3-rd International Conference
"Homo sapiens liberatus"

Moscow, Russia, February 20-21, 2020

Section 4. Aging programs vs anti-aging programs

Matters of Life and Death: What can we learn about aging from mortality and longevity studies?

Leonid A. Gavrilov,
Natalia S. Gavrilova

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

Brief historical note

Our early publication on aging topic in 1978 at Moscow State University

Т. XXXIX, № 5 ЖУРНАЛ ОБЩЕЙ БИОЛОГИИ 1978

УДК 612.6

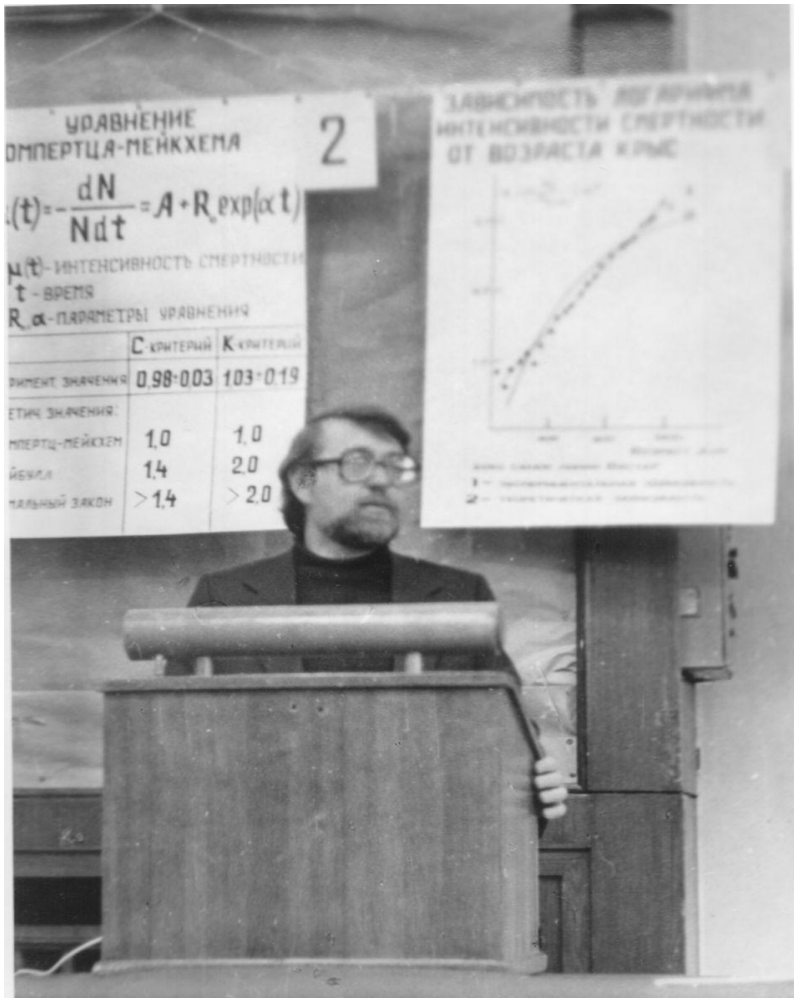
ОСНОВНЫЕ ЗАКОНОМЕРНОСТИ СТАРЕНИЯ И ГИБЕЛИ ЖИВОТНЫХ С ТОЧКИ ЗРЕНИЯ ТЕОРИИ НАДЕЖНОСТИ

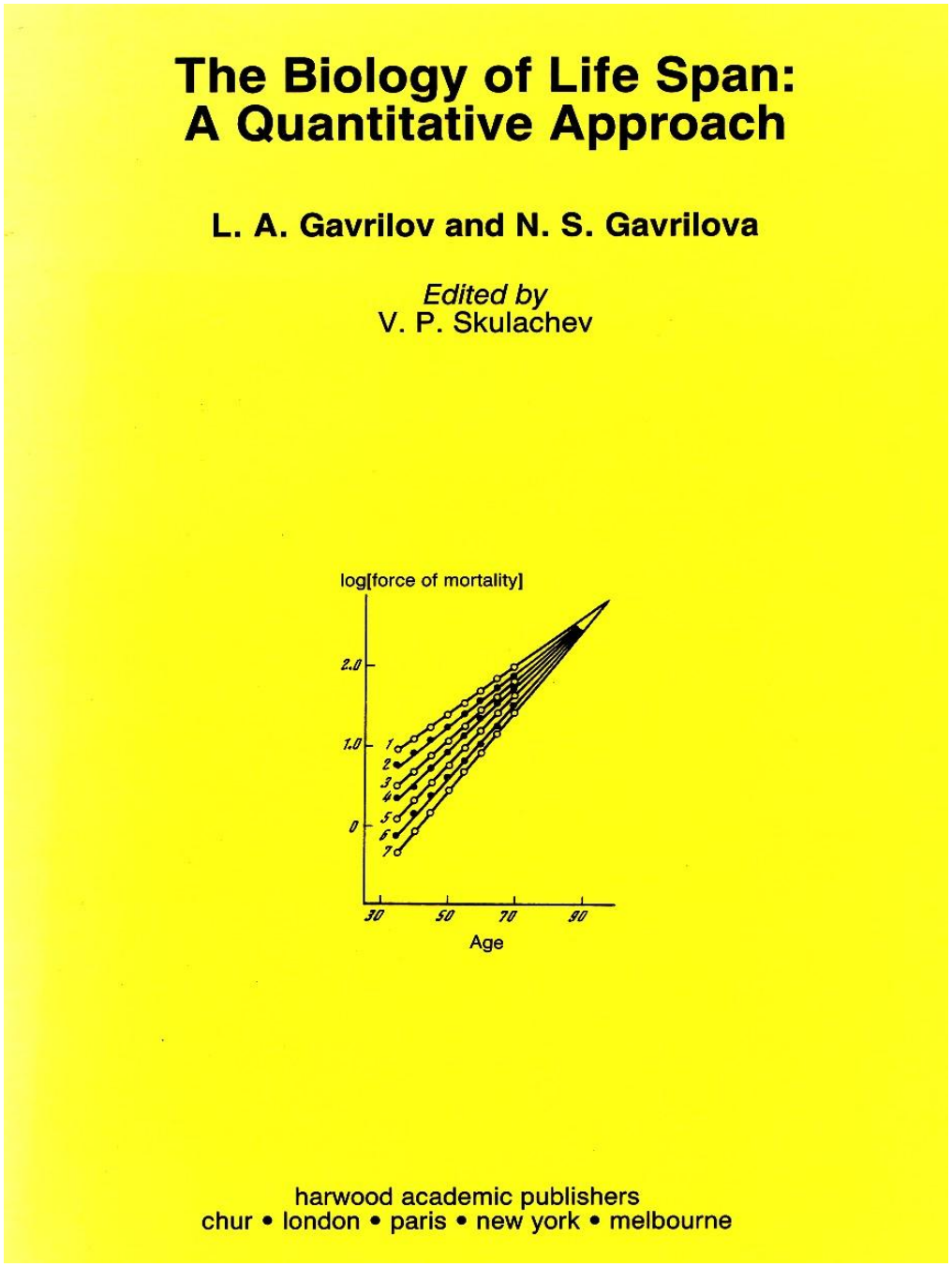
Л. А. ГАВРИЛОВ, Н. С. ГАВРИЛОВА, Л. С. ЯГУЖИНСКИЙ

