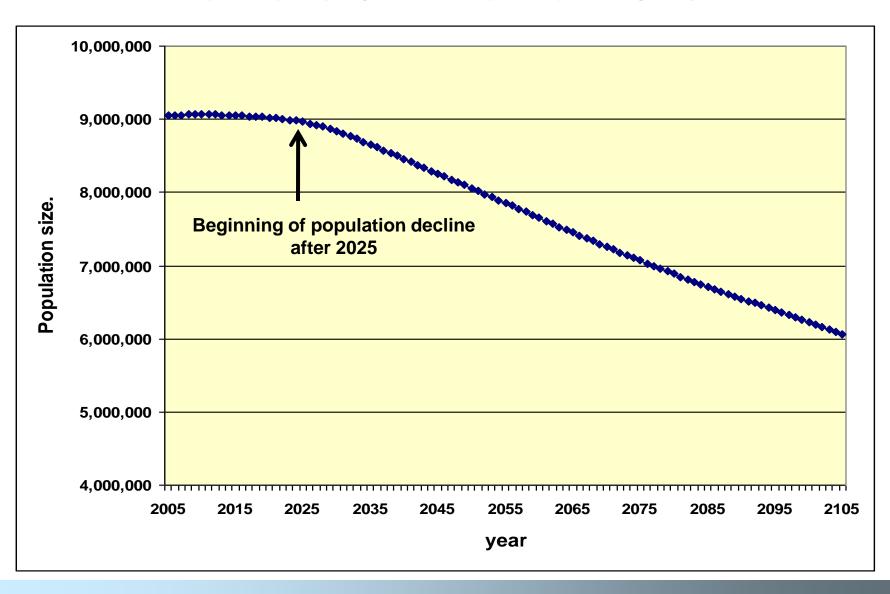
Study population: Sweden 2005



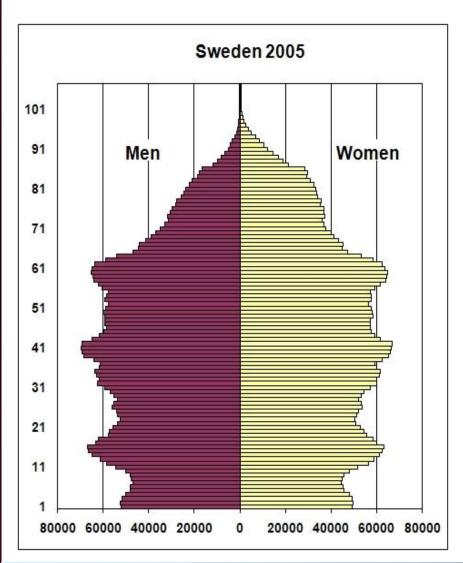
Mortality in the study population

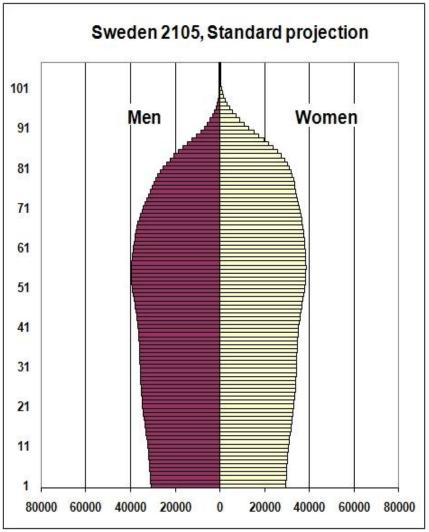


Population projection without life extension interventions



Projected changes in population pyramid 100 years later





Accelerated Population Aging is the Major Impact of Longevity on our Demography

It is also an opportunity if society is ready to accept it and properly adapt to population aging.

Why Life-Extension is a Part of the Solution, rather than a Problem

Many developed countries (like the studied Sweden) face dramatic decline in native-born population in the future (see earlier graphs), and also risk to lose their cultural identity due to massive immigration.

Therefore, extension of healthy lifespan in these countries may in fact prevent, rather than create a demographic catastrophe.

Scenarios of life extension

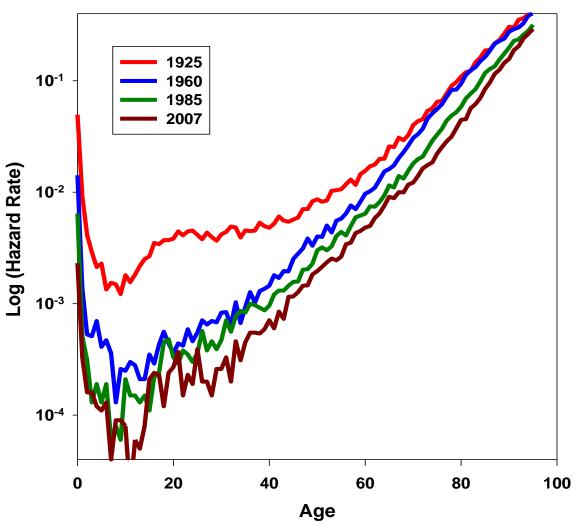
- 1. Continuation of current trend in mortality decline
- 2. Negligible senescence
- 3. Negligible senescence for a part of population (10%)
- 4. Rejuvenation (Gompertz alpha = -0.0005)

All anti-aging interventions start at age 60 years with 30-year time lag

Scenario 1 Modest scenario: Continuous mortality decline

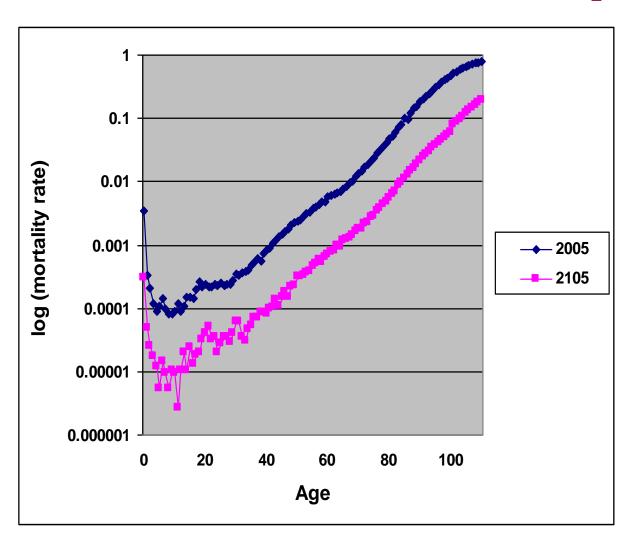
Mortality continues to decline with the same pace as before (2 percent per year)

Changes in Mortality, 1925-2007



Swedish Females. Data source: Human Mortality Database

Modest scenario: Continuous mortality decline

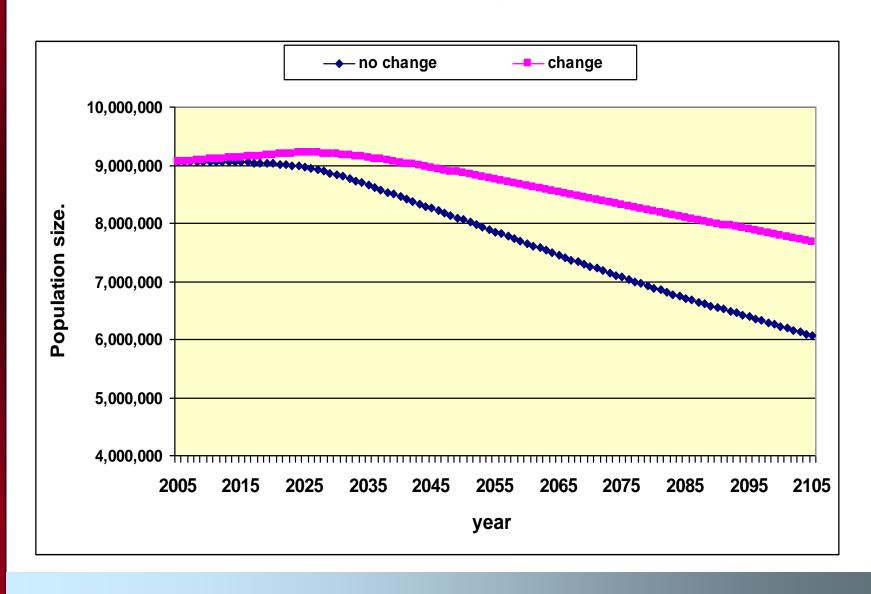


An example for Swedish females.

Median life span increases from 86 years in 2005 to 102 years in 2105

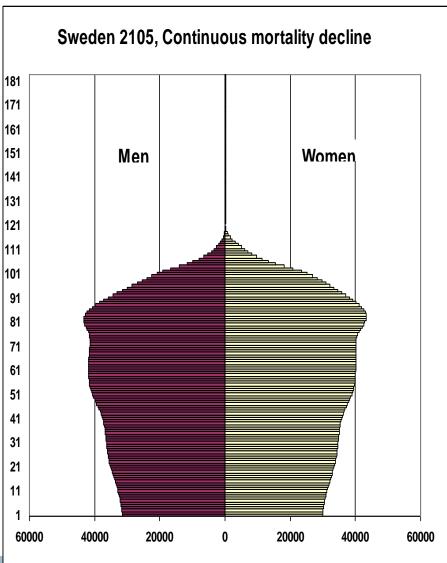
Data Source: Human mortality database

Population projection with continuous mortality decline scenario



Changes in population pyramid 100 years later

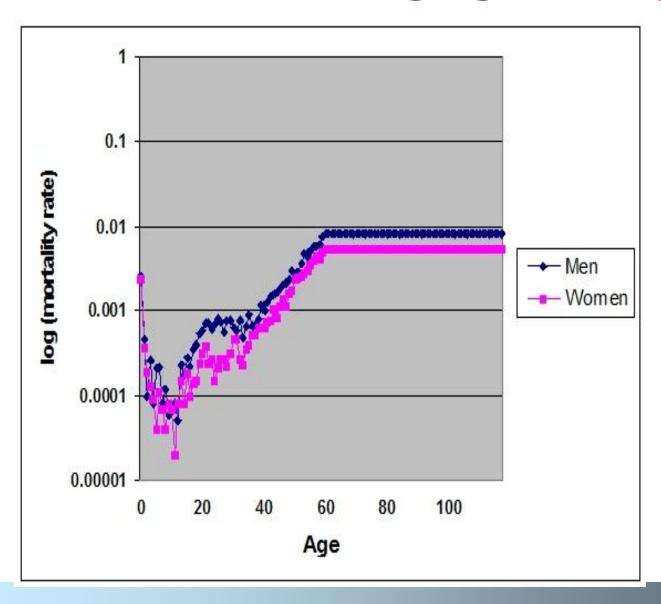




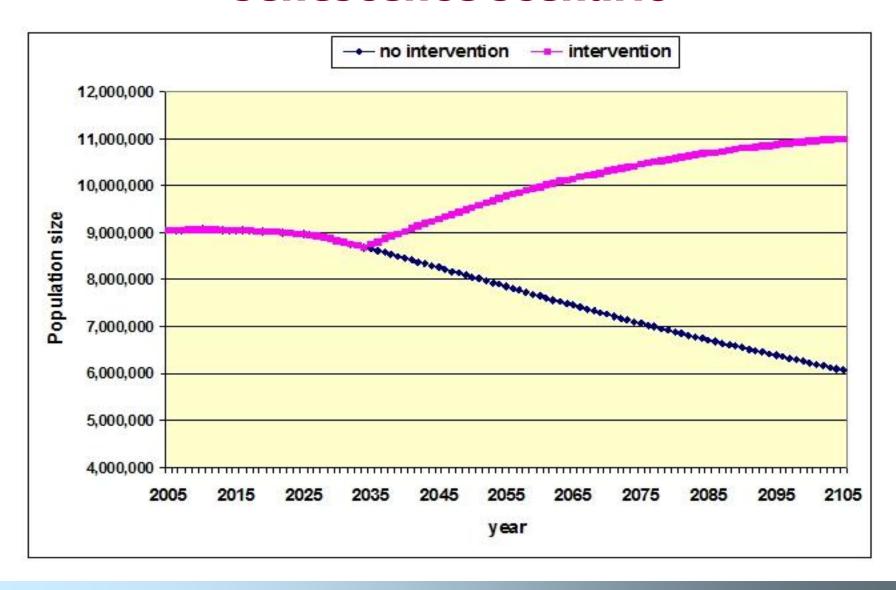
Scenario 2

Negligible senescence after age 60

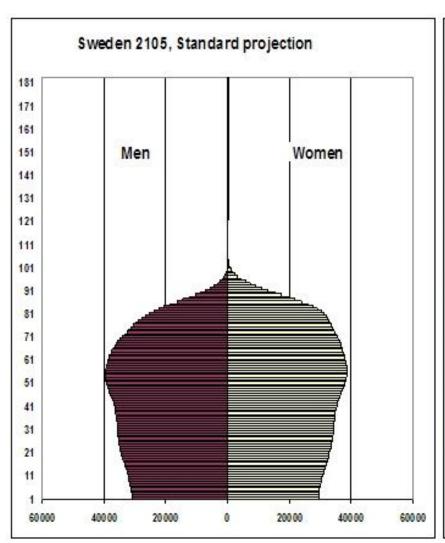
Radical scenario: No aging after age 60

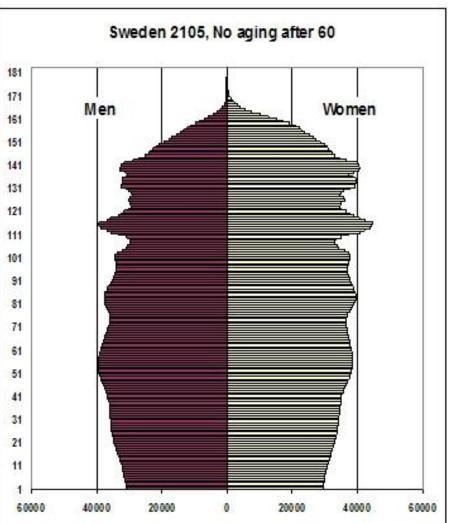


Population projection with negligible senescence scenario



Changes in population pyramid 100 years later





Conclusions on radical scenario

Even in the case of defeating aging (no aging after 60 years) the natural population growth is relatively small (about 20% increase over 70 years)

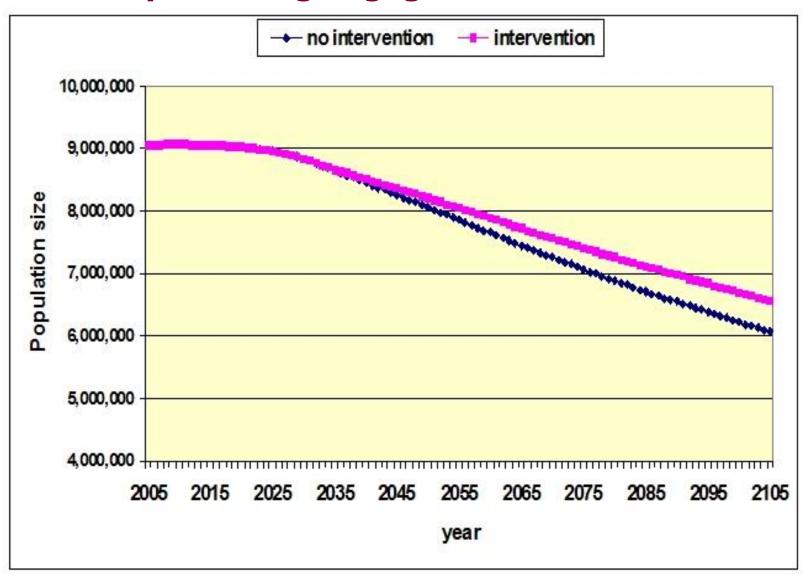
Moreover, defeating aging helps to prevent natural population decline in developed countries

Scenario 3

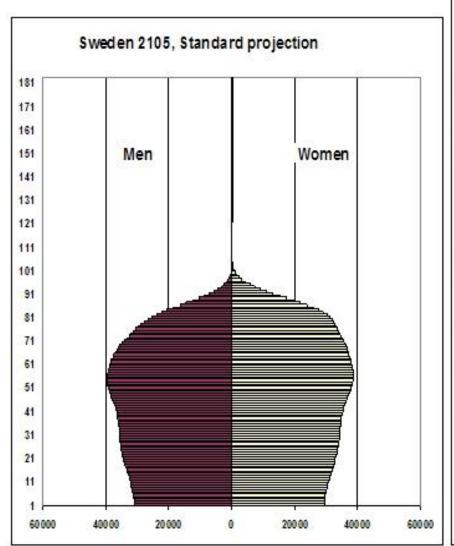
Negligible senescence for a part of population (10%)

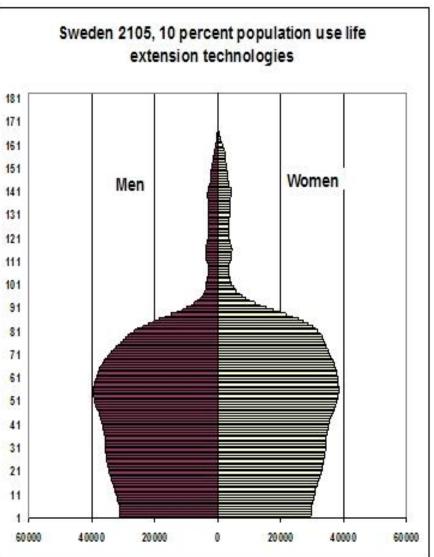
What if only a small fraction of population accepts anti-aging interventions?

