

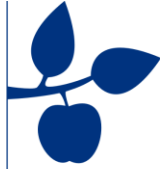


THEORIES OF LONGEVITY

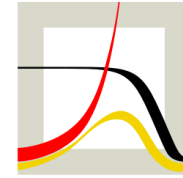
Robert L. Brown, PhD
FCIA, FSA, ACAS, FIA (Hons)

President: International Actuarial Association

University of Waterloo
Retired



SYDDANSK UNIVERSITET
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The Advancing Frontier of Survival: With a Focus on the Future of US Mortality

by James W. Vaupel

Member of the National Academy of Sciences of the United States
*Max Planck Institute for Demographic Research, Rostock, Germany,
University of Southern Denmark, Odense, Denmark
and Duke University, Durham NC, USA*



The Frontier of Survival: Three Views

View 1: The Fixed Frontier of Survival

→ Limited lifespans

Aristotle 350 BC, James Fries *NEJM* 1980

View 2: Breaking through the Frontier of Survival

→ Secrets of longevity

Luigi Cornaro *The Art of Living Long* 1558

View 3: The Advancing Frontier of Survival:

→ Unrecognized progress

Vaupel, Manton, Stallard *Demography* 1979

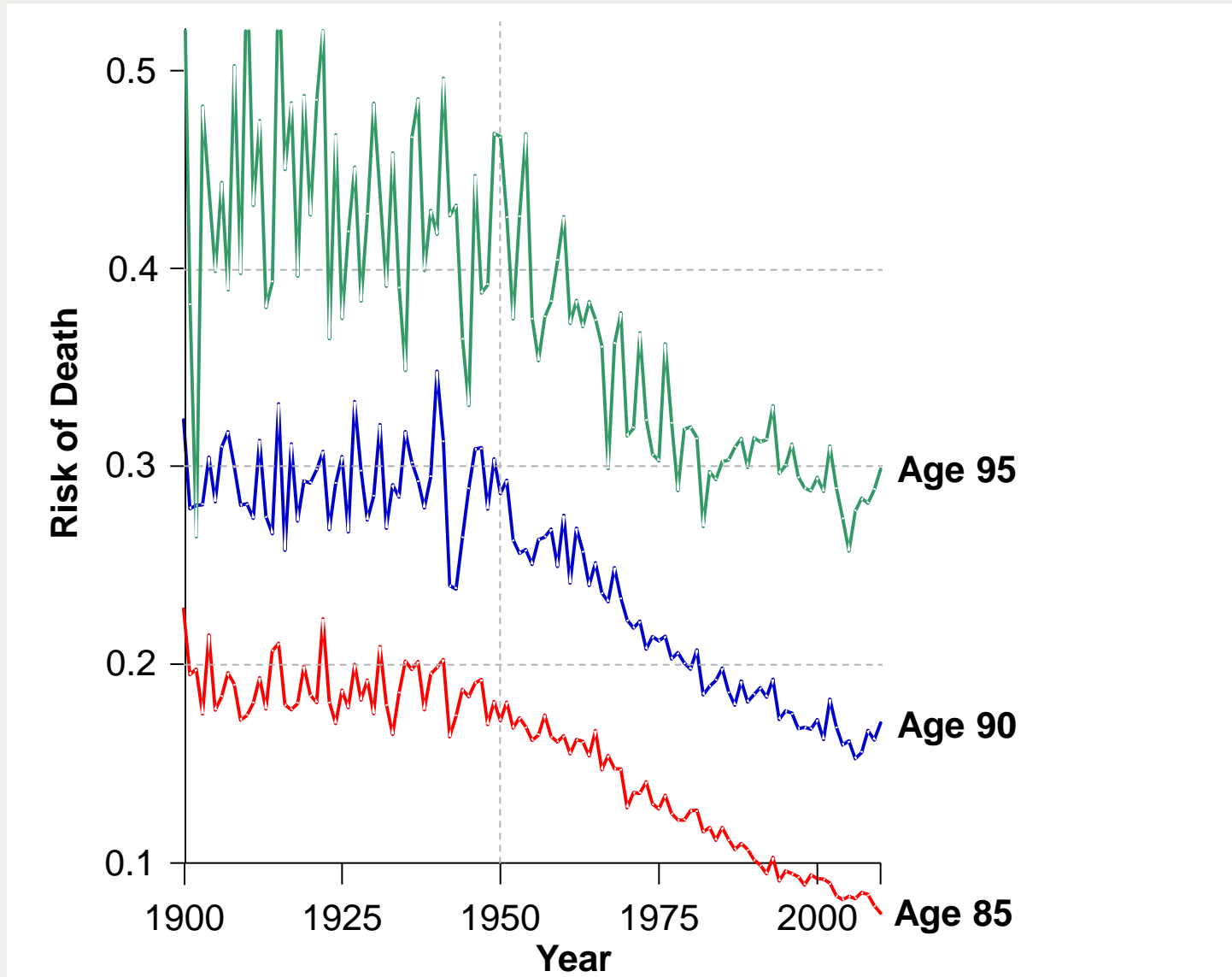


Discovery of the Advancing Frontier of Survival

Vaupel and Lundström 1992/4, extended

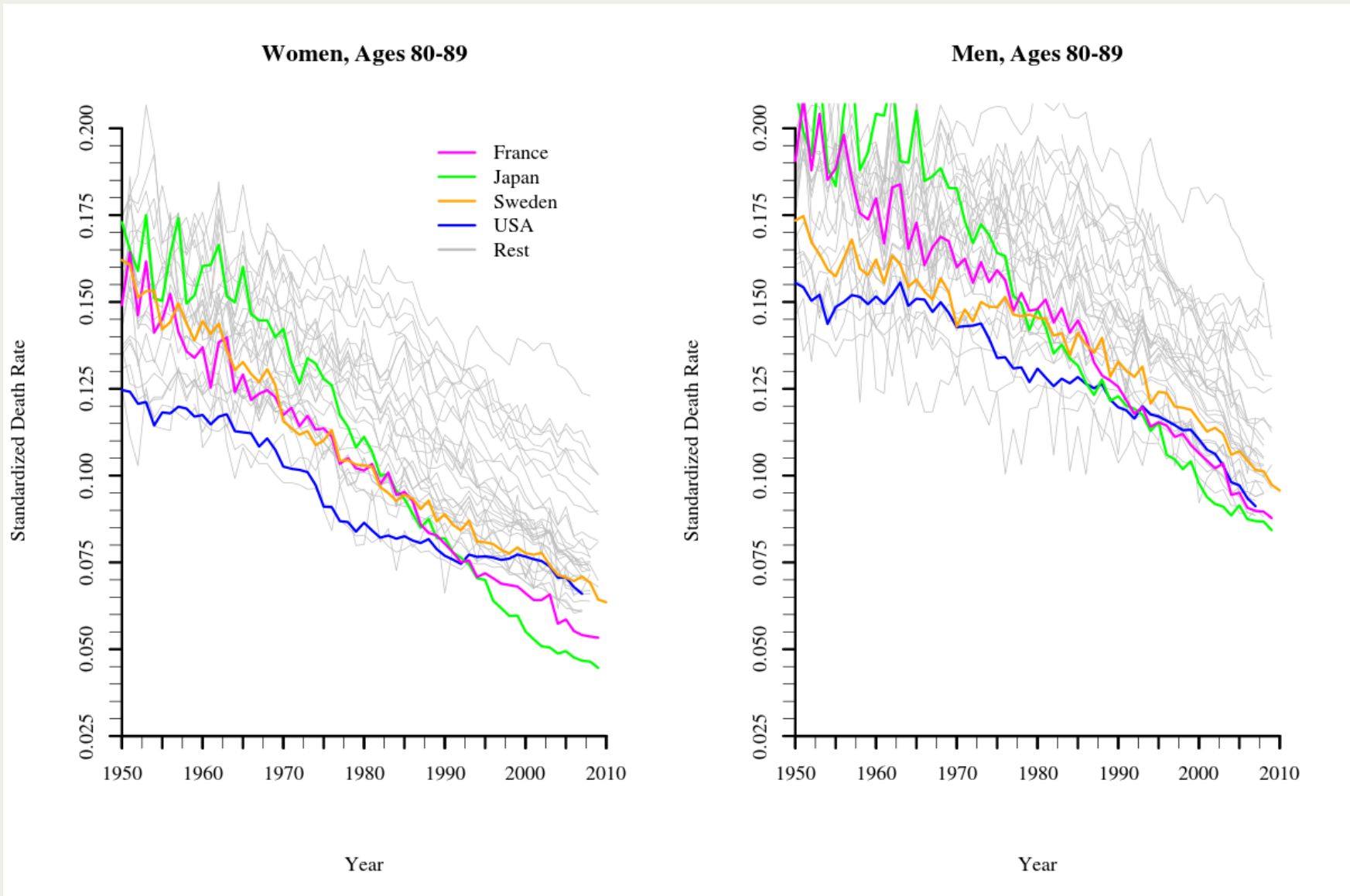


Mortality at ages 85, 90 and 95 for Swedish Females





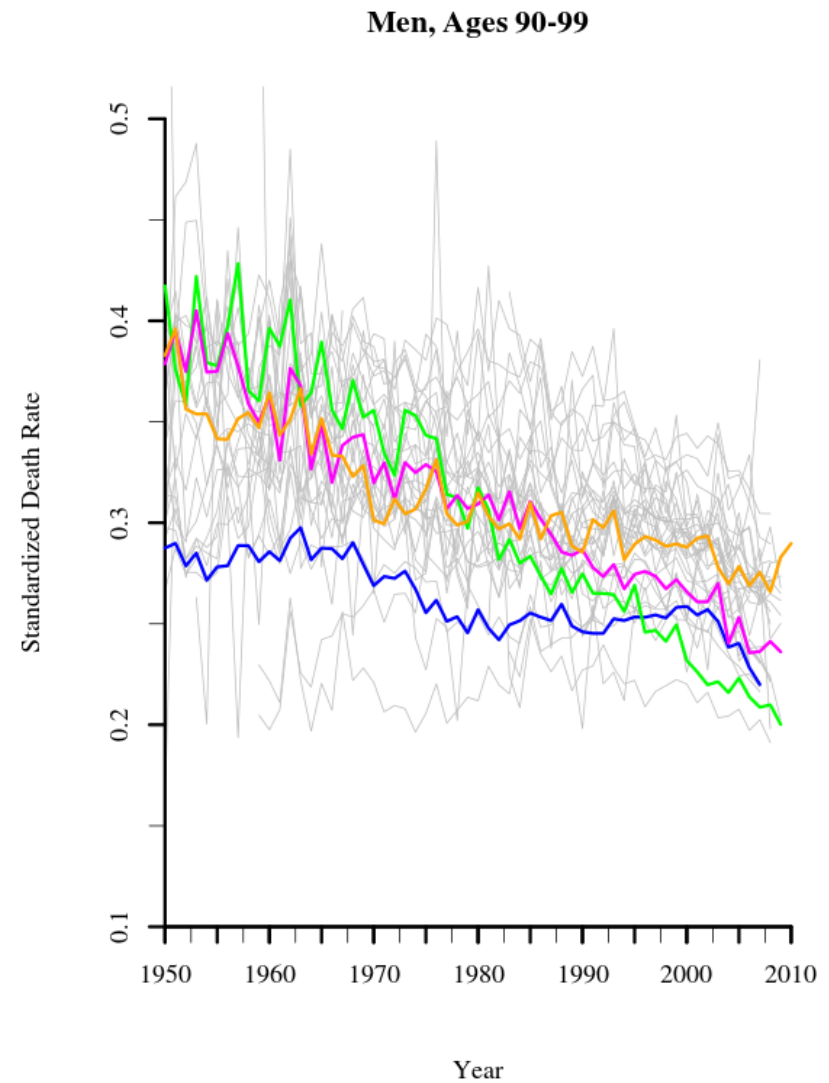
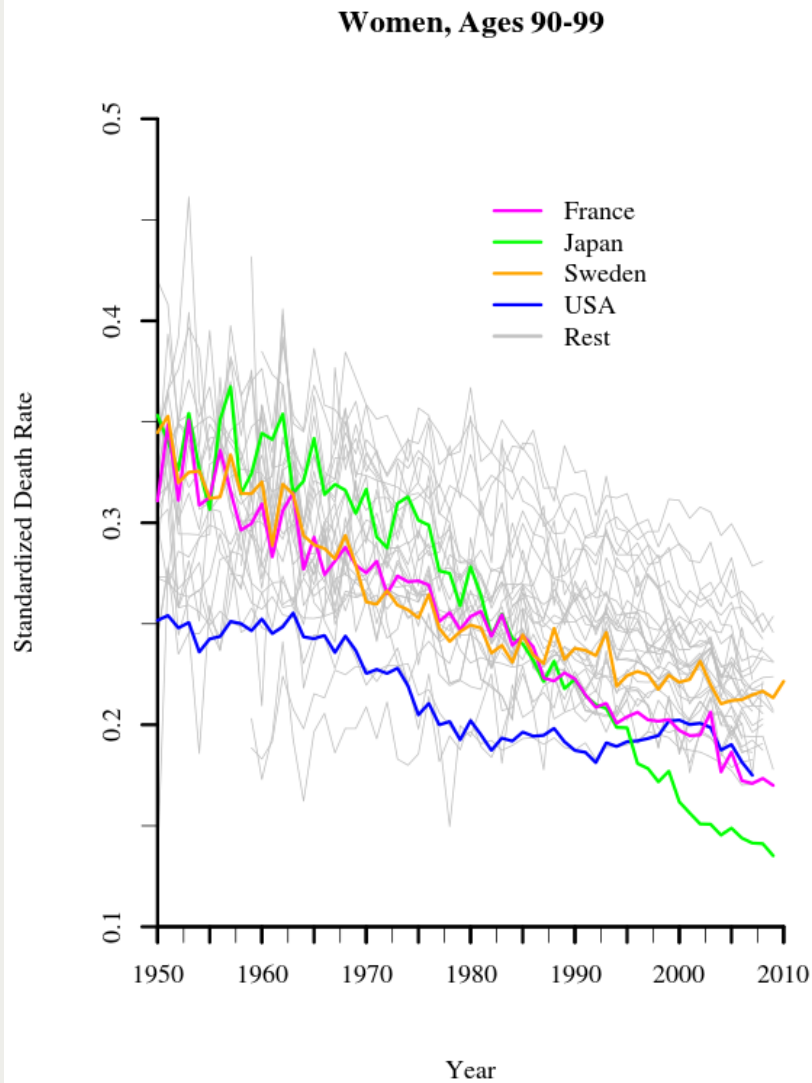
Discovery of the Advancing Frontier of Survival: The Decline in Octogenarian Mortality



Source: Calculations by Roland Rau (unpublished) based on Human Mortality Data Base



Discovery of the Advancing Frontier of Survival: The Decline in Nonagenarian Mortality

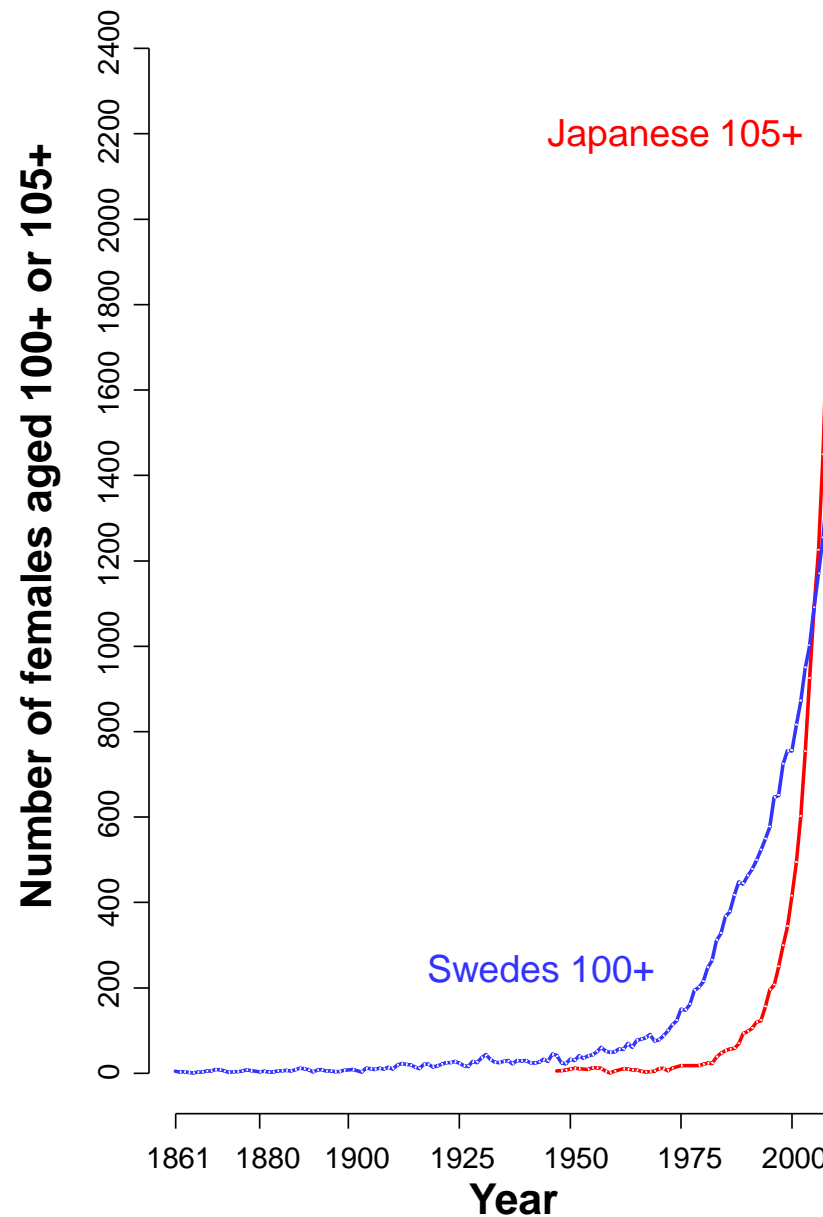


Source: Calculations by Roland Rau (unpublished) based on Human Mortality Data Base



Discovery of the Advancing Frontier of Survival:

Further Evidence: The Explosion of Centenarians, Vaupel *Nature* 2010





Mechanisms of Human Longevity



→ **The major discovery— The advancing frontier of survival.**

Supplemental discoveries

- 1. The frontier of survival is advancing because senescence (the increase of mortality with age) is being postponed.**



Question 1:



Compared with U.S. men 50 years ago, do 70-year-old U.S. males today suffer the same chance of death as

- 1) 67-year-olds did then?
- 2) 65-year-olds did then?
- 3) 60-year-olds did then?