Московский государственный университет им. М. В. Ломоносова

Показано, что применение теории надежности позволяет объяснить основные закономерности старения и гибели животных: уравнение Гомпертца — Макегама, компенсационный эффект и уменьшение числа функционирующих элементов с возрастом. Установлена справедливость уравнения Гомпертца — Макегама для людей (на примере 86 популяций), а также линейных крыс (19 популяций), домашних мух и дрозофил. Предложен новый способ линеаризации статистических данных по смертности животных, позволивший строго доказать существование компенсационного эффекта у людей и точно определить возрастной диапазон, в котором выполняется уравнение Гомпертца — Макегама.

Vladimir P. Skulachev in 1980: My Ph.D. defense at MSU on aging topic





Our book on aging published in 1991 (inspired and edited by V.P. Skulachev).

This book got over 700 scientific citations by now

Recent Collaboration

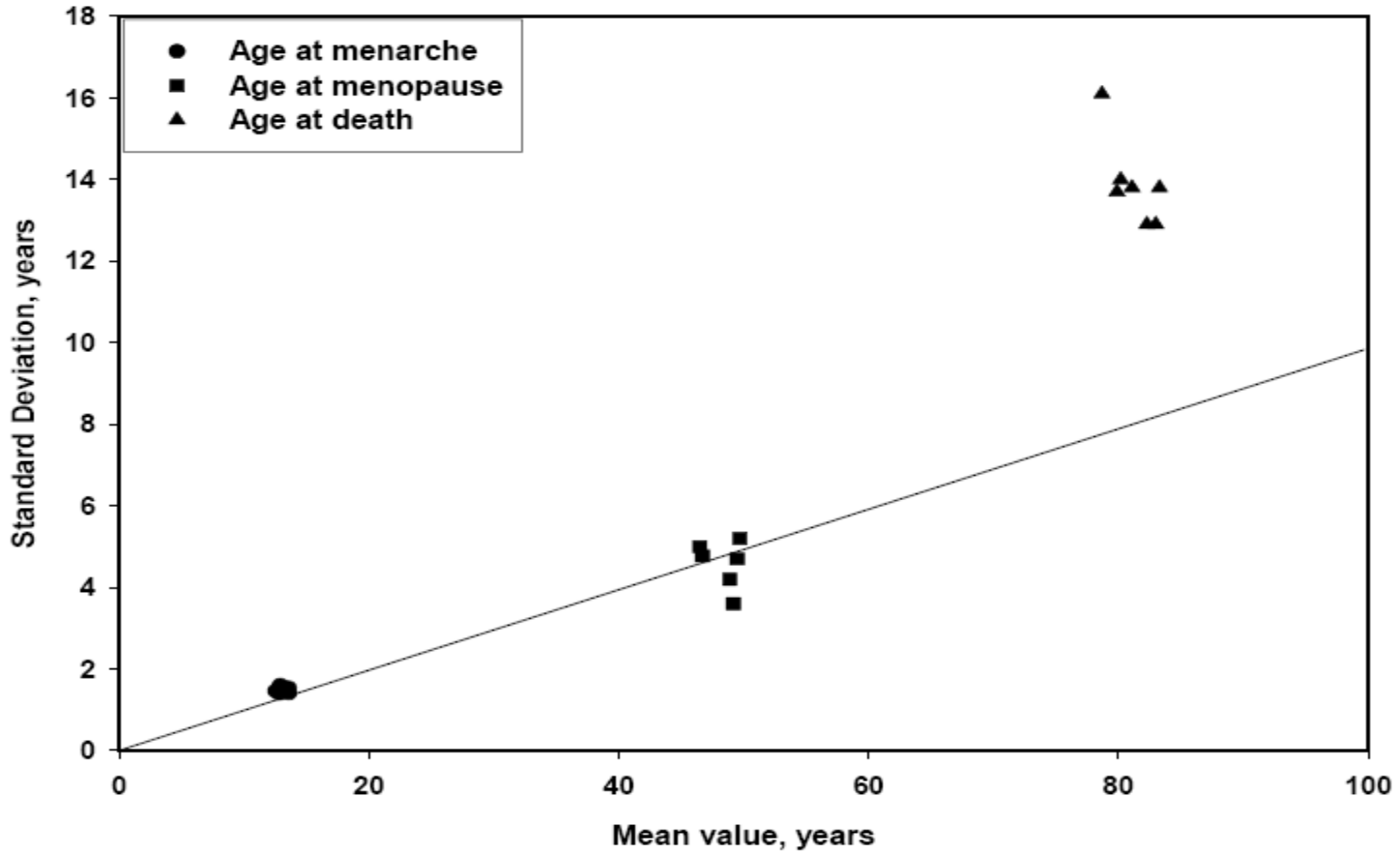
ISSN 0006-2979, Biochemistry (Moscow), 2012, Vol. 77, No. 7, pp. 754-760. © Pleiades Publishing, Ltd., 2012.
Published in Russian in Biokhimiya, 2012, Vol. 77, No. 7, pp. 907-914.