Population projection with 10 percent of population experiencing negligible senescence



Changes in population pyramid 100 years later



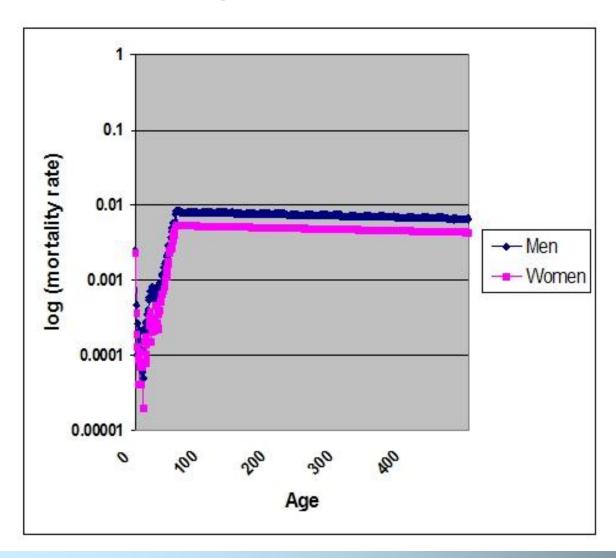


Scenario 4: Rejuvenation Scenario

Mortality declines after age 60 years until the levels observed at age 10 are reached; mortality remains constant thereafter

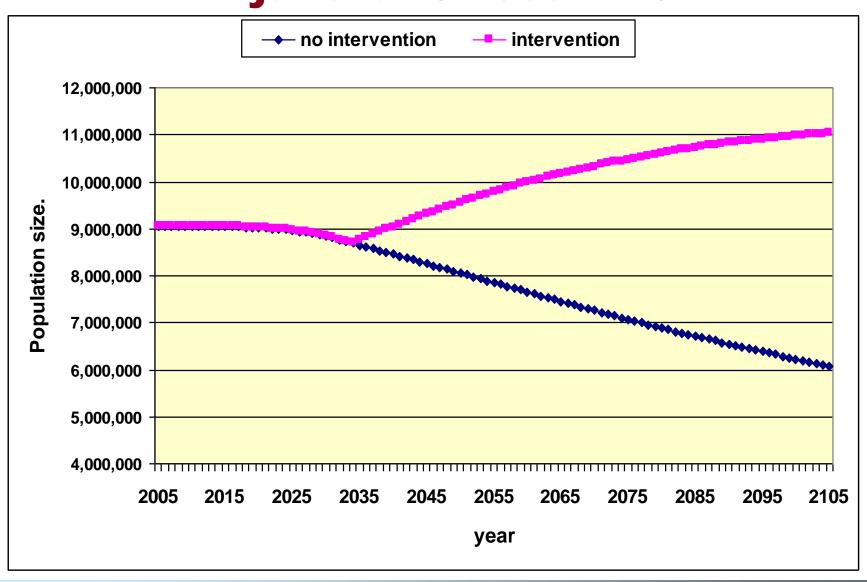
Negative Gompertz alpha (alpha = -0.0005 per year)

Radical scenario: rejuvenation after 60

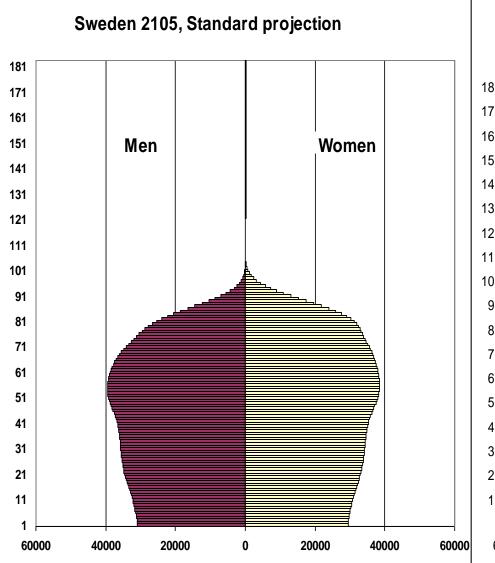


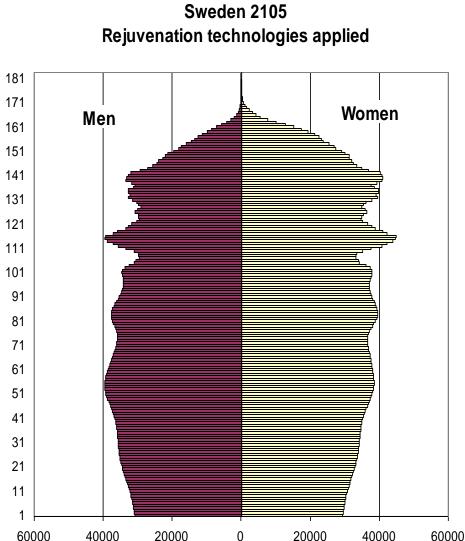
According to this scenario, mortality declines with age after age 60 years

Population projection with rejuvenation scenario



Changes in population pyramid 100 years later





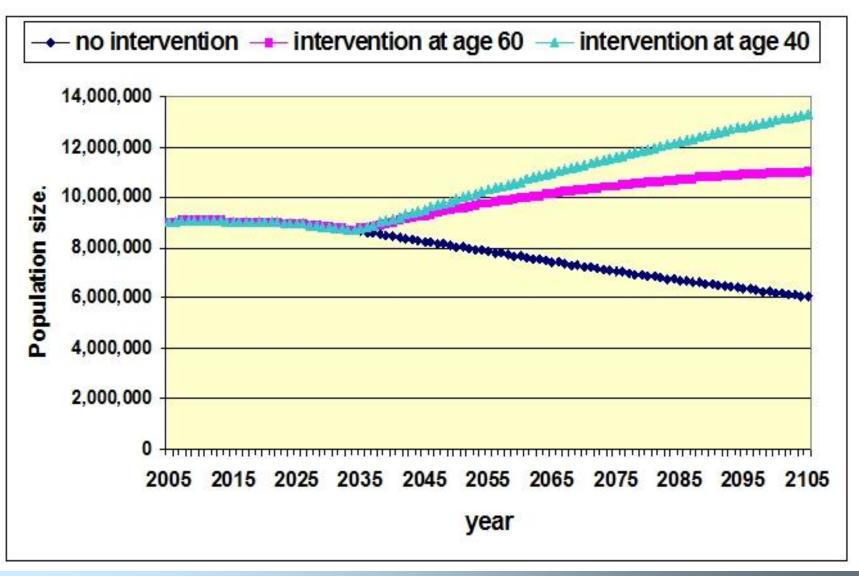
Conclusions on rejuvenation scenario

Even in the case of rejuvenation (aging reversal after 60 years) the natural population growth is still small (about 20% increase over 70 years)

Moreover, rejuvenation helps to prevent natural population decline in developed countries

What happens when rejuvenation starts at age 40 instead of age 60?

Population projection with rejuvenation at ages 60 and 40

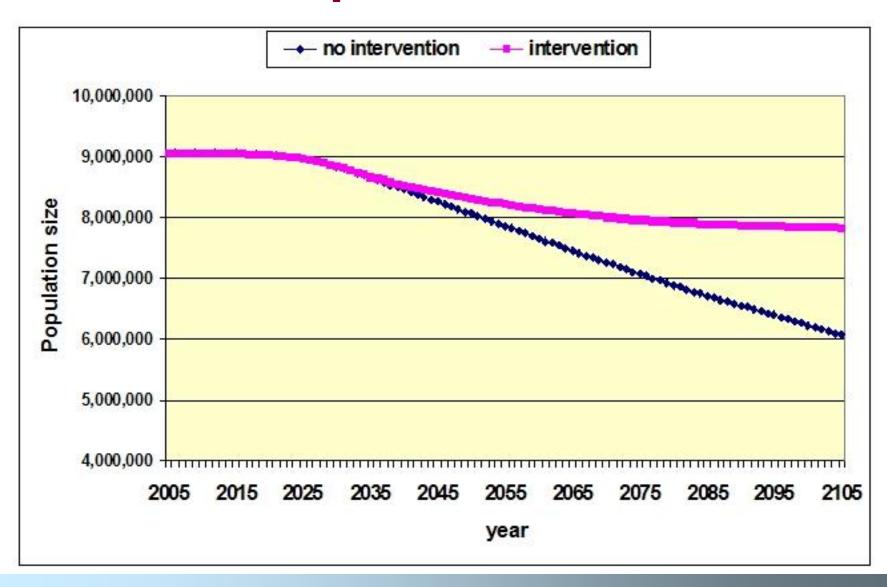


Scenario 5: What happens in the case of growing acceptance of anti-aging interventions (negligible senescence after age 60)?

Additional one percent of population starts using life extension technologies every year

The last remaining five percent of population refuse to apply these technologies in any circumstances

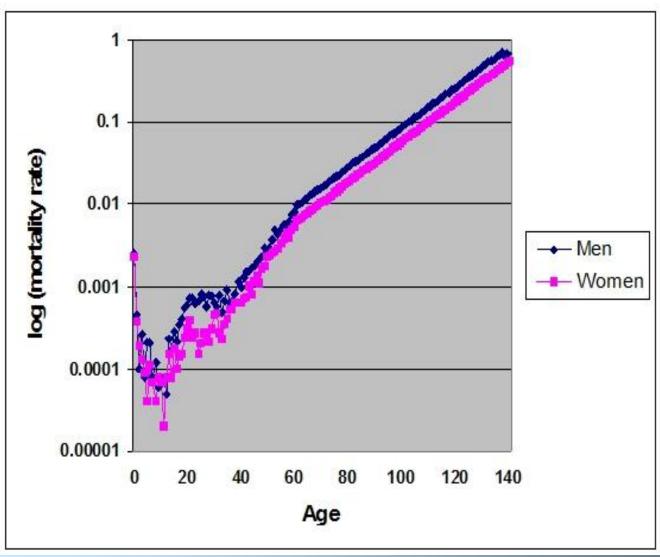
Population projection with growing acceptance scenario



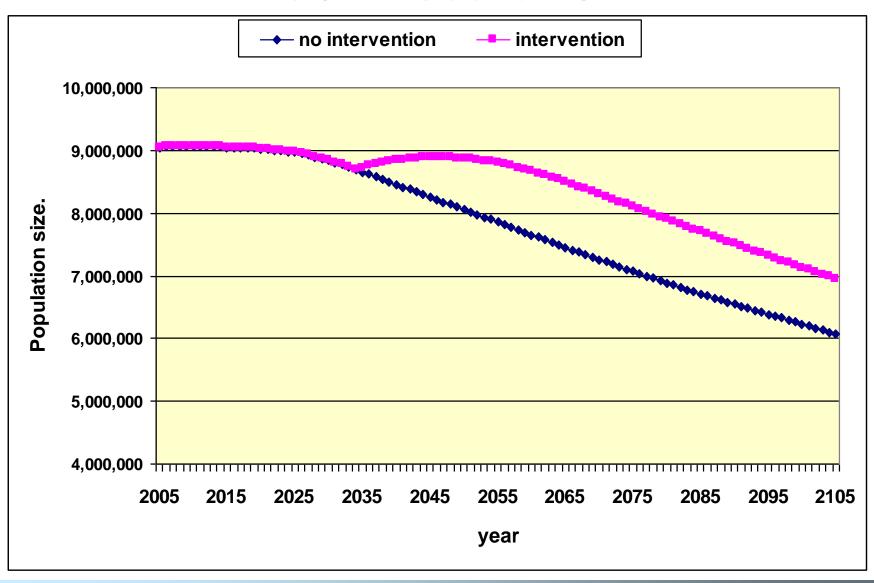
Scenario 6 More modest scenario: Aging slow down

Gompertz alpha decreases by one half

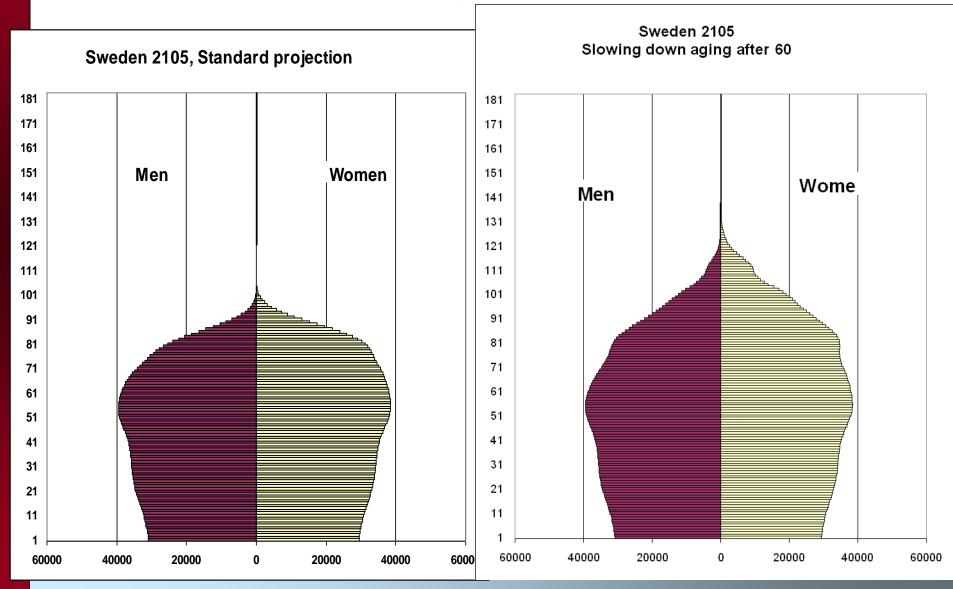
Modest scenario: slowing down aging after 60



Population projection with aging slow down scenario



Changes in population pyramid 100 years later



Conclusions

A general conclusion of this study is that population changes are surprisingly small and slow in their response to a dramatic life extension.

Even in the case of the most radical life extension scenario, population growth could be relatively slow and may not necessarily lead to overpopulation.

Therefore, the real concerns should be placed not on the threat of catastrophic population consequences (overpopulation), but rather on such potential obstacles to a success of biomedical war on aging, as scientific, organizational and financial limitations.

New Estimates of Mortality Trajectories at Extreme Old Ages

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Chicago, Illinois, USA

The growing number of persons living beyond age 80 underscores the need for accurate measurement of mortality at advanced ages.

Recent projections of the U.S. Census Bureau significantly overestimated the actual number of centenarians

Views about the number of centenarians in the United States 2009

Centenarians are the fastest-growing age segment: Number of 100-year-olds to hit 6 million by 2050

BY THE ASSOCIATED PRESS

TUESDAY, JULY 21, 2009, 10:27 AM

New estimates based on the 2010 census are two times lower than the U.S. Bureau of Census forecast

Far fewer centenarians than expected in



Posted Sept. 24, 2011, at 6:19 a.m. Last modified Sept. 24, 2011, at 7:06 a.m.

NEW YORK — Reports of Americans living beyond the ripe old age of 100, it appears, were greatly exaggerated.

The Census Bureau predicted six years ago that the country would be home to 114,000 centenarians by 2010. The actual number was 53,364, the census reported recently. That represented an increase of 5.8 percent since 2000, compared with a 9.7 percent gain in the nation's population as a whole.



The same story recently happened in the Great Britain

Financial Times

September 11, 2012 8:20 pm

Long-lived Britons increasing slower than forecast

By Norma Cohen, Economics Correspondent



The rate at which Britons are living into very old age is rising much more slowly than had been forecast only two years ago, a blow for those hoping for a very long life but good news for pension providers and the Treasury which spend hefty sums on the oldest old.

The first comprehensive study of mortality at advanced ages was published in 1939

HUMAN BIOLOGY

a record of research

FEBRUARY, 1939

VOL. 11



No. 1

THE BIOSTATISTICS OF SENILITY

BY MAJOR GREENWOOD AND J. O. IRWIN

M. Greenwood, J. O. Irwin. BIOSTATISTICS OF SENILITY

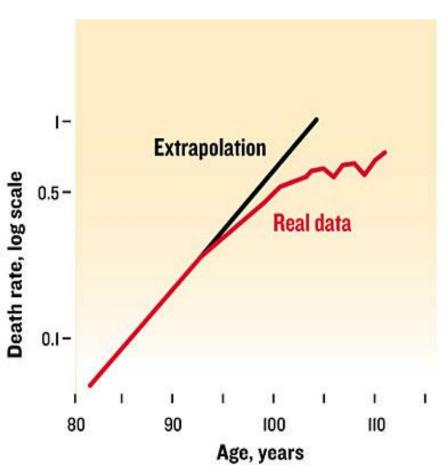
"the increase of mortality rate with age advances at a slackening rate, that nearly all, perhaps all, methods of graduation of the type of Gompertz's formula over-state senile mortality."