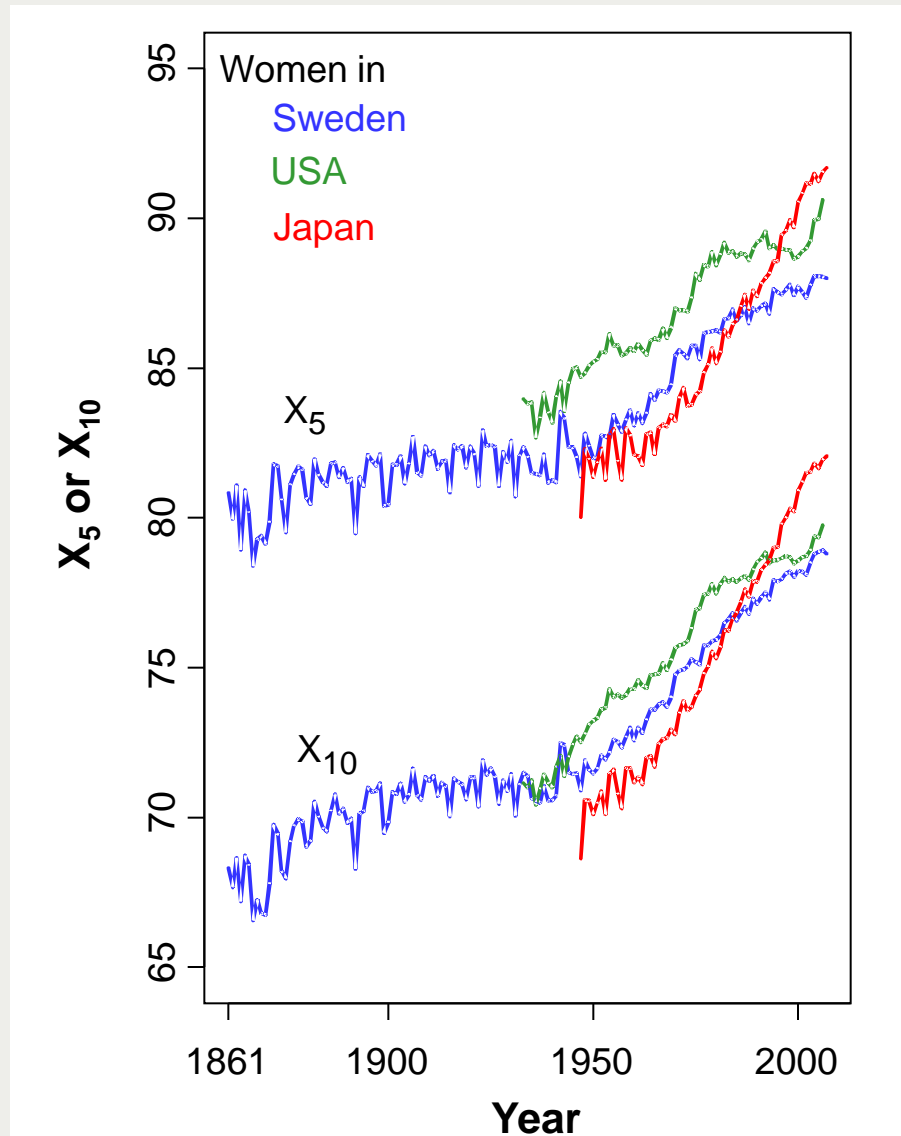


Discovery of the **Postponement** of Senescence

Vaupel and Lundström 1992/4, extended in Vaupel *Nature* 2010

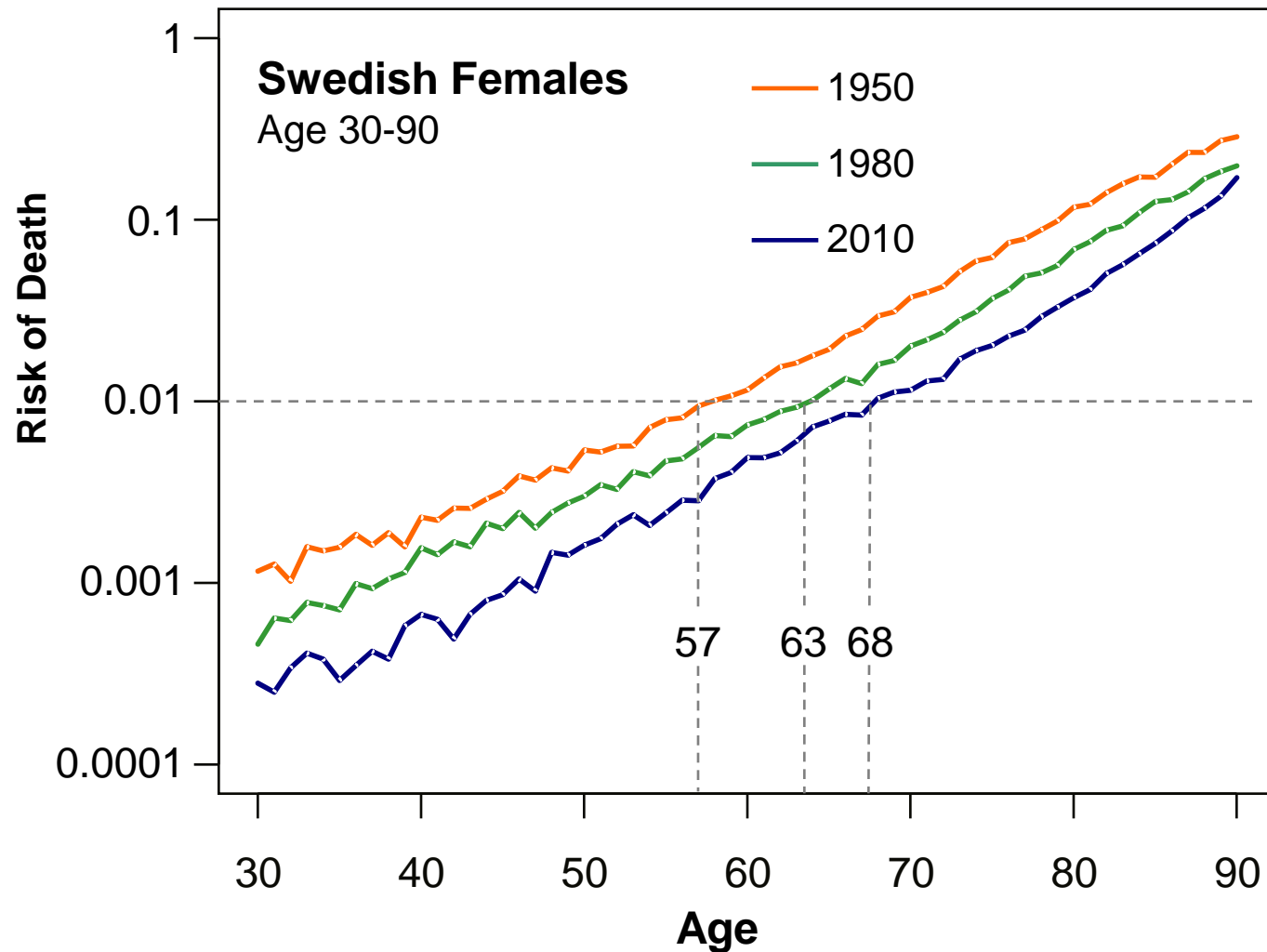


Ages when remaining life expectancy = 5 or 10





The Postponement of Senescence: Evidence from Sweden





Current age and age of equivalent mortality 50 years ago.



Age	Equivalent Age 50 Years Ago							
	Female				Male			
	France	Swe den	USA	Japan	France	Swe den	USA	Japan
50	42	40	44	23	44	43	44	39
60	49	52	53	43	51	53	51	50
<u>70</u>	59	62	63	53	59	62	<u>60</u>	57
80	71	72	74	67	71	73	73	70
90	83	85	85	79	84	87	85	81



Mechanisms of Human Longevity



→ The major discovery— The advancing frontier of survival.

Supplemental discoveries

1. The frontier of survival is advancing because senescence is being postponed.
2. **The advancing frontier of survival is part of the larger, long-term Life Expectancy Revolution.**



Question 2a:



On average, since 1840,
how much has female life expectancy in
the countries with the longest female
life expectancy,
increased per day?

- 1) 1 hour per day?
- 2) 3 hours per day?
- 3) 6 hours per day?



Question 2b:



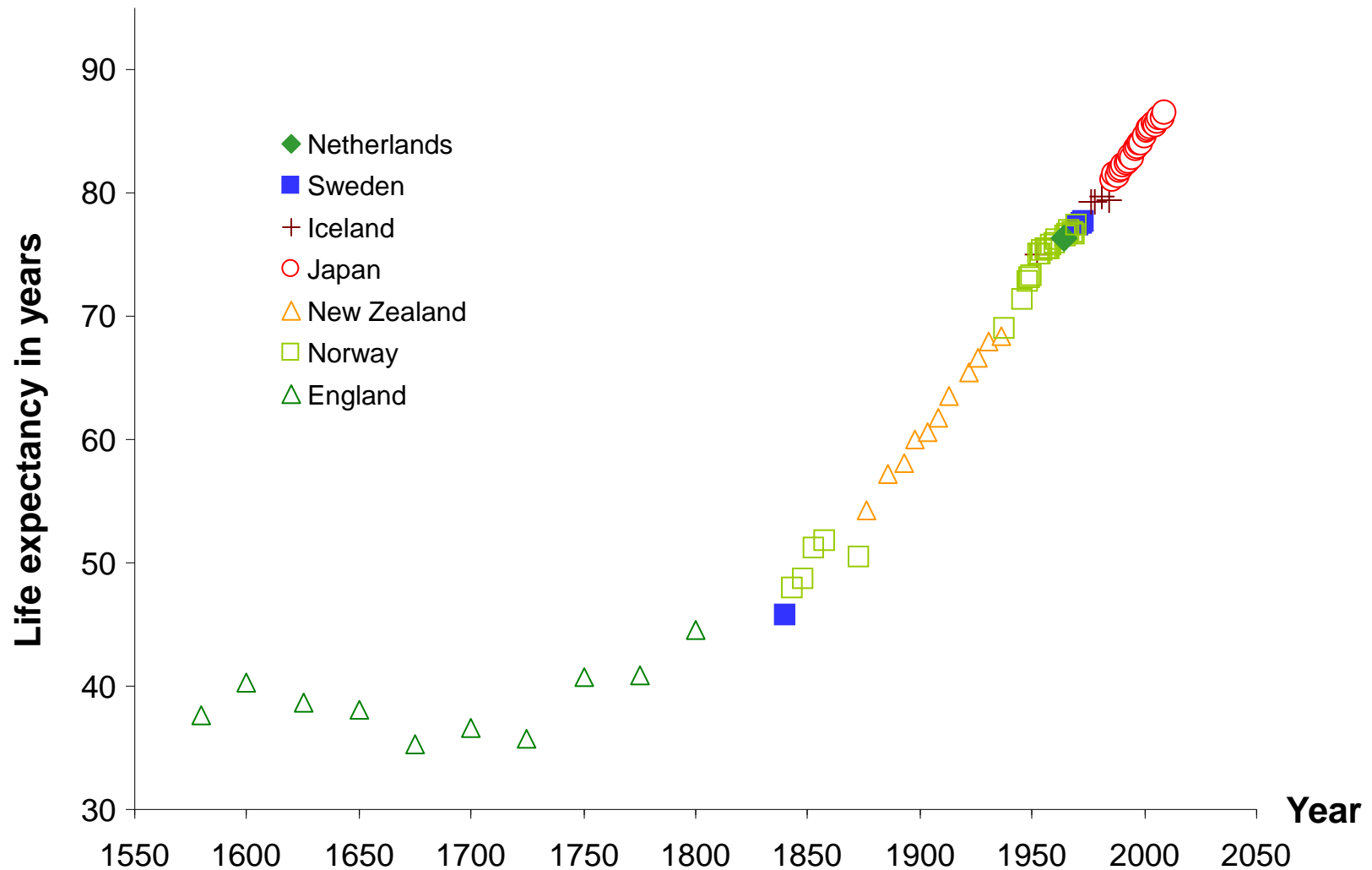
On average, since 1950,
how much has female life expectancy,
in the countries with the
longest female life expectancy,
increased per day?

- 1) 1 hour per day?
- 2) 3 hours per day?
- 3) 6 hours per day?



The Revolution in Record Life Expectancy

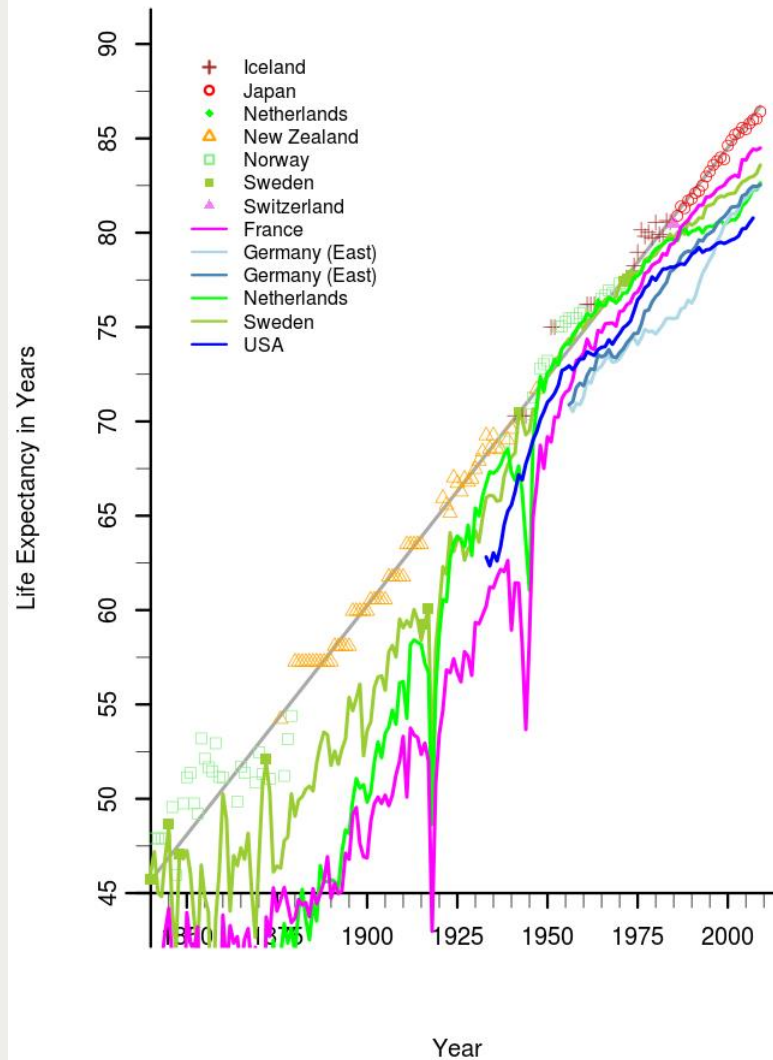
Oeppen & Vaupel *Science* 2002





The Linear Rise of **Record** Life Expectancy

Oeppen & Vaupel *Science* 2002: extended 2010





Question 3:



How much will U.S. life expectancy at birth, for males and females combined, currently about 78 years, increase over the next 40 years?

- 1) Less than two years
- 2) More than 2 years but less than 5
- 3) More than 5 years but less than 8
- 4) More than 8 years.



The Best Forecasting Strategy



At present the best way to forecast U.S. life expectancy is to extrapolate long-term historical trends from countries with high life expectancy.

And then to ask: why might progress be faster? Why might it be slower?

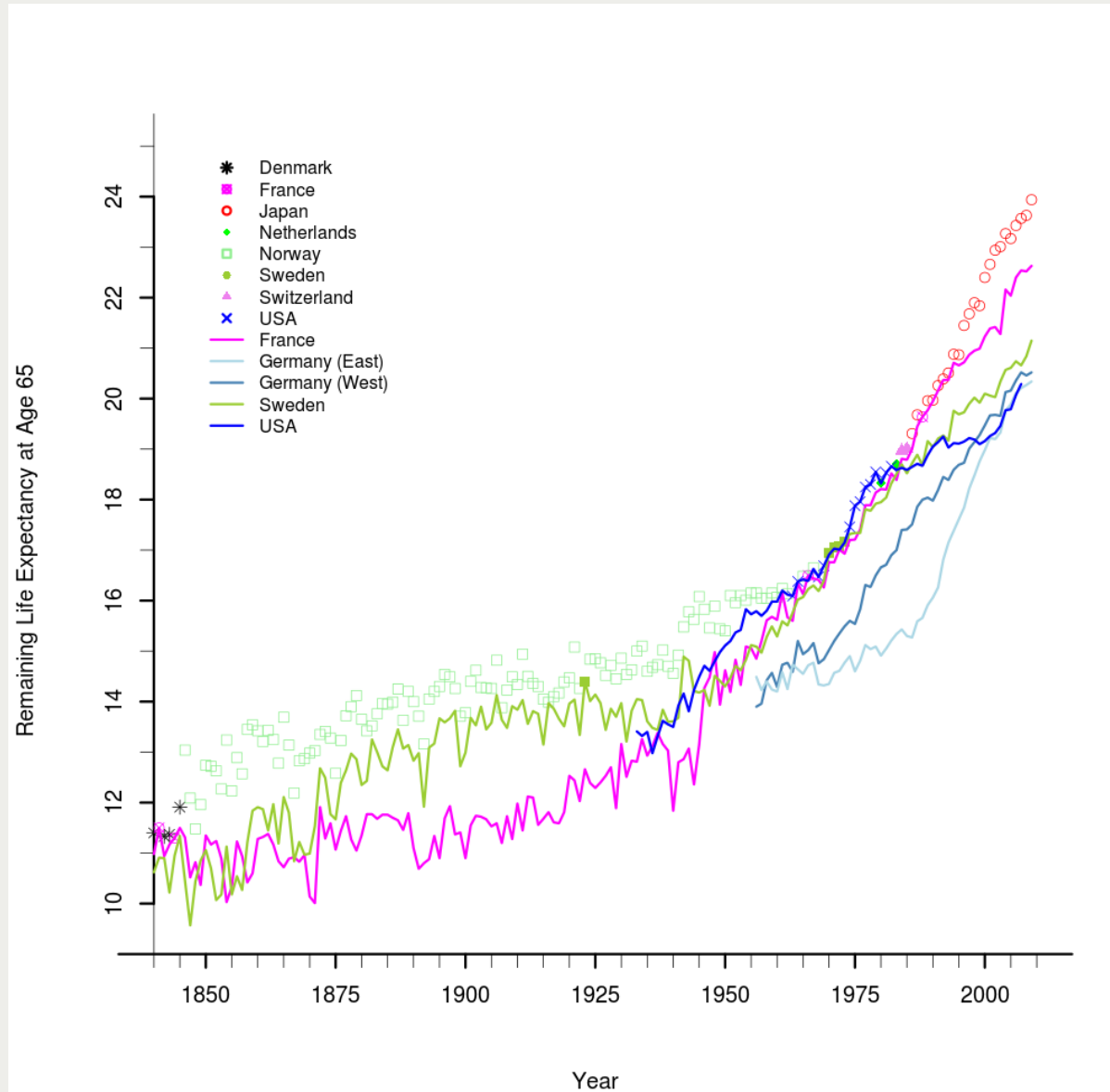


U.S. life expectancy at birth, for males and for females, may increase by 3 months per year over the rest of the 21st century, rising a full decade in the next 40 years.

Remaining life expectancy at age 65 may increase almost as much.



The Rise in **Record** Life Expectancy at Age 65





For U.S. birth cohorts, life expectancy may increase by 4 months per year.

If so, most Americans born since 2000 will celebrate their 100th birthdays.



