Gompertz 200. Celebrating Two Centuries of Longevity Research

Fifty Years of Research on the Gompertz Law: Key Insights and Lessons Learned

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

NORC at The University of Chicago
Chicago, Illinois, USA

Our brief self-introduction

This year marks the 50th anniversary of our scientific union

- We met as students at the Moscow State University (Chemistry department), Russia, and found a common interest in understanding the mechanisms of human aging, with a hope to find ways for extending healthy life.

- We were inspired by the scientific approach of Nobel laureate Nikolay Semyonov, who demonstrated that the mechanisms of chemical reactions can be studied through the clever quantitative analysis of reaction kinetics over time.

Moscow, March 14 ,1975

We decided to apply this approach to studies of aging and mortality by quantitative analysis of mortality kinetics (mortality laws). And the Gompertz law was the most important mortality law.

Our first publication in Journal of General Biology (1978) on reliability model explaining three empirical mortality laws

› Zh Obshch Biol. 1978 Sep-Oct;39(5):734-42.

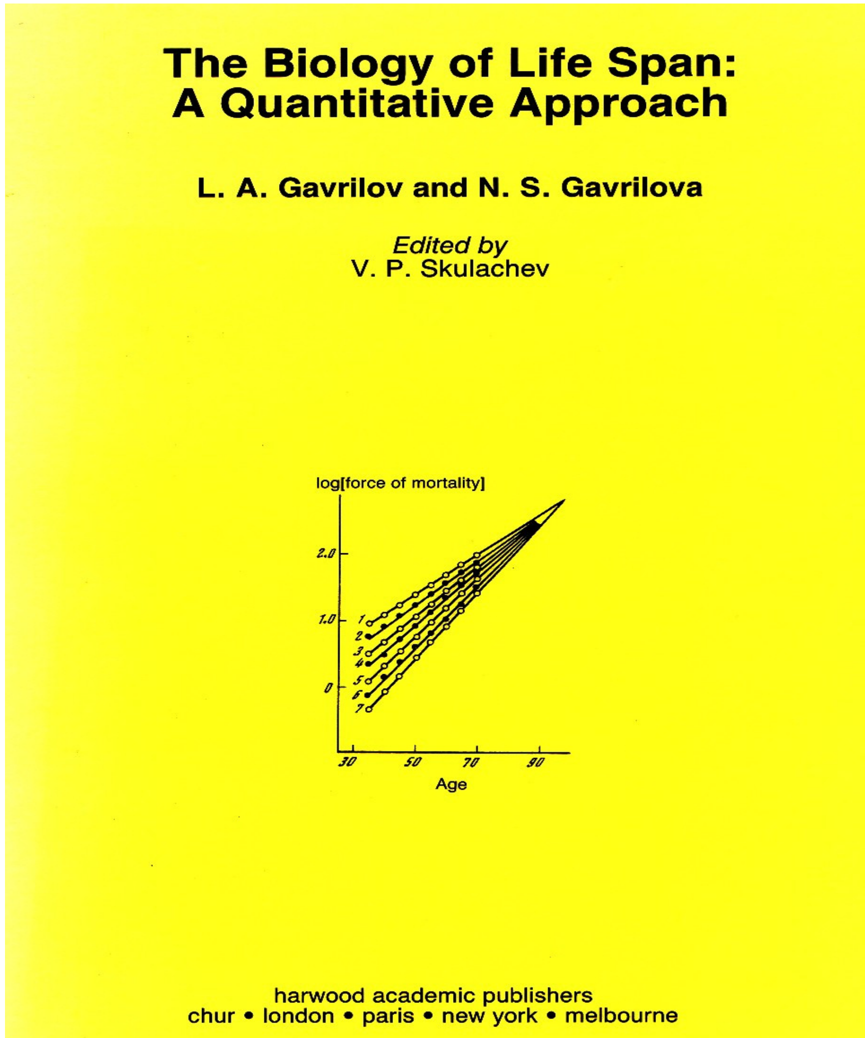
[Basic patterns of aging and death in animals from the standpoint of reliability theory]

[Article in Russian]

L A Gavrilov, N S Gavrilova, L S Iaguzhinskiĭ

PMID: 716614

This book published in 1991 summarized our earlier studies of the Gompertz law



The Gompertz Law

Risk of death increases exponentially with age.

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

R – intercept coefficient (in semi-log scale)

α – slope coefficient (in semi-log scale)

x - age

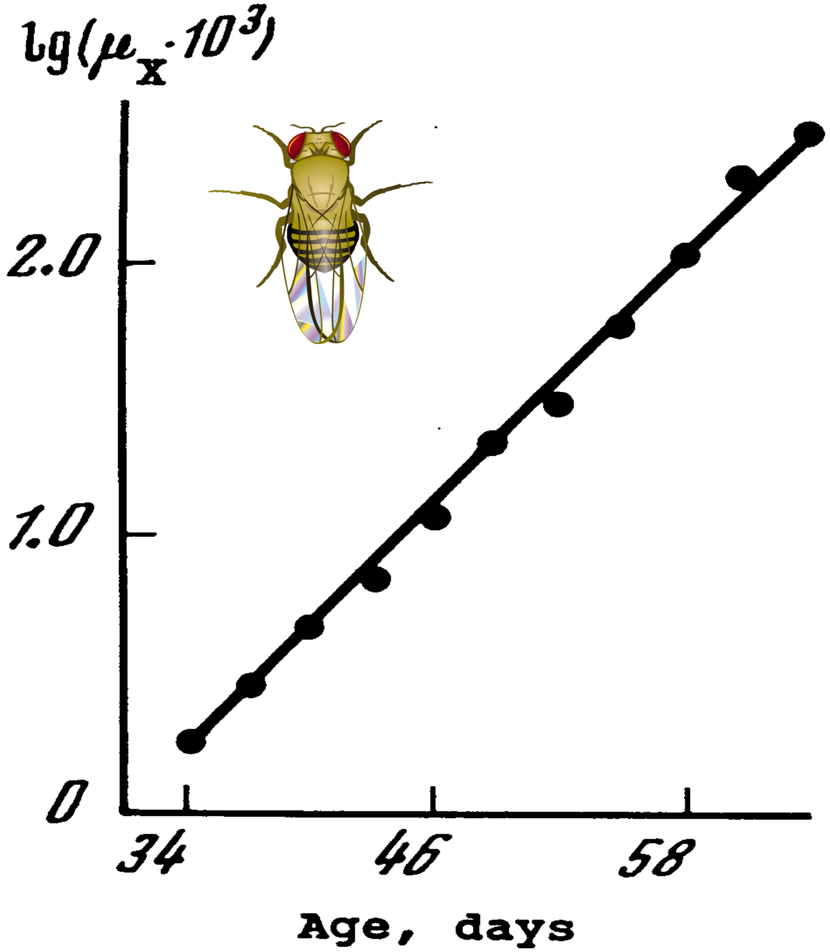
Our “Zoo of Death”

Collection of published life tables for various species

Collection of human complete life tables

We believe that this collection inspired John Wilmoth to create his Berkeley Mortality Database (later transformed to the Human Mortality Database)

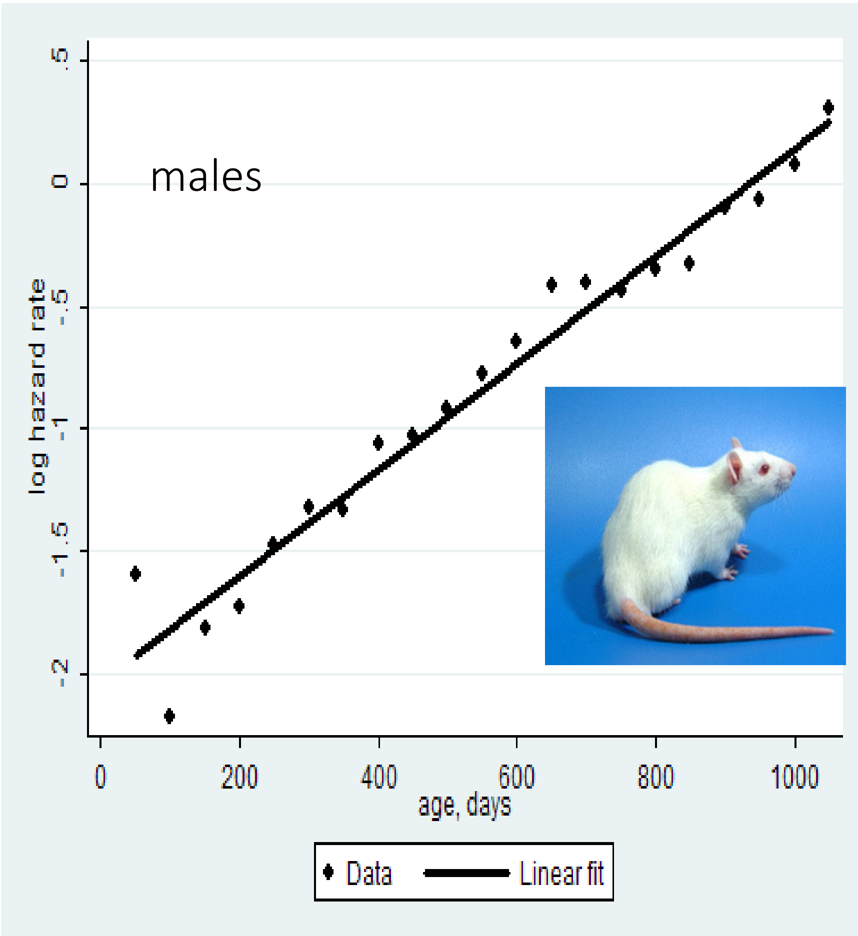
Gompertz Law of Mortality in Fruit Flies

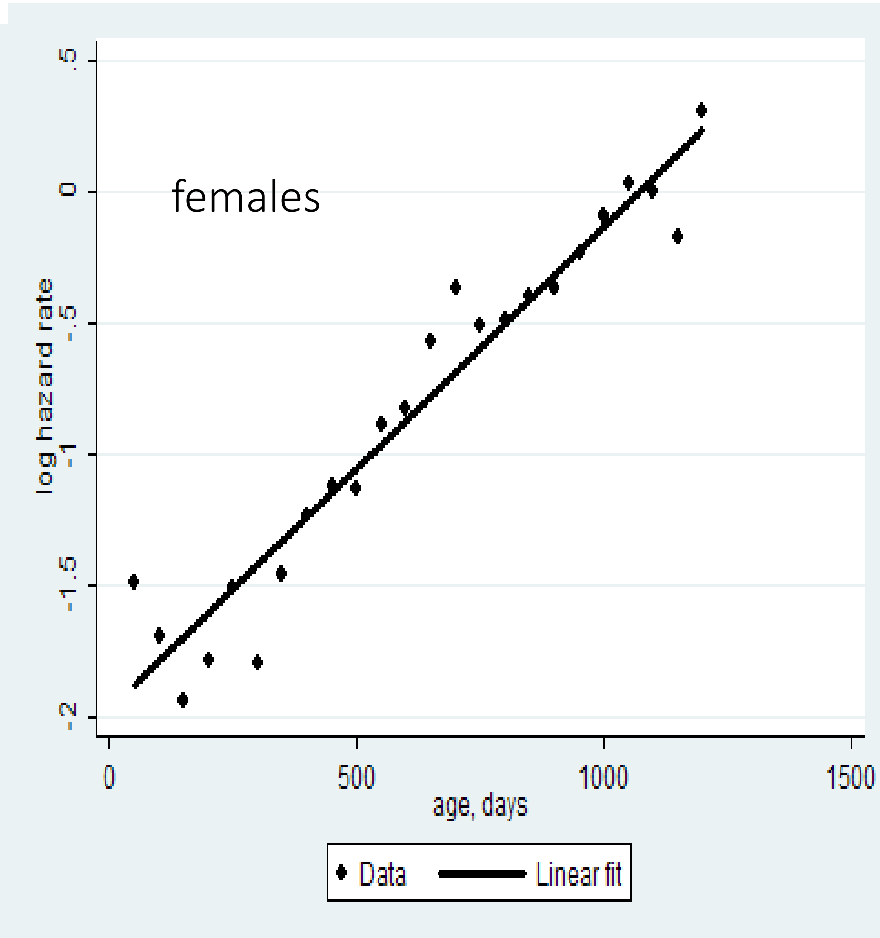


Based on the life table for 2400 females of *Drosophila melanogaster* published by Hall (1969).