"... possibility that with advancing age the rate of mortality asymptotes to a finite value. "

"... The limiting values of q_{σ} are 0.439 for women and 0.544 for men. Some tests of the ultimate mortalities in non-human experience were not unfavorable."

Earlier studies suggested that the exponential growth of mortality with age (Gompertz law) is followed by a period of deceleration, with slower rates of mortality increase.

Mortality deceleration at advanced ages.



After age 95, the observed risk of death [red line] deviates from the values predicted by the Gompertz law [black line].

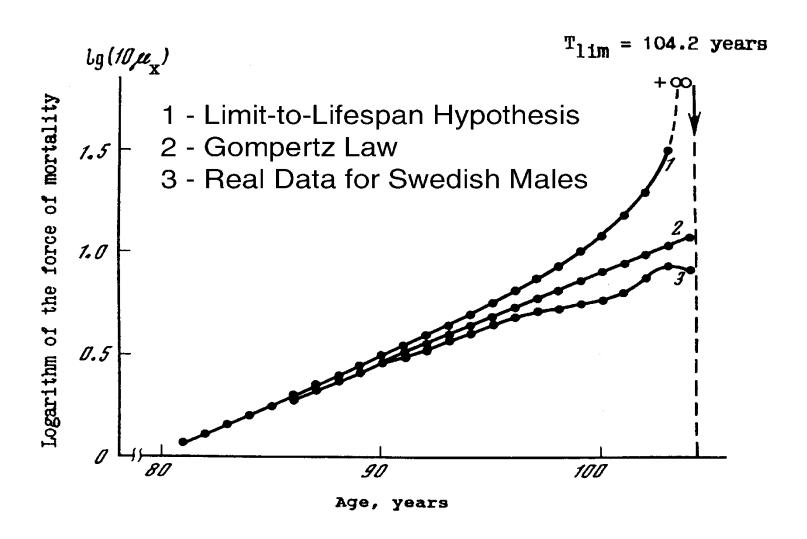
Mortality of Swedish women for the period of 1990-2000 from the Kannisto-Thatcher Database on Old Age Mortality

Source: Gavrilov, Gavrilova, "Why we fall apart. Engineering's reliability theory explains human aging". *IEEE Spectrum*. 2004.

Implications

- There is no fixed upper limit to human longevity - there is no special fixed number, which separates possible and impossible values of lifespan.
- This conclusion is important, because it challenges the common belief in existence of a fixed maximal human life span.

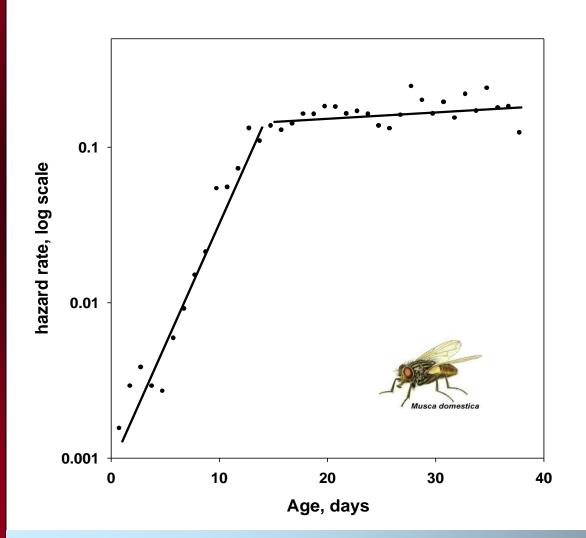
Mortality at Advanced Ages – over 20 years ago



Source: Gavrilov L.A., Gavrilova N.S. The Biology of Life Span:

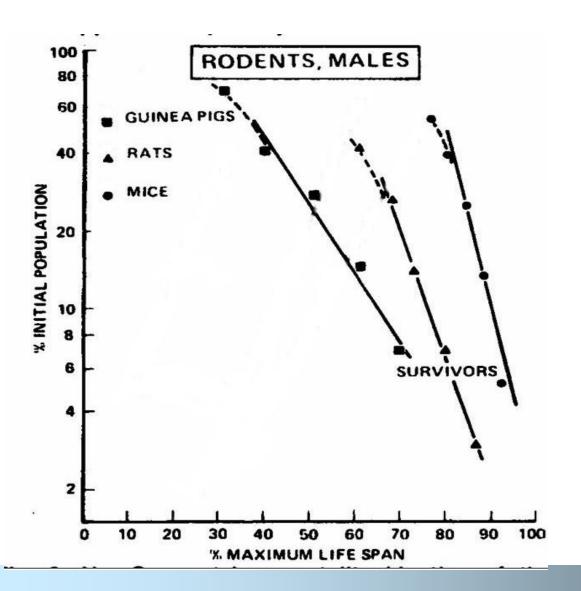
A Quantitative Approach, NY: Harwood Academic Publisher, 1991

Mortality Leveling-Off in House Fly Musca domestica



Based on life table of 4,650 male house flies published by Rockstein & Lieberman, 1959

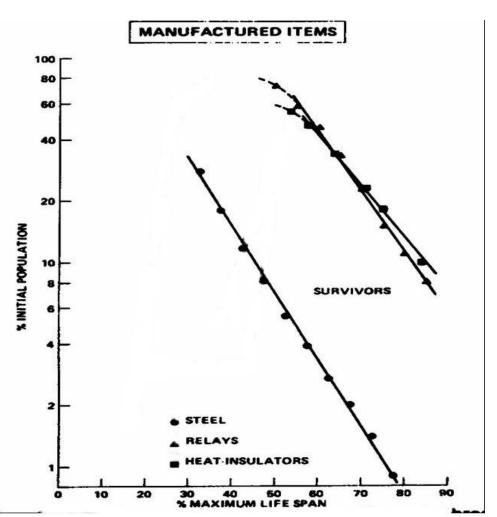
Non-Aging Mortality Kinetics in Later Life



Source: A. Economos.
A non-Gompertzian paradigm for mortality kinetics of metazoan animals and failure kinetics of manufactured products. AGE, 1979, 2: 74-76.

Non-Aging Failure Kinetics of Industrial Materials in 'Later Life'

(steel, relays, heat insulators)



Source:

A. Economos.

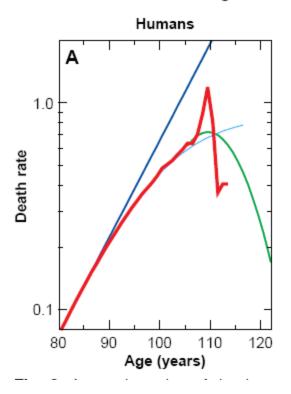
A non-Gompertzian paradigm for mortality kinetics of metazoan animals and failure kinetics of manufactured products. AGE, 1979, 2: 74-76.

Nature (1998)

Biodemographic Trajectories of Longevity



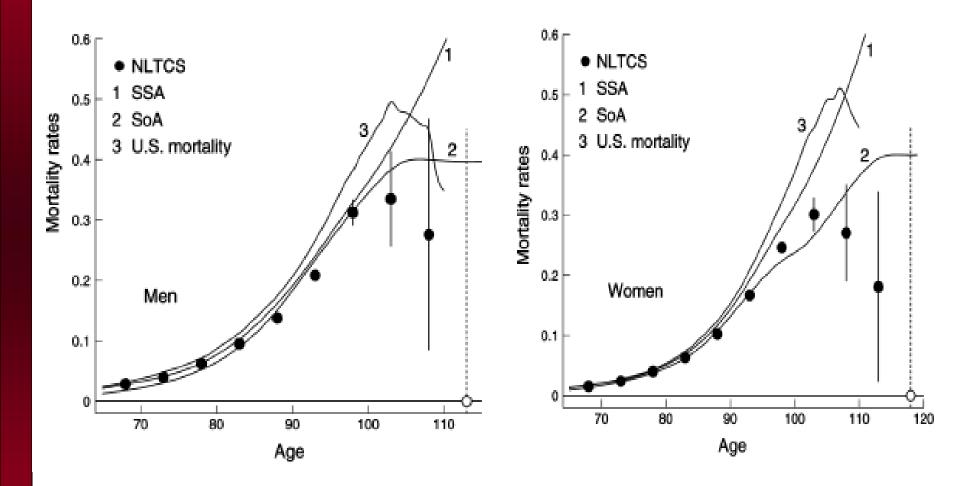
James W. Vaupel,* James R. Carey, Kaare Christensen, Thomas E. Johnson, Anatoli I. Yashin, Niels V. Holm, Ivan A. Iachine, Väinö Kannisto, Aziz A. Khazaeli, Pablo Liedo, Valter D. Longo, Yi Zeng, Kenneth G. Manton, James W. Curtsinger



For humans (Fig. 3A), death rates increase at a slowing rate after age 80. A logistic curve that fits the data well from age 80 to 105 indicates that death rates may reach a plateau (16). A quadratic curve fit to the data at ages 105+ suggests a decline in mortality after age 110.

Aggregated data for 14 countries over the period 1950-1990

Mortality at Advanced Ages, Recent Study



Source: Manton et al. (2008). Human Mortality at Extreme Ages: Data from the NLTCS and Linked Medicare Records. *Math.Pop.Studies*

Existing Explanations of Mortality Deceleration

- **Population Heterogeneity (Beard, 1959; Sacher, 1966).** "... sub-populations with the higher injury levels die out more rapidly, resulting in progressive selection for vigour in the surviving populations" (Sacher, 1966)
- Exhaustion of organism's redundancy (reserves) at extremely old ages so that every random hit results in death (Gavrilov, Gavrilova, 1991; 2001)
- Lower risks of death for older people due to less risky behavior (Greenwood, Irwin, 1939)
- **Evolutionary explanations** (Mueller, Rose, 1996; Charlesworth, 2001)

Mortality force (hazard rate) is the best indicator to study mortality at advanced ages

$$\mu_x = -\frac{dN_x}{N_x dx} = -\frac{d\ln(N_x)}{dx} \approx -\frac{\Delta\ln(N_x)}{\Delta x}$$

Does not depend on the length of age interval

Has no upper boundary and theoretically can grow unlimitedly

Famous Gompertz law was proposed for fitting age-specific mortality force function (Gompertz, 1825)

Problems in Hazard Rate Estimation At Extremely Old Ages

- 1. Mortality deceleration in humans may be an artifact of mixing different birth cohorts with different mortality (heterogeneity effect)
- 2. Standard assumptions of hazard rate estimates may be invalid when risk of death is extremely high
- 3. Ages of very old people may be highly exaggerated

Study of the Social Security Administration Death Master File

MORTALITY MEASUREMENT AT ADVANCED AGES: A STUDY OF THE SOCIAL SECURITY ADMINISTRATION DEATH MASTER FILE

Leonid A. Gavrilov* and Natalia S. Gavrilova[†]

ABSTRACT

Accurate estimates of mortality at advanced ages are essential to improving forecasts of mortality and the population size of the oldest old age group. However, estimation of hazard rates at extremely old ages poses serious challenges to researchers: (1) The observed mortality deceleration

NORTH AMERICAN ACTUARIAL JOURNAL, VOLUME 15, NUMBER 3

North American Actuarial Journal, 2011, 15(3):432-447

Social Security Administration's Death Master File (SSA's DMF) Helps to Alleviate the First Two Problems

Allows to study mortality in large, more homogeneous single-year or even single-month birth cohorts

Allows to estimate mortality in onemonth age intervals narrowing the interval of hazard rates estimation

What Is SSA's DMF?

- As a result of a court case under the Freedom of Information Act, SSA is required to release its death information to the public. SSA's DMF contains the complete and official SSA database extract, as well as updates to the full file of persons reported to SSA as being deceased.
- SSA DMF is no longer a publicly available data resource (now is available from Ancestry.com for fee)
- We used DMF full file obtained from the National Technical Information Service (NTIS). Last deaths occurred in September 2011.

SSA's DMF Advantage

Some birth cohorts covered by DMF could be studied by the method of extinct generations

Considered superior in data quality compared to vital statistics records by some researchers

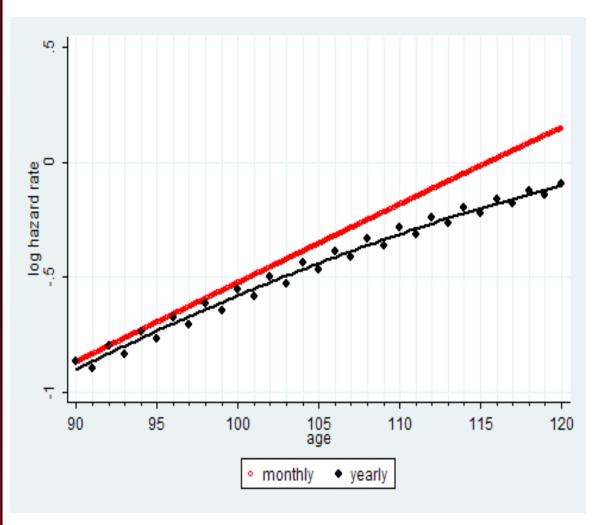
Social Security Administration's Death Master File (DMF) Was Used in This Study:

To estimate hazard rates for relatively homogeneous single-year extinct birth cohorts (1890-1899)

To obtain monthly rather than traditional annual estimates of hazard rates

To identify the age interval and cohort with reasonably good data quality and compare mortality models

Monthly Estimates of Mortality are More Accurate Simulation assuming Gompertz law for hazard rate



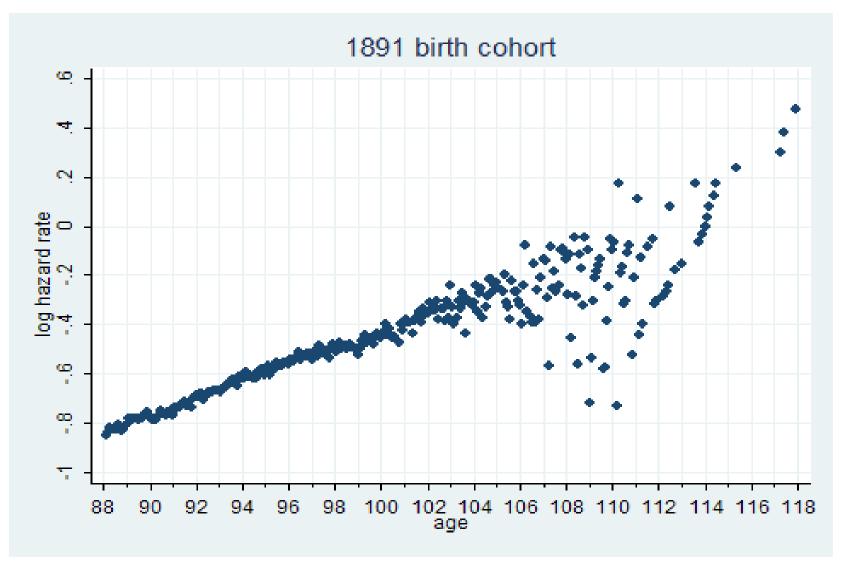
Stata package uses the Nelson-Aalen estimate of hazard rate:

$$\mu_x = H(x) - H(x - 1) = \frac{d_x}{n_x}$$

H(x) is a cumulative hazard function, d_x is the number of deaths occurring at time x and n_x is the number at risk at time x before the occurrence of the deaths. This method is equivalent to calculation of probabilities of death:

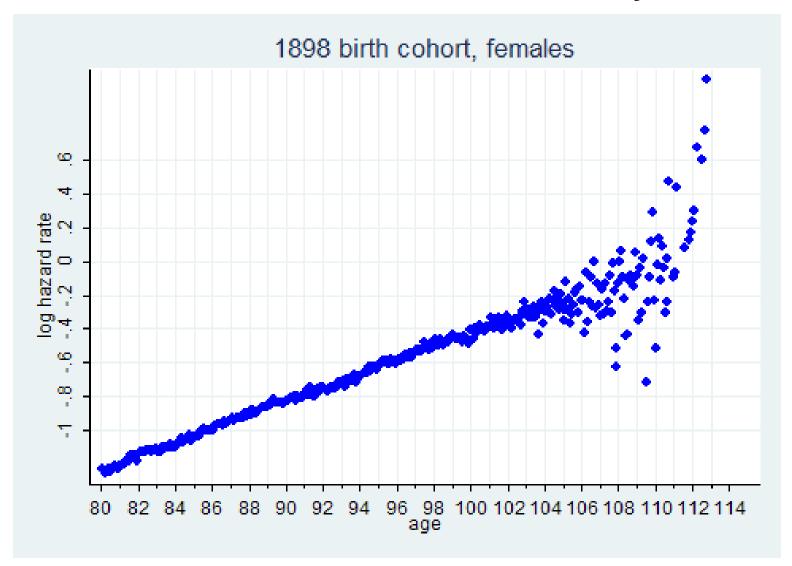
$$q_x = \frac{d_x}{l_x}$$

Hazard rate estimates at advanced ages based on DMF



Nelson-Aalen monthly estimates of hazard rates using Stata 11

More recent birth cohort mortality



Nelson-Aalen monthly estimates of hazard rates using Stata 11

Hypothesis

Mortality deceleration at advanced ages among DMF cohorts may be caused by poor data quality (age exaggeration) at very advanced ages