Oldest Age at which at least 50% of a Birth Cohort is Still Alive

Christensen, Doblhammer, Rau & Vaupel *Lancet* 2009, extended



<i>Year of Birth: 2000</i>		<i>2005</i>	<i>2010</i>
France	102	104	105
Germany	100	101	103
Great Britain	102	103	105
Japan	105	107	108
Sweden	101	102	104
USA	101	103	105

Data are ages in years. Baseline data were obtained from the Human Mortality Database and refer to the total population of the respective countries.



Why did the U.S. do so poorly for men in the 1970s and 1980s and for women in the 1980s and 1990s.

The three main reasons are

smoking, smoking and smoking

followed by the syndrome of obesity, poor diet, lack of exercise and failure to get and follow good medical advice.

The key underlying reason is social inequality.



The Failure of Expert Imagination

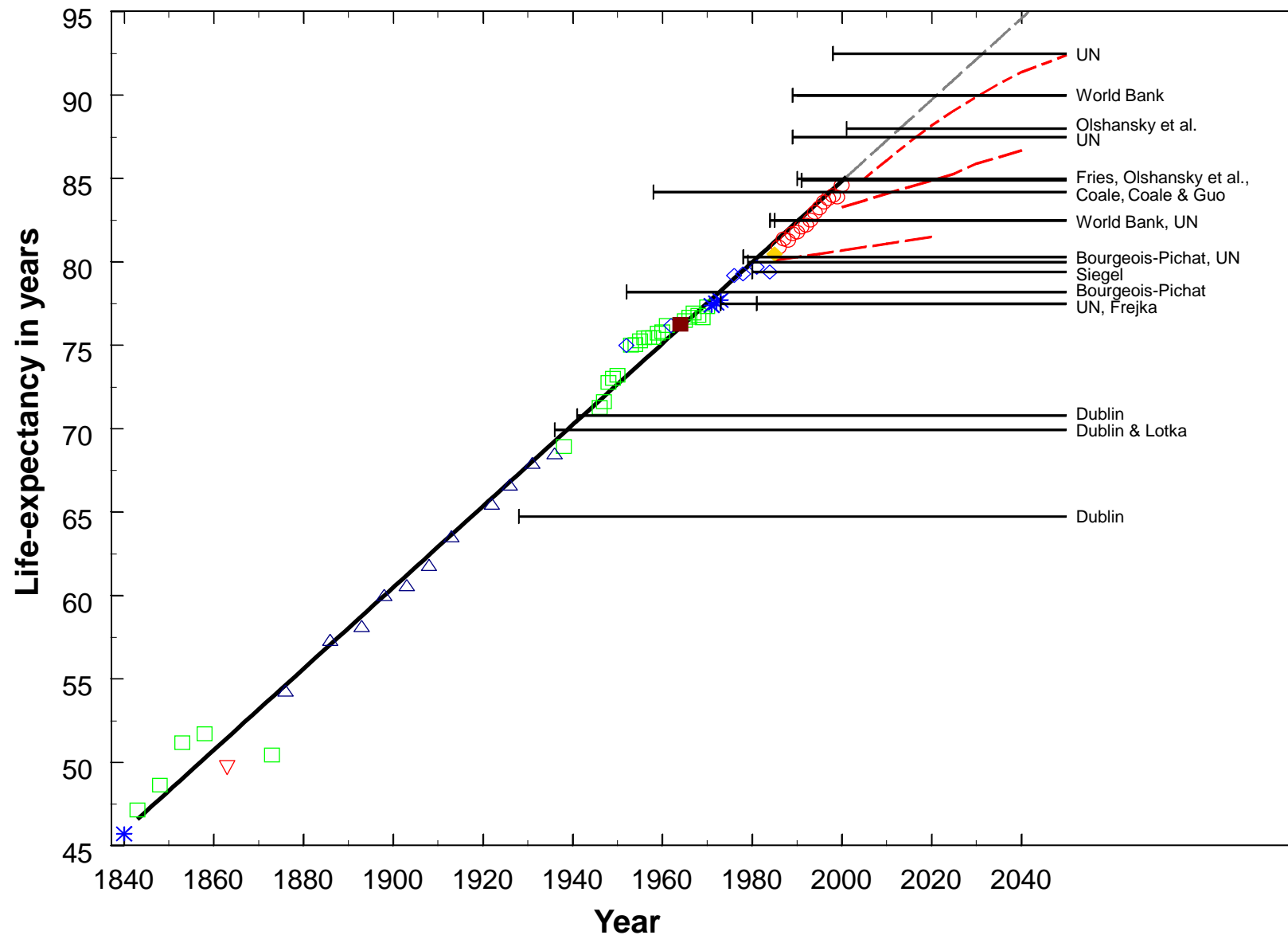


Mortality forecasts based on expert judgment have been less accurate than extrapolation.



The Sorry Saga of Looming Limits to Life Expectancy

Oeppen and Vaupel *Science* 2002





The Future Will Be Different from the Past



- In next decade or two, progress against **cancer** and **dementia** and in developing **genotype-specific therapies**
- Then progress in **regenerating** and eventually **rejuvenating** tissues and organs
- Accompanied by progress in **replacing deleterious genes**
- Aided by **nanotechnologies** (nanobots)
- Perhaps in a decade or two, probably later, progress in **slowing the rate of aging** (as opposed to further postponing aging).



The Future will be different from the past



Since 1840, future progress in extending life expectancy has been different from past progress.

- The country with the longest life expectancy has shifted from Sweden to Japan
- The causes of death against which progress has been made have shifted from infectious diseases to chronic diseases
- The ages at which mortality has been reduced have shifted from childhood to old age



Age-Specific Contributions to the Increase of Record Life Expectancy among Women 1850 to 2009 in %



Age group	1850-1901	1901-1925	1925-1950	1950-1975	1975-1990	1990-2009
0	14	32	15	21	10	4
1-14	55	8	16	12	4	2
15-49	25	38	39	20	7	4
50-64	3	13	19	17	20	11
65-79	2	8	11	24	41	37
80+	0	1	0	6	17	41
Total	100	100	100	100	100	100



The Future will be different from the past



BECAUSE since 1840 future progress in extending life expectancy has been different from past progress,

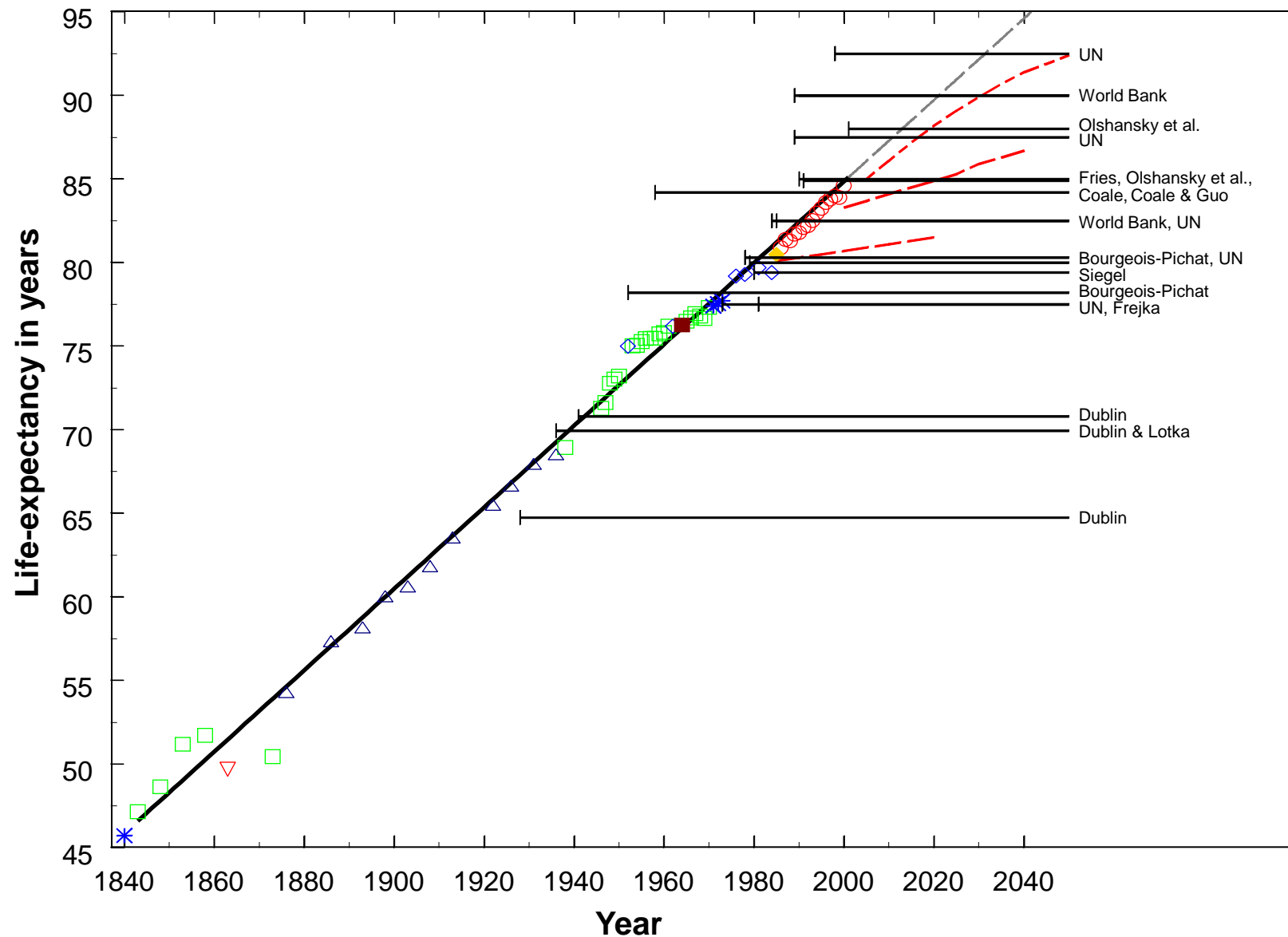
and because experts understand the past but have difficulty foreseeing future advances,

the best strategy for forecasting the future of mortality is to extrapolate past trends, which incorporate all the unforeseen advances and shocks in the past.



The Sorry Saga of Looming Limits to Life Expectancy

Oeppen and Vaupel *Science* 2002





Leonard Hayflick
Professor of Anatomy
University of California, San Francisco

1. Aging
2. Longevity Determination
3. Age-associated Diseases
4. Death



THERE ARE ONLY TWO WAYS IN WHICH AGE CHANGES CAN OCCUR

(1) A purposeful program driven by genes.

or

(2) A stochastic or randomly occurring cascade of accidental events.



EVIDENCE THAT AGING IS A STOCHASTIC PROCESS



- (1) There is no **direct** evidence that supports the notion that aging is the result of a genetic program. No gene that codes for a generally accepted biomarker of aging has been found.
- (2) Animate and inanimate objects require no instructions to age.
- (3) A huge body of knowledge exists indicating that age changes are characterized by the loss of molecular fidelity in both animate and inanimate objects.



SO, WHAT IS AGING?



Aging is the random, systemic, loss of molecular fidelity that occurs from life's beginning. Repair, maintenance and synthesis processes are capable of maintaining the balance in favor of sustaining molecular fidelity until reproductive maturity.

If not, the species would vanish.

After reproductive maturation and the great probability of species survival, the energy states of molecules, evolved through natural selection diminishes.

Thus, the balance slowly shifts to favor the continued accumulation of un-repaired or un-replaced dysfunctional molecules. This accumulation is expressed at higher levels of organization as age changes.

The progressive loss of molecular fidelity increases vulnerability to age-associated diseases.



WHY ARE MOST DISEASES AGE-ASSOCIATED?

Age-associated changes and pathology result from secondary modifications that occur after the basic unrepaired age changes have modified molecular structures.

Unlike what occurs in young cells, the increasing accumulation and vulnerability of dysfunctional molecules that have undergone unrepaired age changes in old cells explains why most chronic diseases occur in old age.

These secondary modifications reveal themselves at higher orders of organization as the manifestations of age-associated diseases such as annoyances (gray hair, age spots, wrinkles) or later as serious pathology, (cardiovascular disease, cancer, stroke).



WHY IS AGING NOT DETERMINED BY GENES?

Age changes occur spontaneously in the molecules of both animate and inanimate objects as molecules dissipate energy, lose structural integrity and finally, within various time frames, lose functional capacity.

Genes are unnecessary to drive a spontaneous process.

Blueprints contain no information instructing a car how to age. Analogously, the genome also does not need to contain similar instructions.

Aging is an artifact of human civilization. It occurs only in humans or in animals we choose to protect.



AGE CHANGES MUST OCCUR IN MOLECULES THAT FIRST EXIST WITHOUT AGE CHANGES

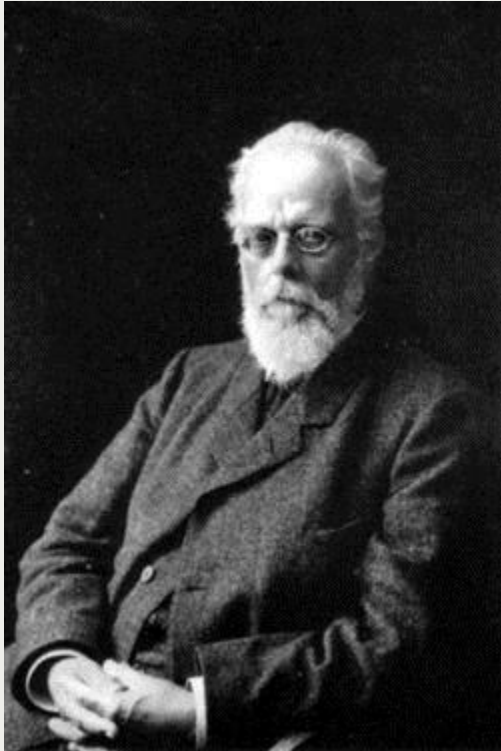
Longevity is determined by the length of time that repair, synthesis and maintenance processes can retain the biologically active state of molecules.

When molecules composing the repair, synthesis and maintenance processes themselves eventually succumb to the same irreparable reduced energy states as does their substrate molecules, the aging process becomes manifest at higher levels of organization.



WE WERE THE FIRST TO DEMONSTRATE THE MORTALITY OF NORMAL CELLS IN THE LABORATORY

In 1980 I LEARNED THAT IN 1881 THE GERMAN BIOLOGIST AUGUST WEISMANN WAS FIRST TO **SPECULATE THAT THIS WAS TRUE:**



“Death takes place because a worn-out tissue cannot forever renew itself, and because a capacity for increase by means of cell division is not everlasting but finite”

A. Weismann. *Clarendon, Oxford* **1881**



THE GENOME INDIRECTLY DETERMINES LONGEVITY

The genome governs events from life's beginning until reproductive maturation after which many of the events that it continues to govern are overtaken by the aging process (The 2nd law, - dispersal of energy).

In youth, the efficiency of repair, synthesis and maintenance of molecules is favored over the continued loss of molecular structure in substrate molecules.

After reproductive success, the balance slowly shifts to a state where the loss of molecular structure begins to exceed repair and maintenance capacity.



THE GENOME INDIRECTLY DETERMINES LONGEVITY



Unlike the stochastic process that characterizes aging, longevity determination is not a random process.

Longevity is governed by the enormous excess, or redundancy, in physiological reserve reached at the time of reproductive maturation.

This redundancy has been achieved through natural selection to better guarantee survival to the age of reproductive success.

Thus, the determination of longevity is incidental to the main goal of the genome which is to reach reproductive maturity.



AGING DETERMINANTS vs. LONGEVITY DETERMINANTS



Longevity determination is an entirely different process from the aging process.

One might think of longevity determination as the energy state of molecules before they incur age changes. (“Why do we live as long as we do?”)

One might think of aging as the state of molecules as they continue to incur irreparable states of dysfunction. (“Why do things eventually go wrong?”)

Aging then is a **catabolic** process that is chance driven.

Longevity determination is an **anabolic** process that, indirectly, is genome driven.



WHAT IF ALL LEADING CAUSES WRITTEN ON DEATH CERTIFICATES WERE TO BE RESOLVED?



In developed countries there could only be an increase in life expectancy of about 13 years.

Average life expectancy at birth in the U.S. today is about 79 years, thus 92 years would be the maximum, - absent the ability to perturb the aging and longevity determining processes.

(Anderson RN, U.S. Decennial Life Tables for 1989–91, Vol. 1, No. 4. US life tables eliminating certain causes of death. Hyattsville, MD: Nat. Ctr. for Health Statistics; 1999:7–8.)



WHAT WOULD BE THE INCREASE IN LIFE EXPECTANCY IF THE LEADING CAUSES OF DEATH ARE RESOLVED?



<i>CAUSE OF DEATH</i>	<i>APPROXIMATE INCREASE IN YEARS</i>	
	<i>At Birth:</i>	<i>At Age 65:</i>
Cardiovascular Disease & Stroke	6.73	6.25
Cancer	3.40	2.19
Accidents	0.92	0.14
All Other Causes	4.29	1.71

(U.S. Decennial Life Tables for 1989-91, vol. 1, no. 4, DHHS Pub. No. PHS-99-1150-4)



IF ALL CAUSES OF DEATH CURRENTLY WRITTEN ON DEATH CERTIFICATES WOULD BE RESOLVED THEN WHAT WOULD CAUSE DEATH?



Manifestations of the aging process would be the cause of most death. (Accidents, homicide, wars and suicide may never be eliminated.)

The aging process, which usually begins well before most age-associated diseases appear, would continue.

A new vocabulary would be required to describe causes of death attributable to the loss of physiological capacity in some vital organ.



WHY IS IT IMPORTANT TO DISTINGUISH AGING FROM DISEASE?



Scientific reasons:

1. Research on the fundamental biology of aging could reveal that the increase in vulnerability to **all** age-associated diseases is rooted in some fundamental property found in old but not in young cells.
2. The probability that this is true is the universal belief that aging is the greatest risk factor for all age-associated diseases.