Testing Predictions of the Programmed and Stochastic Theories of Aging: Comparison of Variation in Age at Death, Menopause, and Sexual Maturation

N. S. Gavrilova[1]*, L. A. Gavrilov[1], F. F. Severin[2], and V. P. Skulachev[2]

We found that coefficients of variation are in the range of 8-13% for age at menarche, 7-11% for age at menopause, and 16-21% for age at death. Thus, the relative variability for the age at death is only twice higher than for the age at menarche, while the relative variability for the age at menopause is almost the same as for the age at menarche.

Relative variability for the age at natural menopause is almost the same as for the age at menarche



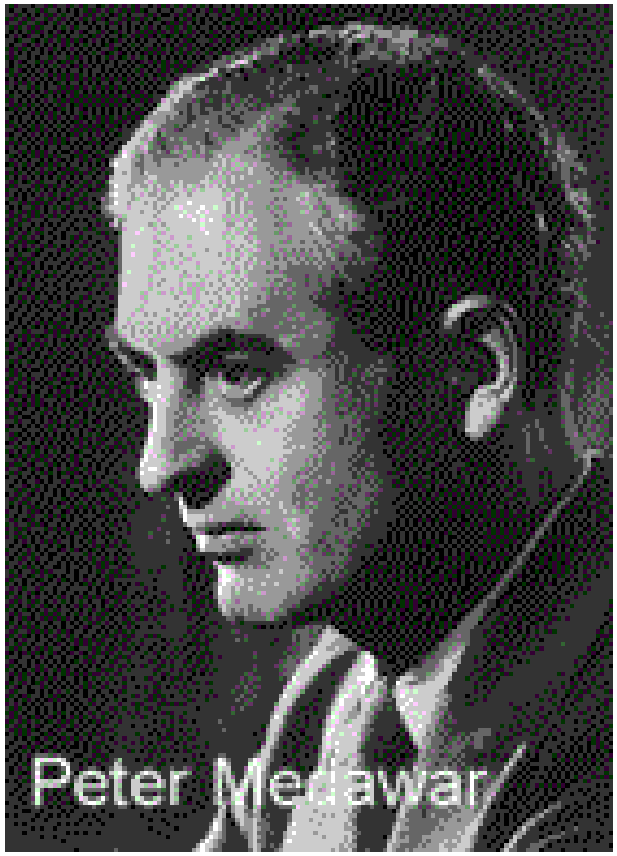
Source: Gavrilova et al., *Biochemistry*, 2012, vol.77, No.7, pp.754-760

Fundamental biological theories of aging can be tested using mortality and longevity data

Traditional evolutionary theory explains aging by a declining force of natural selection with age.

Mutation Accumulation Theory of Aging (Medawar, 1946)

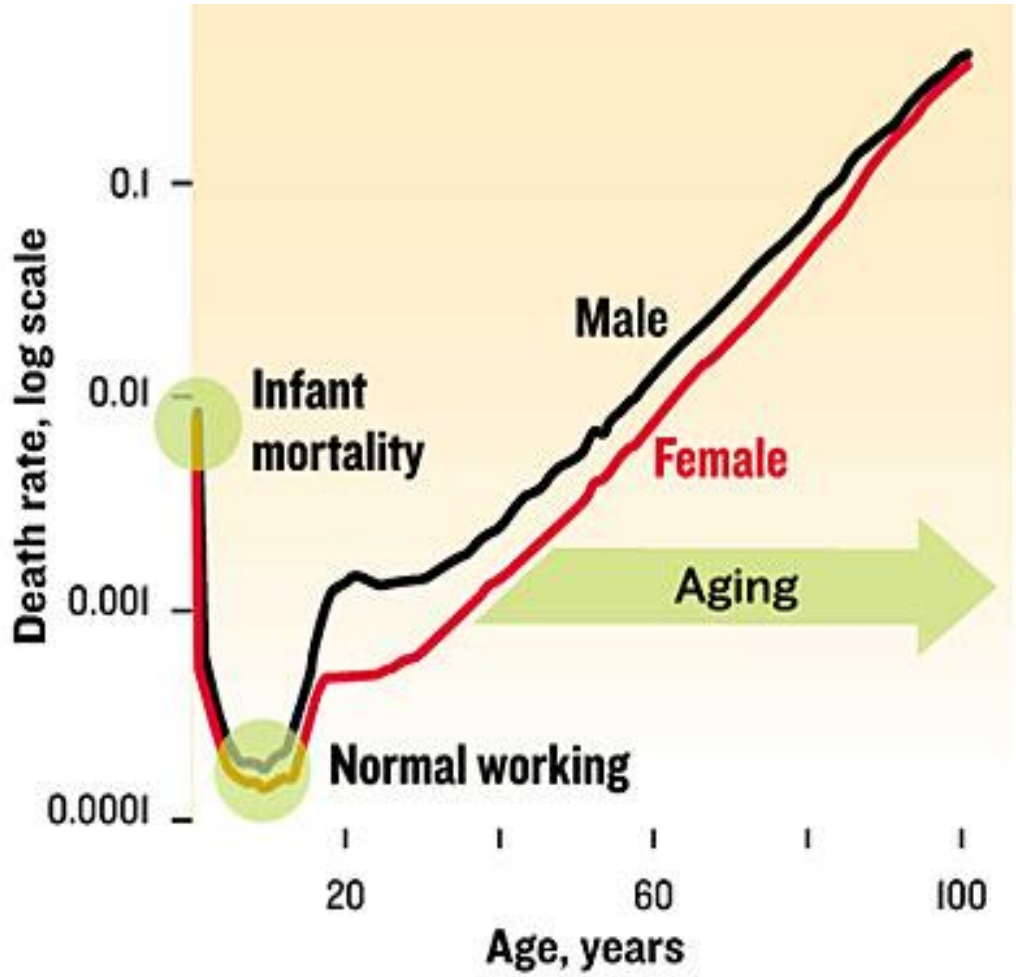
- From the evolutionary perspective, aging is an inevitable result of the declining force of natural selection with age.
- The equilibrium frequency of deleterious mutations is higher for later acting mutations (LAM), because selection against LAM is weaker and mutation-selection balance is shifting to higher LAM levels.