If this hypothesis is correct then mortality deceleration at advanced ages should be less expressed for data with better quality

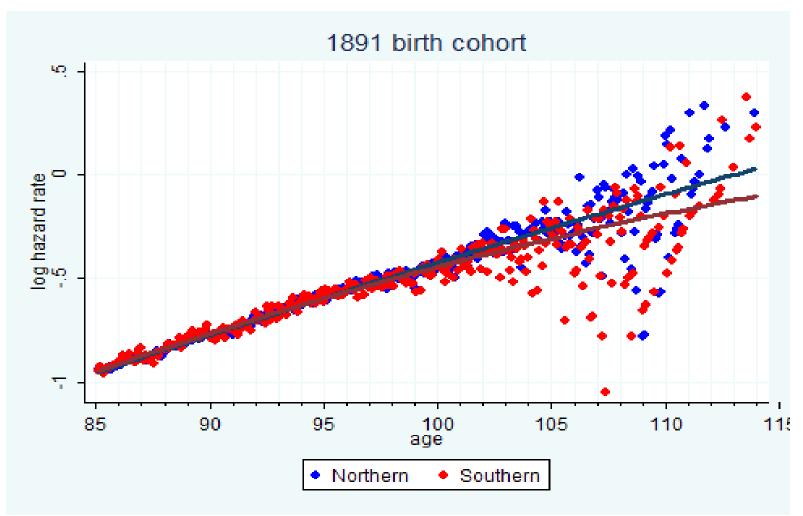
Quality Control (1)

Study of mortality in the states with different quality of age reporting:

Records for persons applied to SSN in the Southern states were found to be of lower quality (Rosenwaike, Stone, 2003)

We compared mortality of persons applied to SSN in Southern states, Hawaii, Puerto Rico, CA and NY with mortality of persons applied in the Northern states (the remainder)

Mortality for data with presumably different quality: Southern and Non-Southern states of SSN receipt



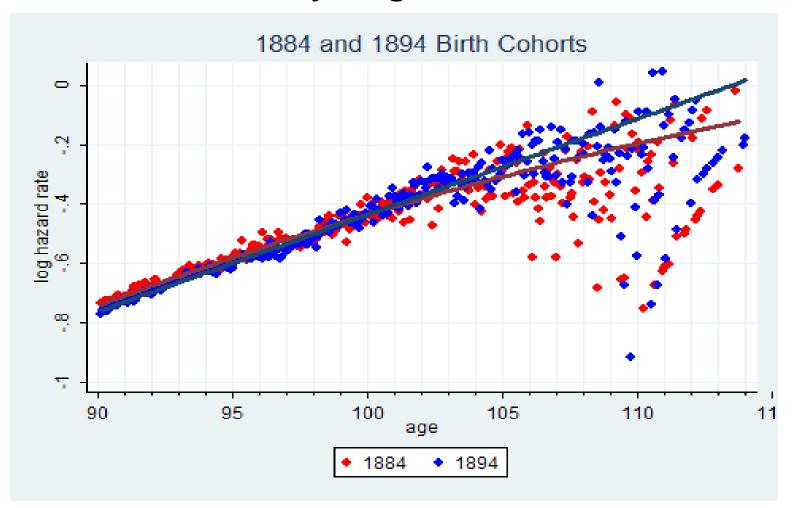
The degree of deceleration was evaluated using quadratic model

Quality Control (2)

Study of mortality for earlier and later single-year extinct birth cohorts:

Records for later born persons are supposed to be of better quality due to improvement of age reporting over time.

Mortality for data with presumably different quality: Older and younger birth cohorts

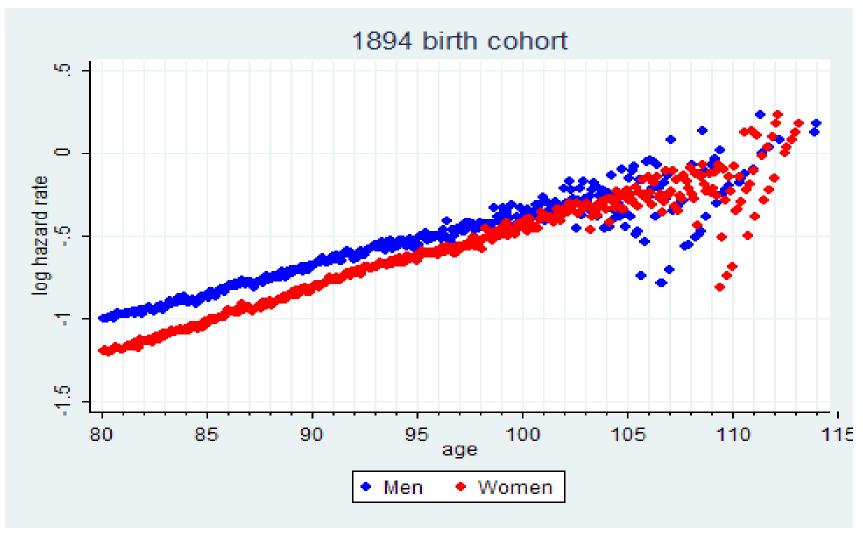


The degree of deceleration was evaluated using quadratic model

At what age interval data have reasonably good quality?

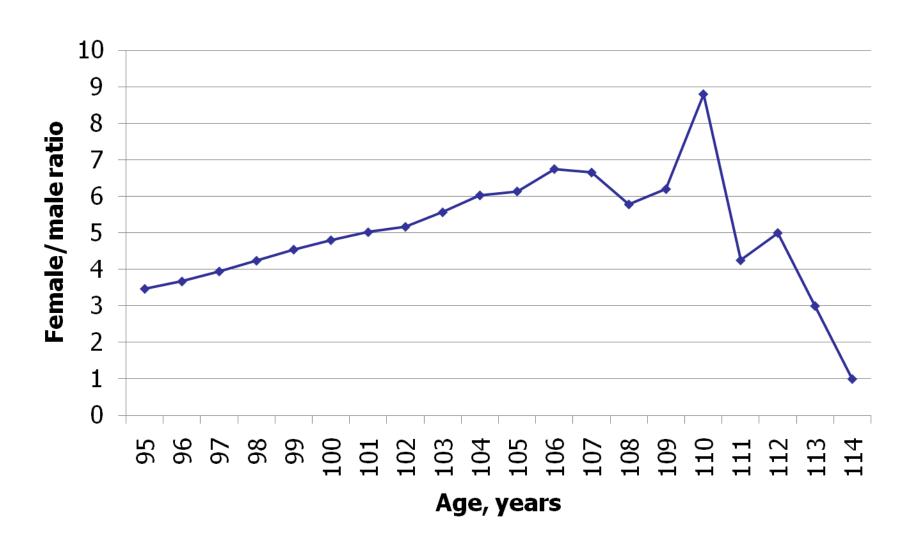
A study of age-specific mortality by gender

Women have lower mortality at advanced ages

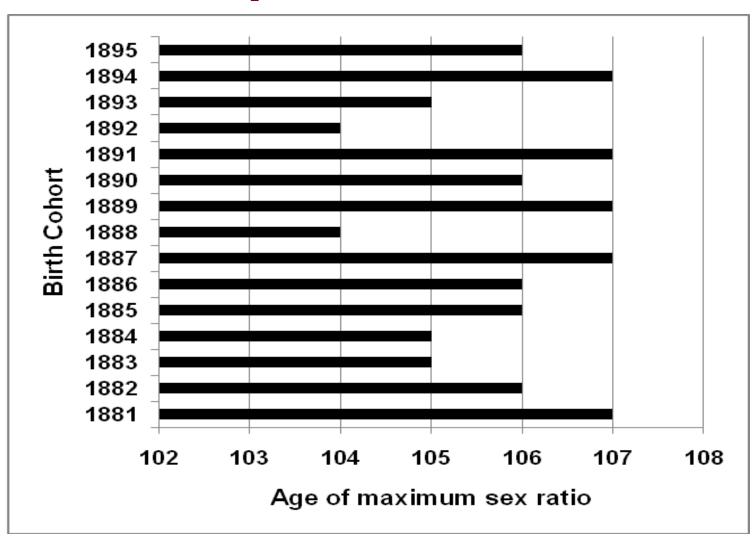


Hence number of females to number of males ratio should grow with age

Observed female to male ratio at advanced ages for combined 1887-1892 birth cohort



Age of maximum female to male ratio by birth cohort



Selection of competing mortality models using DMF data

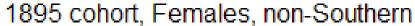
Data with reasonably good quality were used: non-Southern states and 85-106 years age interval

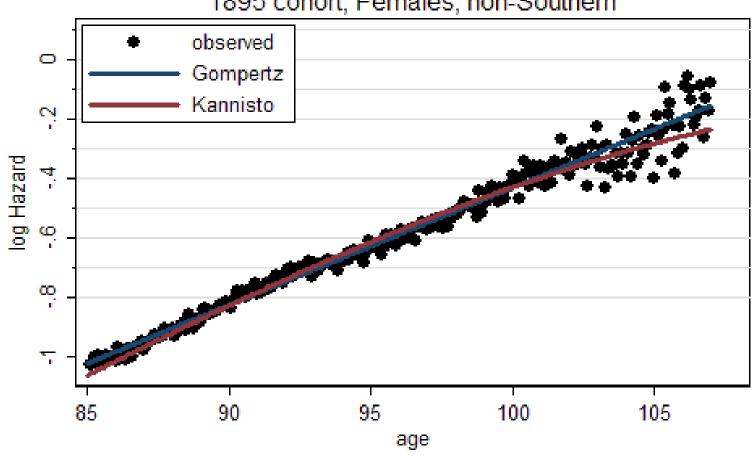
Gompertz and logistic (Kannisto) models were compared

Nonlinear regression model for parameter estimates (Stata 11)

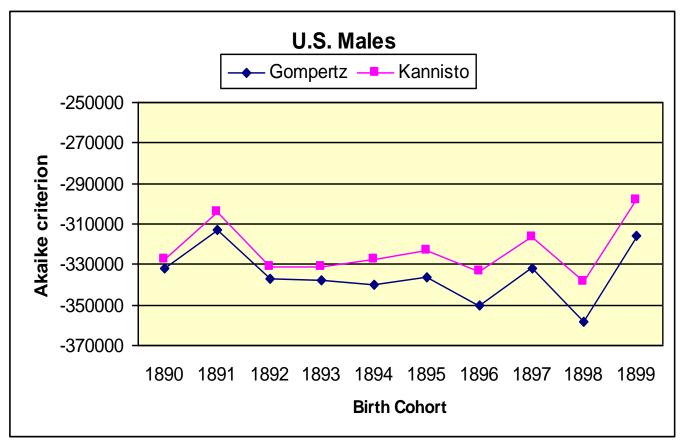
Model goodness-of-fit was estimated using AIC and BIC

Fitting mortality with Kannisto and **Gompertz models**



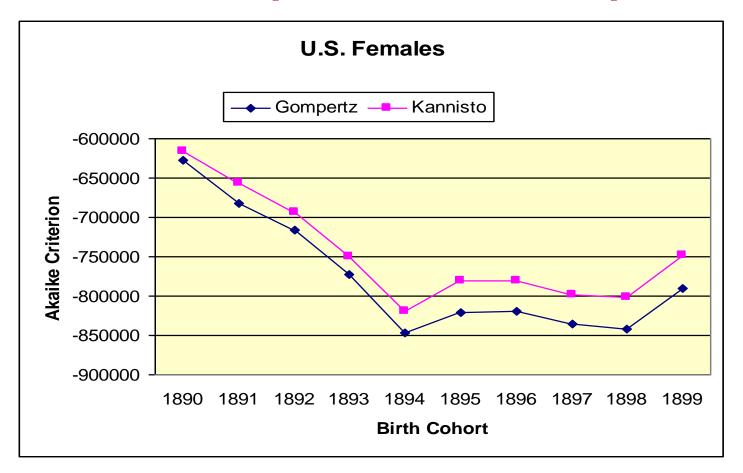


Akaike information criterion (AIC) to compare Kannisto and Gompertz models, men, by birth cohort (non-Southern states)



Conclusion: In all ten cases Gompertz model demonstrates better fit than logistic model for men in age interval 85-106 years

Akaike information criterion (AIC) to compare Kannisto and Gompertz models, <u>women</u>, by birth cohort (non-Southern states)



Conclusion: In all ten cases Gompertz model demonstrates better fit than logistic model for men in age interval 85-106 years

Conclusions from our study of Social Security Administration Death Master File

Mortality deceleration at advanced ages among DMF cohorts is more expressed for data of lower quality

Mortality data beyond ages 106-107 years have unacceptably poor quality (as shown using female-to-male ratio test). The study by other authors also showed that beyond age 110 years the age of individuals in DMF cohorts can be validated for less than 30% cases (Young et al., 2010)

Source: Gavrilov, Gavrilova, *North American Actuarial Journal*, 2011, 15(3):432-447

Mortality at advanced ages is the key variable for understanding population trends among the oldest-old

THE WALL STREET JOURNAL

WWwgg

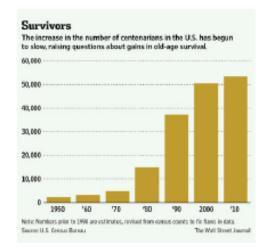
THE NUMBERS GUY | March 2, 2012, 7:00 p.m. ET

Death Gets in the Way of Old-Age Gains



A new research paper, and a census surprise, are calling into question some long-held beliefs about a morbid bit of math: how much mortality rates increase with age.

It's no surprise that the older a group of people get, the higher the percentage of them who will die in any given time period. Benjamin Gompertz, a 19th-century British mathematician, charted the increase in mortality rates as very regular. His Gompertz law of mortality says that each additional period brings a constant percentage increase in mortality rates.



In the 20th century, though, as the world population aged and demographers' data improved, Gompertz started to look fallible. Researchers have found that, starting around age 80, mortality keeps increasing, but more slowly. More 100-year-olds die before turning 101 than 80-year-olds do before their 81st birthday, but the difference was less than Gompertz predicted.

But Gompertz may be right after all. In a study published last year and publicized last month, two longtime researchers of aging and believers in the late-life mortality slowdown reported that they and others were wrong. Death rates among Americans born between 1875 and 1895 kept on climbing steadily as they aged, they found, all the way through age 106, when their numbers got too sparse to follow.

This is bad news for anyone who wants to reach the century mark, but could provide an odd measure of relief for pensions, retirement programs and medical insurers, whose costs rise as people live longer.