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The Future Course of Longevity

S. Jay Olshansky, Ph.D.

University of Illinois at Chicago



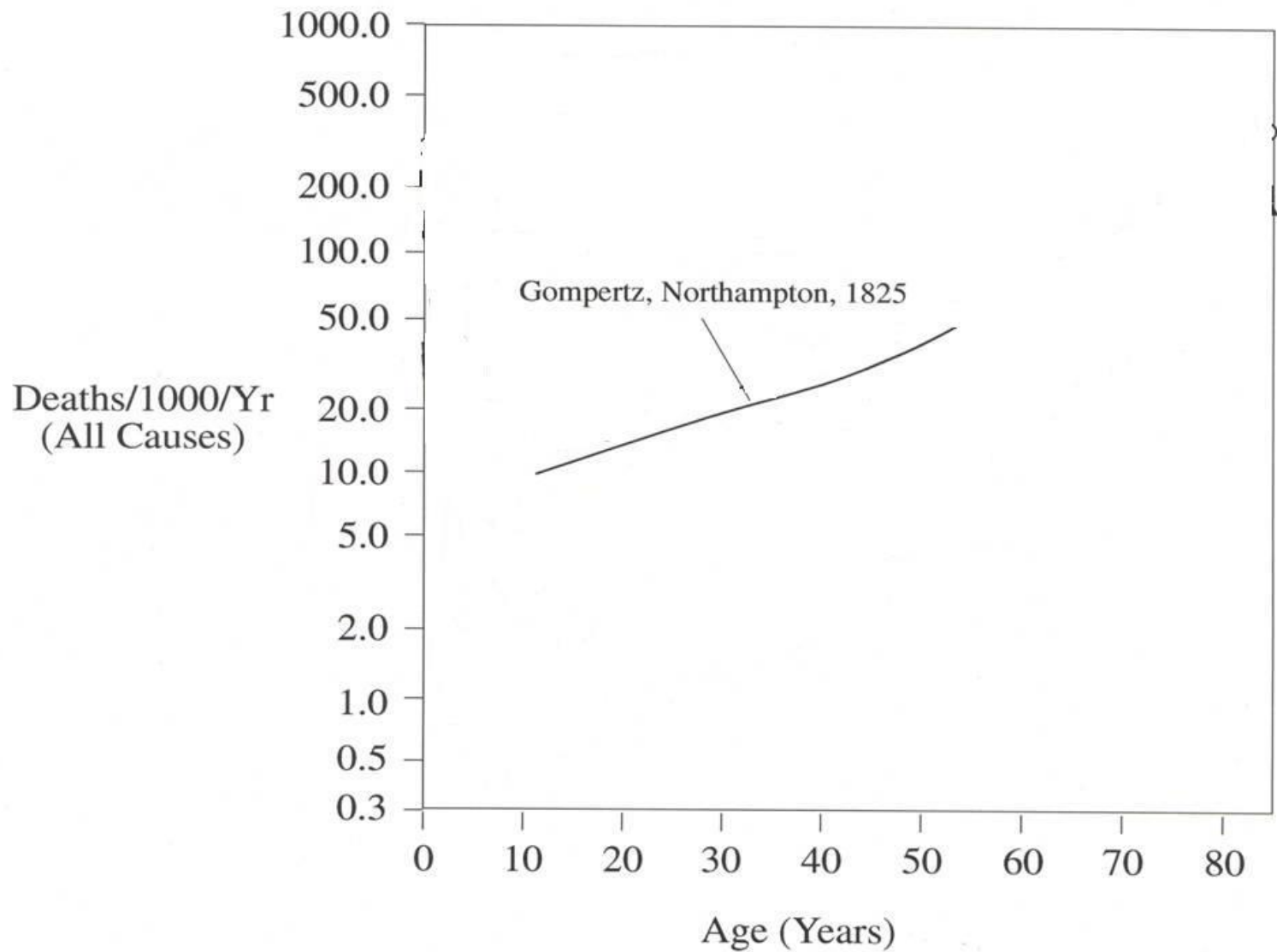
Summary

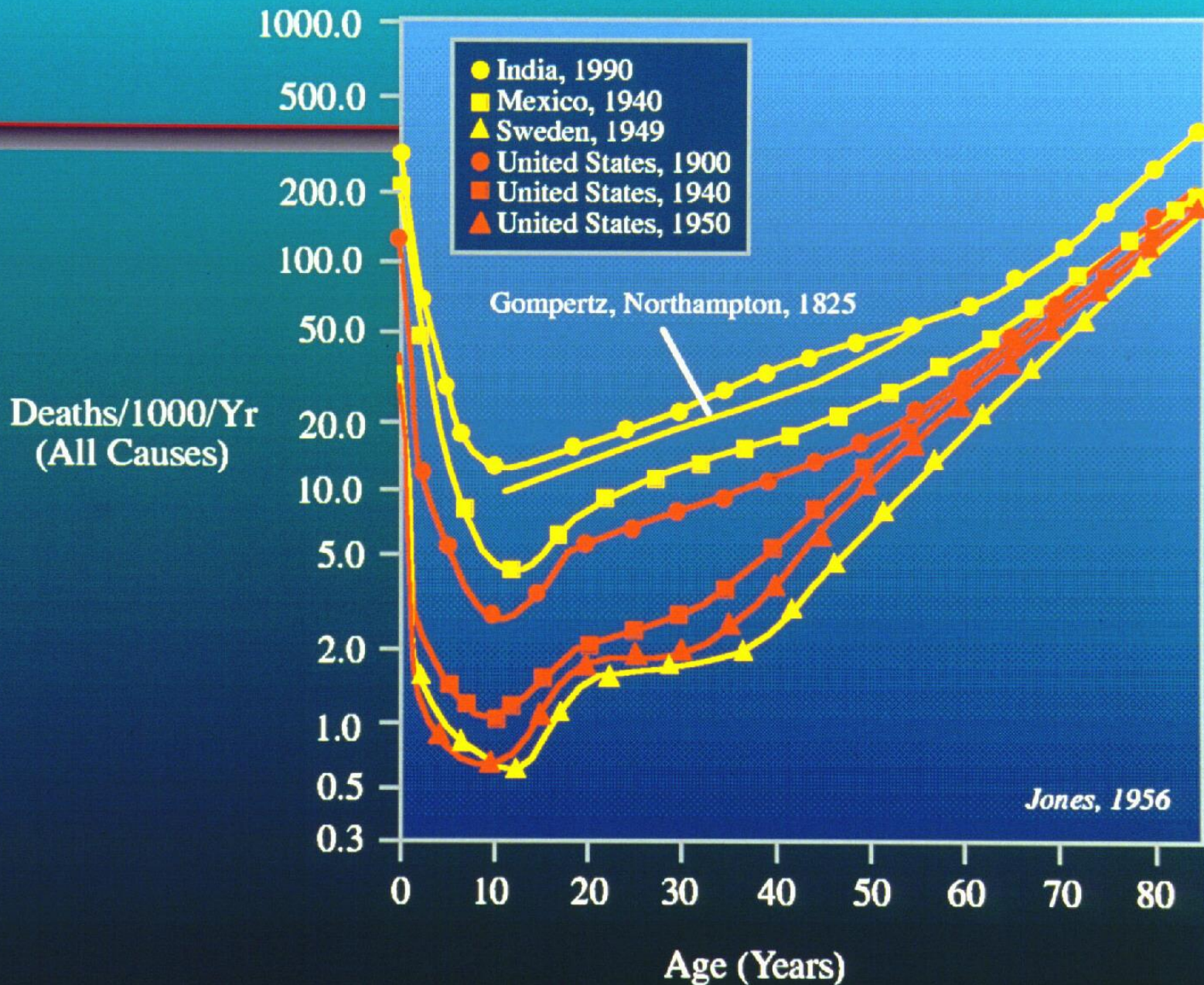
Message 1 Gompertz saw biology in the life table, and he was right – there is a law of mortality.

Message 2 Future trends in mortality and longevity will be driven by biology, not past trends. Linear thinking got us in trouble in the past, and it's still getting us in trouble today.

Message 3 A life expectancy of 100 is highly unlikely, but the number of centenarians will rise dramatically.

Message 4 Life expectancy is likely to rise rapidly for some, and decline dramatically for others. Education is a longevity trump card.





VI. A COMPARISON OF THE LAWS OF MORTALITY IN *DROSOPHILA* AND IN MAN

PROFESSOR RAYMOND PEARL

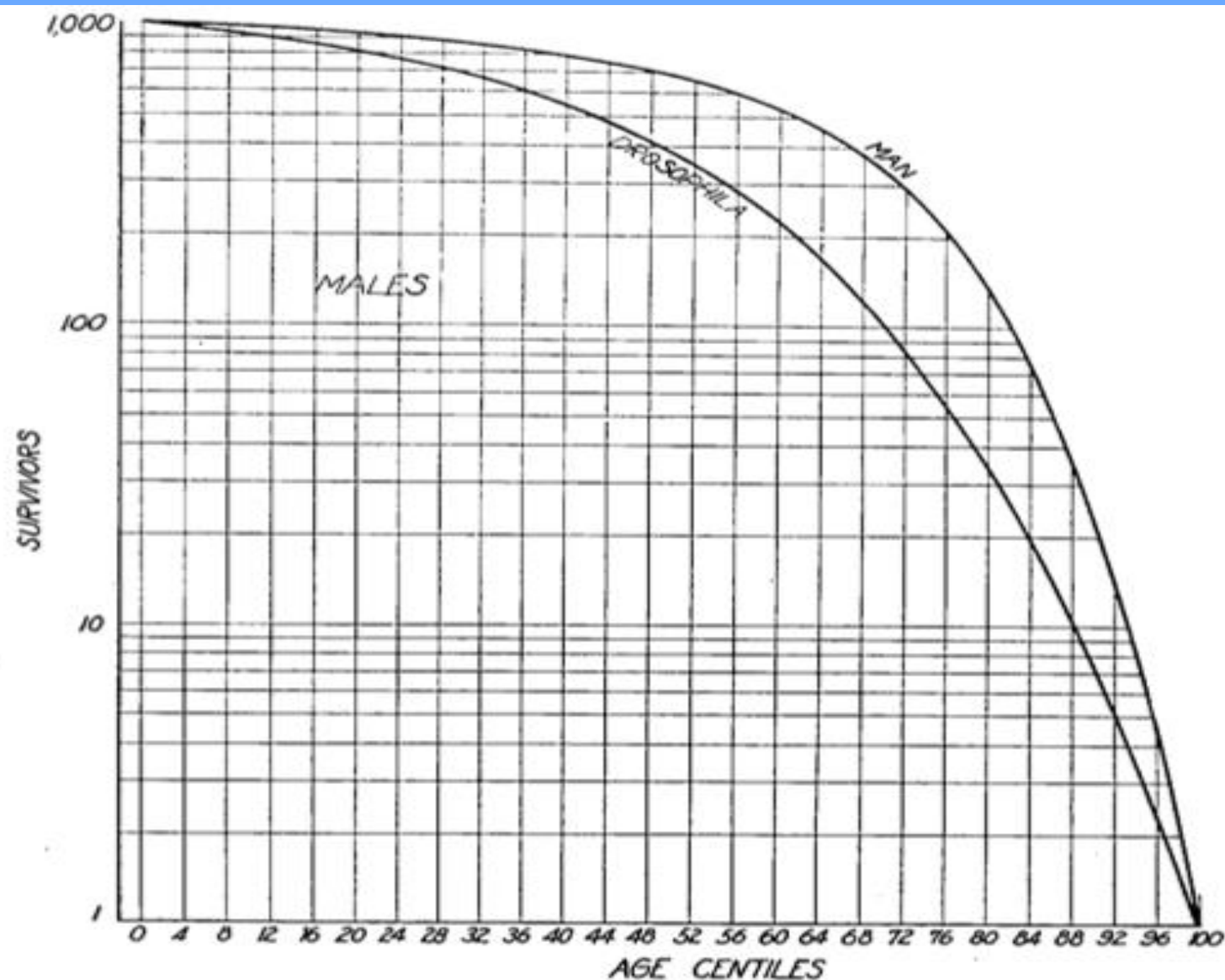


FIG. 1. Comparing the survivorship distributions of *Drosophila* and man (males in both cases) over the equivalent life spans.

Solving the law of mortality required conditions that were difficult to overcome

- The ability to reliably measure Intrinsic Mortality
- Access to reliable intrinsic mortality rates for different species
- Scaling Time

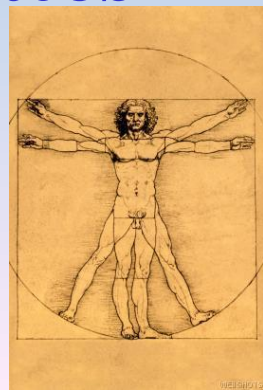
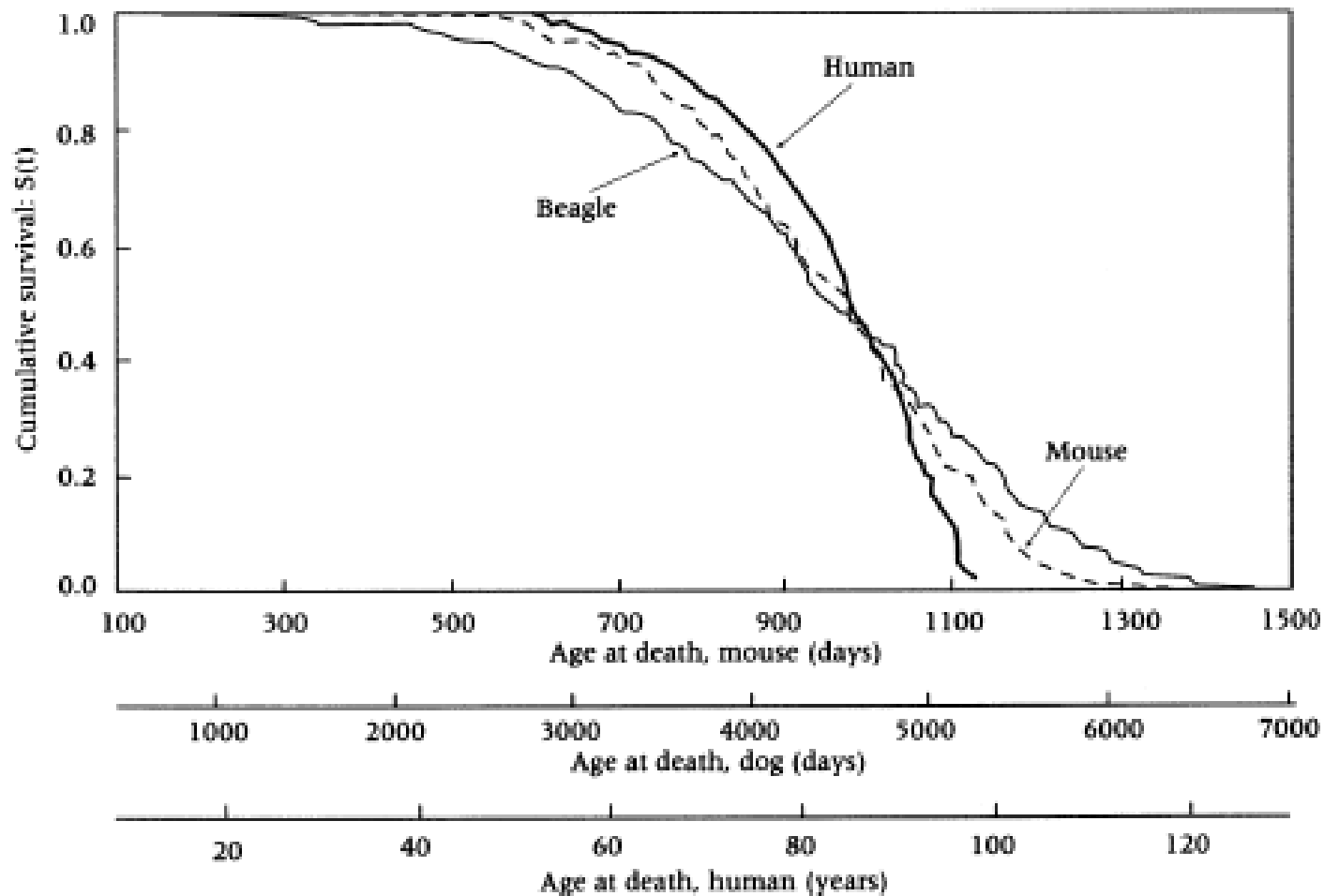
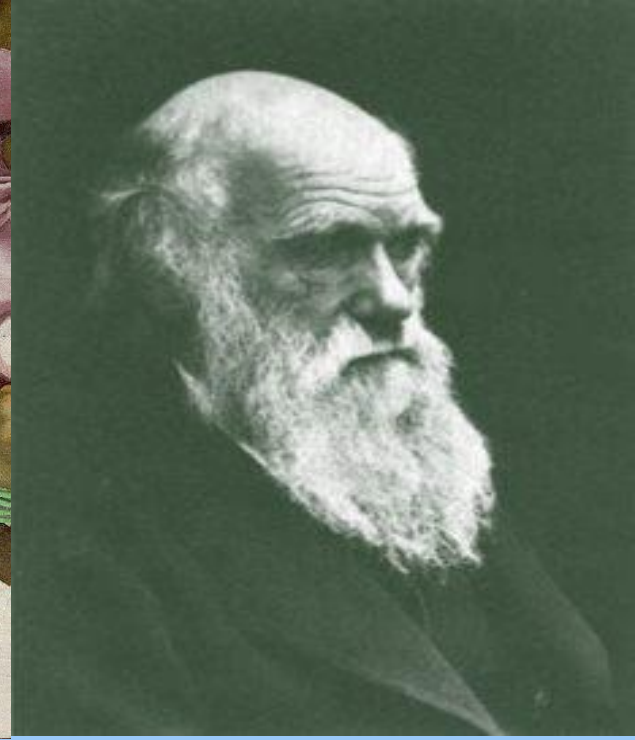
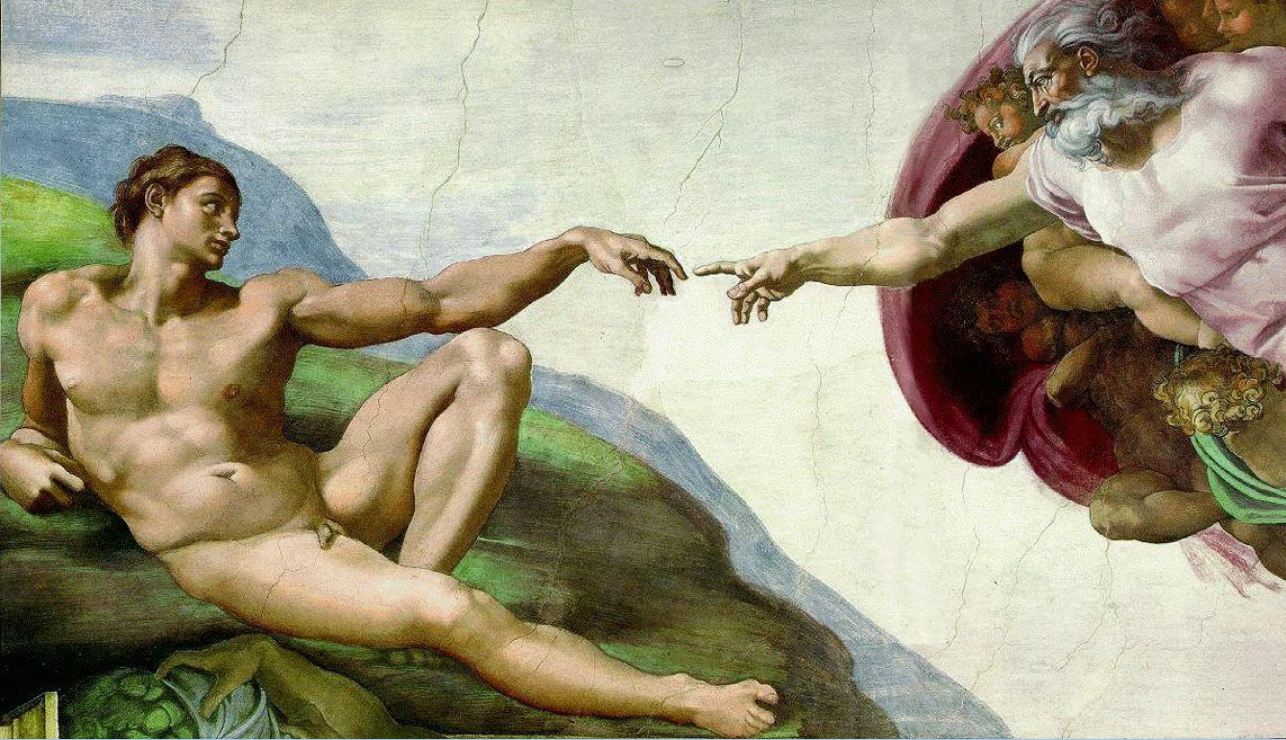