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

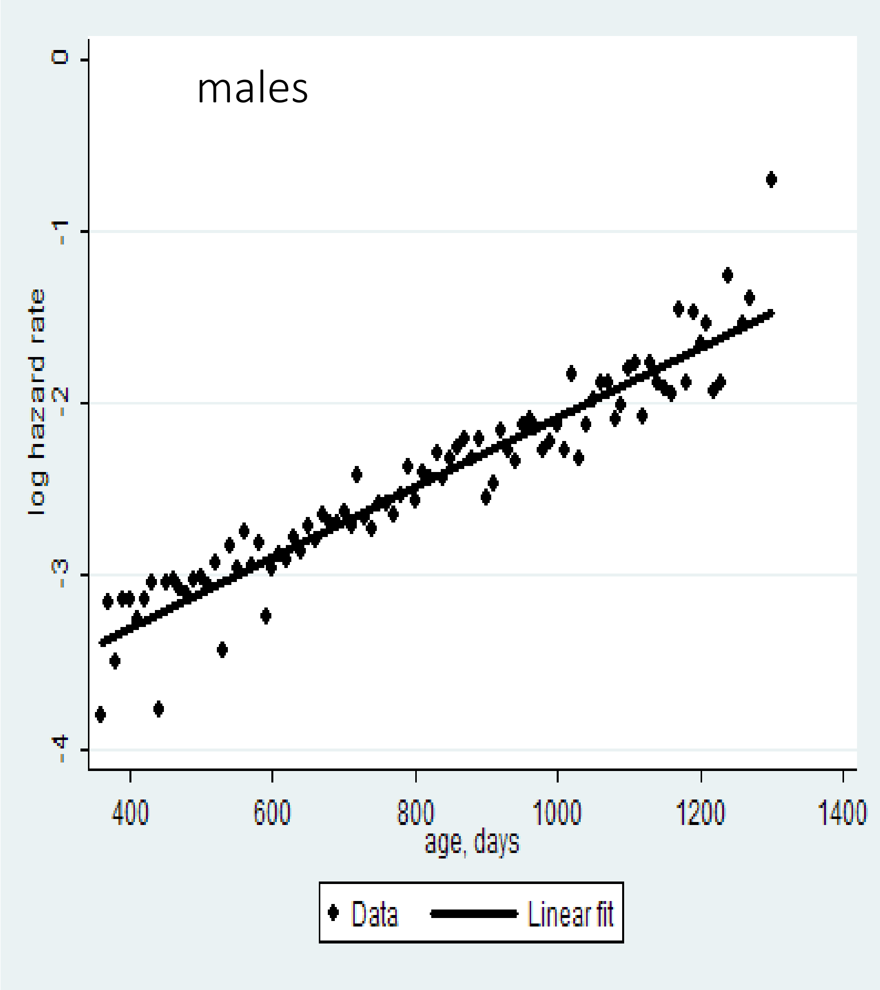
Mortality of Wistar rats

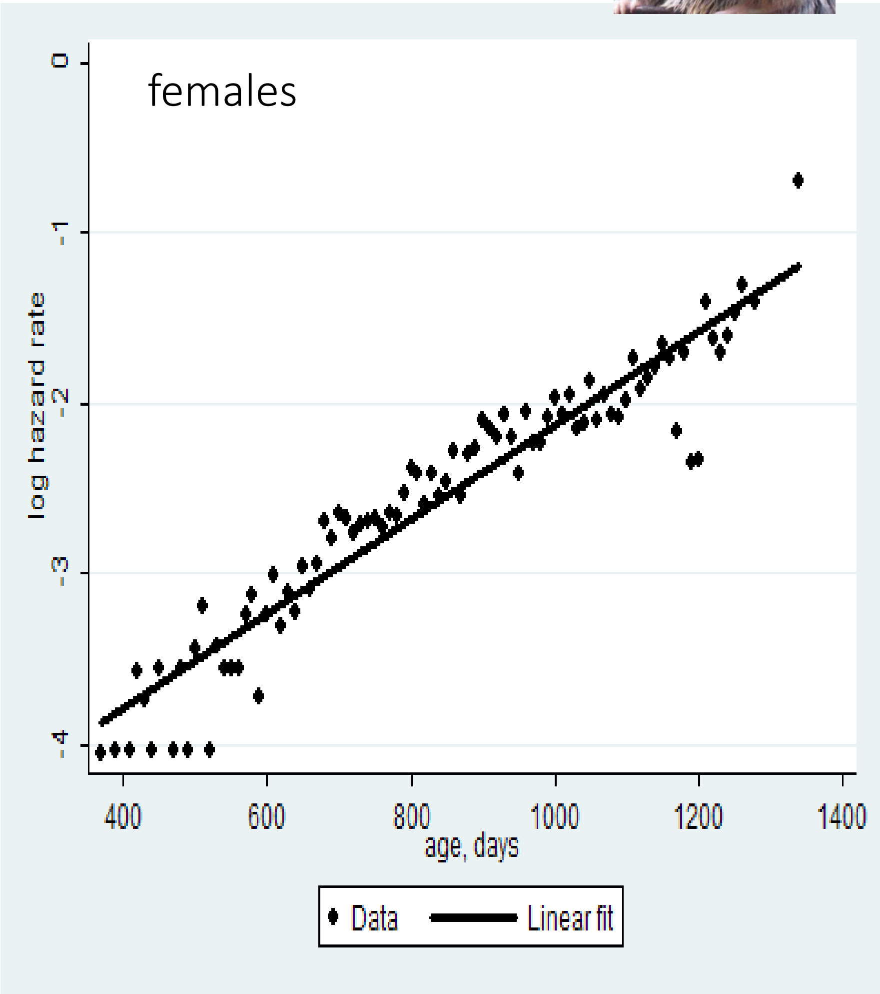




- Actuarial estimate of hazard rate with 50-day age intervals
- Data source: Weisner, Sheard, 1935

Mortality of mice (log scale)
Miller data





- **Actuarial estimate of hazard rate with 10-day age intervals**

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. Important for historical human data.