Testable prediction from the evolutionary theory

- One may expect a fundamental change in age dynamics of mortality at very old post-reproductive ages, when the force of natural selection becomes negligible and there is no room for its further decline.
- For example, a prediction could be made that mortality dynamics at reproductive ages (20-40 years in humans) should be fundamentally different from mortality dynamics at extreme post-reproductive ages (90-105 years).

Mortality grows with age according to the Gompertz law



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

Study of U.S. mortality

United States has the largest number of centenarians among the advanced economies

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

Leonid A. Gavrilov* and Natalia S. Gavrilova†

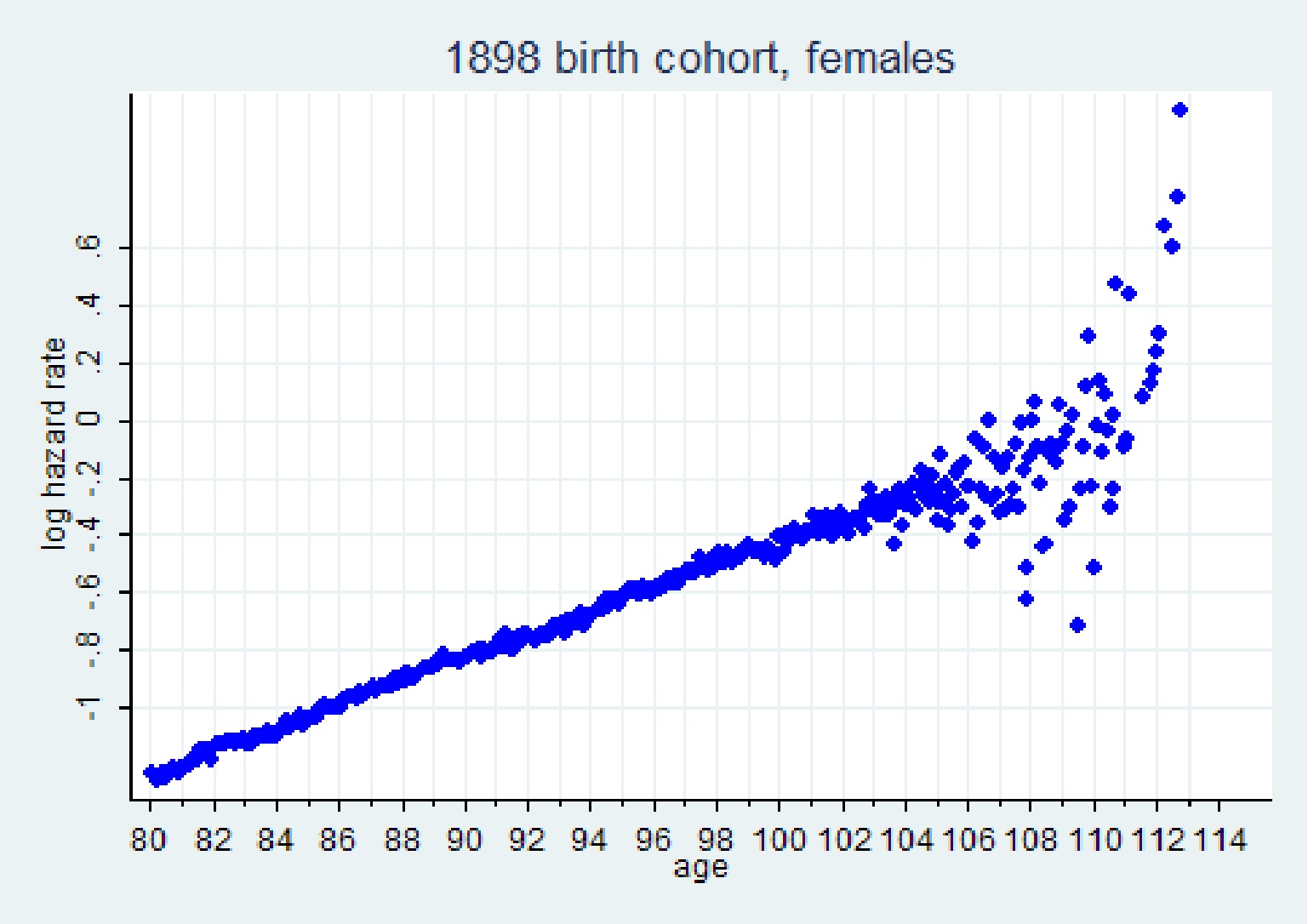