FIGURE 3 Comparison of cumulative survival curves for the mouse, beagle, and human populations plotted on the time scale for the B6CF₁ mouse strain. Additional time axes are shown for the beagle and human to demonstrate the effect of scaling

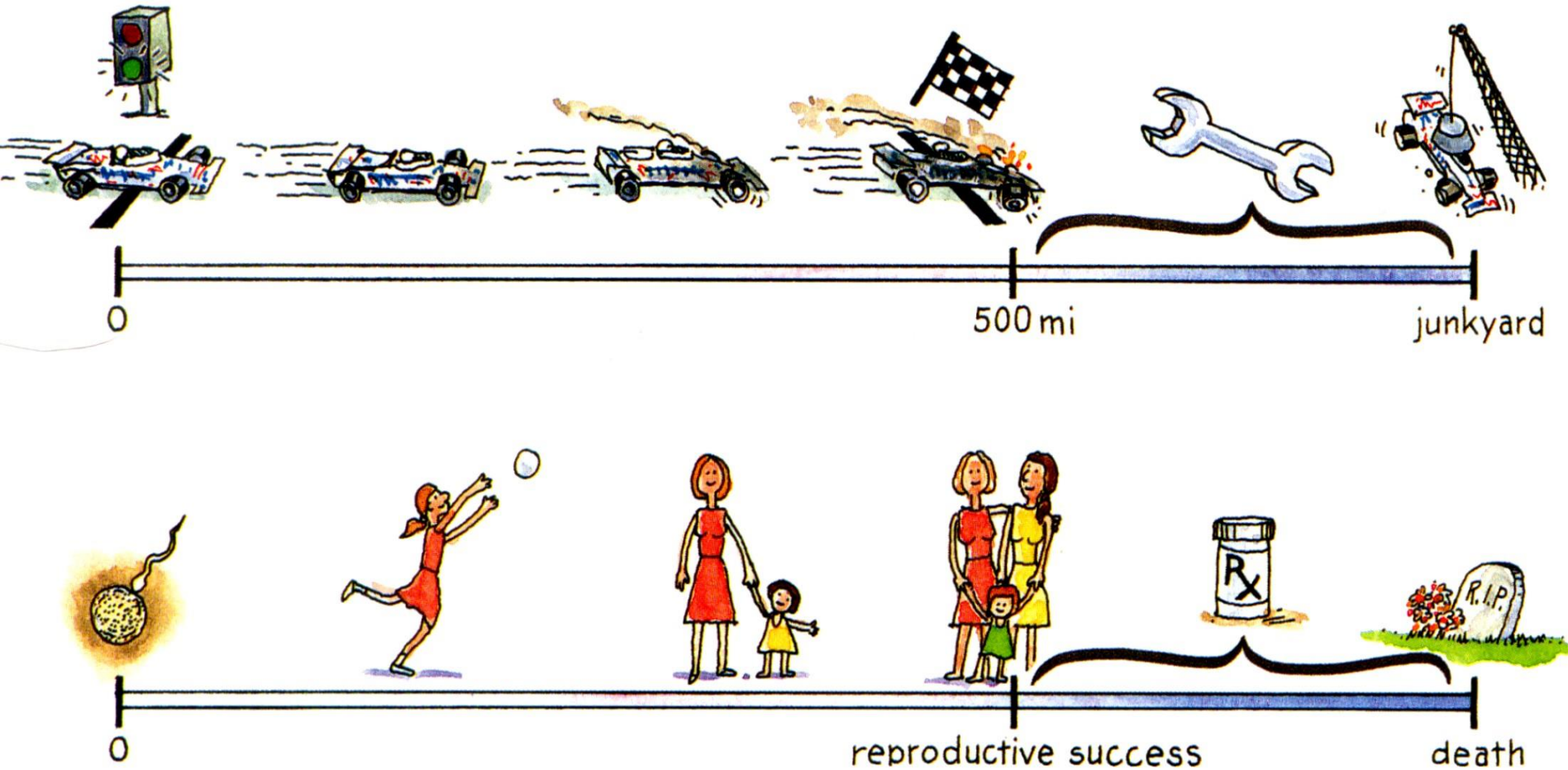


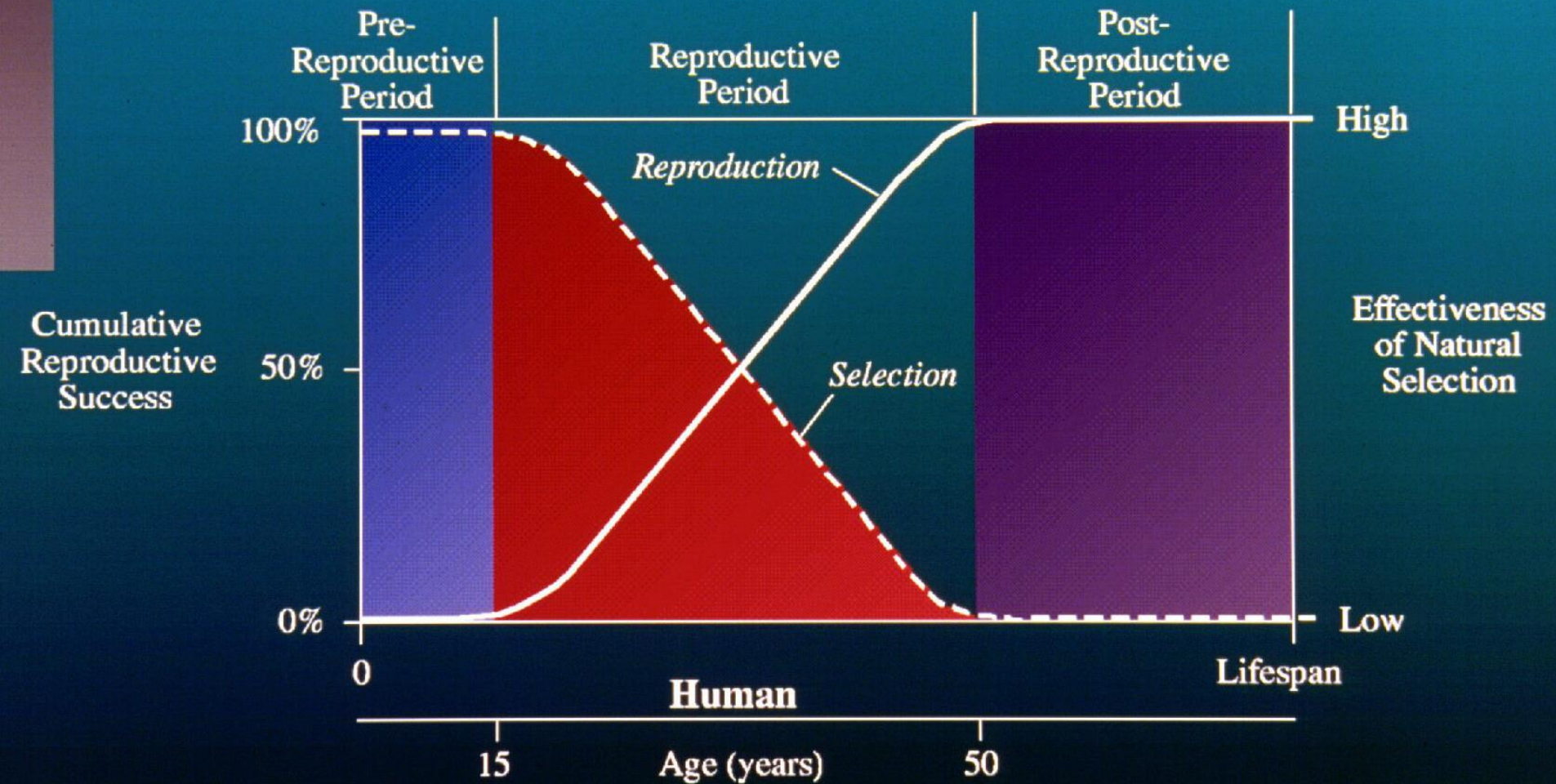


BOTH Michelangelo and Darwin WERE RIGHT

The human body is a miraculous machine that works with near artistic perfection – for a while. Time reveals the “flaws” in a body design that was not intended for long-term use.

WHY DO WE LIVE AS LONG AS LONG AS WE DO?





There is a remarkable consistency to the timing of death across species.

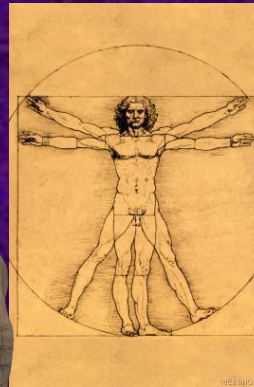
Duration of life is calibrated to the onset and length of a species' reproductive window.



77,000 days
Bowhead
Whale



55,000 days
Sea Turtle



29,000 days
Human



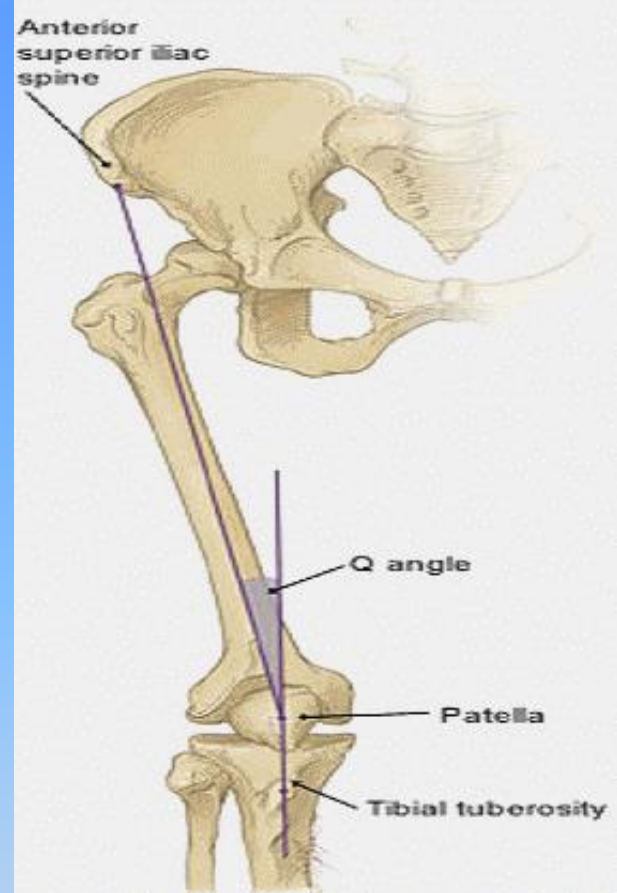
26,000 days
Elephant



5,000 days
Dog



1,000 days
Mouse



Although there is no genetic program that limits how fast humans are capable of running, there are nevertheless biomechanical constraints on running speed.

Although there is no genetic program that limits the duration of life, there are nevertheless biomechanical constraints on the functioning of body parts that influence how long we live.

Can most live to 100?

Can we really add decades of life to people aged 70+ today faster than we added decades of life to children born in the early 20th century?

SPECIAL

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EDITION

HOW TO LIVE TO 100

WHAT SCIENCE
REVEALS ABOUT
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IS YOUR JOB
KILLING
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HOW TO KEEP YOUR
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THIS BABY
WILL LIVE TO BE
120*



Bridge on Whangai Island 10
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Fossilize the World 14
Building the New Gumbata 16
China's Great Canal 18

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THIS BABY
WILL LIVE TO BE
120*