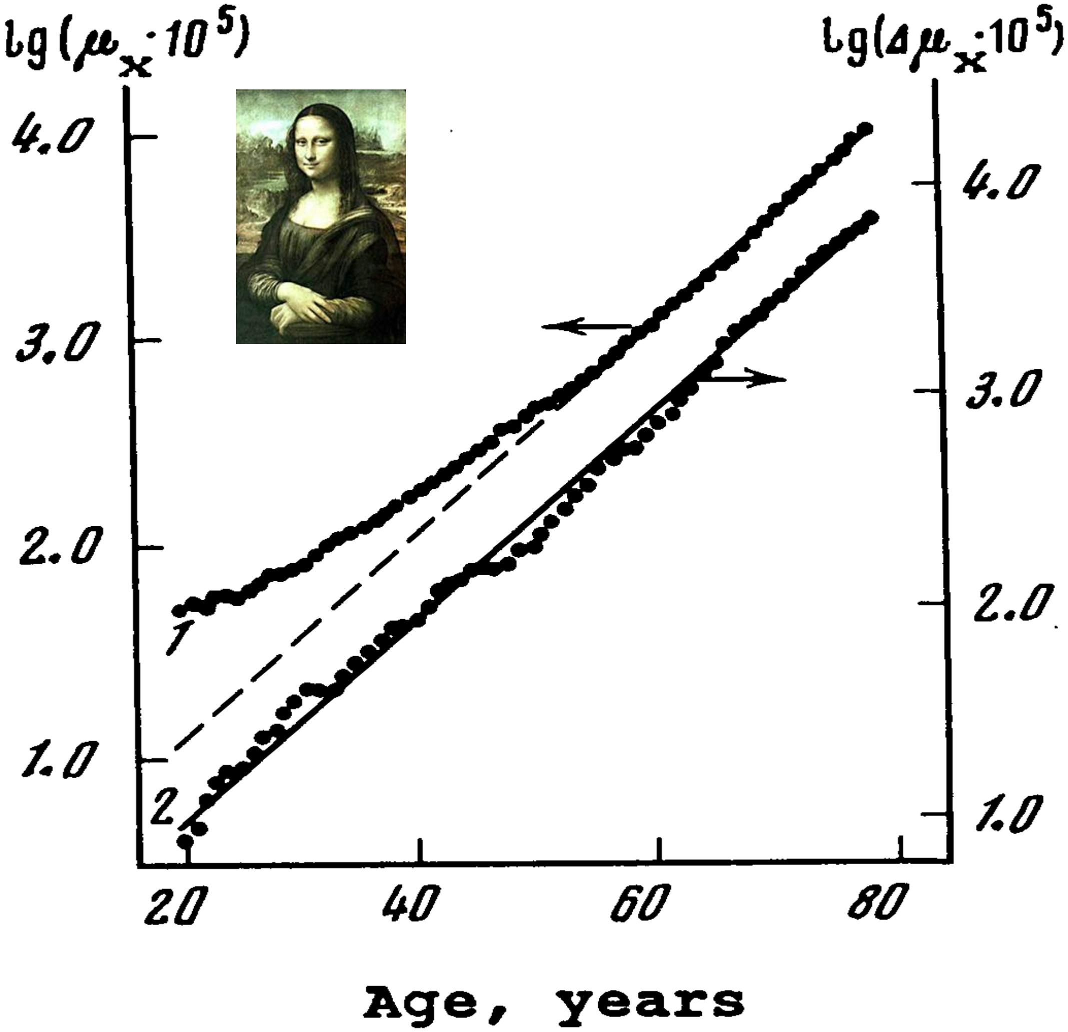
$$\mu(x) = A + R e^{ax}$$

risk of death

A – Makeham term or background mortality

$R e^{ax}$ – age-dependent mortality; x - age

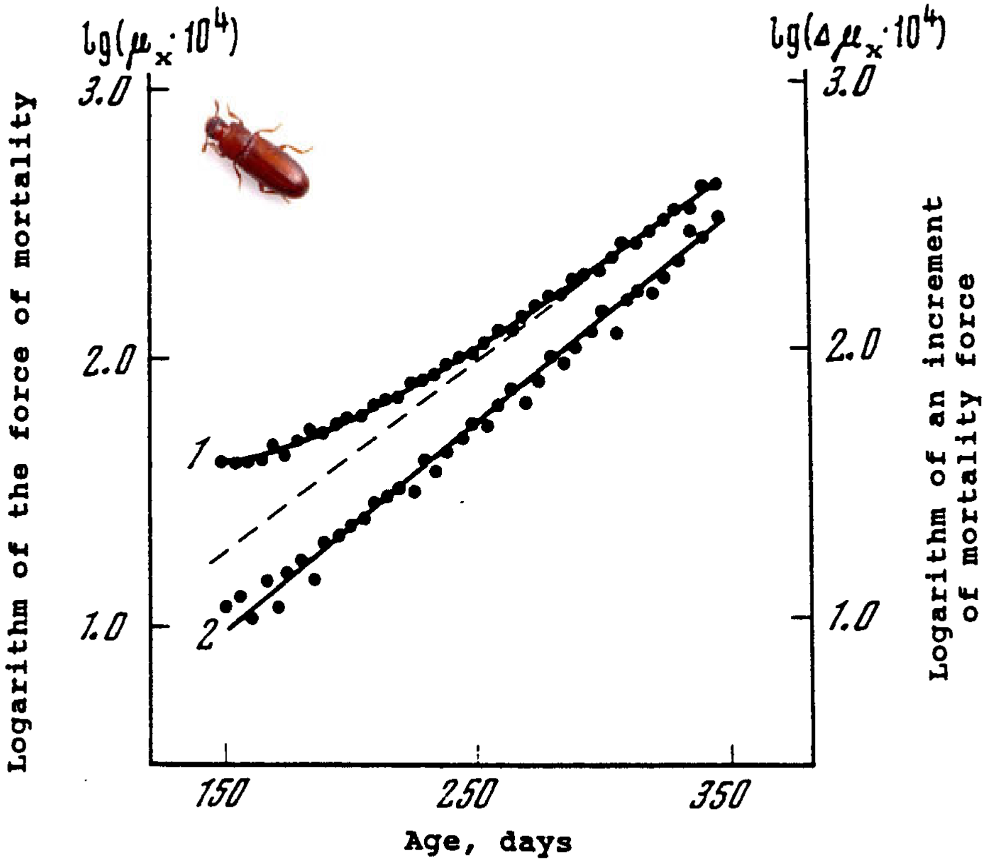
Gompertz-Makeham Law of Mortality in Italian Women



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

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

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

Comparison of Gompertz law with competing Weibull mortality law

Statistical analysis of 290 human populations and 129 life tables of fruit flies revealed that the Gompertz law describes mortality better than competing Weibull law used to fit failure rates of technical systems (Gavrilov, Gavrilova, 1991).

The Strehler-Mildvan Correlation (*Science*, 1960): Inverse correlation between the Gompertz parameters

Limitation: Did not take into account the Makeham parameter that leads to spurious correlation.

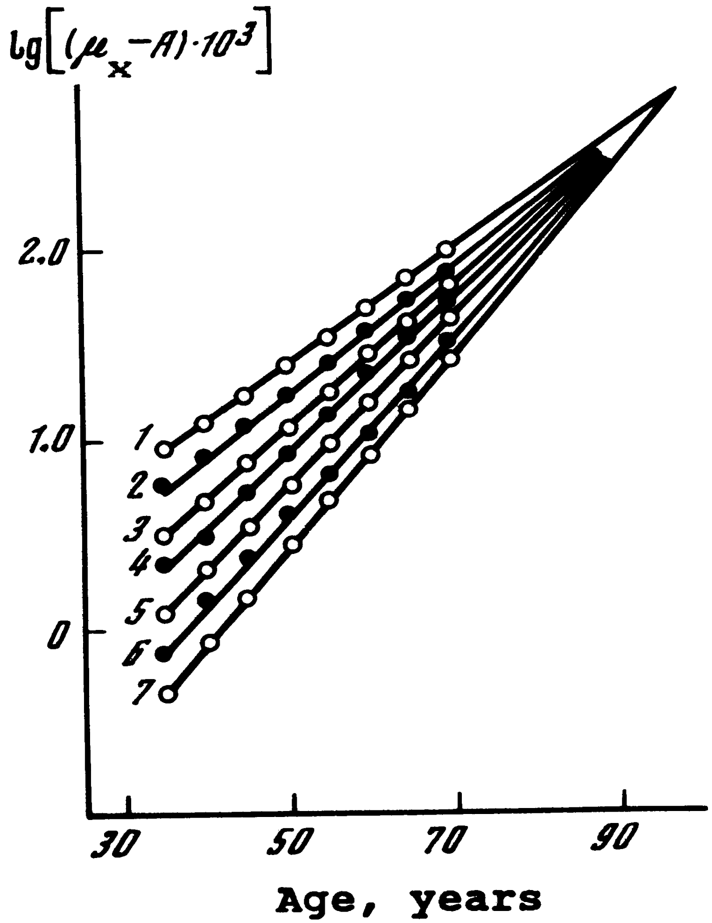
Our simulation study showed that this correlation was caused by varying values of the Makeham term

The Second Mortality Law: Compensation Law of Mortality (late-life mortality convergence)

In 1978, we described the phenomenon of the compensation effect of mortality, where Gompertz mortality trajectories tend to converge in semi-logarithmic coordinates around age 95.

Compensation Law of Mortality

Convergence of Mortality Rates with Age

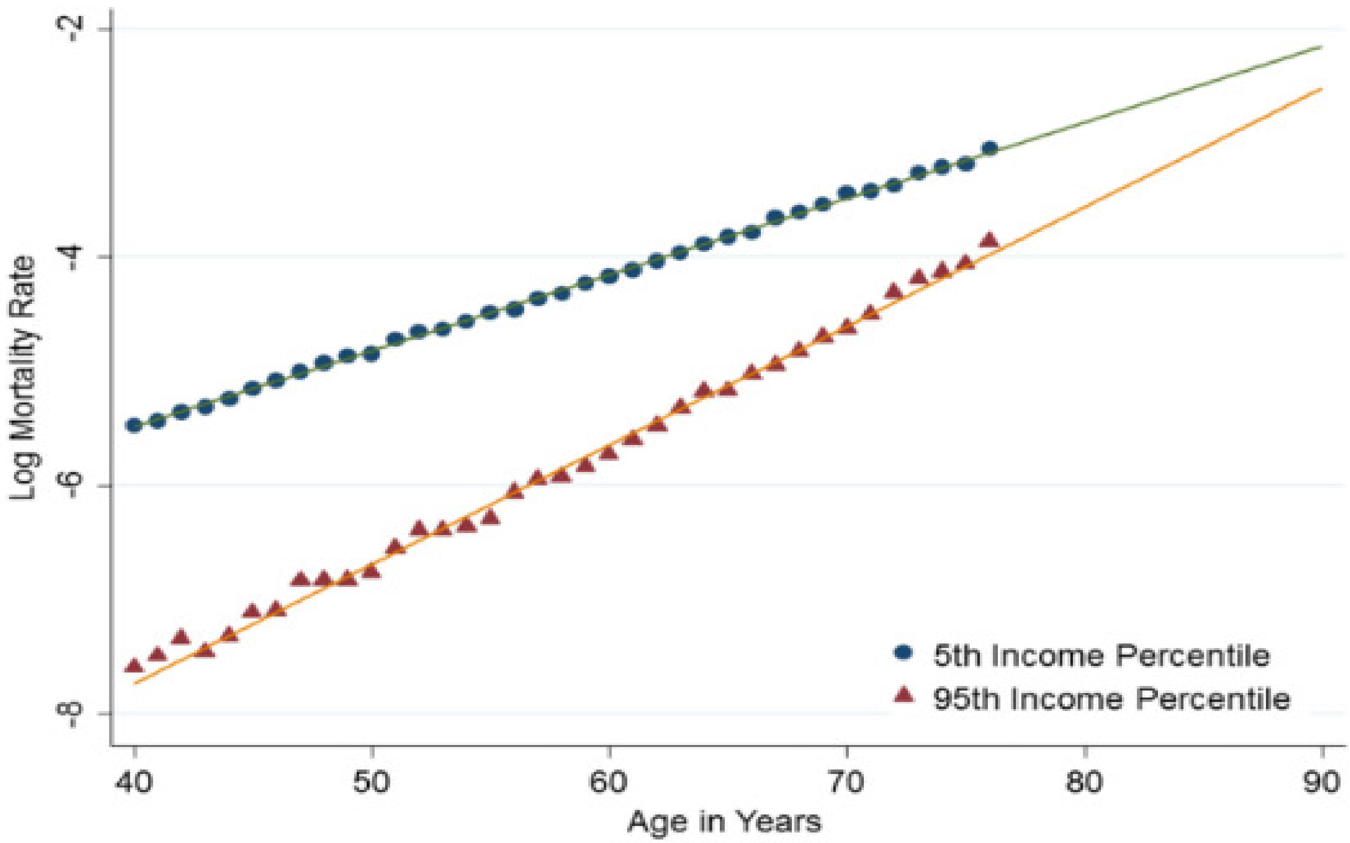


1 – India, 1941-1950, males
2 – Turkey, 1950-1951, males
3 – Kenya, 1969, males
4 - Northern Ireland, 1950-1952, males
5 - England and Wales, 1930-1932, females
6 - Austria, 1959-1961, females
7 - Norway, 1956-1960, females

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

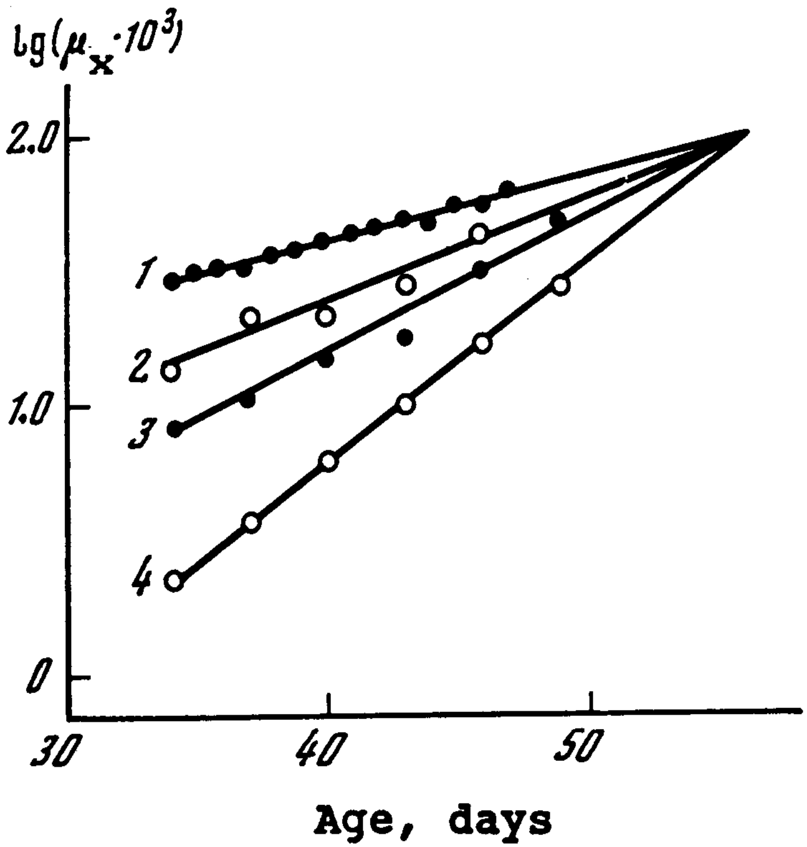
Compensation Law of Mortality

The Association Between Income and mortality of men in the United States, 2001-2014