ABSTRACT

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**

U.S. birth cohort mortality, DMF data



Nelson-Aalen monthly estimates of hazard rates using Stata 11

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

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

Biodemography of Old-Age Mortality in Humans and Rodents

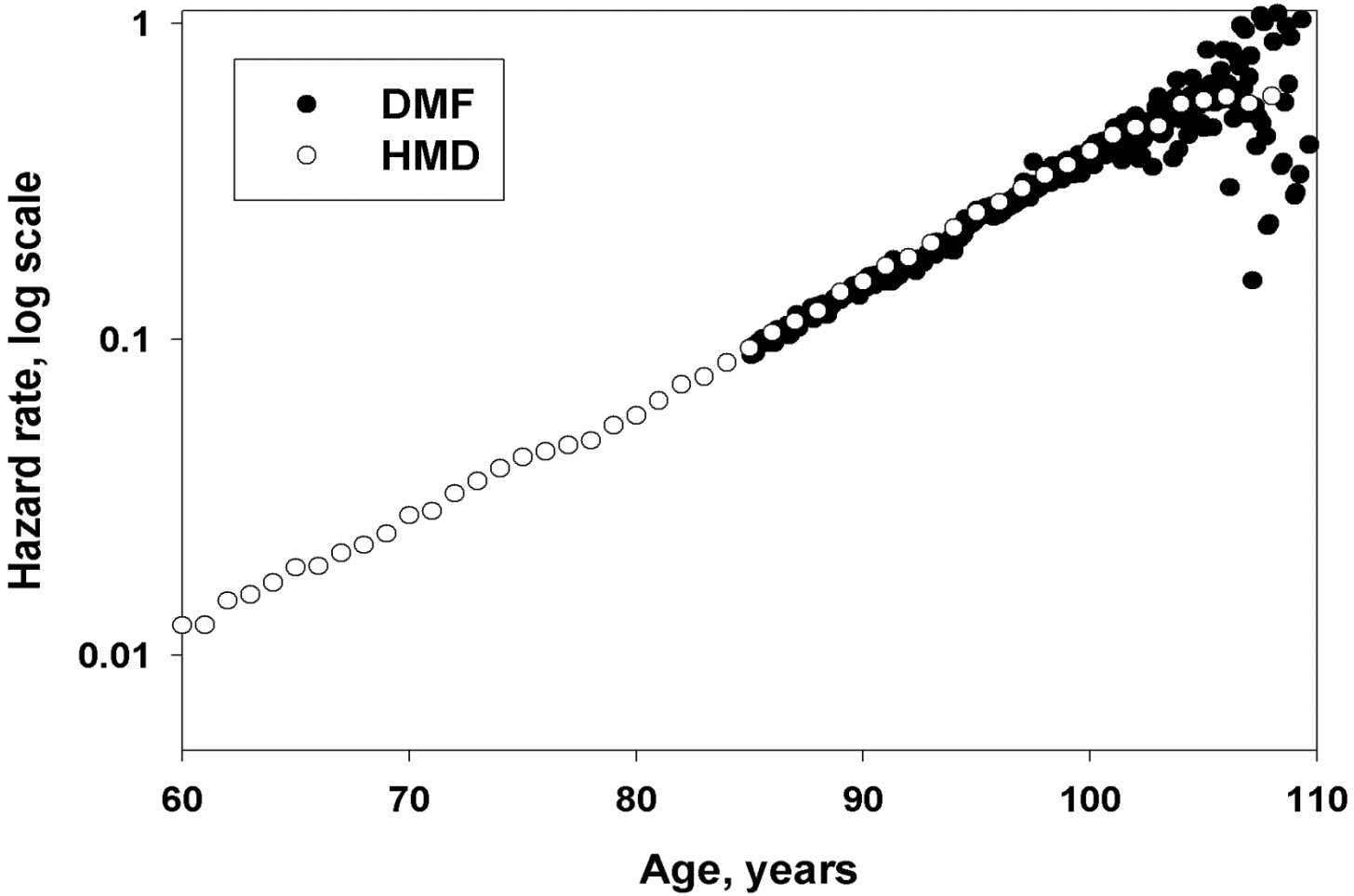
Natalia S. Gavrilova and Leonid A. Gavrilov

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

No deviations from the Gompertz model at extreme old ages



U.S. women, 1898 birth cohort. Source: Gavrilova, Gavrilov, J.Gerontology, 2015

Challenge to evolutionary theories

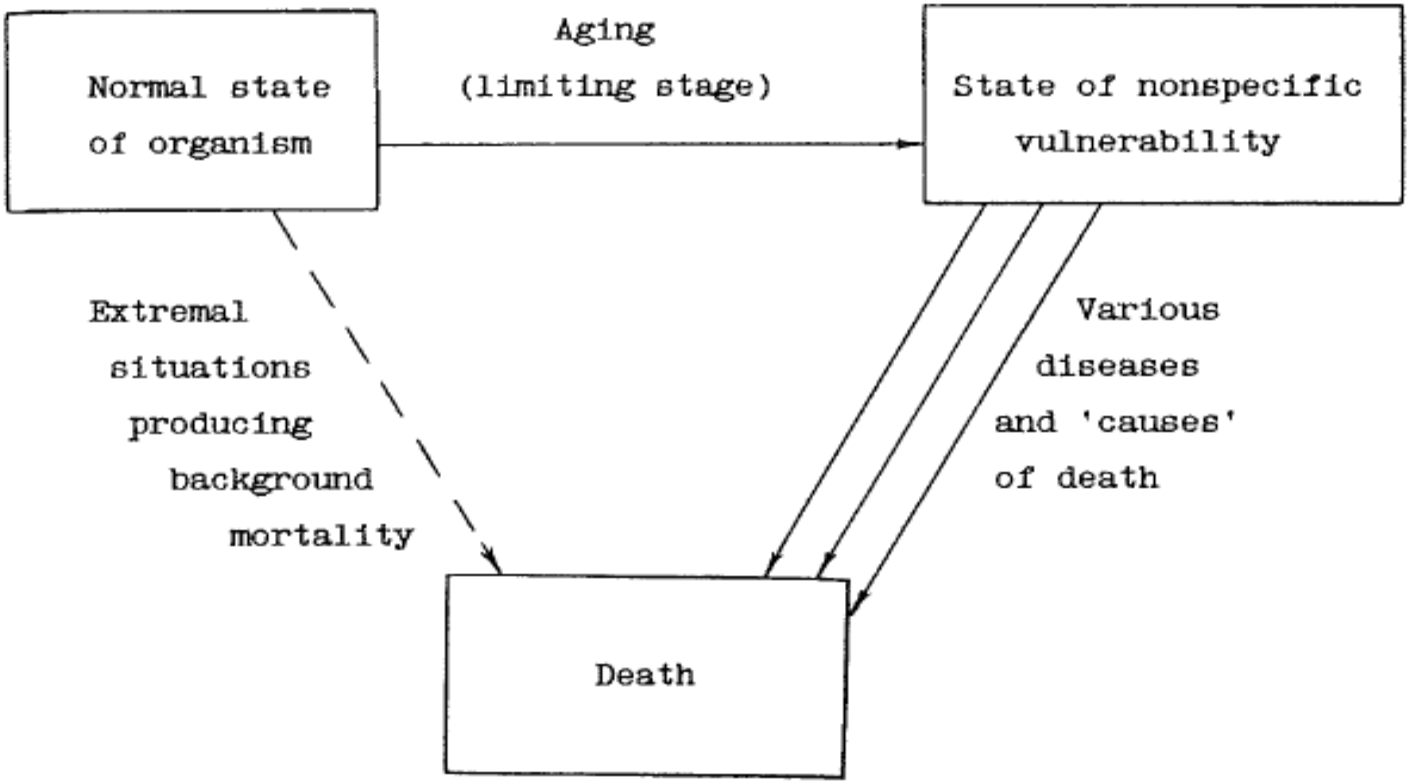
- **We see no difference in mortality kinetics at extremely old post-reproductive ages compared to young reproductive ages**