The second studied dataset: U.S. cohort death rates taken from the Human Mortality Database

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Biodemography of Old-Age Mortality in Humans and Rodents

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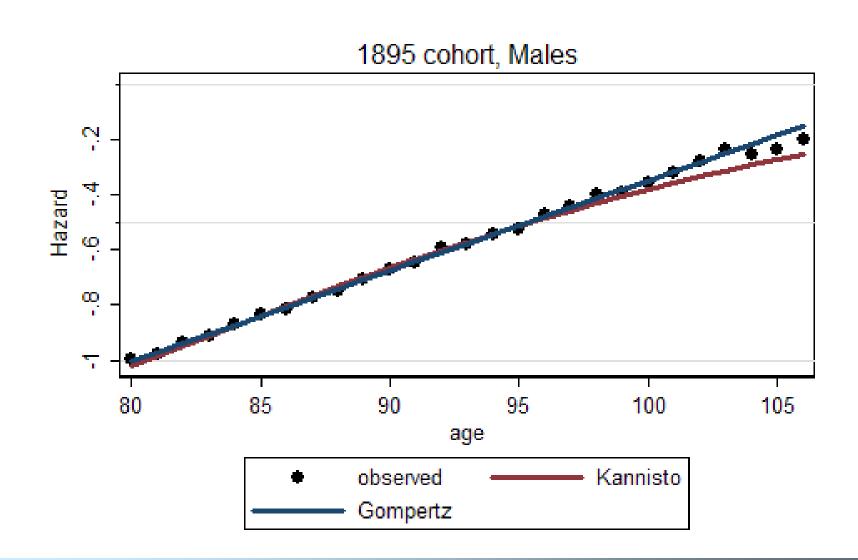
The growing number of persons living beyond age 80 underscores the need for accurate measurement of mortality at advanced ages and understanding the old-age mortality trajectories. It is believed that exponential growth of mortality

The second studied dataset: U.S. cohort death rates taken from the Human Mortality Database

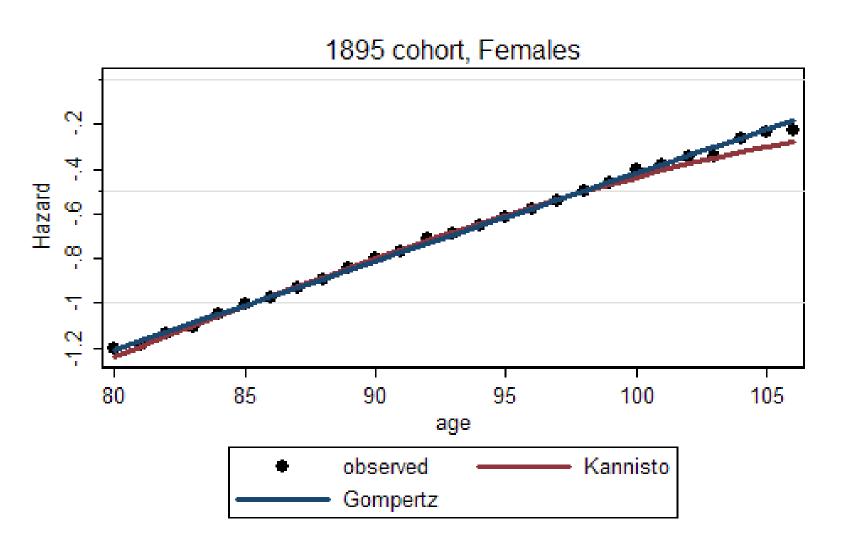
Selection of competing mortality models using HMD data

- Data with reasonably good quality were used: 80-106 years age interval
- Gompertz and logistic (Kannisto) models were compared
- Nonlinear weighted regression model for parameter estimates (Stata 11)
- Age-specific exposure values were used as weights (Muller at al., Biometrika, 1997)
- Model goodness-of-fit was estimated using AIC and BIC

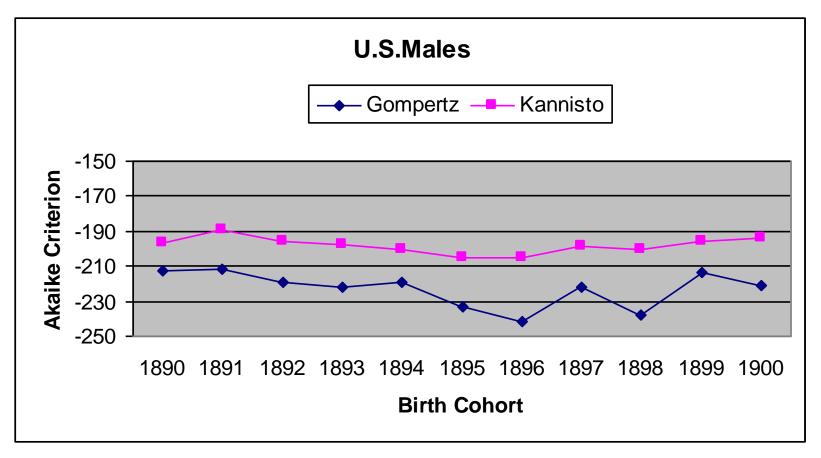
Fitting mortality with Kannisto and Gompertz models, HMD U.S. data



Fitting mortality with Kannisto and Gompertz models, HMD U.S. data

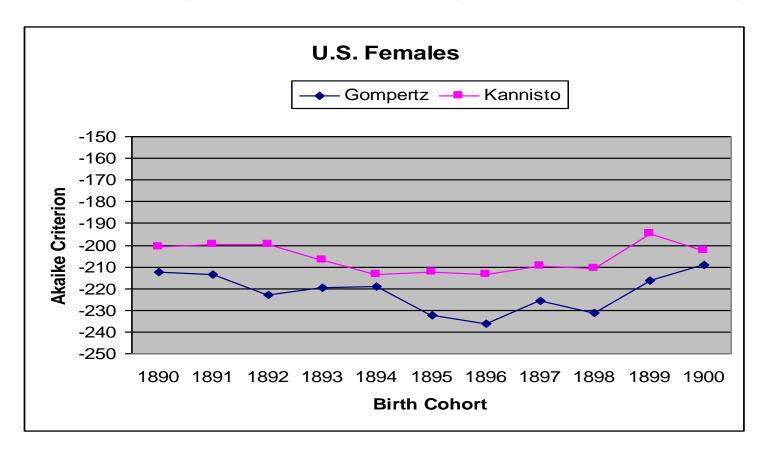


Akaike information criterion (AIC) to compare Kannisto and Gompertz models, men, by birth cohort (HMD U.S. data)



Conclusion: In all ten cases Gompertz model demonstrates better fit than logistic model for men in age interval 80-106 years

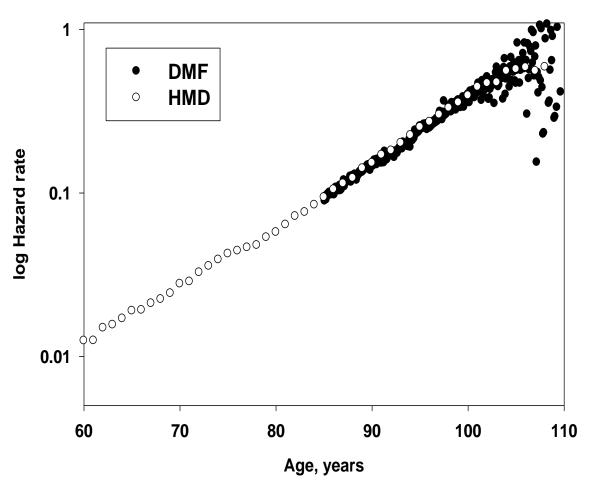
Akaike information criterion (AIC) to compare Kannisto and Gompertz models, men, by birth cohort (HMD U.S. data)



Conclusion: In all ten cases Gompertz model demonstrates better fit than logistic model for men in age interval 80-106 years

Compare DMF and HMD data

Females, 1898 birth cohort



Hypothesis about two-stage Gompertz model is not supported by real data

Which estimate of hazard rate is the most accurate?

Simulation study comparing several existing estimates:

- Nelson-Aalen estimate available in Stata
- Sacher estimate (Sacher, 1956)
- Gehan (pseudo-Sacher) estimate (Gehan, 1969)
- Actuarial estimate (Kimball, 1960)

Simulation study to identify the most accurate mortality indicator

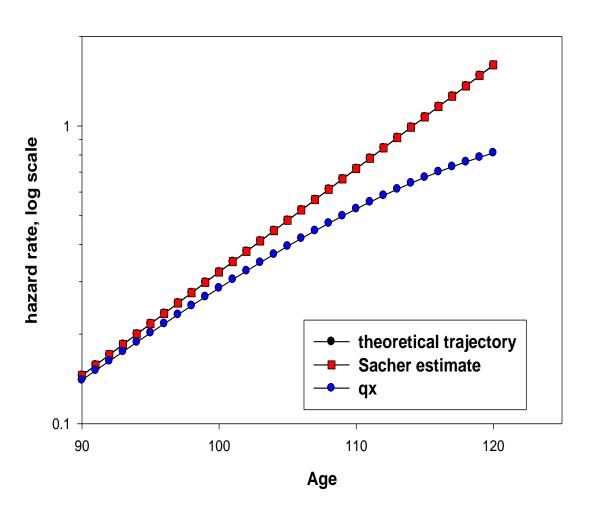
Simulate yearly I_x numbers assuming Gompertz function for hazard rate in the entire age interval and initial cohort size equal to 10^{11} individuals

Gompertz parameters are typical for the U.S. birth cohorts: slope coefficient (alpha) = 0.08 year^{-1} ; $R_0 = 0.0001 \text{ year}^{-1}$

Focus on ages beyond 90 years

Accuracy of various hazard rate estimates (Sacher, Gehan, and actuarial estimates) and probability of death is compared at ages 100-110

Simulation study of Gompertz mortality Compare Sacher hazard rate estimate and probability of death in a yearly age interval



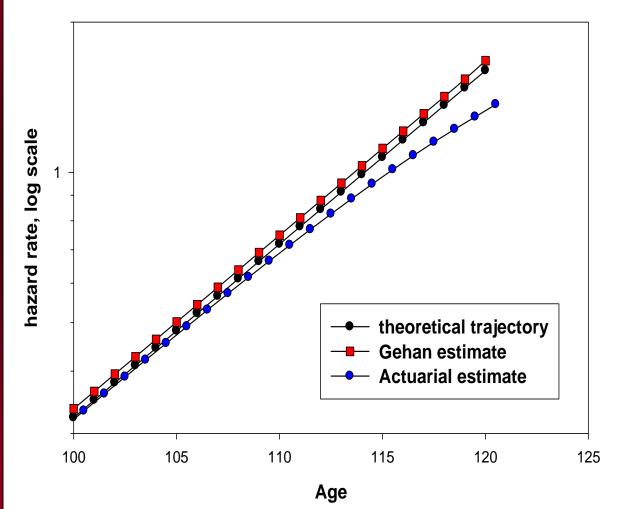
Sacher estimates practically coincide with theoretical mortality trajectory

$$\mu_x = \frac{1}{2\Delta x} \ln \frac{l_{x - \Delta x}}{l_{x + \Delta x}}$$

Probability of death values strongly undeestimate mortality after age 100

$$q_x = \frac{d_x}{l_x}$$

Simulation study of Gompertz mortality Compare Gehan and actuarial hazard rate estimates



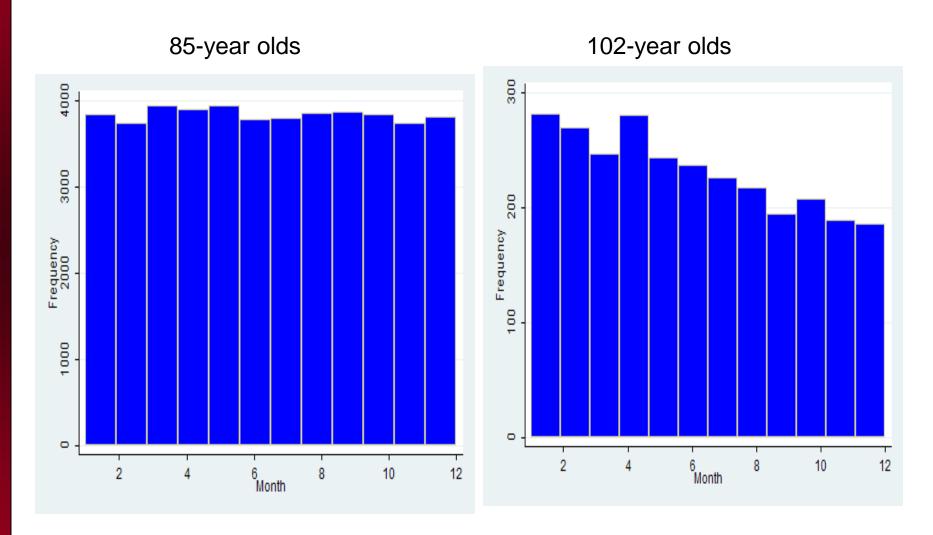
Gehan estimates slightly overestimate hazard rate because of its half-year shift to earlier ages

$$\mu_x = -\ln(1 - q_x)$$

Actuarial estimates undeestimate mortality after age 100

$$\mu_{x + \frac{\Delta x}{2}} = \frac{2}{\Delta x} \frac{l_{x} - l_{x + \Delta x}}{l_{x} + l_{x + \Delta x}}$$

Deaths at extreme ages are not distributed uniformly over one-year interval



1894 birth cohort from the Social Security Death Index

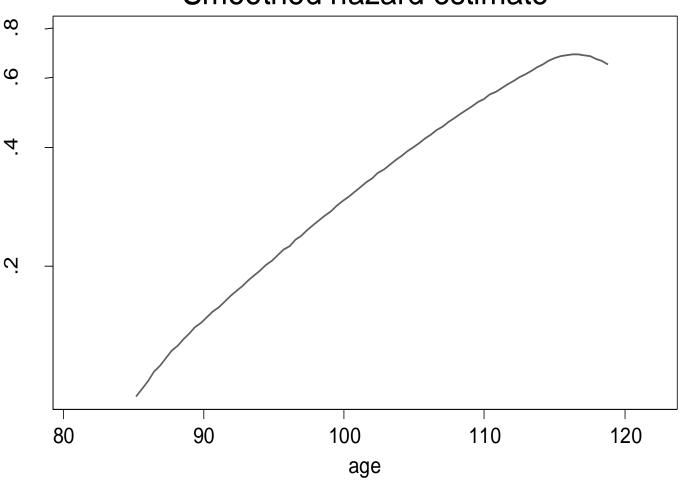
Accuracy of hazard rate estimates

Relative difference between theoretical and observed values, %

Estimate	100 years	110 years
Probability of death	11.6%, understate	26.7%, understate
Sacher estimate	0.1%, overstate	0.1%, overstate
Gehan estimate	4.1%, overstate	4.1%, overstate
Actuarial estimate	1.0%, understate	4.5%, understate

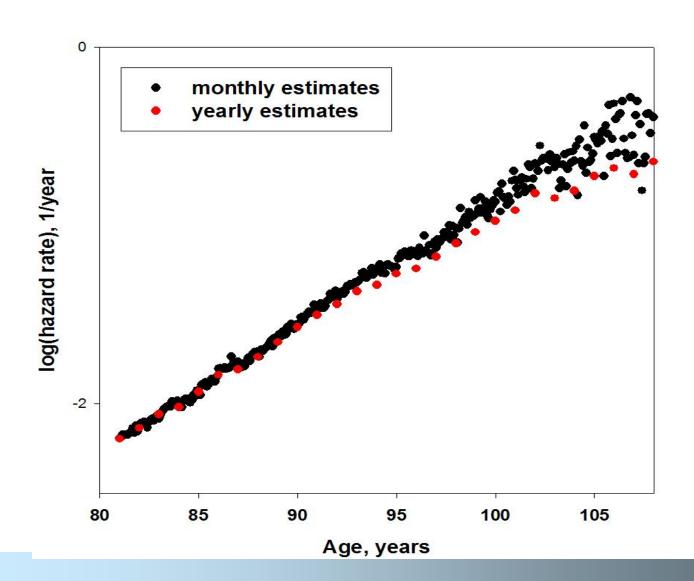
Simulation study of the Gompertz mortality Kernel smoothing of hazard rates





Mortality of 1894 birth cohort

Monthly and Yearly Estimates of Hazard Rates using Nelson-Aalen formula (Stata)



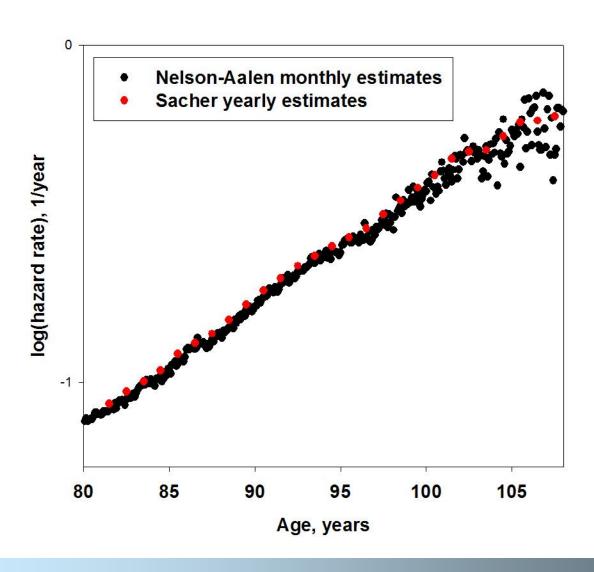
Sacher formula for hazard rate estimation (Sacher, 1956; 1966)

$$\mu_x = \frac{1}{\Delta x} \left(\ln l_{x - \frac{\Delta x}{2}} - \ln l_{x + \frac{\Delta x}{2}} \right) = \frac{1}{2\Delta x} \ln \frac{l_{x - \Delta x}}{l_{x + \Delta x}}$$
Hazard rate
$$l_x - \text{survivor function at age x; } \Delta x - \text{age interval}$$

Simplified version suggested by Gehan (1969):

$$\mu_{\scriptscriptstyle X} = -\ln(1-q_{\scriptscriptstyle X})$$

Mortality of 1894 birth cohort Sacher formula for yearly estimates of hazard rates



Conclusions

Deceleration of mortality in later life is more expressed for data with lower quality. Quality of age reporting in DMF becomes poor beyond the age of 107 years

Below age 107 years and for data of reasonably good quality the Gompertz model fits mortality better than the logistic model (no mortality deceleration)

Sacher estimate of hazard rate turns out to be the most accurate and most useful estimate to study mortality at advanced ages

What about mortality deceleration in other species?