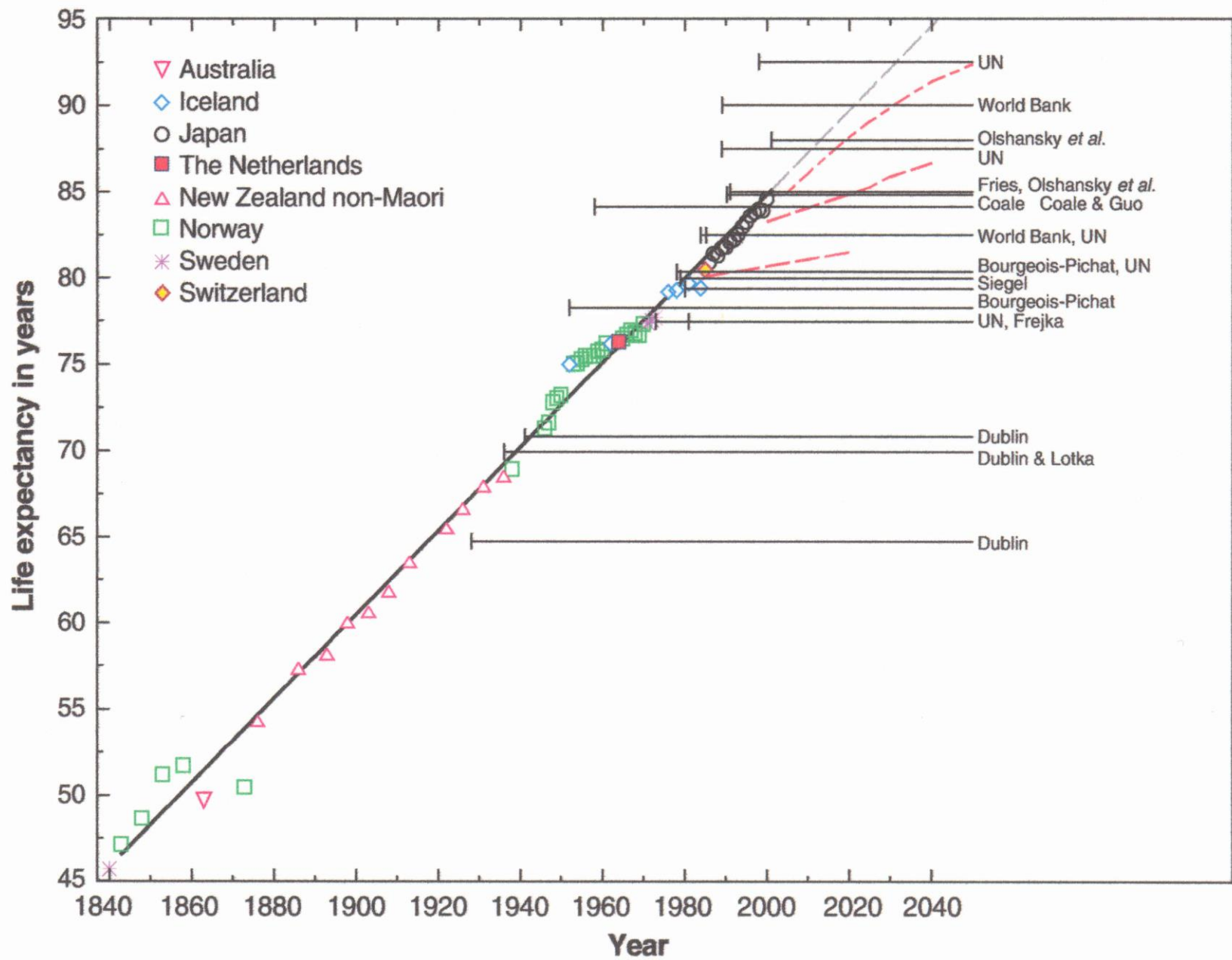
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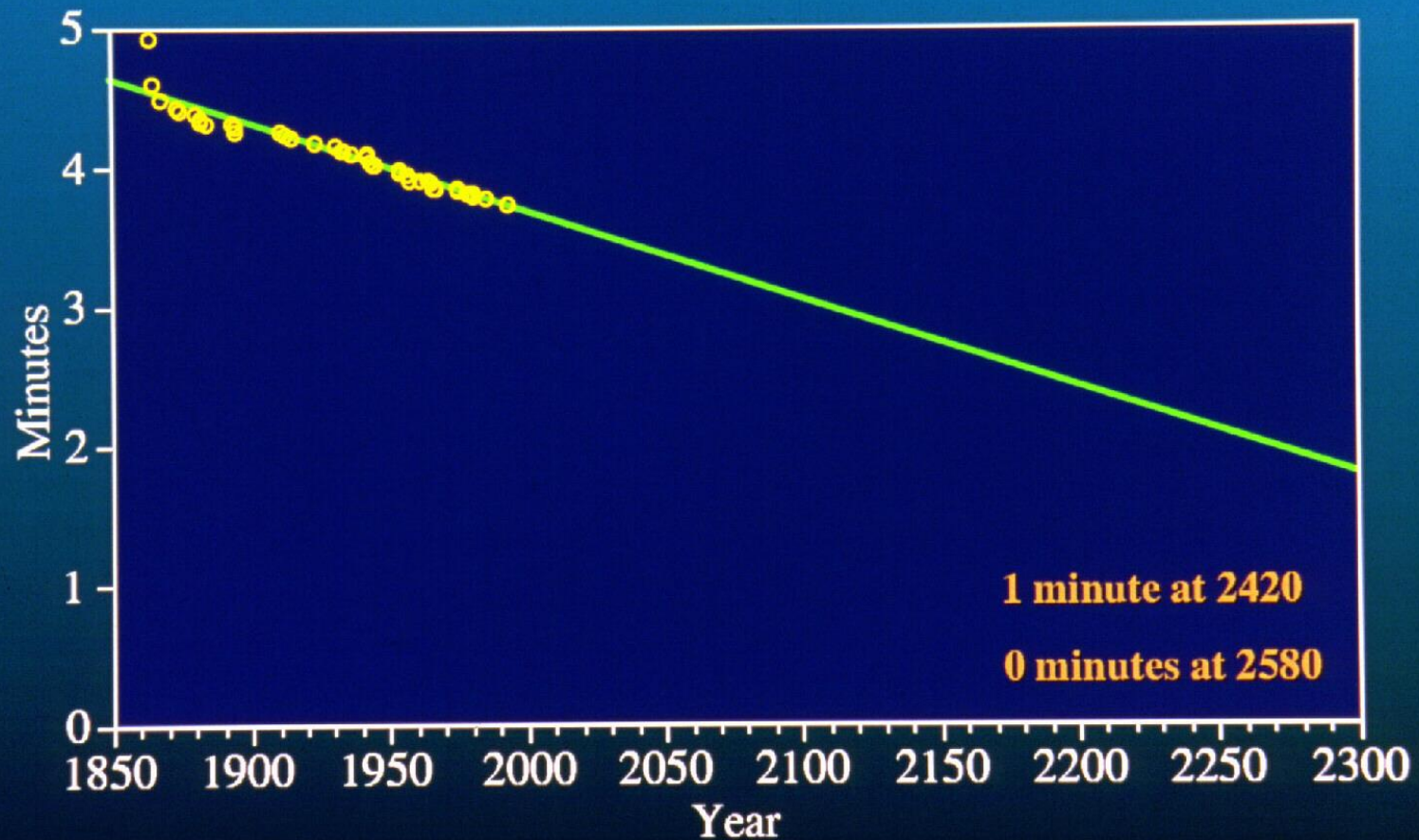
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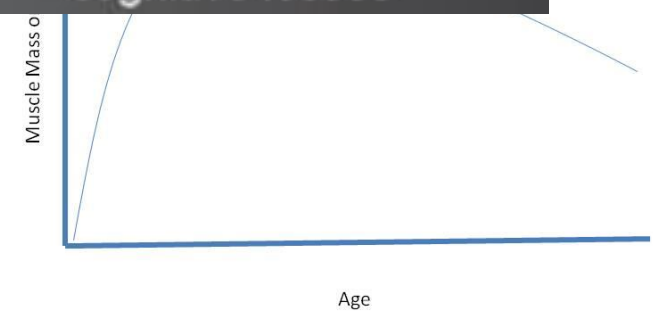
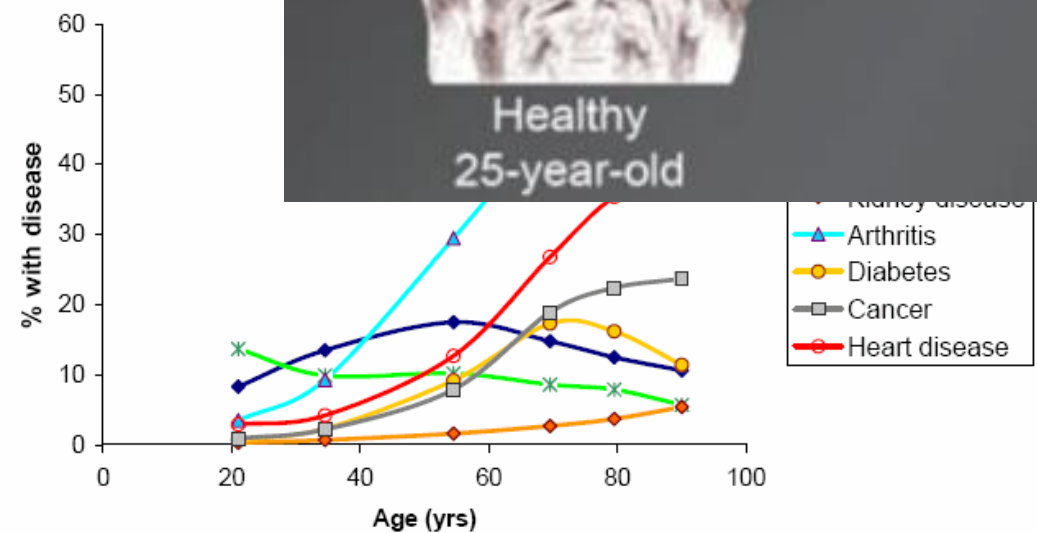
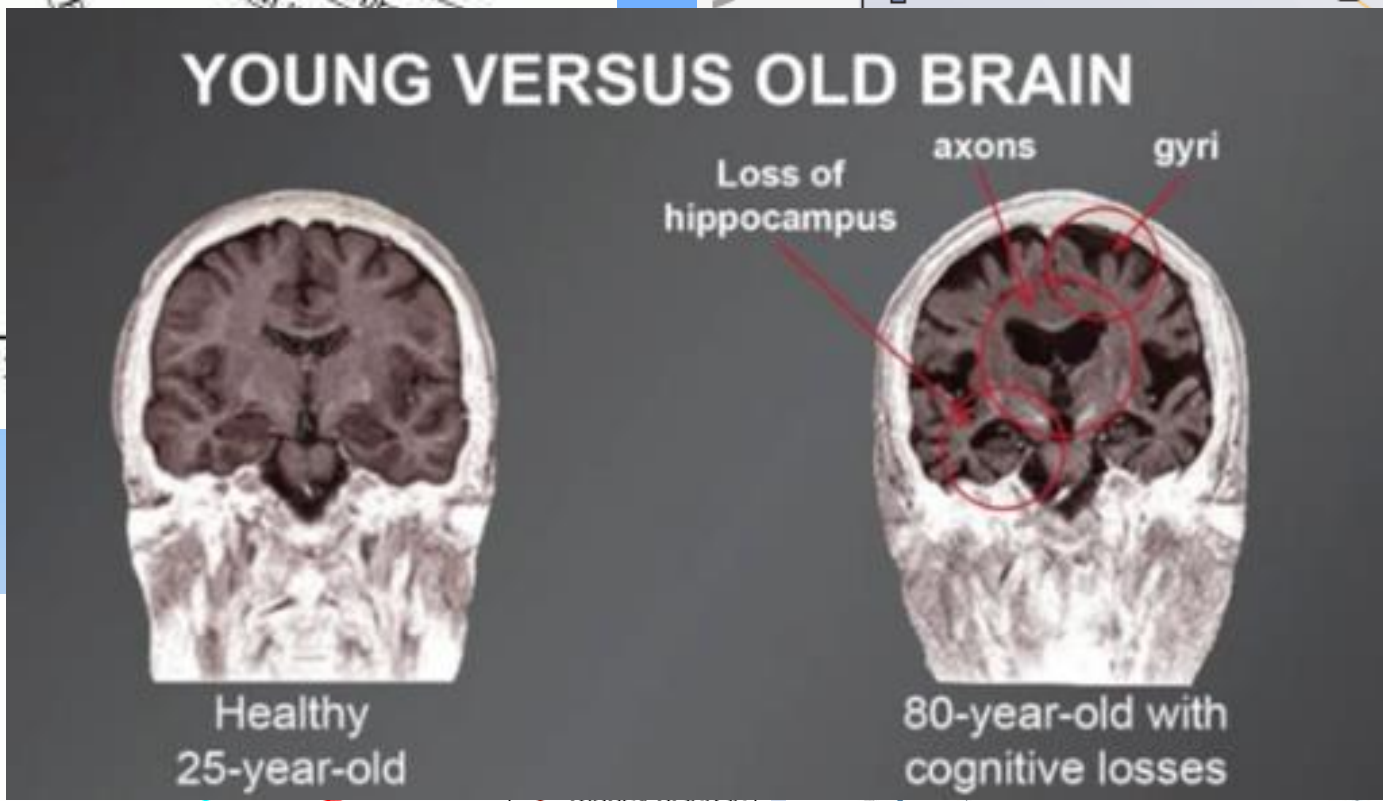
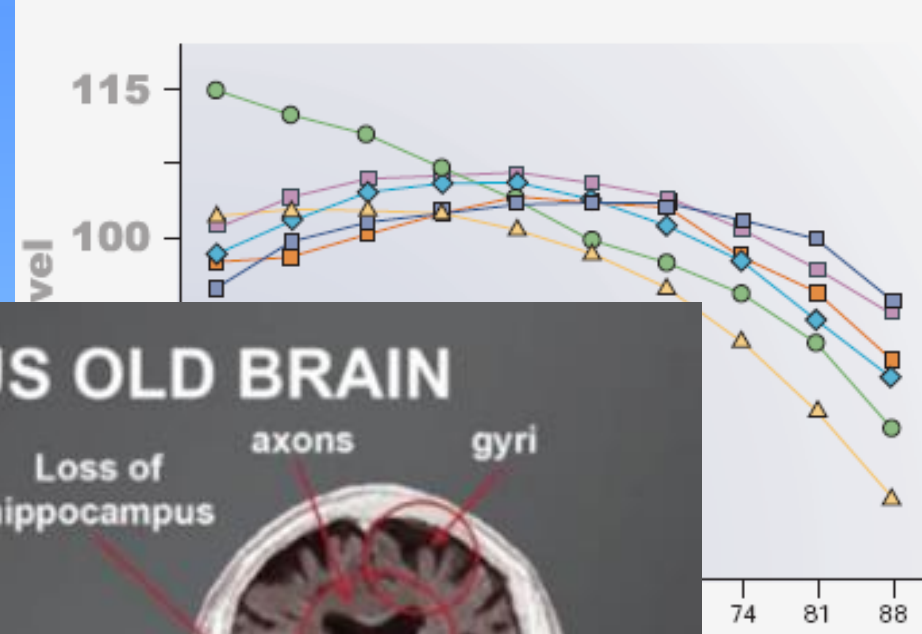
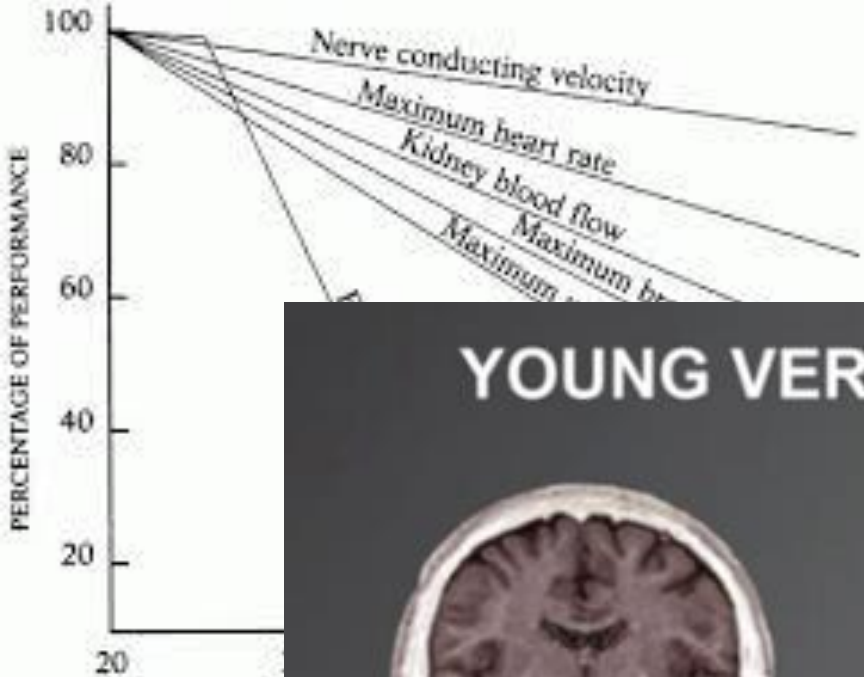
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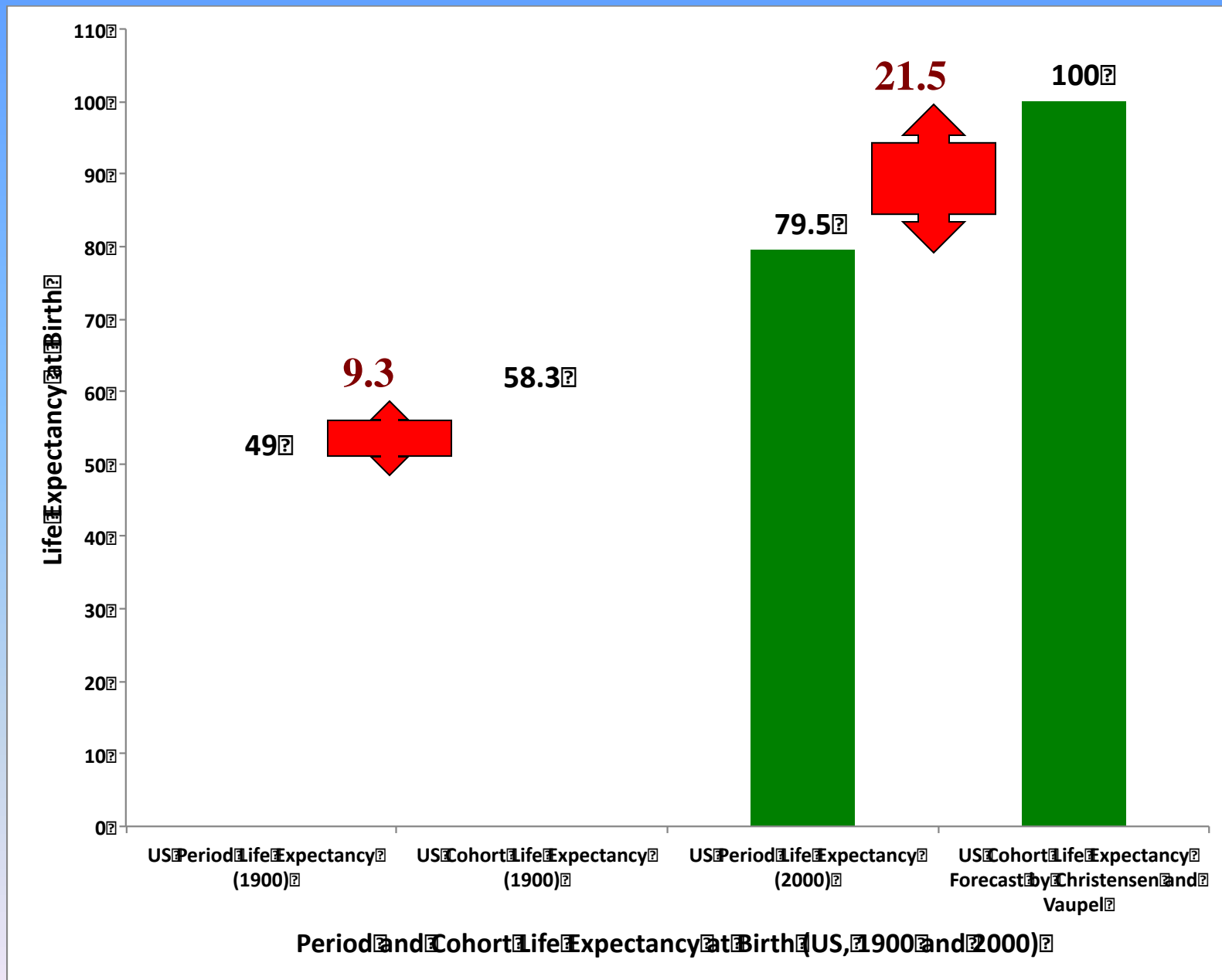


World Record for the 1-Mile Run (Males)



Source: World Almanac, 1985; 1990; 1995





Source: US Social Security Administration and Christensen et al., 2009

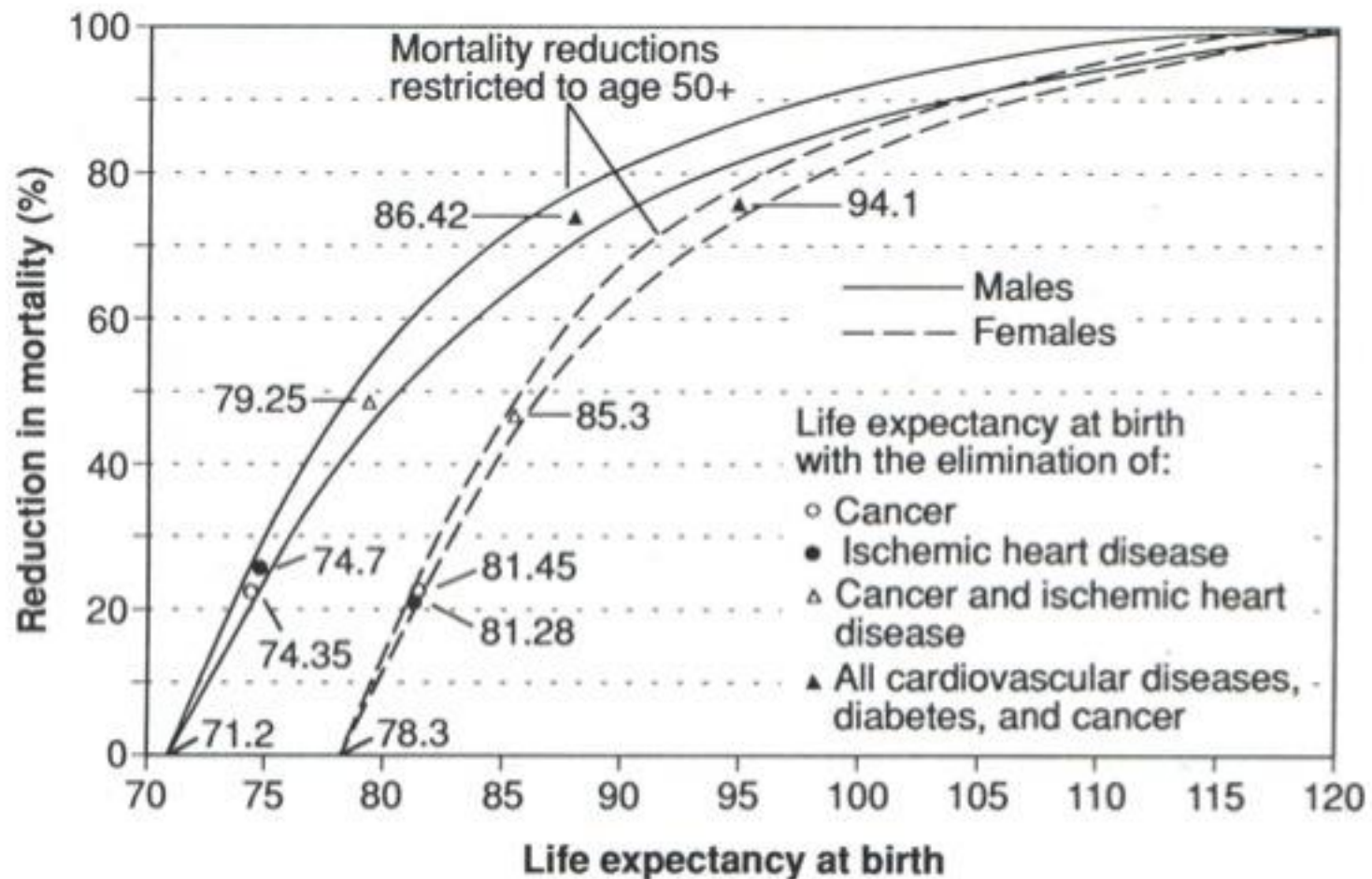
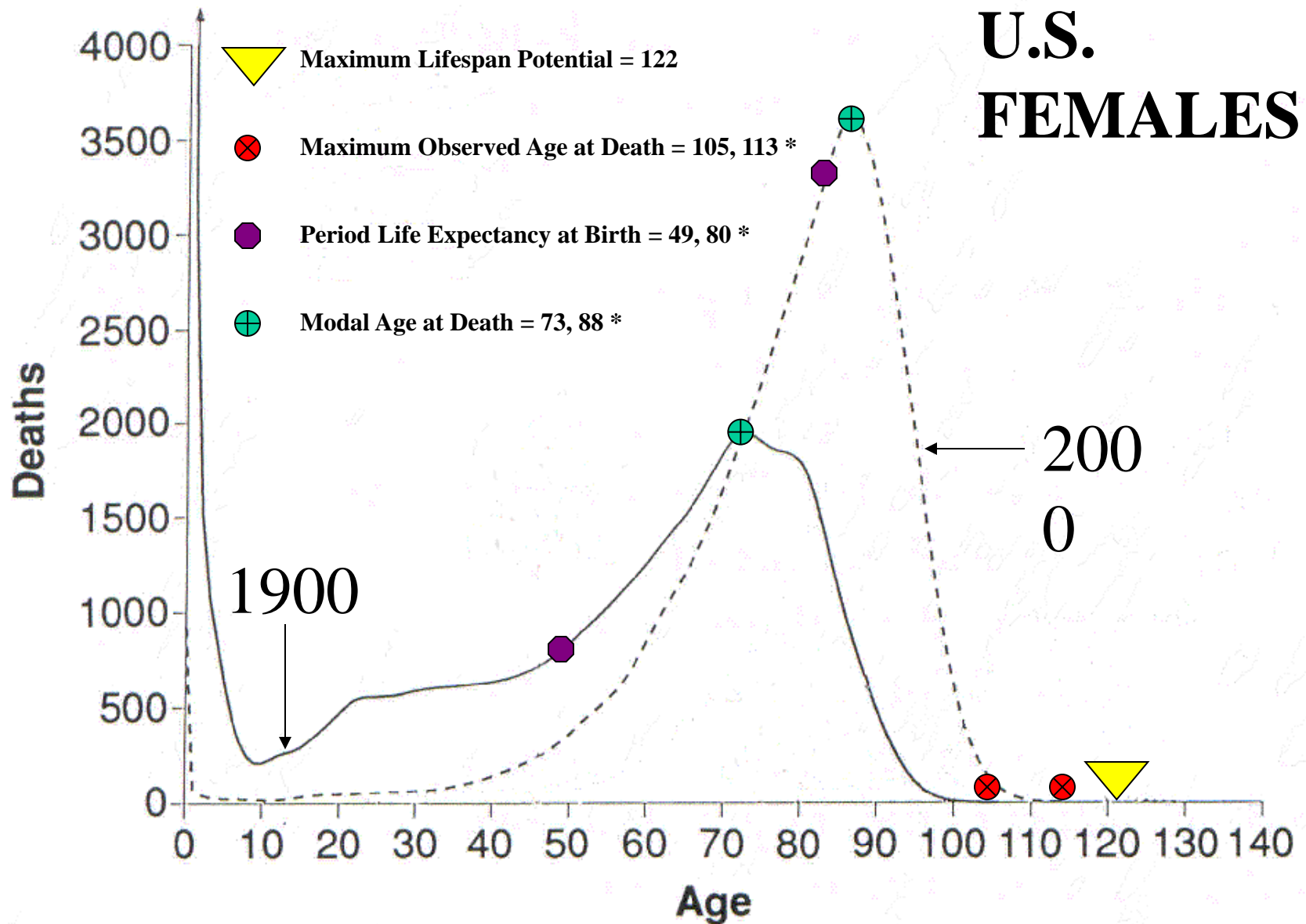


Fig. 2. Percentage of reduction in the conditional probability of death for the United States (from 1985 levels) required to produce a life expectancy at birth from 80 to 120 years.