Another Challenge

- **Wide applicability of the Gompertz law to almost all adult ages leads to another burning research question for future studies:**
- **How is it possible for different diseases and causes of death to "negotiate" with each other in order to produce a simple exponential function for all-cause mortality (given that contribution of different causes of death in all-cause mortality changes dramatically with age)?**

Simplified schema explaining the existing phenomenon

Hypothesis of the state of non-specific vulnerability ("нежилец")



Source: Gavrilov, L.A. & Gavrilova, N.S. 1991. The Biology of Life Span: A Quantitative Approach. Harwood Academic Publisher, New York.

New Vision of Aging-Related Diseases

High Initial Damage Load (HIDL) Idea

"Adult organisms already have an exceptionally high load of initial damage, ***which is comparable with the amount of subsequent aging-related deterioration, accumulated during the rest of the entire adult life.****"*

Source: Gavrilov, L.A. & Gavrilova, N.S. 1991. The Biology of Life Span: A Quantitative Approach. Harwood Academic Publisher, New York.

Practical implications from the HIDL hypothesis:

"Even a small progress in optimizing the early-developmental processes can potentially result in a remarkable prevention of many diseases in later life, postponement of aging-related morbidity and mortality, and significant extension of healthy lifespan."

Source: Gavrilov, L.A. & Gavrilova, N.S. 1991. The Biology of Life Span: A Quantitative Approach. Harwood Academic Publisher, New York.

Older Moms More Likely to Pass Along Mitochondrial DNA with Mutations, Study Finds

The older the mother, the higher is the risk that mutated, disease-causing mitochondrial DNA will be passed along to offspring.

Burgstaller et al. *Nature Communications, 2018,* volume 9, Article number: 2488, doi: 10.1038/s41467-018-04797-2

Our two studies on the effects of maternal age on human longevity

Biodemography and Social Biology, 58:14–39, 2012

ISSN: 1948-5565 print / 1948-5573 online
DOI: 10.1080/19485565.2012.666121

Routledge
Taylor & Francis Group

Biodemography of Exceptional Longevity: Early-Life and Mid-Life Predictors of Human Longevity

LEONID A. GAVRILOV AND NATALIA S. GAVRILOVA
Center on Aging, NORC at the University of Chicago, Chicago, Illinois, USA

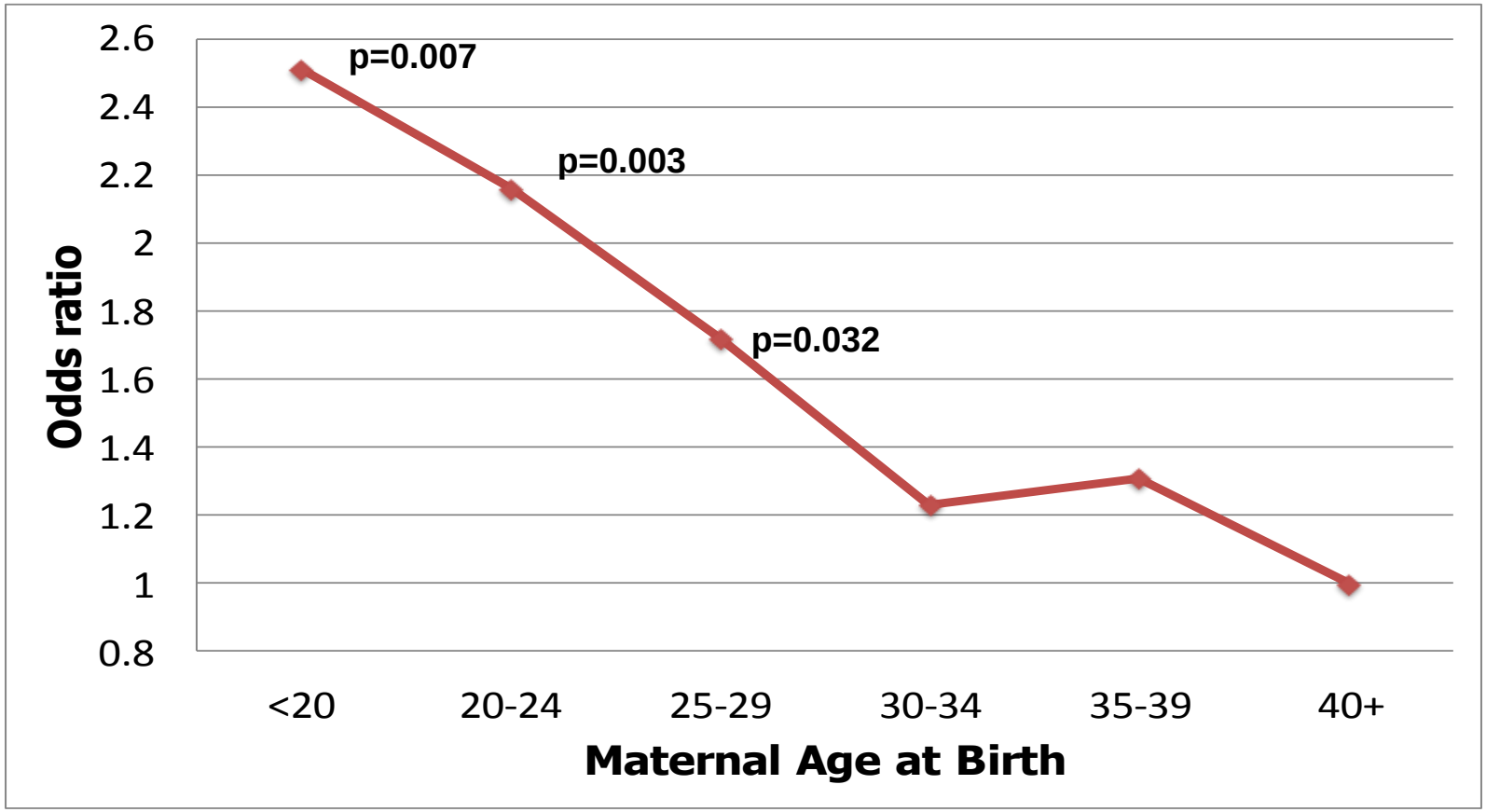
Vienna Yearbook of Population Research 2013 (Vol. 11), pp. 295–323