Source: Chetty et al., JAMA. 2016;315(16):1750-1766. doi:10.1001/jama.2016.4226

Compensation Law of Mortality in Laboratory *Drosophila*



1 – drosophila of the Old Falmouth, New Falmouth, Sepia and Eagle Point strains (1,000 virgin females)

2 – drosophila of the Canton-S strain (1,200 males)

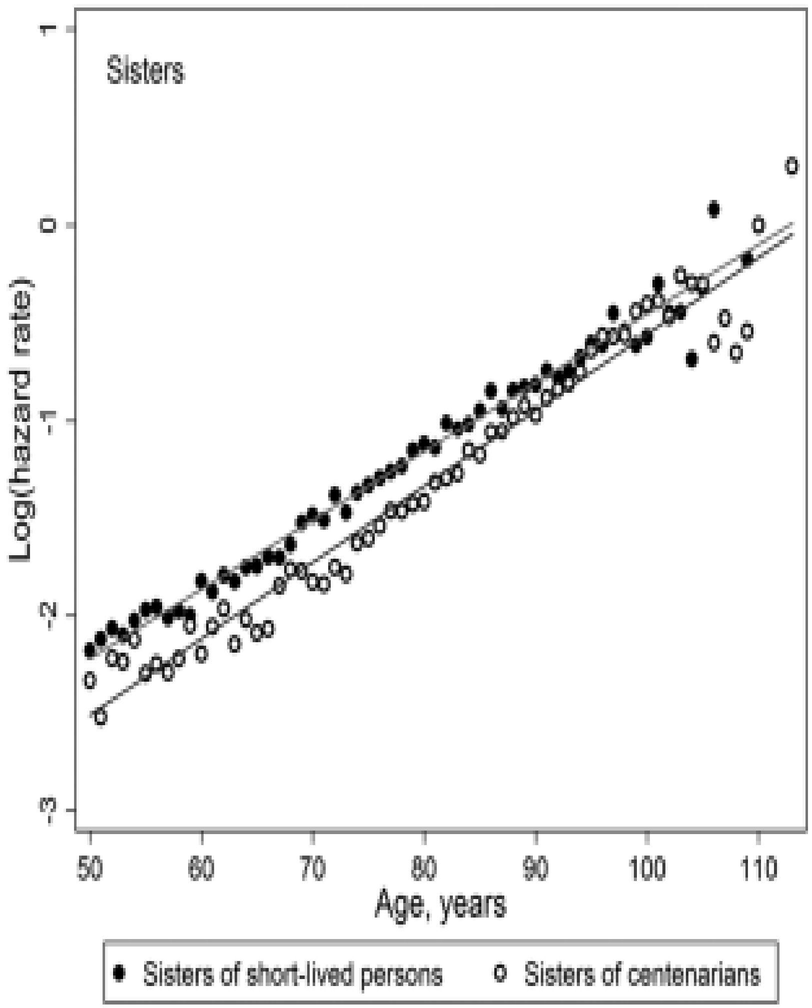
3 – drosophila of the Canton-S strain (1,200 females)

4 - drosophila of the Canton-S strain (2,400 virgin females)

Mortality force was calculated for 6-day age intervals.

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

Compensation effect of mortality is a challenge to life extension



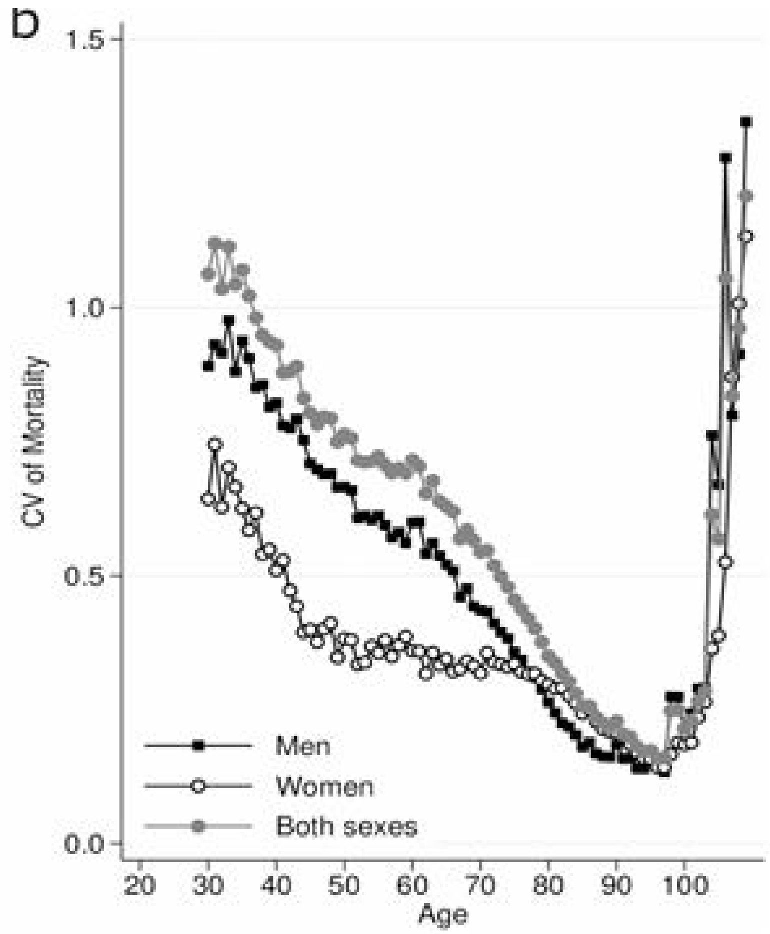
Even familial longevity does not help to decrease mortality after age 100 years.

Source: Gavrilova N.S., Gavrilov L.A. Protective Effects of Familial Longevity Decrease With Age and Become Negligible for Centenarians. Journal of Gerontology – Series A, 2022, Vol.77(4): 736-743.

Some researchers challenged this finding, suggesting that the effect was merely an artifact of spurious correlation between biased estimates of Gompertz parameters (Tarkhov, 2017).

However, our recent studies confirmed the existence of the compensation effect, with the convergence point aligning with minimal mortality variation.

The age of convergence point called the species-specific lifespan did not change over the last 50 years and is equal to 95-98 years (Gavrilov et al., 1978, Gavrilov, Gavrilova, 2022, Milevsky, 2020)



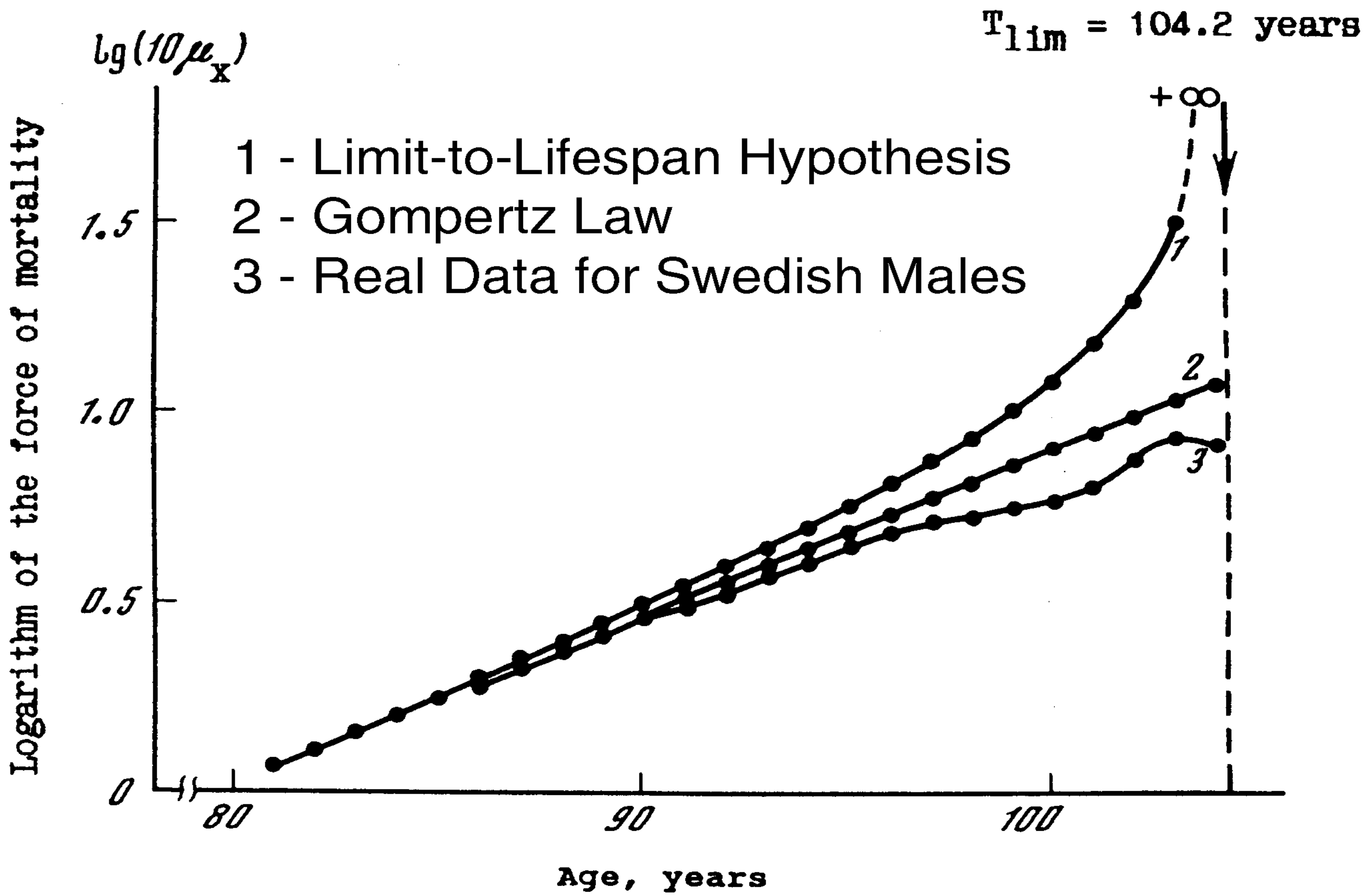
Mortality data for 44 human populations.
Data Source: Human Mortality Database
Source: Gavrilova, Gavrilov, Biogerontology, 2024

The Third Mortality Law: The Late-Life Mortality Deceleration

(Mortality Leveling-off, Mortality Plateaus)