Mortality Deceleration in Other Species

Invertebrates:

Nematodes, shrimps, bdelloid rotifers, degenerate medusae (Economos, 1979)

Drosophila melanogaster (Economos, 1979; Curtsinger et al., 1992)

Medfly (Carey et al., 1992)

Housefly, blowfly (Gavrilov, 1980)

Fruit flies, parasitoid wasp (Vaupel et al., 1998)

Bruchid beetle (Tatar et al., 1993)

Mammals:

Mice (Lindop, 1961; Sacher, 1966; Economos, 1979)

Rats (Sacher, 1966)

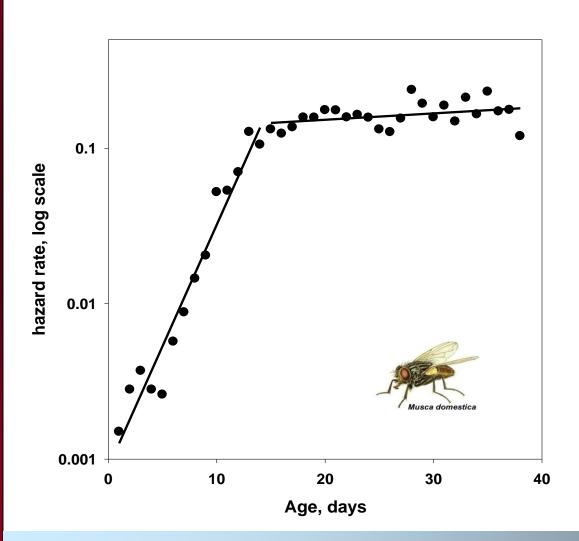
Horse, Sheep, Guinea pig (Economos, 1979; 1980)

However no mortality deceleration is reported for

Rodents (Austad, 2001)

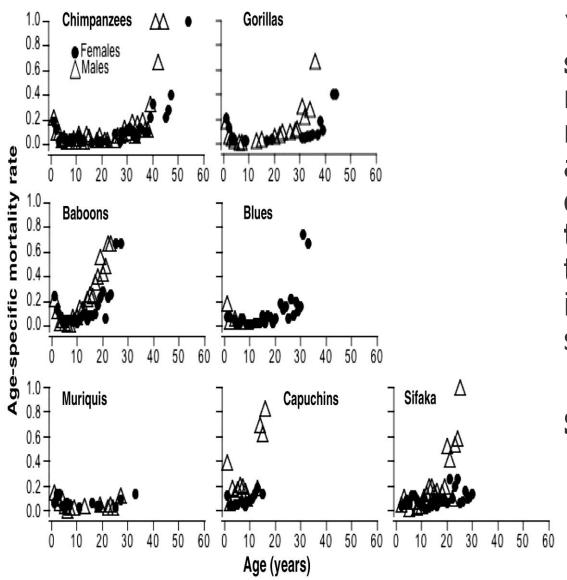
Baboons (Bronikowski et al., 2002)

Mortality Leveling-Off in House Fly Musca domestica



Based on life table of 4,650 male house flies published by Rockstein & Lieberman, 1959

Recent developments



"none of the agespecific mortality
relationships in our
nonhuman primate
analyses
demonstrated the
type of leveling off
that has been shown
in human and fly data
sets"

Bronikowski et al., Science, 2011

What about other mammals?



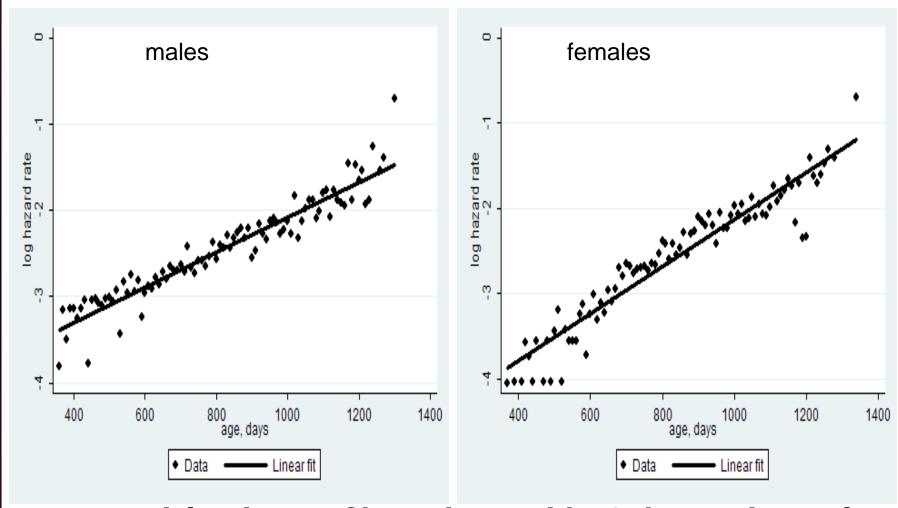
Mortality data for mice:

Data from the NIH Interventions Testing Program, courtesy of Richard Miller (U of Michigan)

Argonne National Laboratory data, of Bruce Carnes (U of Oklahoma)

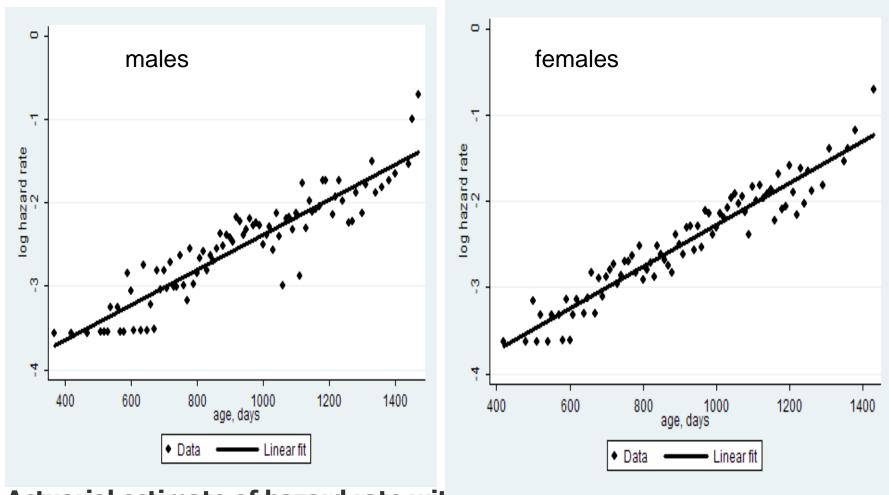
courtesy

Mortality of mice (log scale) Miller data



Actuarial estimate of hazard rate with 10-day age intervals

Mortality of mice (log scale) Carnes data



Actuarial estimate of hazard rate witn 10-day age intervals

Data were collected by the Argonne National Laboratory, early experiments shown

Bayesian information criterion (BIC) to compare the Gompertz and logistic models, mice data

Dataset	Miller data Controls		Miller data Exp., no life extension		Carnes data Early controls		Carnes data Late controls	
Sex	М	F	M	F	М	F	М	F
Cohort size at age one year	1281	1104	2181	1911	364	431	487	510
Gompertz	-597.5	-496.4	-660.4	-580.6	-585.0	-566.3	-639.5	-549.6
logistic	-565.6	-495.4	-571.3	-577.2	-556.3	-558.4	-638.7	-548.0

Better fit (lower BIC) is highlighted in red

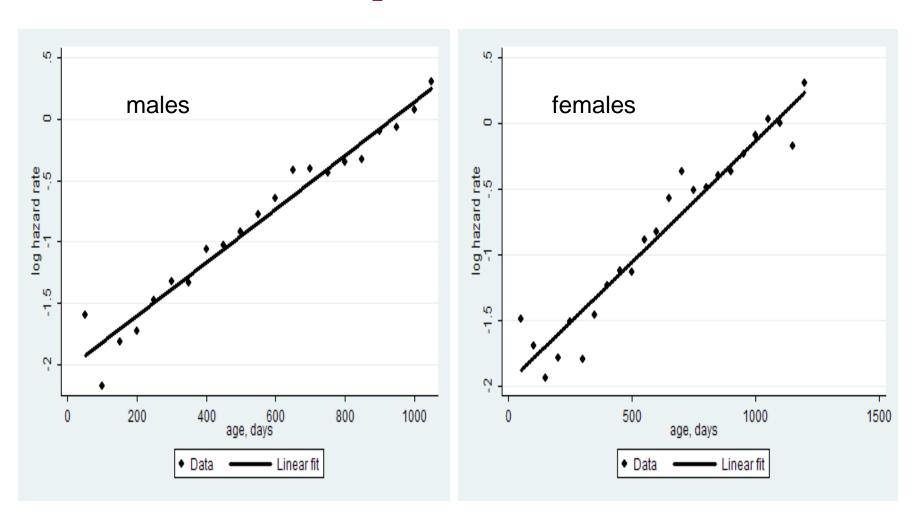
Conclusion: In all cases Gompertz model demonstrates better fit than logistic model for mortality of mice after one year of age

Laboratory rats



Data sources: Dunning, Curtis (1946); Weisner, Sheard (1935), Schlettwein-Gsell (1970)

Mortality of Wistar rats



Actuarial estimate of hazard rate with 50-day age intervals Data source: Weisner, Sheard, 1935

Bayesian information criterion (BIC) to compare logistic and Gompertz models, rat data

Line	Wistar (1935)		Wistar (1970)		Copenhagen		Fisher		Backcrosses	
Sex	М	F	М	F	М	F	М	F	М	F
Cohort size	1372	1407	1372	2035	1328	1474	1076	2030	585	672
Gompertz	-34.3	-10.9	-34.3	-53.7	-11.8	-46.3	-17.0	-13.5	-18.4	-38.6
logistic	7.5	5.6	7.5	1.6	2.3	-3.7	6.9	9.4	2.48	-2.75

Better fit (lower BIC) is highlighted in red

Conclusion: In all cases Gompertz model demonstrates better fit than logistic model for mortality of laboratory rats

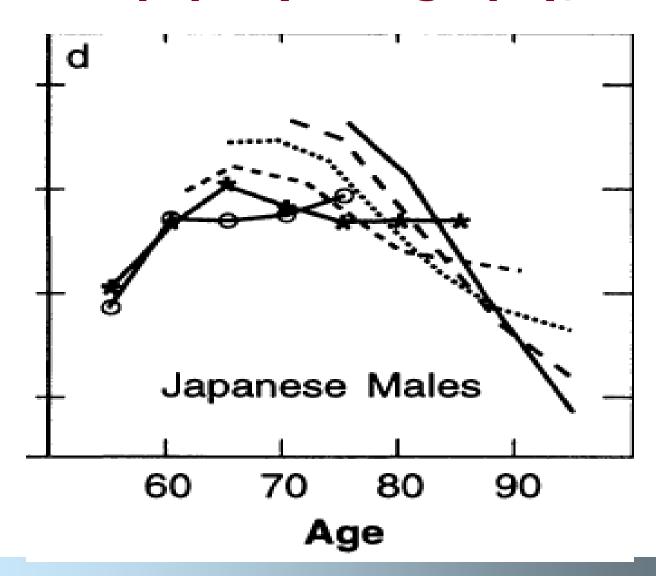
Alternative way to study mortality trajectories at advanced ages: Age-specific rate of mortality change

Suggested by Horiuchi and Coale (1990), Coale and Kisker (1990), Horiuchi and Wilmoth (1998) and later called 'life table aging rate (LAR)'

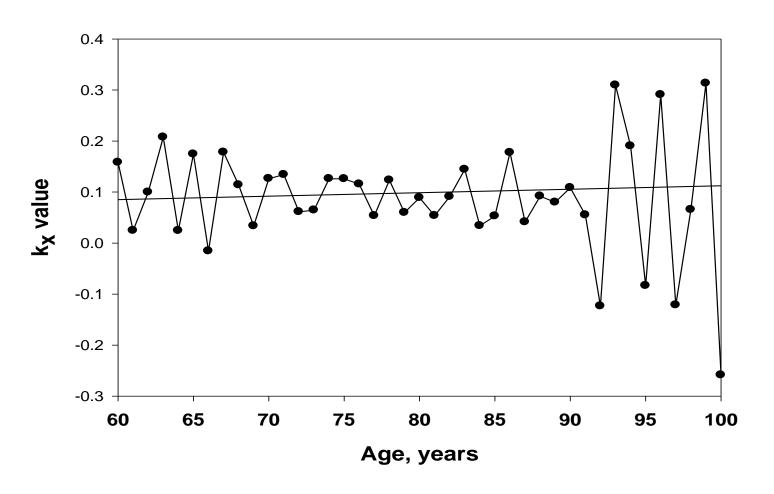
$$k(x) = d \ln \mu(x)/dx$$

- Constant k(x) suggests that mortality follows the Gompertz model.
- Earlier studies found that k(x) declines in the age interval 80-100 years suggesting mortality deceleration.

Typical result from Horiuchi and Wilmoth paper (Demography, 1998)



Age-specific rate of mortality changeSwedish males, 1896 birth cohort



Flat k(x) suggests that mortality follows the Gompertz law

Slope coefficients (with p-values) for linear regression models of k(x) on age

Country	Sex							
		1894		18	96	1898		
		slope	p-value	slope	p-value	slope	p-value	
Canada	F	-0.00023	0.914	0.00004	0.984	0.00066	0.583	
	M	0.00112	0.778	0.00235	0.499	0.00109	0.678	
France	F	-0.00070	0.681	-0.00179	0.169	-0.00165	0.181	
	M	0.00035	0.907	-0.00048	0.808	0.00207	0.369	
Sweden	F	0.00060	0.879	-0.00357	0.240	-0.00044	0.857	
	M	0.00191	0.742	-0.00253	0.635	0.00165	0.792	
USA	F	0.00016	0.884	0.00009	0.918	0.000006	0.994	
	M	0.00006	0.965	0.00007	0.946	0.00048	0.610	

All regressions were run in the age interval 80-100 years.

Can data aggregation result in mortality deceleration?

Age-specific 5-year cohort death rates taken from the Human Mortality Database

Studied countries: Canada, France, Sweden, United States

Studied birth cohorts: 1880-84, 1885-89, 1895-99

k(x) calculated in the age interval 80-100 years

k(x) calculated using one-year (age) mortality rates

Slope coefficients (with p-values) for linear regression models of k(x) on age

Country	Sex	Birth cohort						
		188	5-89	189	0-94	1895-99		
		slope	p-value	slope	p-value	slope	p-value	
Canada	F	-0.00069	0.372	0.00015	0.851	-0.00002	0.983	
	M	-0.00065	0.642	0.00094	0.306	0.00022	0.850	
France	F	-0.00273	0.047	-0.00191	0.005	-0.00165	0.002	
	M	-0.00082	0.515	-0.00049	0.661	-0.00047	0.412	
Sweden	F	-0.00036	0.749	-0.00122	0.185	-0.00210	0.122	
	M	-0.00234	0.309	-0.00127	0.330	-0.00089	0.696	
USA	F	-0.00030	0.654	-0.00027	0.685	0.00004	0.915	
	M	-0.00050	0.417	-0.00039	0.399	0.00002	0.972	

All regressions were run in the age interval 80-100 years.

In previous studies mortality rates were calculated for five-year age intervals

$$k_x = \frac{\ln(m_x) - \ln(m_{x-5})}{5}$$

- Five-year age interval is very wide for mortality estimation at advanced ages.
- Assumption about uniform distribution of deaths in the age interval does not work for 5-year interval
- Mortality rates at advanced ages are biased downward

Simulation study of mortality following the Gompertz law

Simulate yearly I_x numbers assuming Gompertz function for hazard rate in the entire age interval and initial cohort size equal to 10^{11} individuals

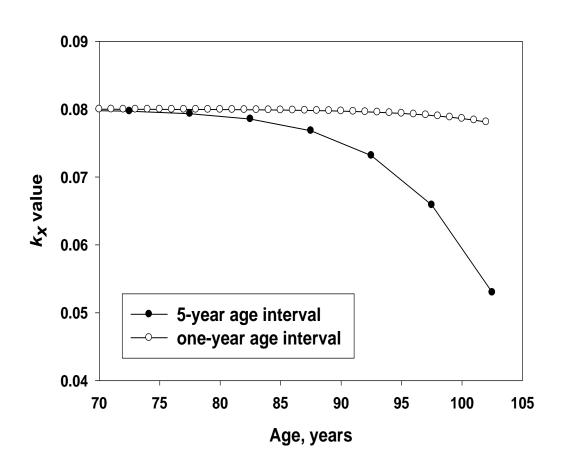
Gompertz parameters are typical for the U.S. birth cohorts: slope coefficient (alpha) = 0.08 year⁻¹; R_0 = 0.0001 year⁻¹

Numbers of survivors were calculated using formula (Gavrilov et al., 1983):

$$\frac{N_x}{N_0} = \frac{N_{x0}}{N_0} \exp\left[\left(-\frac{a}{b}\right) \left(e^{bx} - e^{bx0}\right)\right]$$

where Nx/N0 is the probability of survival to age x, i.e. the number of hypothetical cohort at age x divided by its initial number N0. a and b (slope) are parameters of Gompertz equation

Age-specific rate of mortality change with age, kx, by age interval for mortality calculation Simulation study of Gompertz mortality



Taking into account that underlying mortality follows the Gompertz law, the dependence of k(x) on age should be flat

Recent claims based on the study of 724 French-Canadian centenarians born in 1870-96

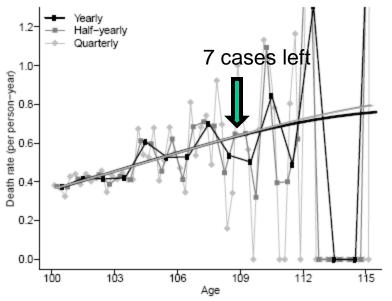
Measurement of Mortality among Centenarians in Canada

Nadine Quellette* and Robert Bourbeau

These

results refute recent findings suggesting that proper hazard rate estimation in relatively homogeneous populations with accurate data leads to a steady death rate increase over age, up to age 106 and possibly beyond (Gavrilov and Gavrilova 2011, 2014).