Determinants of exceptional human longevity: new ideas and findings

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

People Born to Young Mothers Have Twice Higher Chances to Live to 100

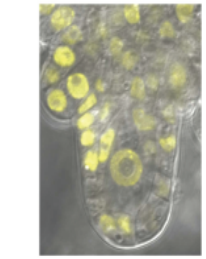
Within-family study of 2,153 centenarians and their siblings survived to age 50. Family size <9 children.



Note: both parents lived 50 years or more.

Source: Gavrilov, Gavrilova, *Gerontology*, 2015

Epigenetic modifications may be a possible mechanism linking maternal age (and early life effects in general) with later health outcomes



Epigenetics

ISSN: 1559-2294 (Print) 1559-2308 (Online) Journal homepage: https://www.tandfonline.com/loi/kepi20

Persistent Epigenetic Changes in Adult Daughters of Older Mothers

Aaron M Moore, Zongli Xu, Ramya T Kolli, Alexandra J White, Dale P Sandler & Jack A Taylor

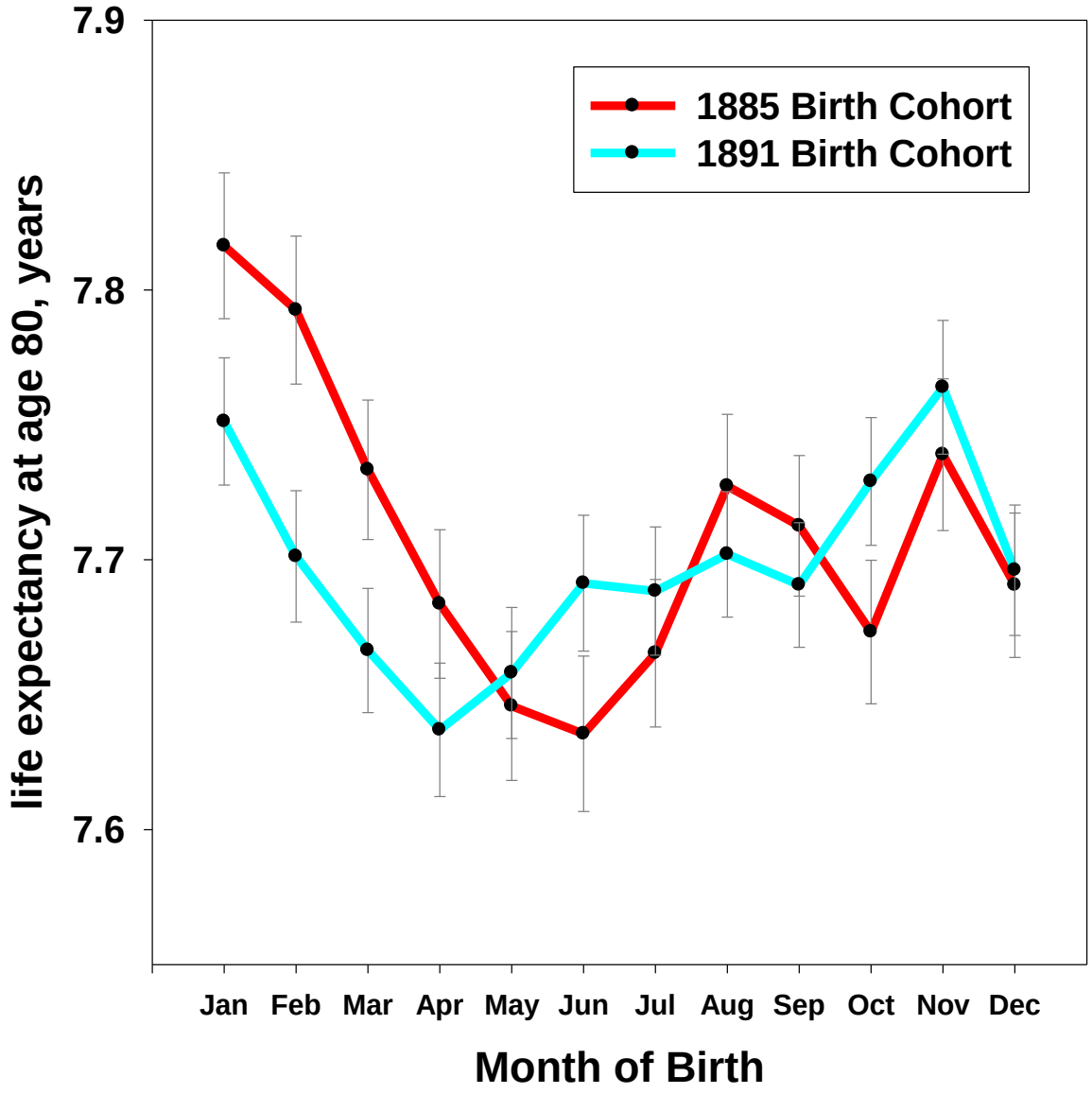
Possible explanation

These findings are consistent with the 'best eggs are used first' hypothesis suggesting that earlier formed oocytes are of better quality, and go to fertilization cycles earlier in maternal life.

Within-Family Study of Season of Birth and Exceptional Longevity

Month of birth is a useful proxy characteristic for environmental effects acting during in-utero and early infancy development

Life Expectancy at Age 80 and Month of Birth



Data source:
Social Security
Death Master File

Published in:

Gavrilova, N.S., Gavrilov, L.A. Search for Predictors of Exceptional Human Longevity. In: "*Living to 100 and Beyond*" Monograph. The Society of Actuaries, Schaumburg, Illinois, USA, 2005, pp. 1-49.