Olshansky et al., 1990. *Science*.

U.S. FEMALES

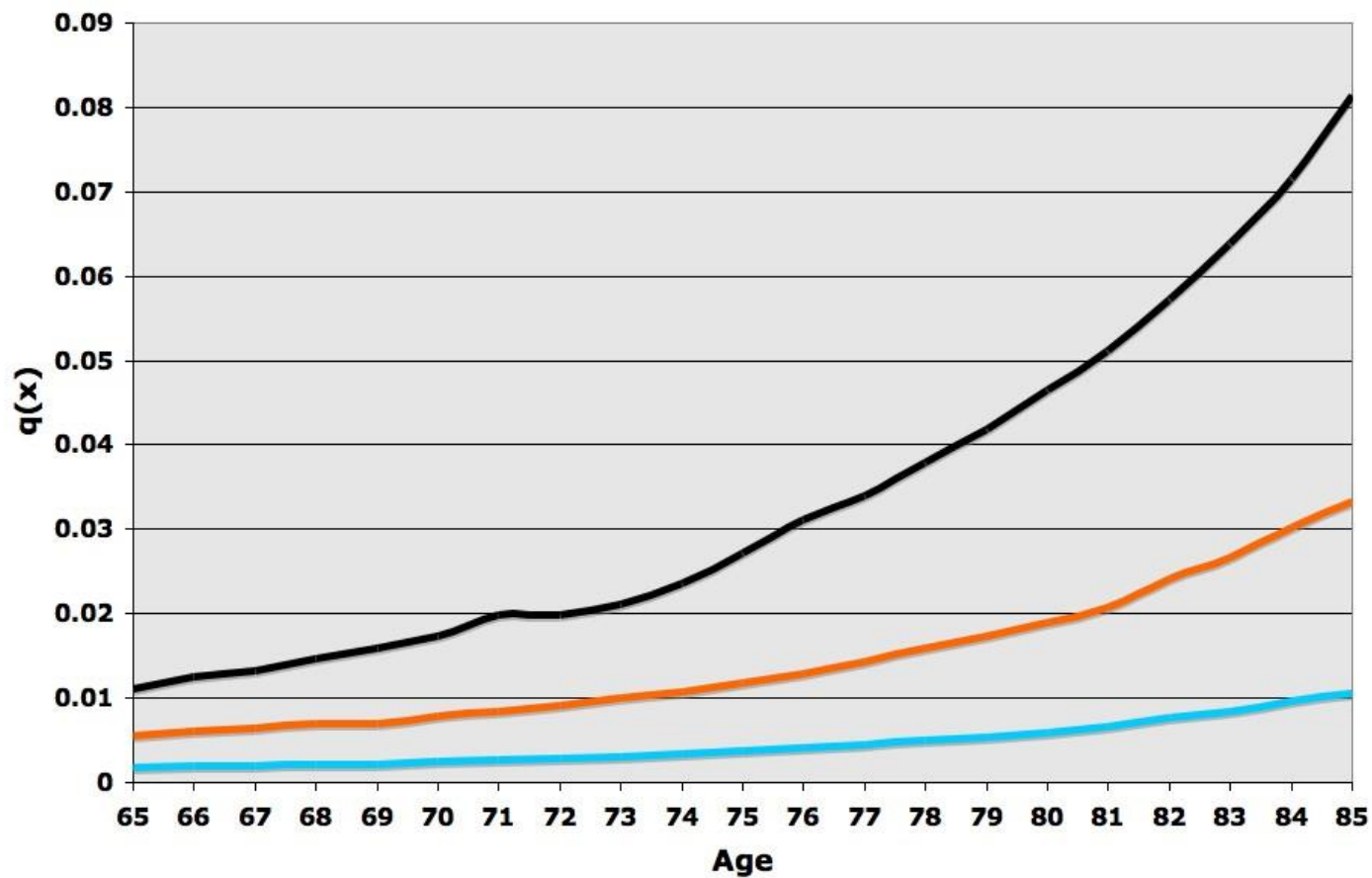


**There is no demographic,
actuarial, or biological
justification for concluding
that most (or even half of the
population) can live to 100**

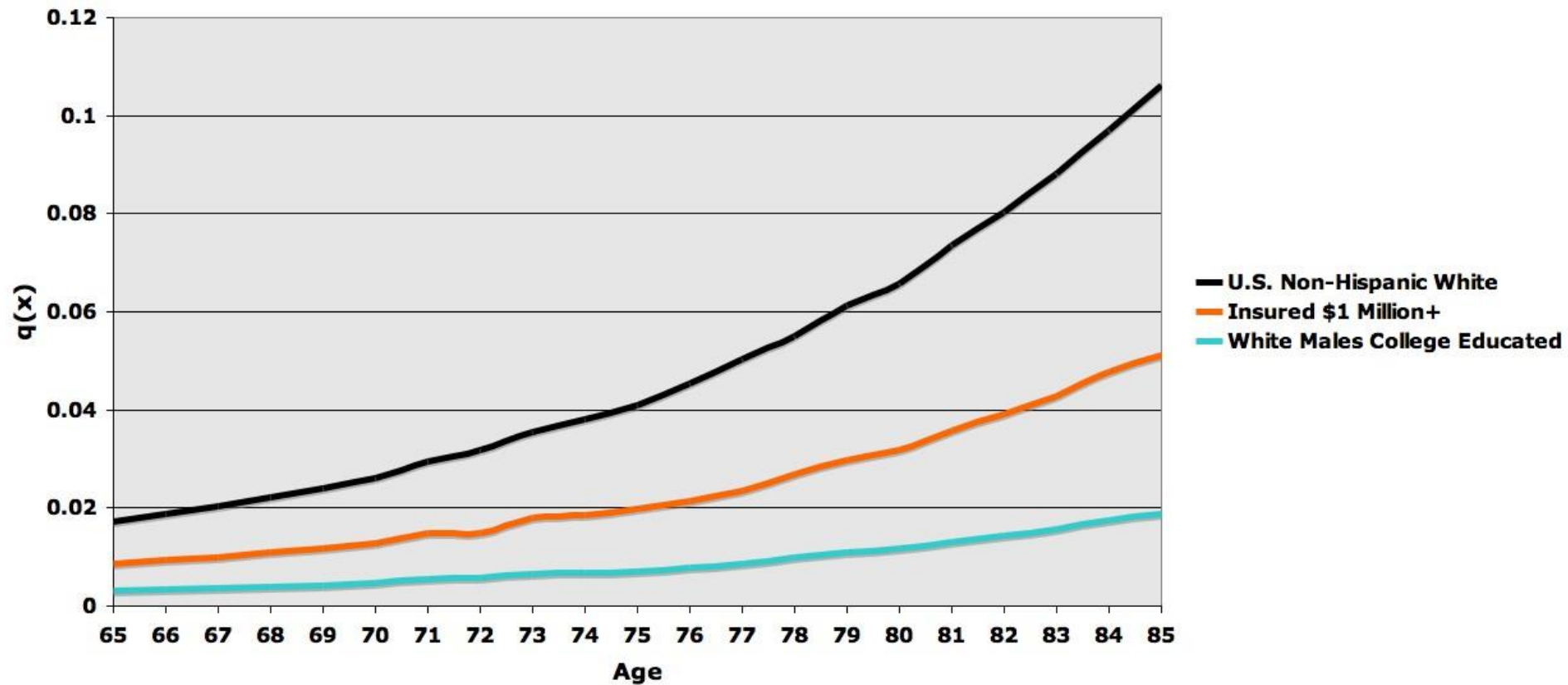
Education

The Longevity Trump Card

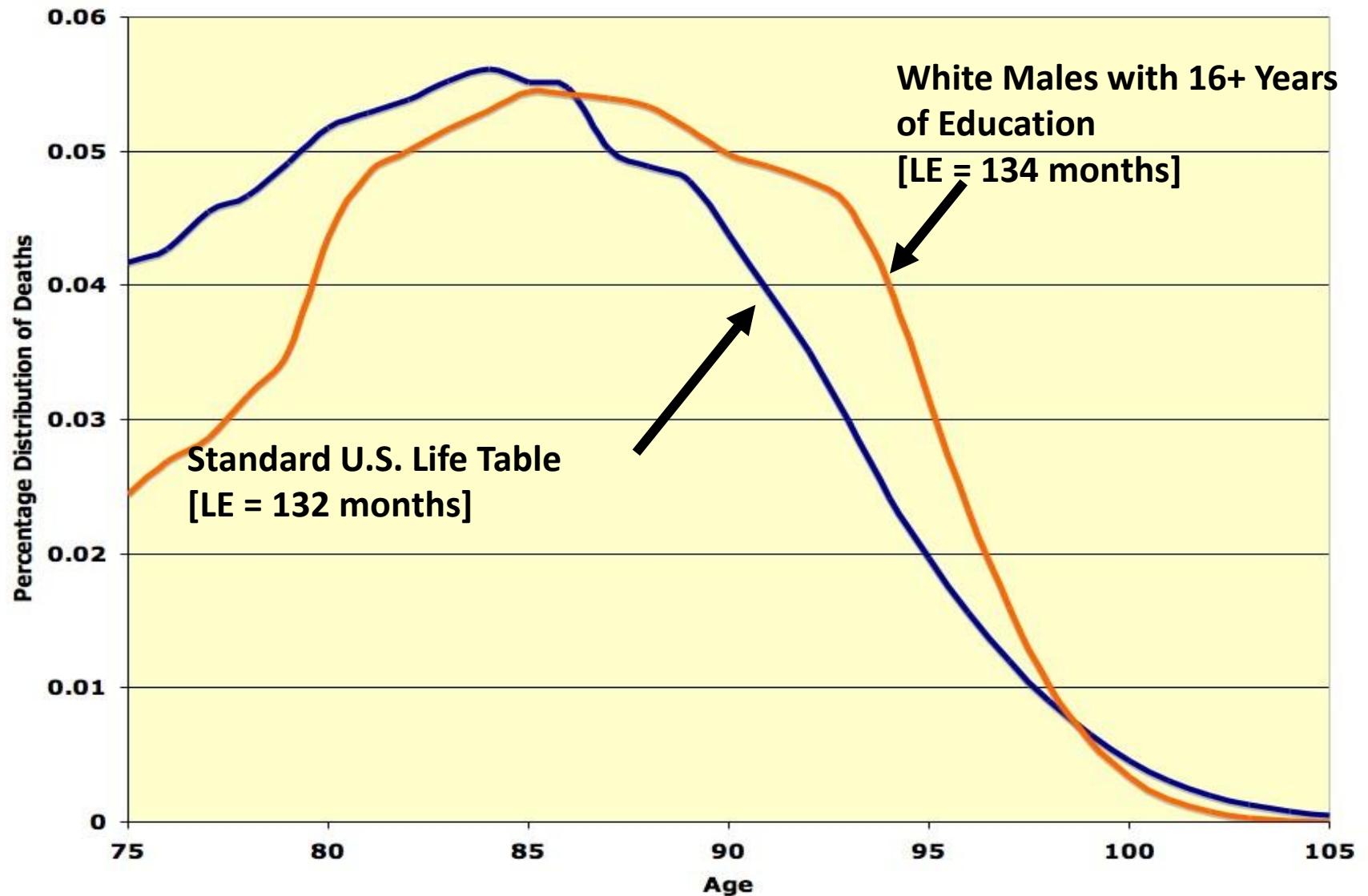
Conditional Probability of Death [$q(x)$] for Females in the U.S. (U.S. Non-Hispanic White, Insured with \$1 Million+ Policies, and Whites with College Education (2005)



Conditional Probability of Death [$q(x)$] for Males in the U.S. (U.S. Non-Hispanic White, Insured with \$1 Million+ Policies, and Whites with College Education (2005)



Percentage Distribution of Deaths for Males Aged 75 and Older (United States, 2007)



The average duration of life will be only 2 months greater, but the distribution of death by age will be dramatically different.

A Possible Decline in Life Expectancy in the United States in the 21st Century?

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Children's Hospital, Boston

New England Journal of Medicine
2005 352:1103-1110.

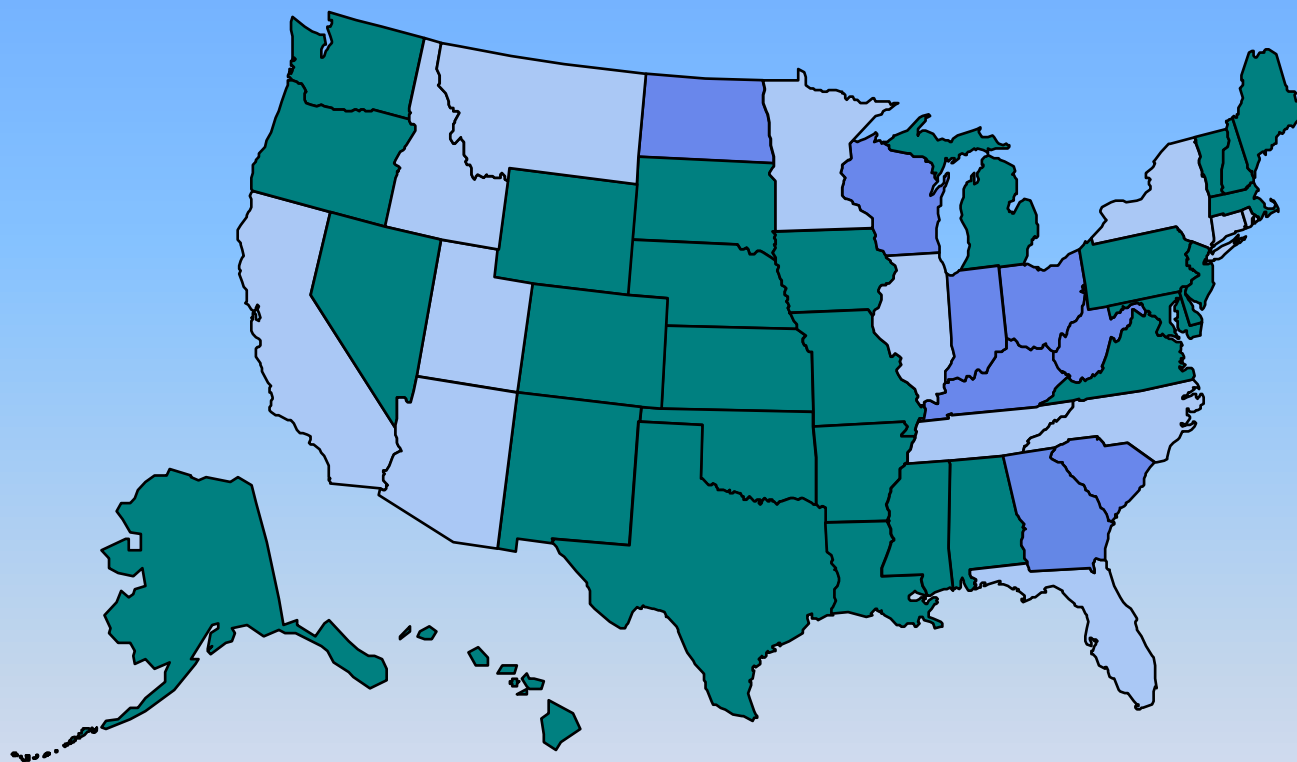


Funding: NIH/NIA; NIDDK; IGPA

Obesity Trends* Among U.S. Adults

1985

(*BMI ≥ 30 , or ~ 30 lbs overweight for 5' 4" person)