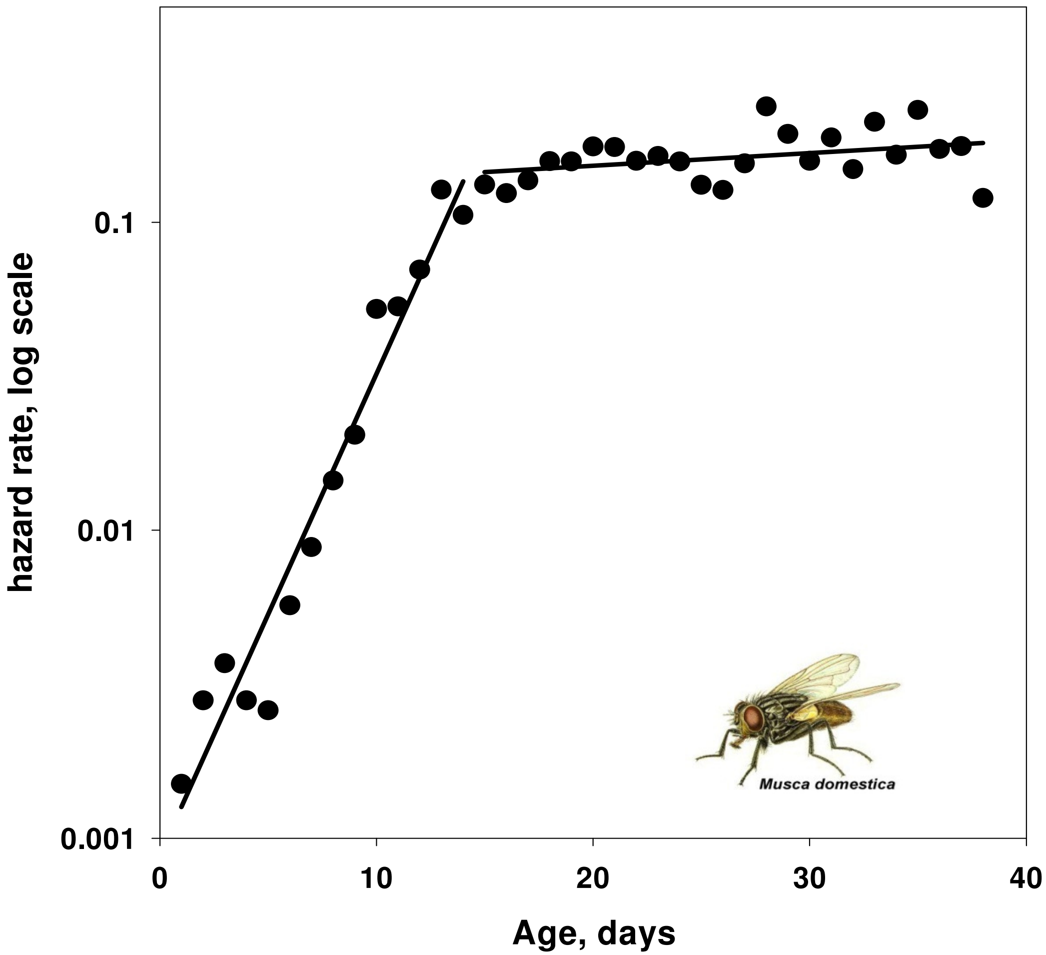
In our 1991 book "The Biology of Life Span", we described the phenomenon of late-life mortality deceleration, where mortality rates deviate downwards from the Gompertz law at very advanced ages.

Testing the “Limit-to-Lifespan” Hypothesis



Source: **Gavrilov L.A., Gavrilova N.S. 1991. *The Biology of Life Span***

Mortality Leveling-Off in House Fly
Musca domestica



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

Studies by demographers after 1991

This concept gained significant attention among demographers in the 1990s. Some demographers believed that they can present mortality deceleration as a kind of their discovery. They published articles on mortality deceleration for insects and humans.

They wrote literally the following: "Mortality deceleration came as a surprise, indeed as a shock, to many biologists and gerontologists..." *Between Zeus and the Salmon*, 1997, p.25

This is despite extensive publications by gerontologists G. Sacher and A. Economos on mortality deceleration in the 1960s and 1970s.

Earlier studies by actuaries (Perks, Beard) were not cited either.

We decided to inform the scientific community at the 2003 International Symposium “Living to 100”

HUMAN BIOLOGY

a record of research

FEBRUARY, 1939

VOL. 11 No. 1

THE BIOSTATISTICS OF SENILITY

BY MAJOR GREENWOOD AND J. O. IRWIN

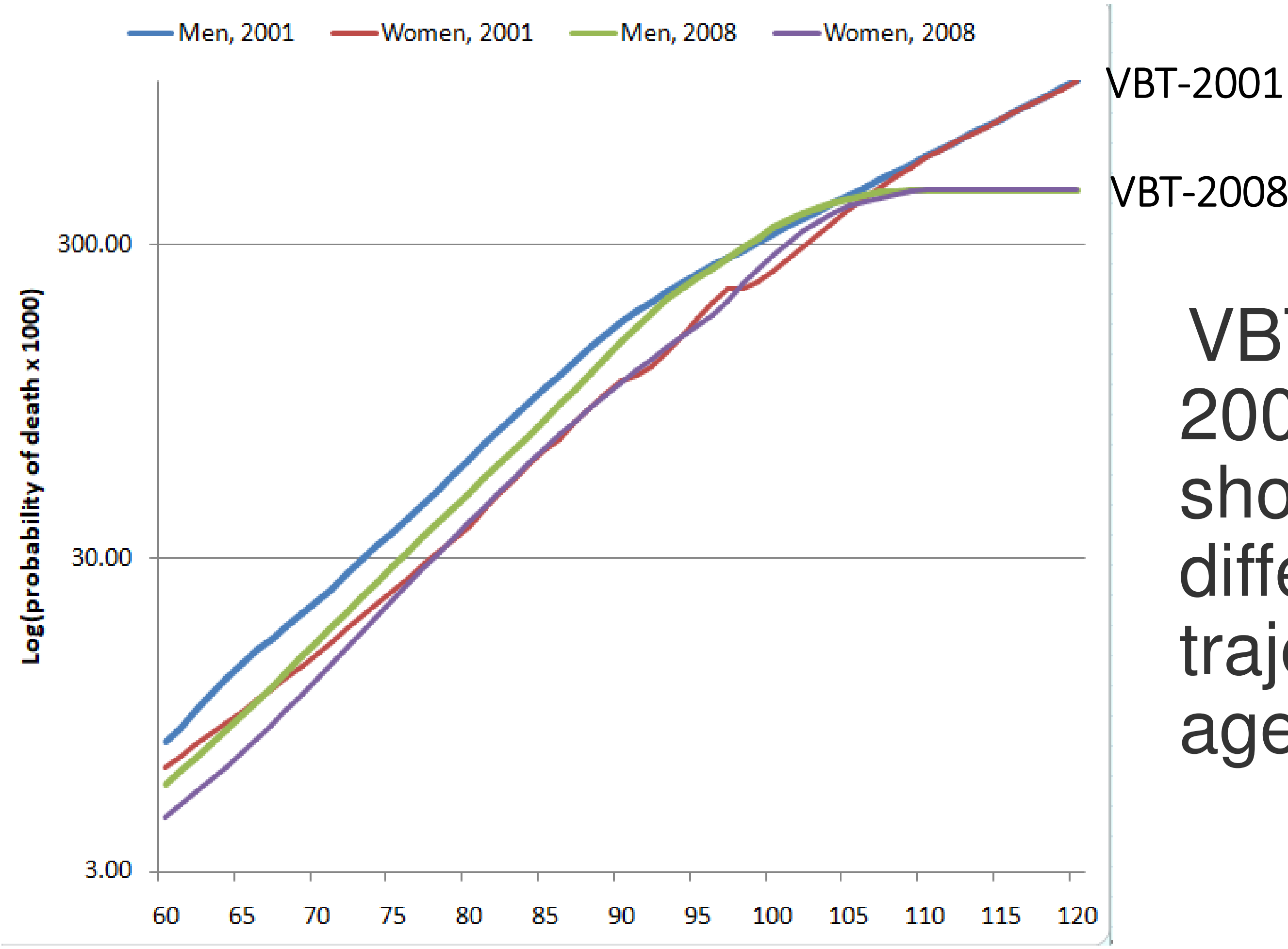
M. Greenwood, J. O. Irwin. BIOSTATISTICS OF SENILITY

" 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_ω are 0.439 for women and 0.544 for men. Some tests of the ultimate mortalities in non-human experience were not unfavorable. "

Mortality in Valuation Basic Tables (VBT) for Non-Smokers by the Society of Actuaries



VBT tables in 2001 and 2008 show totally different trajectories after age 100 years

Further Developments

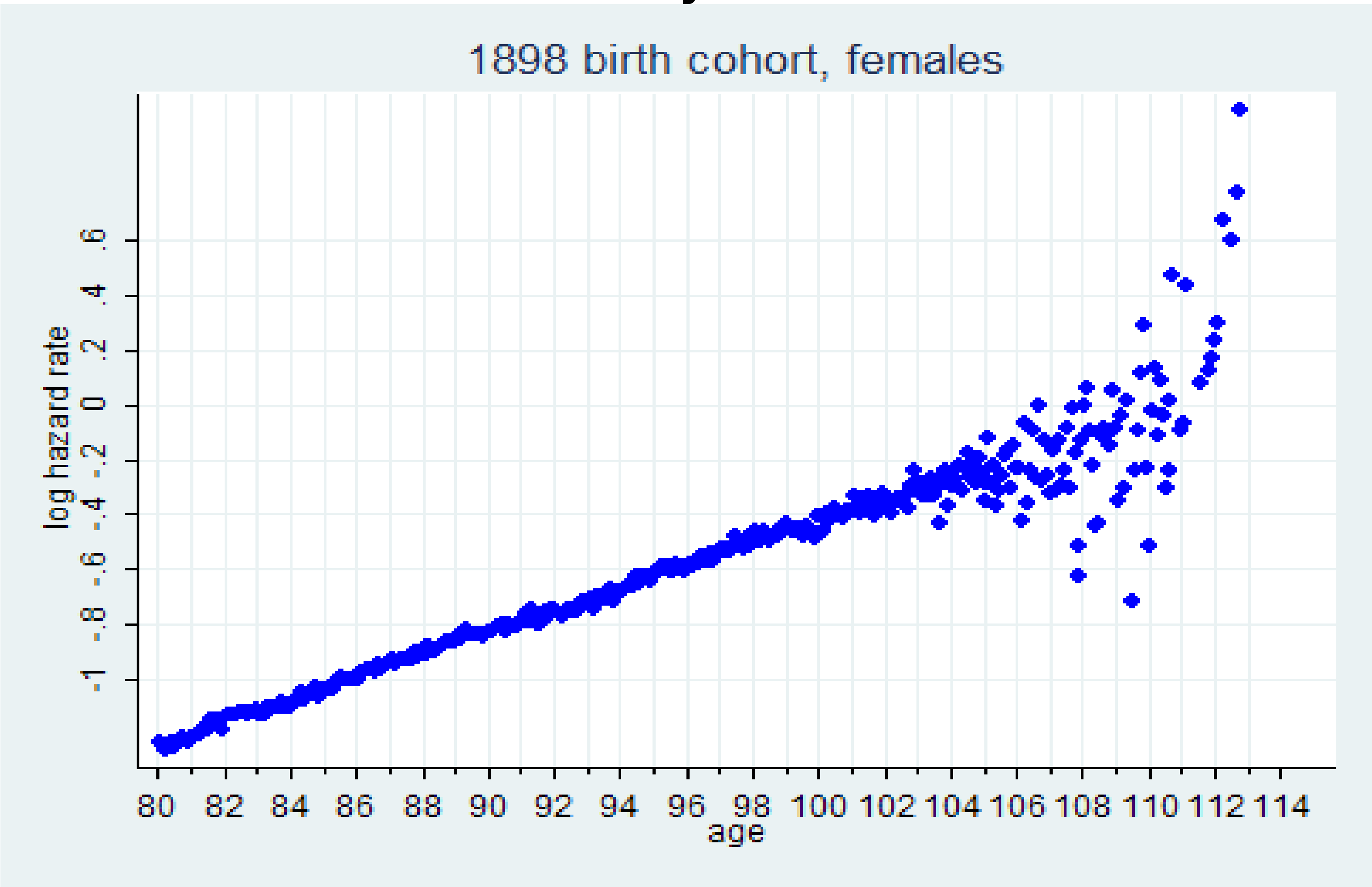
A Study of Extinct Birth Cohorts in the United States (2004)