Within-family study of month-of-birth effects

SAGE-Hindawi Access to Research
Journal of Aging Research
Volume 2011, Article ID 104616, 11 pages
doi:10.4061/2011/104616

Research Article

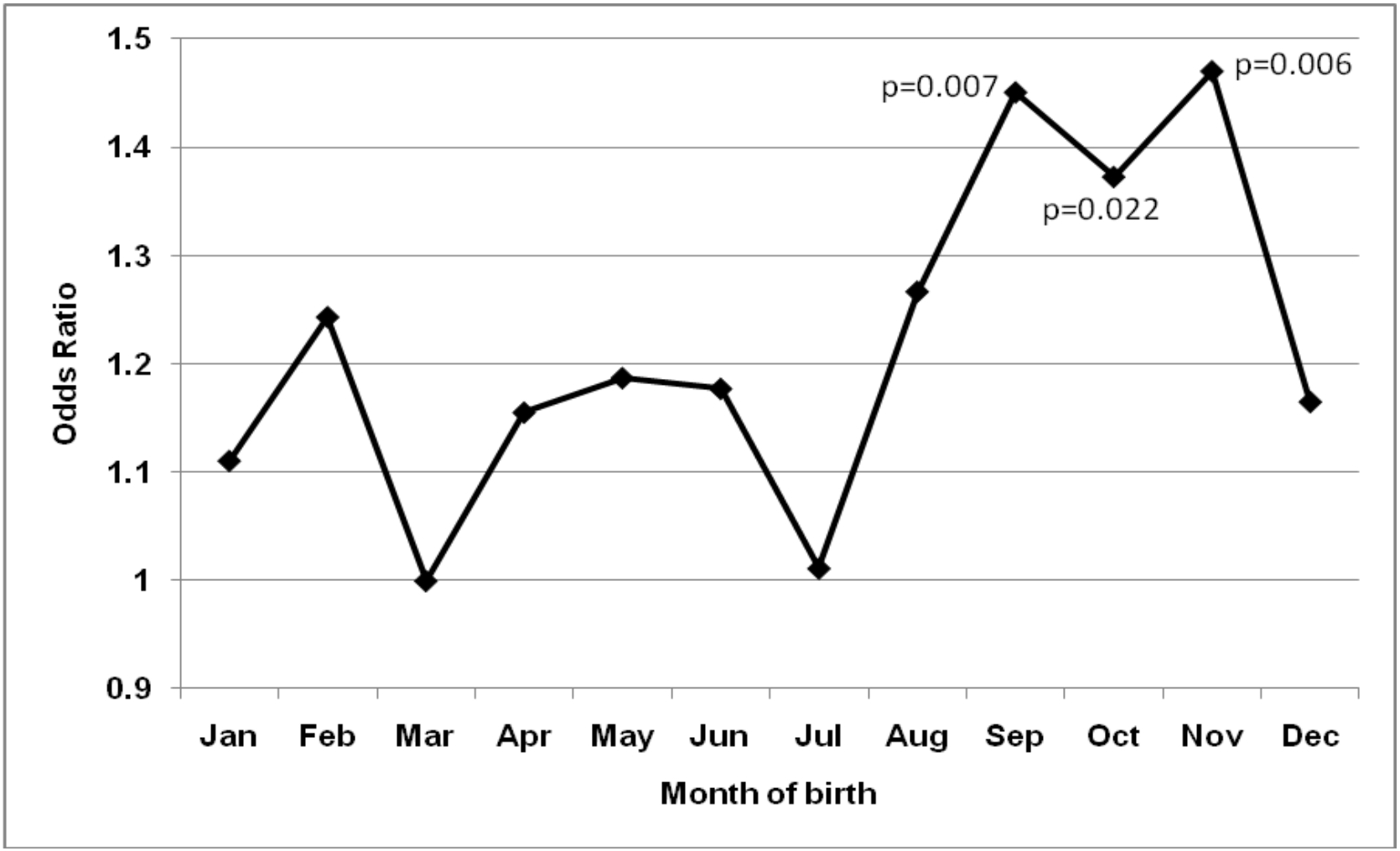
Season of Birth and Exceptional Longevity: Comparative Study of American Centenarians, Their Siblings, and Spouses

Leonid A. Gavrilov and Natalia S. Gavrilova

Center on Economics and Demography of Aging, NORC at the University of Chicago, 1155 East 60th Street, Chicago, IL 60637, USA

Siblings Born in September-November Have Higher Chances to Live to 100

Within-family study of 9,724 centenarians born in 1880-1895 and their siblings survived to age 50



Possible explanations

These are several explanations of season-of birth effects on longevity pointing to the effects of early-life events and conditions:

- **seasonal exposure to infections,**
- **nutritional deficiencies,**
- **environmental temperature and sun exposure.**

All these factors were shown to play role in later-life health and longevity.

Conclusion

- Early-life effects (including epigenetic changes) may have important long-term health consequences

IDEAS & TRENDS

For Centenarians, It All Begins at Birth

By HENRY FOUNTAIN

CENTENARIANS are different from the rest of us, and it's not just that they are a lot older. They are a select group, having persisted through wars, disasters, diseases and accidents that kill tens of millions of ordinary mortals every year.

In looking at what makes a 100-year-old so special — fewer than 2 in every 10,000 Americans live to that age or older — those who study aging cite factors like genetics (particularly having two X chromosomes, as 85 percent of centenarians are women) and environmental influences like good nutrition and health habits.

In a statistical study of centenarians by researchers at the University of Chicago [illegible] found some other potential predictors of extreme longevity. Women and men who were the first born in large families, the study found, were two or three times more likely to reach 100 than later-born children. Those raised in the rural West had a better chance of reaching that age. And people of advanced age who were born in October and November had longer life expectancy than those born in April through June.

So if you are a tall baby, the first child of a [illegible] people from Texas, are you a safe

Genes and environment still rule when it comes to living an ultralong life.

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

- **http://longevity-science.org**

Thank you for your attention!