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

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Brief historical note

Our early publication on aging topic in 1978 at Moscow State University
Vladimir P. Skulachev in 1980: My Ph.D. defense at MSU on aging topic

This book got over 700 scientific citations by now.
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.

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

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

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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
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

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
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")

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."

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."

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.

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

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

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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
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:
Within-family study of month-of-birth effects

Research Article

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

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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.
Early-life effects (including epigenetic changes) may have important long-term health consequences.
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 bit older. They are a select group, having persisted through wars, depressions, disasters and accidents that kill tens of millions of ordinary mortals every year.

Looking at what makes a 100-year-old so special — fewer than 3 in every 10,000 Americans live to that age or older — those who study aging can hardly disagree: particularly having two X chromosomes, as 85 percent of centenarians are women and environmental and lifestyle factors like good nutrition and health habits.

Yet a statistical study of centenarians by researchers at the University of Chicago has found some other potential predictors of extreme longevity. Women and men who were the first born in large families, the study found, were two to three times more likely to make it to 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 Brazil and Somalia had longer life expectancy than those born in April through June.

If you are a tall baby, the first child of a farming family from Maine, 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!