Data from the Social Security Death Index. In 2004 it was publicly available on website. We collected data using web fetching technique

Later the last complete version of SSA Death Master File was officially obtained from the U.S. National Technical Information Service (NTIS)

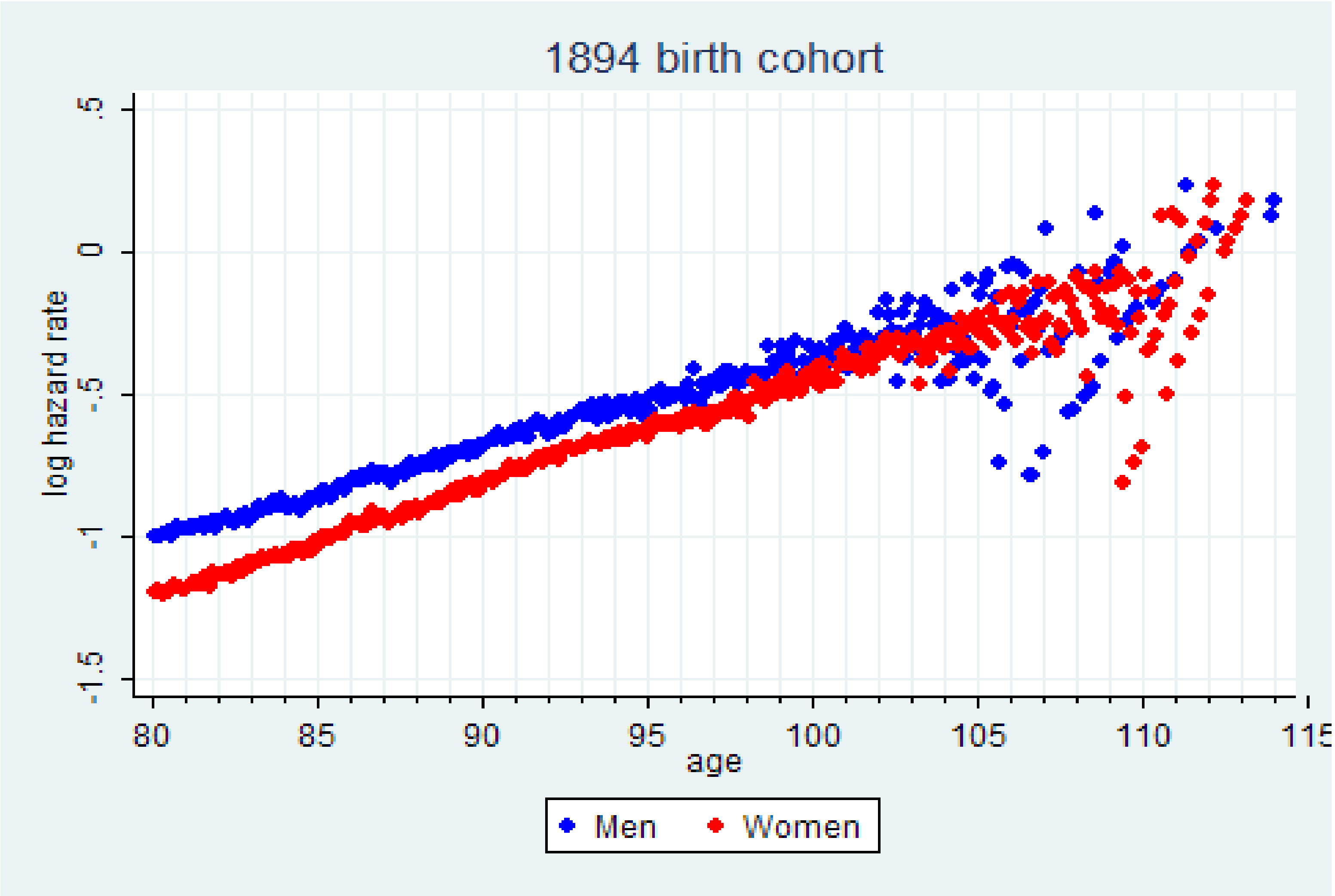
Birth cohort mortality, SSA Death Master File (DMF) data

Where is Mortality Deceleration?



Nelson-Aalen monthly estimates of hazard rates using Stata 11

Mortality of men and women converge at very old age



Gompertz model of old-age mortality

Study of 20 single-year extinct U.S. birth cohorts based on the Social Security Administration Death Master File (DMF) found no mortality deceleration up to ages 105-106 years (Gavrilova, Gavrilov, 2011).

However, data quality problems did not allow us to study mortality trajectories after age 107 or 110 years using this source of data.

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

Featured in the Wall Street Journal:

THE WALL STREET JOURNAL.
WSJ.com

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

Death Gets in the Way of Old-Age Gains

By CARL BIALIK

The second studied dataset: U.S. cohort death rates taken from the Human Mortality Database, our 2014 study

Journals of Gerontology: BIOLOGICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci
doi:10.1093/gerona/glu009

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Biodemography of Old-Age Mortality in Humans and Rodents

Natalia S. Gavrilova and Leonid A. Gavrilov

Center on Aging, NORC at the University of Chicago, Chicago, Illinois.

Address correspondence to Natalia S. Gavrilova, PhD, Center on Aging, NORC at the University of Chicago, 1155 East 60th Street, Chicago, IL 60637.
Email: gavrilova@longevity-science.org

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

Problem of mortality estimation at older ages

Age misreporting

Study by Preston group found that age misreporting results in spurious mortality deceleration

Hypothesis

Mortality deceleration at advanced ages among old DMF cohorts (born before 1886) 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

What is the quality of age reporting in SSA Death Master File across ages and birth cohorts?

Our 2018 study of data quality for five single-year birth cohorts

Supported by the Society of Actuaries

More details are available in a special report by the SOA

SOCIETY OF ACTUARIES®

Study Design

Five single-year birth cohorts:
1898, 1899, 1900, 1901, 1902

Direct age validation of DMF samples randomly selected at ages 100, 103, 105 and 109+ years

Sample sizes: 100 records for ages 100-105 years
For age group 109+ years – all records

Age validation procedure

Age validation was conducted by linkage of DMF records to early historical sources (U.S. censuses, birth and marriage records, draft registration cards).

DMF records were scored according to reliability of age reporting. The scoring system included the following scores:

1 – several early historical sources agree about birth date

2 – one early historical sources agrees about birth date

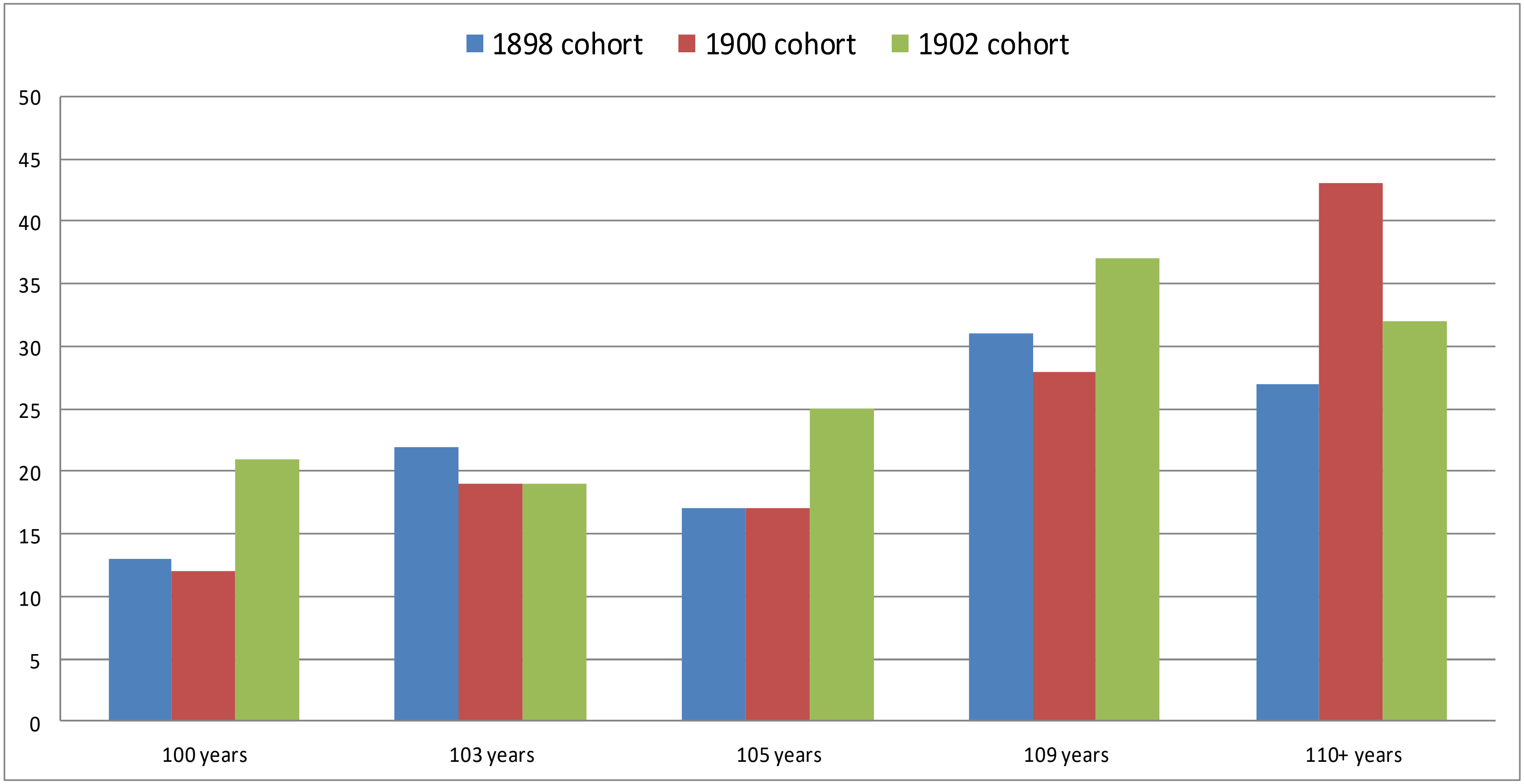
3 – later sources agree about birth date

4 – early sources disagree

5 – foreign-born individual arrived in the U.S. later in life

6 – not found in any sources

Percent of records with questionable quality as a function of age. 1898, 1900 and 1902 birth cohorts



Results of age validation study for samples of 100 records, by age group.