Observed and smoothed death rates



Where is a refutation of 'steady death rate increase?'

724 centenarians born in 1870-96 (Ouellette, Bourbeau, 2014)

12,987 centenarians born in 1898 (Gavrilov, Gavrilova, 2011) – one out of 10 female birth cohorts

Mortality of Supercentenarians: Does It Grow with Age?

Natalia S. Gavrilova, Ph.D. Leonid A. Gavrilov, Ph.D.

Center on Aging
NORC and The University of Chicago
Chicago, Illinois, USA

Biodemography of human ageing

James W. Vaupel^{1,2,3}

Most reported cases of a person being a centenarian — and to an even greater extent a supercentenarian — are erroneous^{73,74}. To verify reputed high ages, correct birth records have to be found. A meticulous research endeavour has yielded a remarkable finding: between the validated ages of 110 and 114, the annual probability of death is constant at a level of 50% per year⁷³. The sparse observations of survival after age 114 are not inconsistent with the hypothesis that mortality stays at this level at all ages after 110. As explained in Box 1, this result implies that at least at advanced ages, human individuals deteriorate at the same rate.

International Database on Longevity (IDL)

This database contains validated records of persons aged 110 years and more from 15 countries with good quality of vital records.

The contributors to IDL performed data collection in a way that avoided ageascertainment bias, which is essential for demographic analysis.

The database was last updated in March 2010. Available at www.supercentenarians.org

Previous studies of mortality using IDL

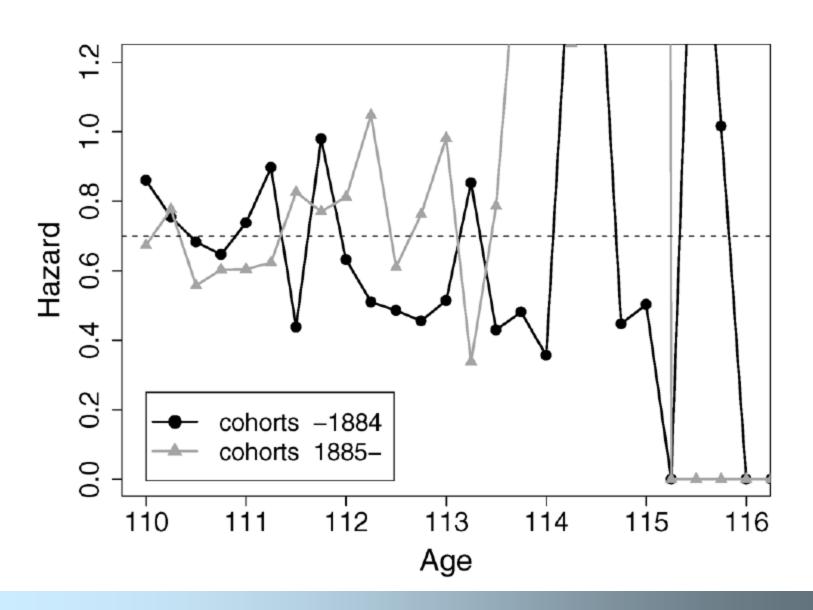
Robine and Vaupel, 2001.

Robine et al. (2005). Used IDL data, calculated age-specific probabilities of death.

Gampe, 2010. Used IDL data. Wrote her own program to estimate hazard rates, which adjusts for censored and truncated data.

Main conclusion from these studies is that hazard rate after age 110 years is flat.

From study by Gampe (2010)



Our study of supercentenarians based on IDL data

IDL database as of January, 2015. Last update in 2010, last deaths in 2007.

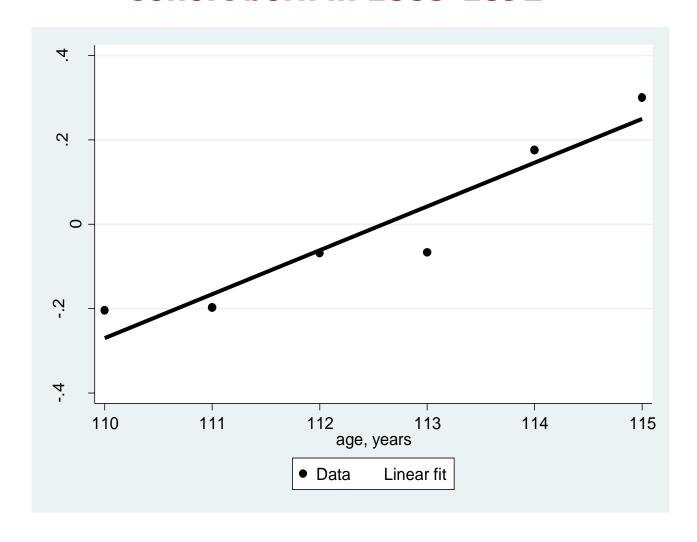
Two extinct birth cohorts (<1885 and 1885-1892), so no censored or truncated records were used.

Hazard rate was estimated using standard Stata package (procedure Itable).

Hazard rate was calculated using actuarial estimate of hazard rate (mortality rate):

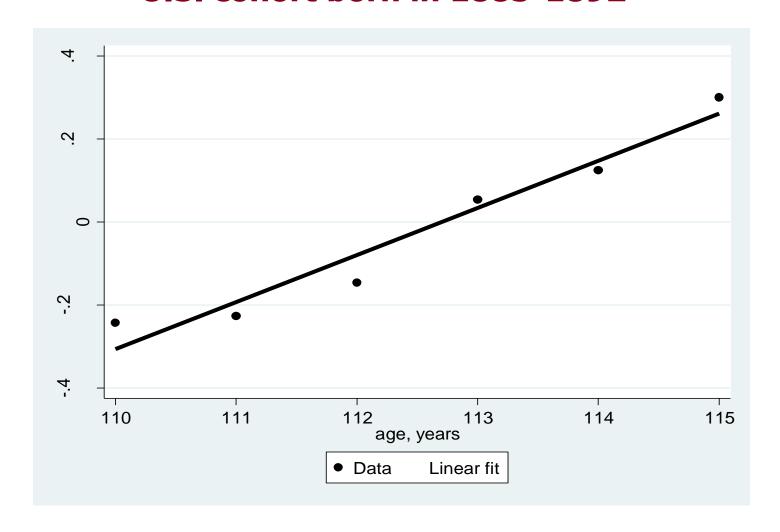
$$\mu_{x+\frac{\Delta x}{2}} = \frac{2}{\Delta x} \frac{l_x - l_{x+\Delta x}}{l_x + l_{x+\Delta x}}$$

Mortality of supercentenarians Cohort born in 1885-1892



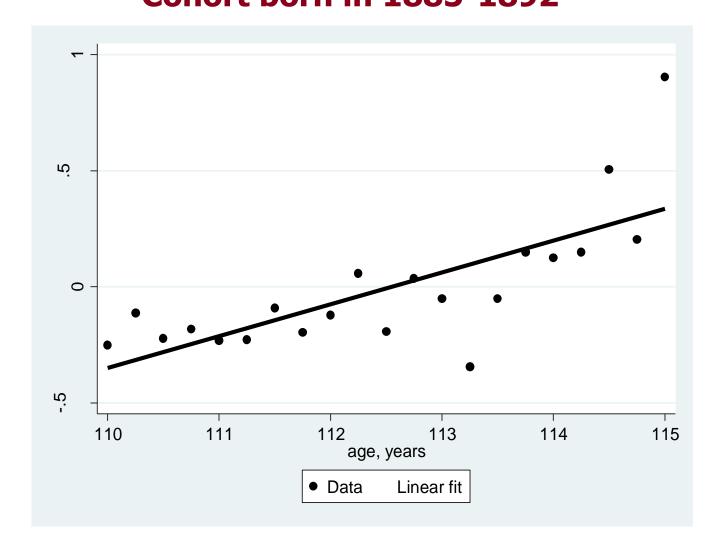
Yearly age intervals

Mortality of supercentenariansU.S. cohort born in 1885-1892



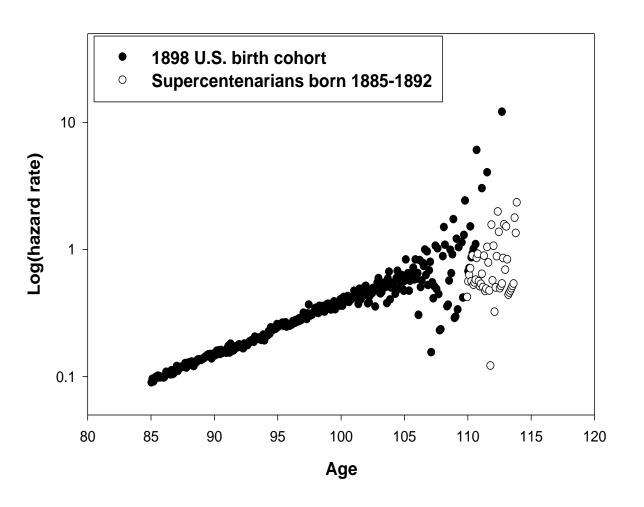
Yearly age intervals

Mortality of supercentenarians Cohort born in 1885-1892



Quarterly age intervals

Mortality after age 85 years

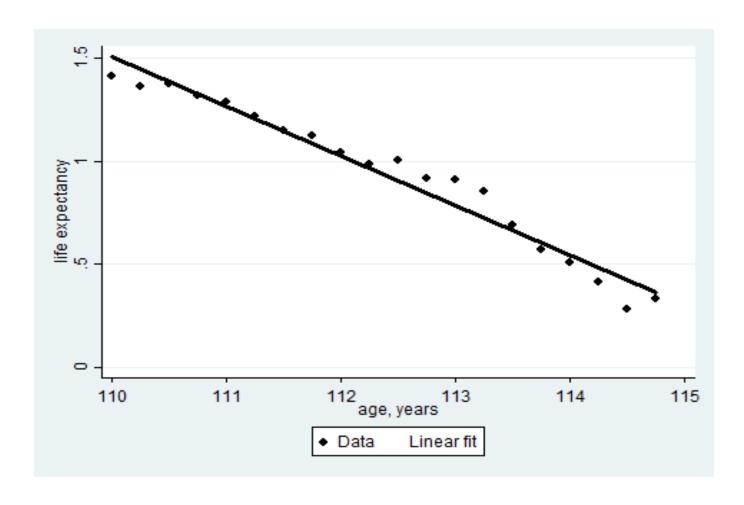


Monthly age intervals

Testing assumption about flat hazard rate after age 110

- Direct estimates of hazard rates at advanced ages are subjected to huge variations.
- More robust ways of testing this assumption come from the properties of exponential distribution:
- 1. Hazard rate, μ = const
- 2. Mean life expectancy (LE) = $1/\mu$ = const
- 3. Coefficient of variation for LE = SD/mean=1

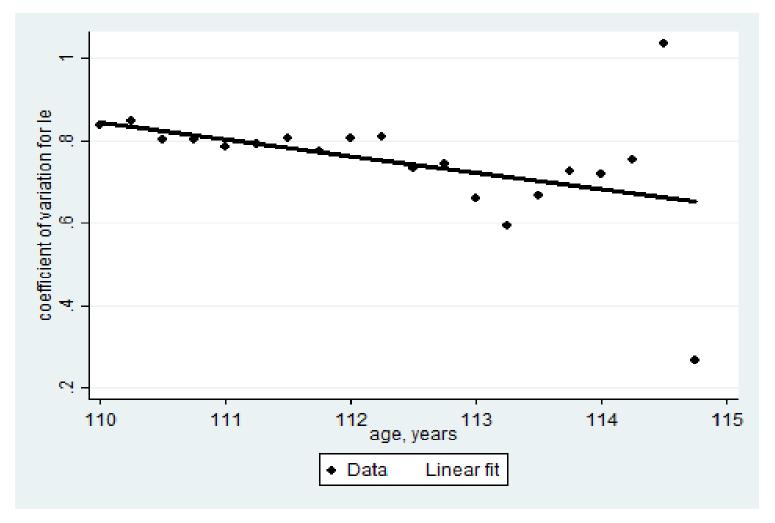
Mean life expectancy vs age Cohort born in 1885-1892



Slope coefficient = -0.24 (p<0.001). Quarterly age intervals

Coefficient of variation for LE vs age

Cohort born in 1885-1892



Slope coefficient = -0.041 (p=0.066). Quarterly age intervals

Conclusions

Assumption about flat hazard rate after age 110 years is not supported by the study of age trajectory for mean life expectancy. Life expectancy after age 110 is declining suggesting that actuarial aging continues.

Coefficient of variation for LE is lower than one and declines rather than increases with age, which does not support the assumption about flat hazard rate.

Hazard rate estimates (mortality rates) after age 110 continue to grow with almost linear trajectory in semi-log coordinates suggesting that Gompertz law is still working

Some other recent studies

Scandinavian Actuarial Journal, 2014 Vol. 2014, No. 3, 189–207, http://dx.doi.org/10.1080/03461238.2012.676562 Taylor & Francis
Taylor & Francis Group

Original Article

Beyond the Gompertz law: exploring the late-life mortality deceleration phenomenon

MARK BEBBINGTON^a*, REBECCA GREEN^a, CHIN-DIEW LAI^a and RIČARDAS ZITIKIS^b

A number of data sets have been explored, with a particular emphasis on those originating from Scandinavia. Although those from Australia, Canada, and the USA are compatible with Gompertzian mortality, those from the other countries examined are not. We find in particular that the onset of mortality deceleration is being progressively delayed in Western societies but that there is evidence of mortality plateauing at earlier ages.

Acknowledgments

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Stimulating working environment at the Center on Aging, NORC/University of Chicago

For More Information and Updates Please Visit Our Scientific and Educational Website on Human Longevity:

http://longevity-science.org

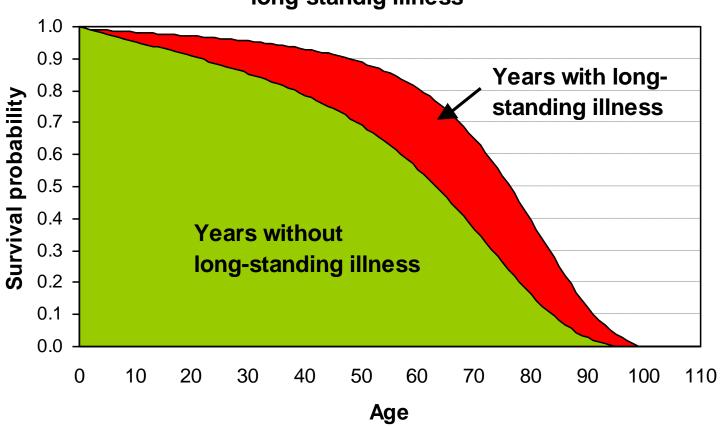
And Please Post Your Comments at our Scientific Discussion Blog:

http://longevity-science.blogspot.com/

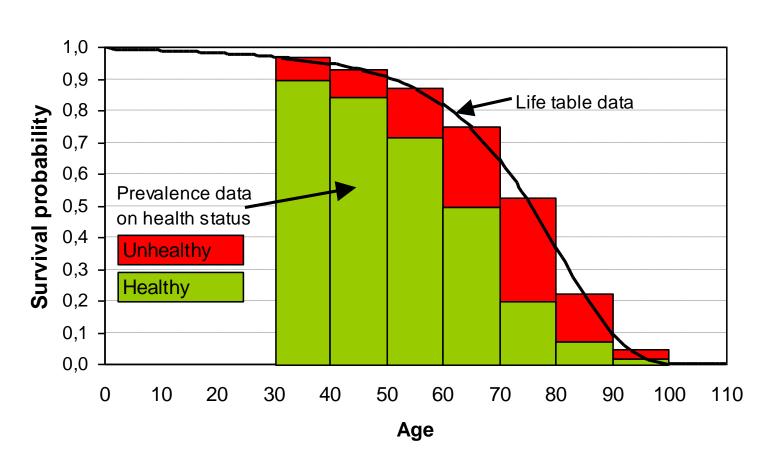
Ожидаемая продолжительность здоровой жизни и ее производные