For ages 109 and 110+ years sample sizes were slightly higher than 100.

Further development

Direct age validation of all records at ages 105 and over for those born in 1900, our 2019 study

PLOS | BIOLOGY

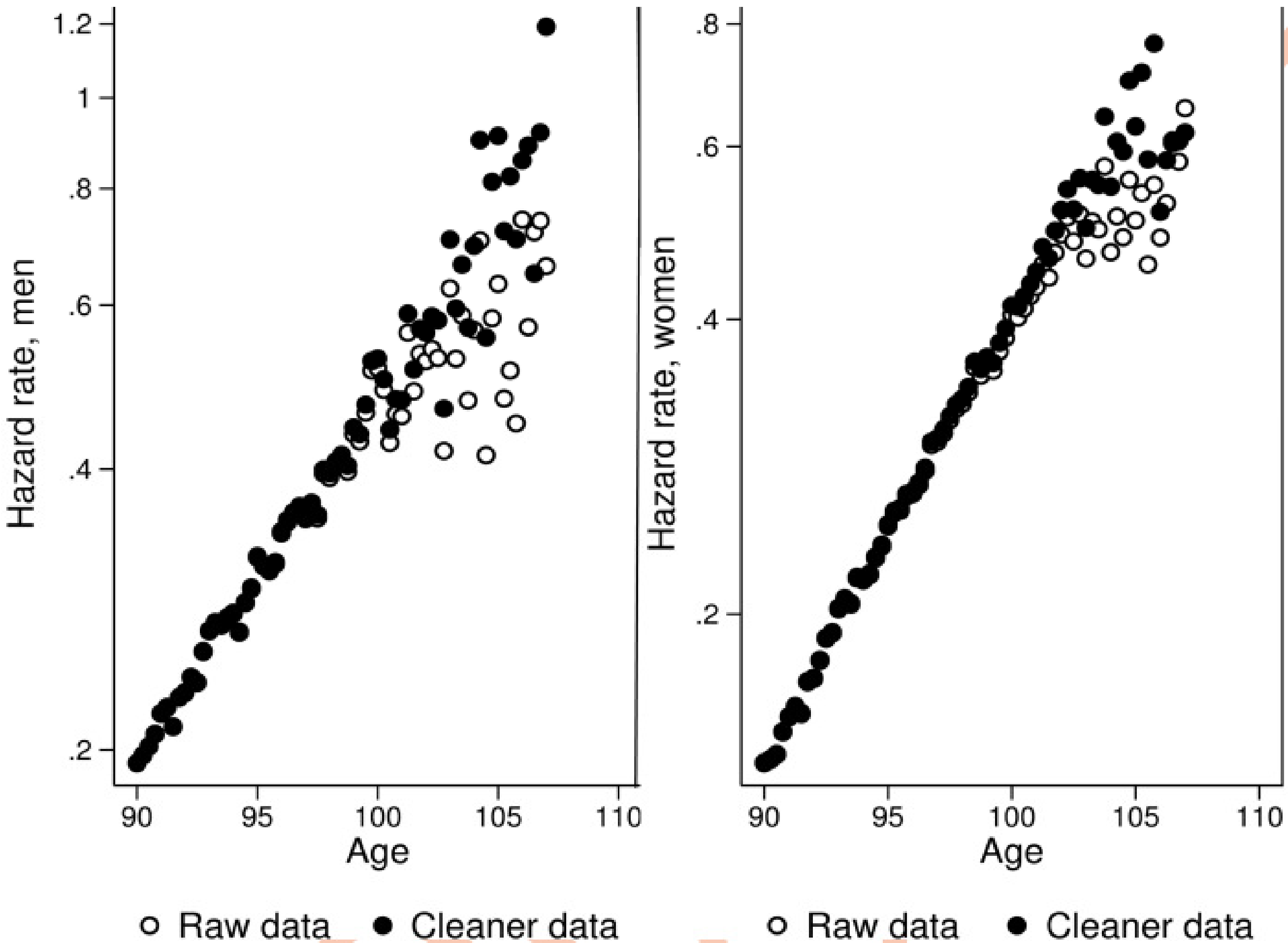
PRIMER

Late-life mortality is underestimated because of data errors

Leonid A. Gavrilov*, **Natalia S. Gavrilova**

NORC at the University of Chicago, Chicago, Illinois, United States of America

Mortality of U.S. men (left) and women (right) born in 1900 before and after data cleaning



Source: Gavrilov, Gavrilova, PLOS Biology, 2019.

Data: 1900 DMF birth cohort cleaned after age 104 years of age using linkage to historical documents

Conclusion:

Age misreporting produces spurious mortality deceleration

Hypothesis

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

If this hypothesis is correct then mortality deceleration should be more prevalent among historically older birth cohorts

In 2019 we found a new trend in old-age mortality using U.S. cohort data: Transition from mortality deceleration to the Gompertz trajectory

Of General Interest / Viewpoint

Gerontology

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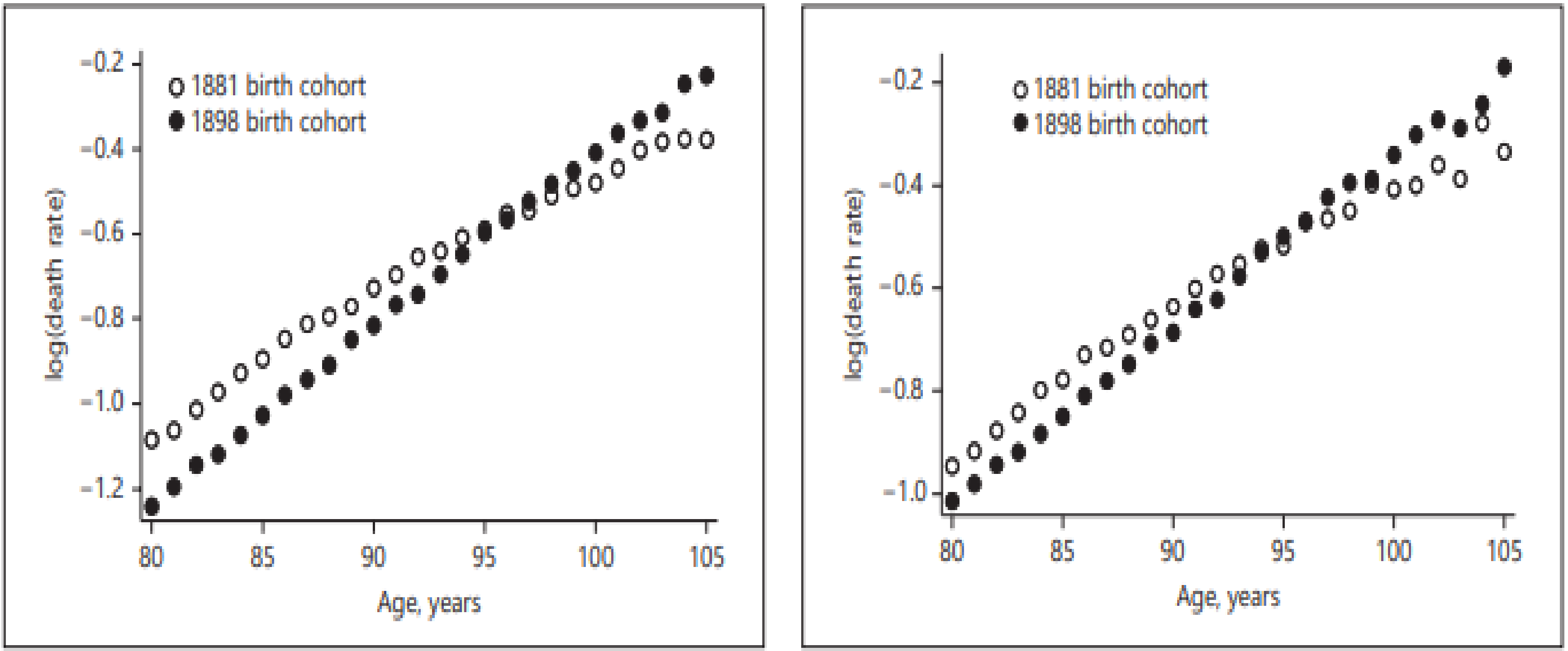
New Trend in Old-Age Mortality: Gompertzialization of Mortality Trajectory

Leonid A. Gavrilov   Natalia S. Gavrilova

Academic Research Centers, NORC at the University of Chicago, Chicago, IL, USA

Transition to the Gompertz model

Mortality of U.S. women (left) and men (right) in earlier and later birth cohorts



Source: Gavrilov, Gavrilova, New Trend in Old-Age Mortality: Gompertzialization of Mortality Trajectory, *Gerontology*, 2019.

Is this trend observed in other countries?

- We analyzed mortality for nine countries with relatively large populations in order to have sufficient number of survivors beyond age 100: Australia, Belgium, Canada, France, Italy, Japan, Spain, United Kingdom and USA.

- For all nine studied countries we analyze mortality of 1880-1902 single-year birth cohorts for men and women separately

Methods

- We fit mortality for two competing models: the Gompertz model and the Kannisto (mortality deceleration) model using weighted non-linear regression method in the age interval 80-105 years (*nlin* procedure in Stata). Values of exposure were used as weights.

- Akaike Information Criterion (AIC) is used to evaluate goodness of fit for the Gompertz and the Kannisto models

Gompertzialization:
Transition from mortality deceleration to the Gompertz model

Best models according to AIC differences for 1880-1902 birth cohorts, by country

Comparison of Gompertz (***G***) and Kannisto (*K*) models. *U* – uncertain result (|ΔAIC| < 5)

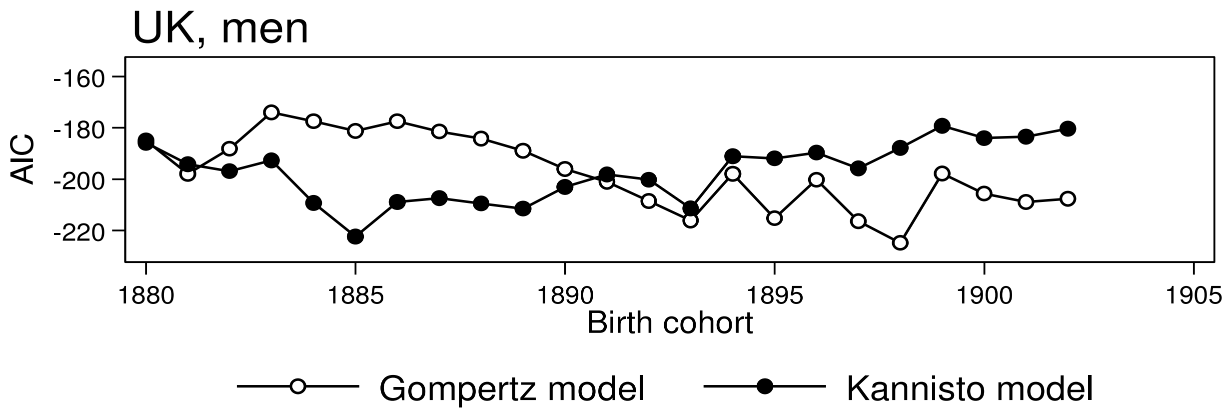
Country	Sex	1880	1881	1882	1883	1884	1885	1886	1887	1888	1889	1890	1891	1892	1893	1894	1895	1896	1897	1898	1899	1900	1901	1902
USA	M	*K*	*K*	*K*	*K*	*K*	*K*	*U*	*U*	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***
	F	*K*	*K*	*K*	*K*	*K*	*K*	*U*	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***
UK	M	*U*	*U*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*U*	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***
	F	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*K*	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***
Canada	M	*K*	*K*	*K*	*K*	*K*	*K*	***G***	*K*	*U*	*U*	*U*	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***
	F	*K*	*K*	*K*	*K*	*K*	*K*	*K*	*U*	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	***G***	*U*	*U*	***G***	*U*