Estimation of health expectancy by Sullivan's method

Life expectancy and expected lifetime with and without long-standig illness



Health expectancy by Sullivan's method

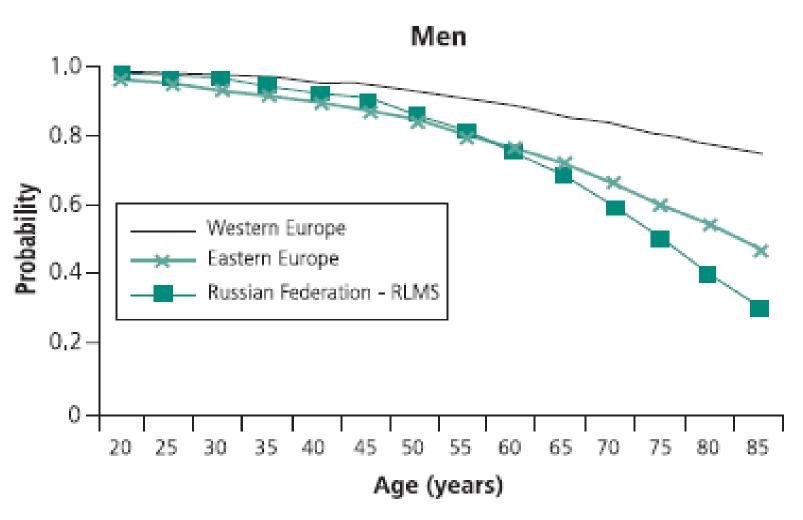


Calculation of health expectancy (Sullivan method)

$$\blacksquare \mathsf{L}_{\mathsf{X}}^{\mathsf{h}} = \mathsf{L}_{\mathsf{X}} \mathsf{X} \; \pi_{\mathsf{x}}$$

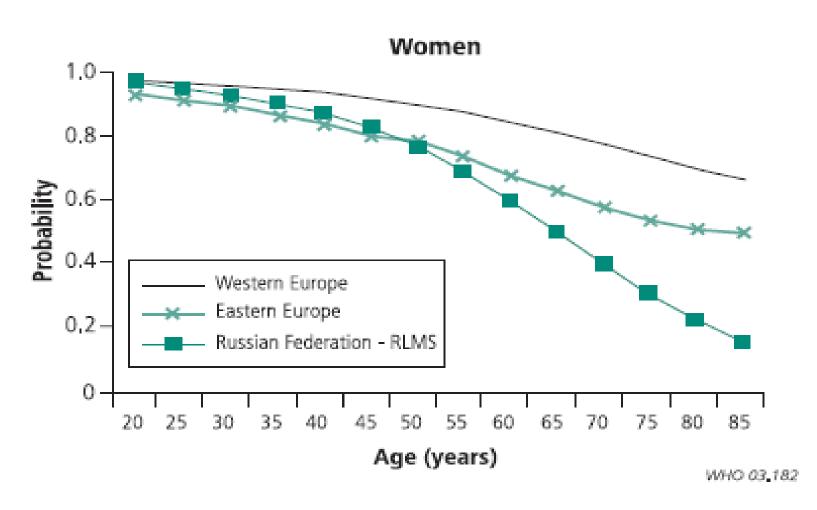
- Where π_x prevalence of healthy individuals at age x
- L_x^h person-years of life in healthy state in age interval (x,x+1)

Probability to be in good or excellent health



Andreyev et al., Bull.WHO, 2003

Probability to be in good or excellent health



Population surveys

- Provide more detailed information on specific topics compared to censuses
- Cover relatively small proportion of population (usually several thousand)
- Population-based survey random sample of the total population; represents existing groups of population

New trends in health surveys

Harmonization of surveys at world scale

Biomarker collection



Large-scale study of health and retirement of older Americans
Survey of more that 22000 Americans older than 55 years every 2 years.
Started in 1992

HRS-harmonizing studies

- UK English Longitudinal Study of Ageing (ELSA)
- Study on Health, Ageing and Retirement in Europe (SHARE)
- WHO Study on global AGEing and adult health (SAGE) including Russia
- Отдельные исследования в Мексике, Китае, Индии, Японии, Корее, Ирландии



Midlife in the United States

A National Study of Health & Well-Being

National survey conducted in 1994/95

7,189 Americans aged 25-74

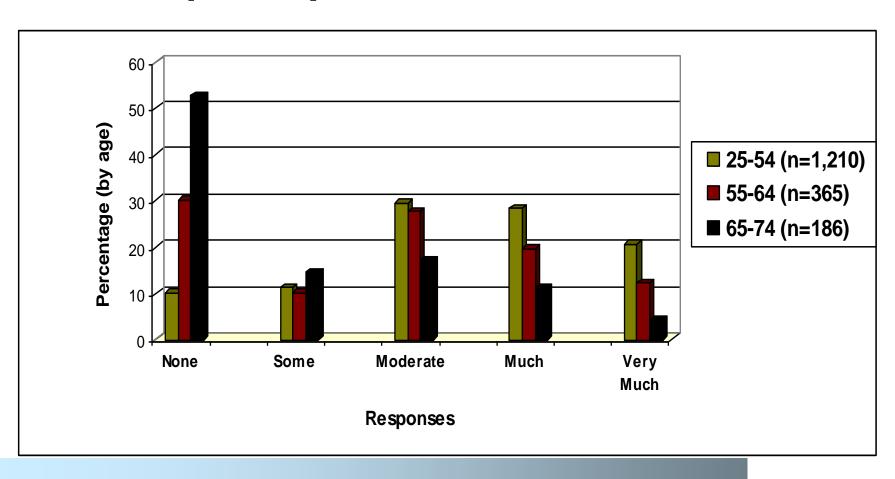
core national sample (N=3,485) city oversamples (N=957)

Strata: age, self-reported health status

Control variables: partner status, partner health, race, education

IS SEX IMPORTANT?

"How much thought and effort do you put into the sexual aspect of your life?"



How to Compare Sexual Activity Across Populations?

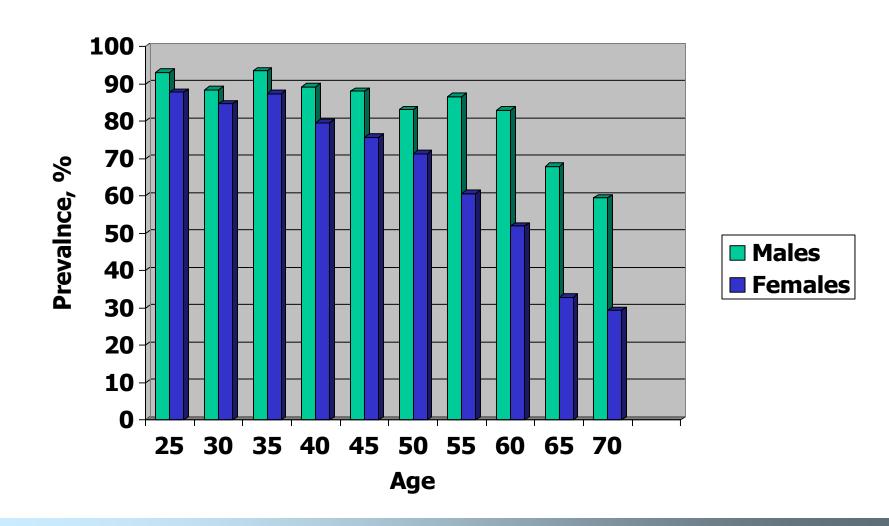
We suggest to use a new measure — Sexually Active Life Expectancy (SALE)

Calculated using the Sullivan method

Based on self-reported prevalence of having sex over the last 6 months (MIDUS and NSHAP studies)

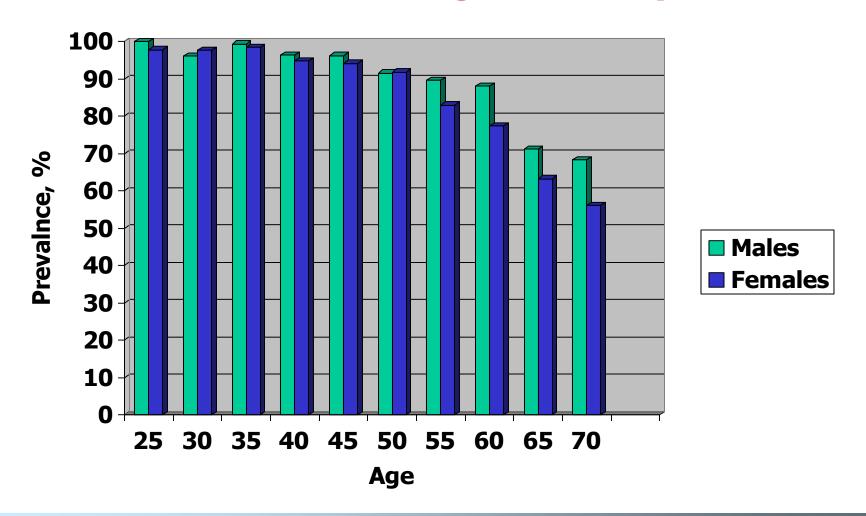
Life tables for the U.S. population in 1995 and 2003 (from Human Mortality Database)

Prevalence of Sexual Activity by Age and Gender (MIDUS 1)



Prevalence of Sexual Activity by Age and Gender (MIDUS 1)

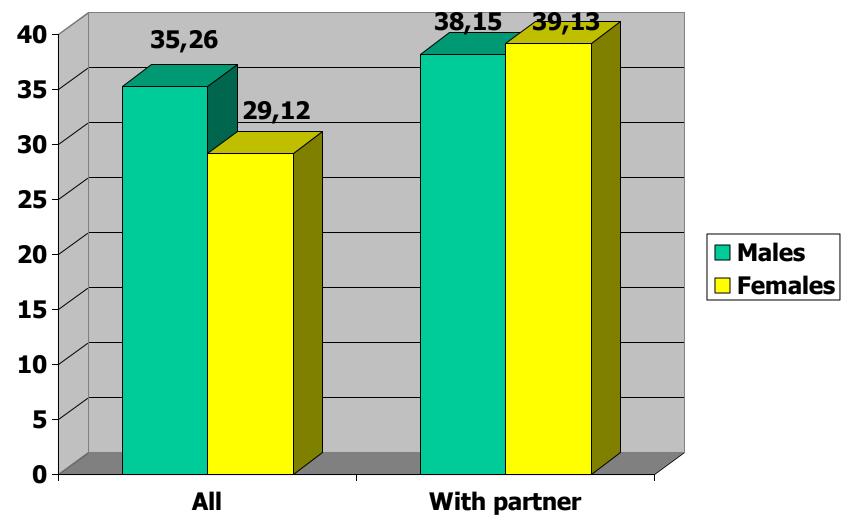
Men and women having intimate partner



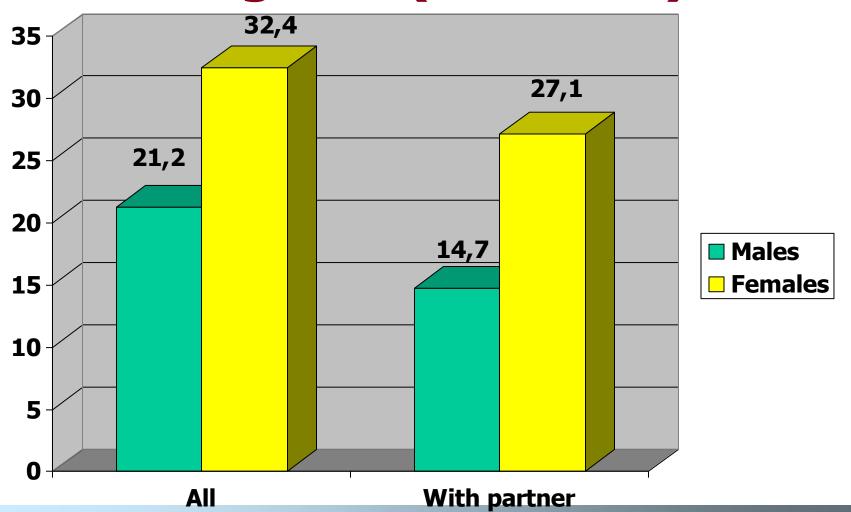
LE and SALE at Age 30 (MIDUS 1)



Sexually Active Life Expectancy at Age 30 (MIDUS 1)



Percent of Expected Life Without Sexual Activity at Age 30 (MIDUS 1)



Comparison with other surveys

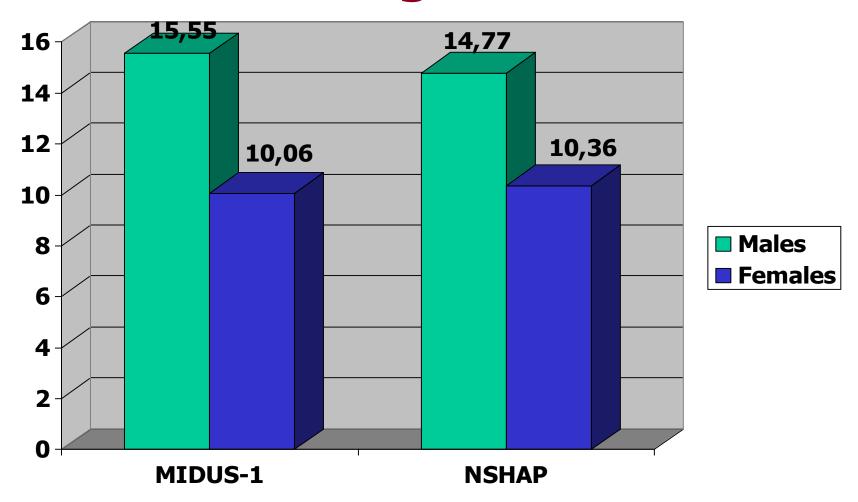
NSHAP - National Social Life, Health, and Aging Project, is an in-home survey of 3,000 persons aged 57 to 84 that collect biomarkers of health and physiological functioning to better characterize the health of survey participants. Rich source of data on sexuality at older ages.

MIDUS-2 – second wave of the MIDUS study conducted in 2004-2006

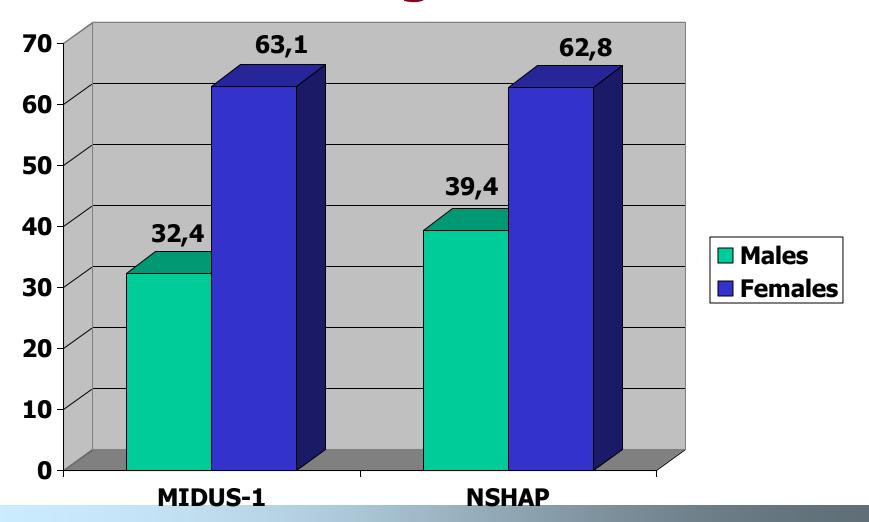
Introduction to:



Sexually Active Life Expectancy at Age 55



Percent of Expected Life Without Sexual Activity at Age 55



Publication on sexuality



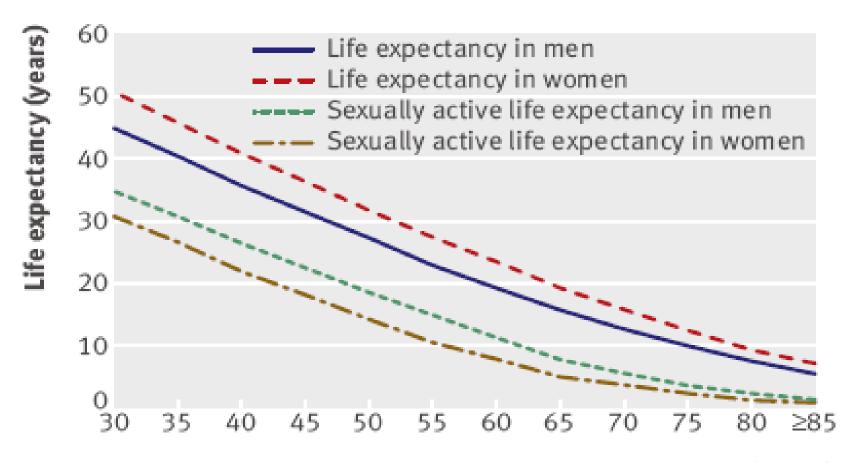
RESEARCH

Sex, health, and years of sexually active life gained due to good health: evidence from two US population based cross sectional surveys of ageing

Stacy Tessler Lindau, associate professor, 12 Natalia Gavrilova, senior research associate1

Lindau, Gavrilova, British Medical Journal, 2010, 340, c810

Life expectancy and sexually active life expectancy (SALE)



Age (years)

Based on the MIDUS study

Sexually active life expectancy and self-rated health



Conclusions

- Proportion of women having sex partner declines with age
- Amount of control over sexual aspect of life declines with age
- Self-rated physical health is higher among sexually active women
- Women have lower sexually active life expectancy compared to men