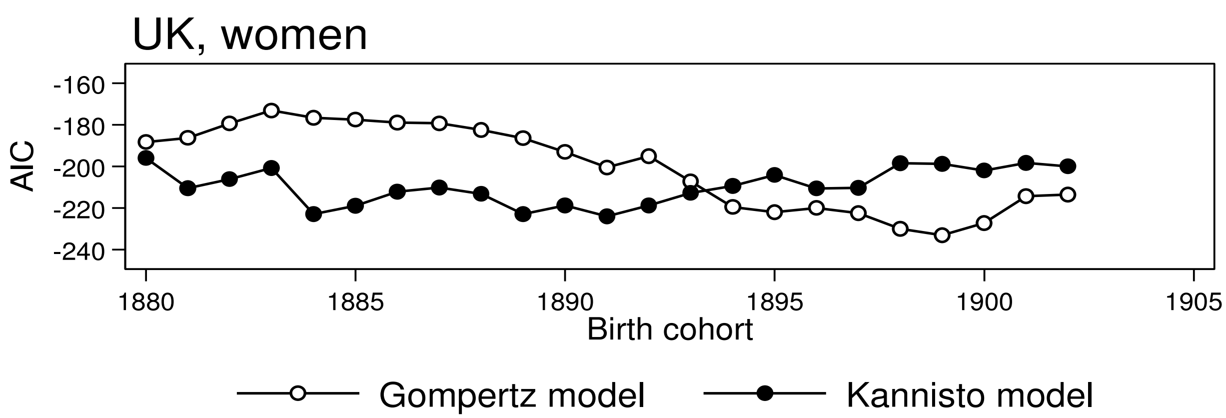
Fitting age-specific cohort death rates taken from the Human Mortality Database

Transition from mortality deceleration to the Gompertz model

1880-1902 UK birth cohorts.

AIC values for fitting Gompertz and Kannisto models



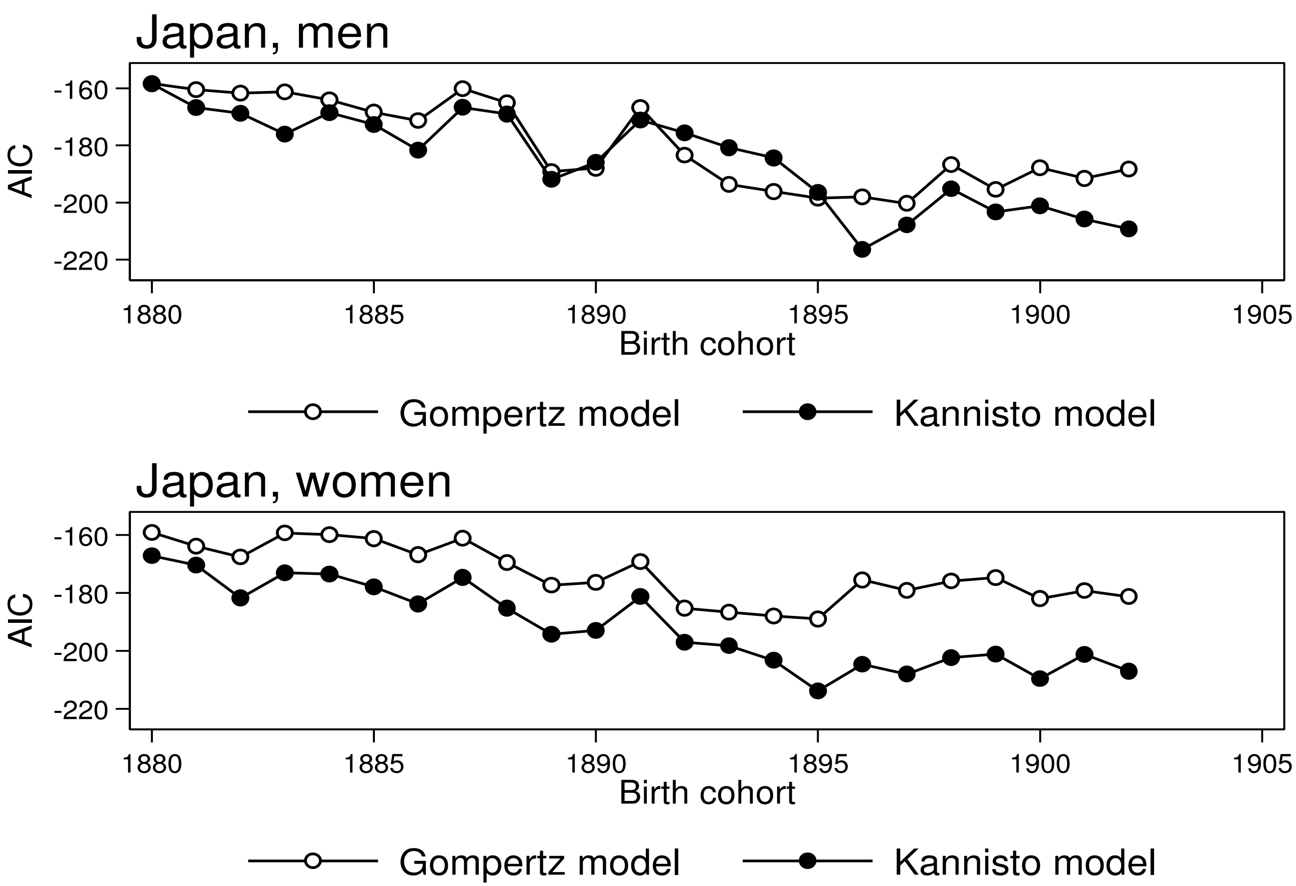


Fitting age-specific cohort death rates taken from the Human Mortality Database

No transition to the Gompertz model

1880-1902 Japanese birth cohorts.

AIC values for fitting Gompertz and Kannisto models

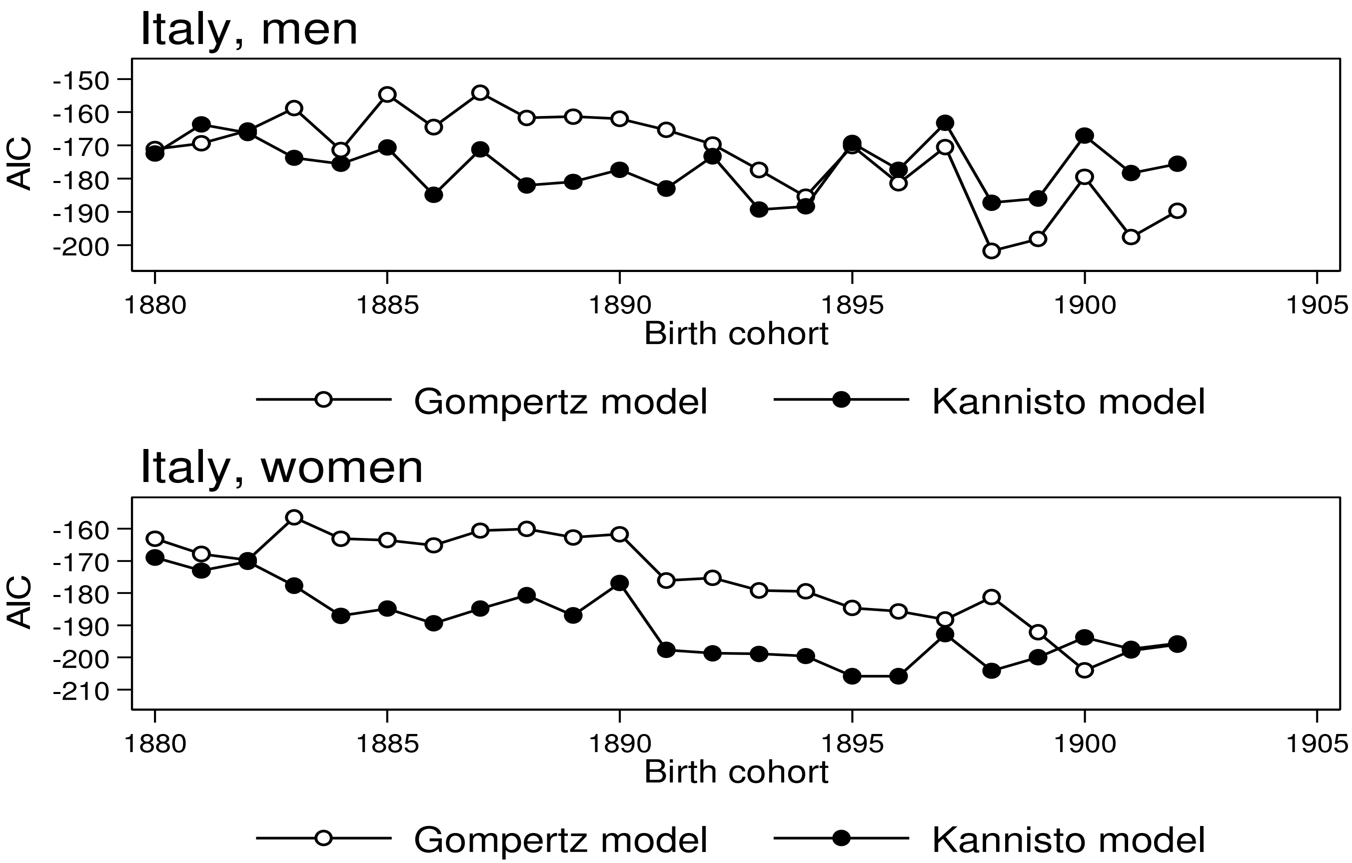


Fitting age-specific cohort death rates taken from the Human Mortality Database

Transition to uncertain model in women

1880-1902 Italian birth cohorts.

AIC values for fitting Gompertz and Kannisto models



Fitting age-specific cohort death rates taken from the Human Mortality Database

Summary of Results (presented at the 2023 SOA Living to 100 Symposium)

Mortality transition pattern	Men	Women
From mortality deceleration to the Gompertz model	Australia, Belgium, Canada, France, Italy, UK, USA	Belgium, UK, USA
From mortality deceleration to uncertain pattern	Spain	Australia, Canada, France, Italy
Mortality deceleration for all studied birth cohorts	Japan	Japan, Spain

Conclusion

These findings reaffirm the enduring relevance of the Gompertz law as a fundamental tool for describing mortality patterns, even at the most advanced ages.

Thank you for your attention!