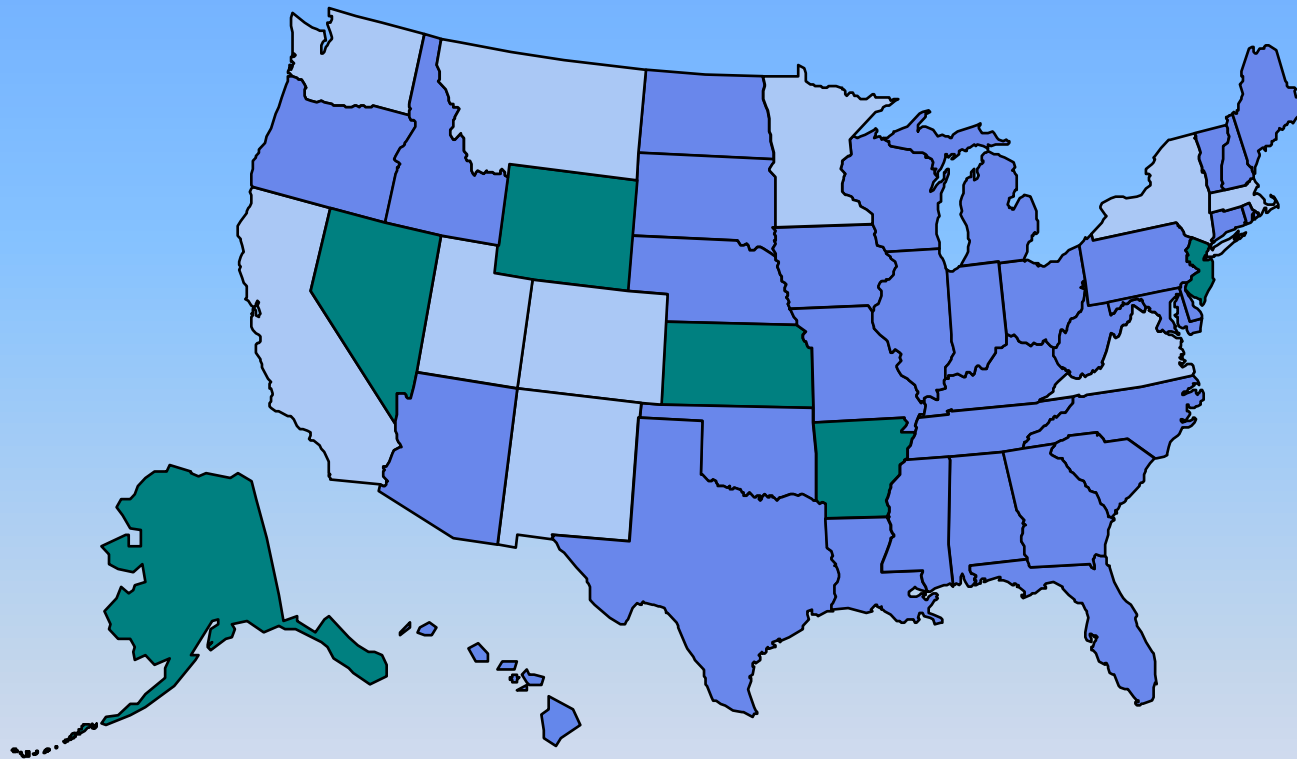


■ No Data ■ <10% ■ 10%–14% ■ 15%–19% ■ 20%–24% ■ $\geq 25\%$

Source: CDC

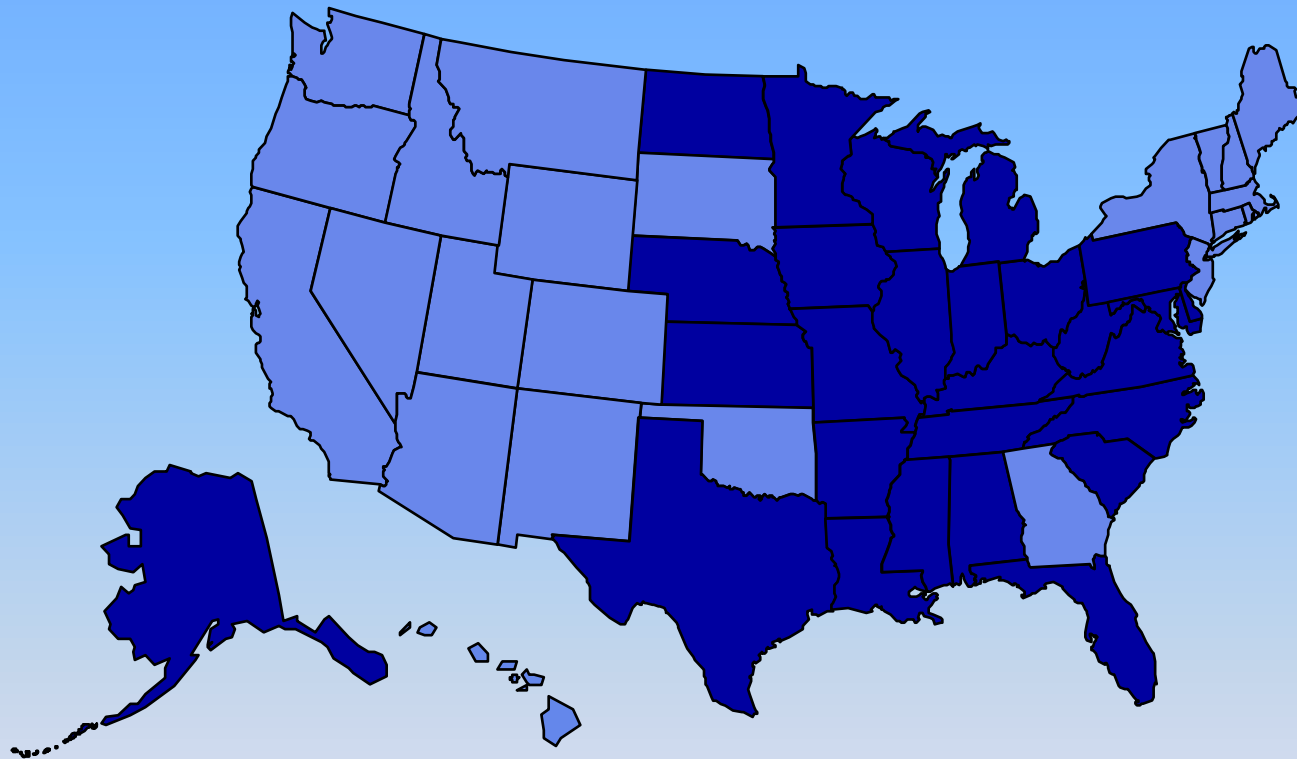
Obesity Trends Among U.S. Adults

1990



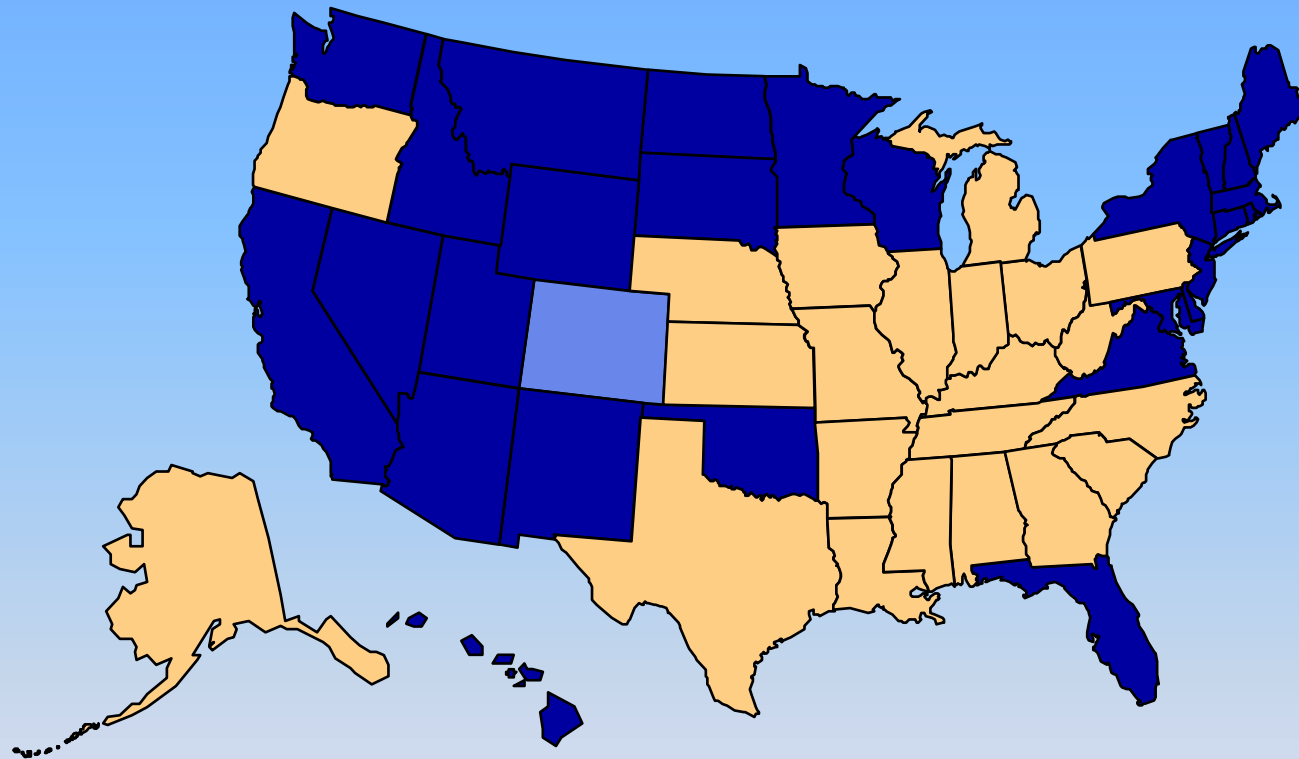
Obesity Trends Among U.S. Adults

1995



Obesity Trends Among U.S. Adults

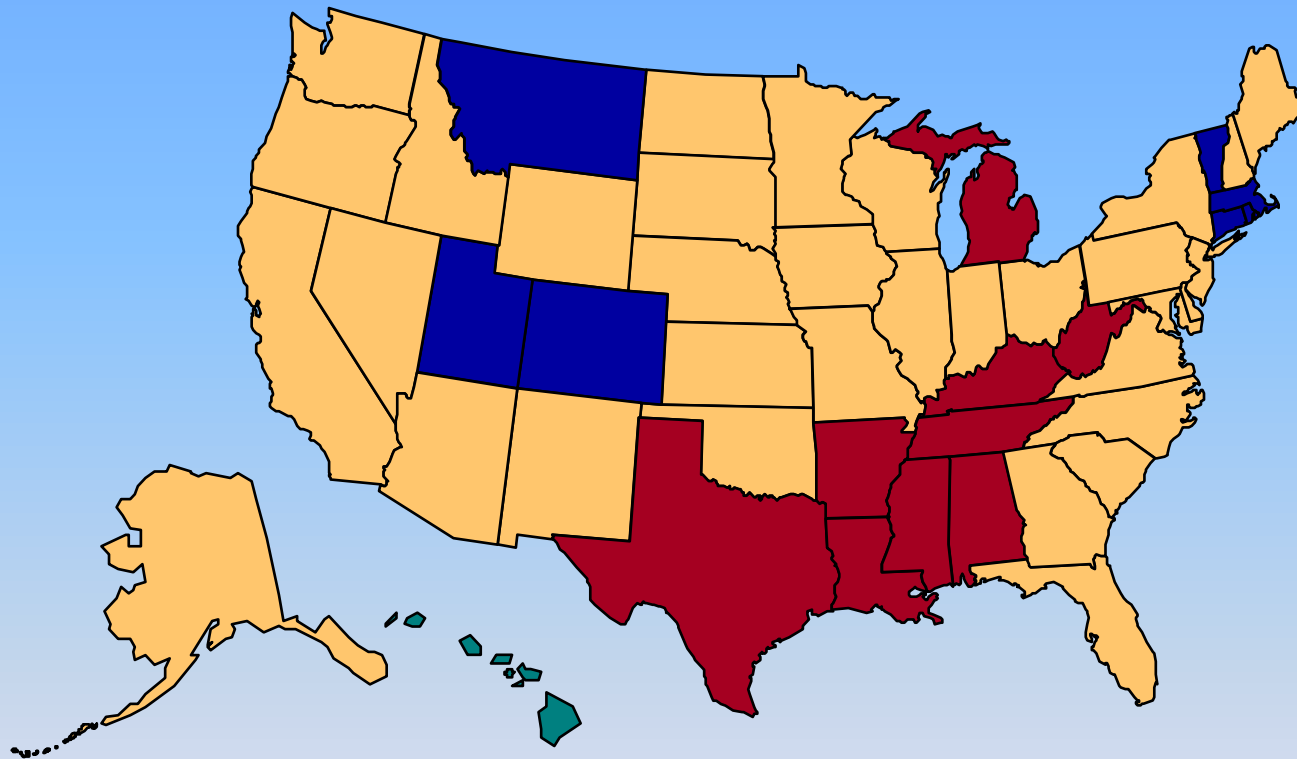
2000



Legend: No Data, <10%, 10%-14%, 15%-19%, 20%-24%, $\geq 25\%$

Obesity Trends Among U.S. Adults

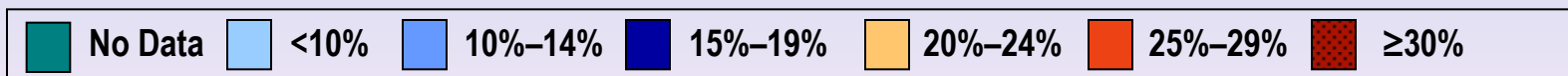
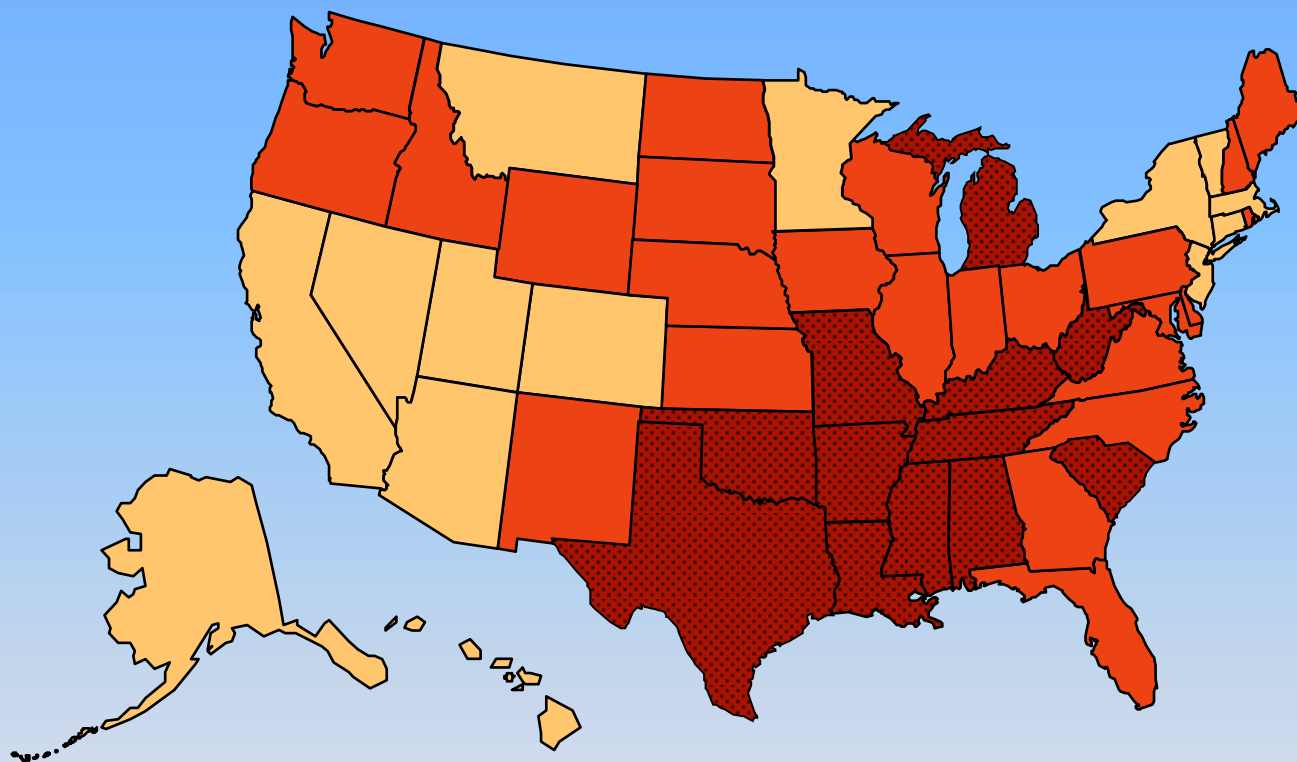
2004



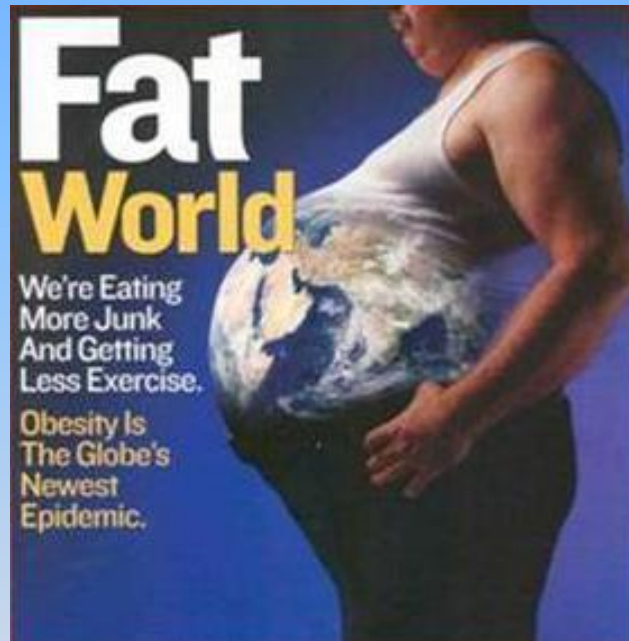
■ No Data ■ <10% ■ 10%–14% ■ 15%–19% ■ 20%–24% ■ ≥25%

Obesity Trends Among U.S. Adults

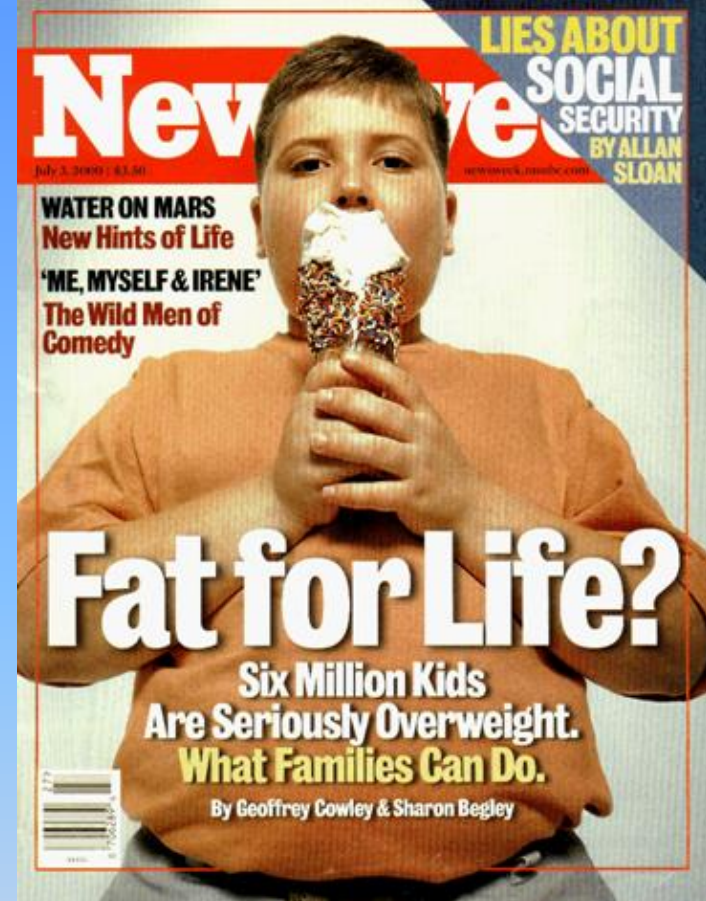
2010



Obesity is a global pandemic



OBESEITY: A Weighty Issue for Children



By Eric N. Reither, S. Jay Olshansky, and Yang Yang

New Forecasting Methodology Indicates More Disease And Earlier Mortality Ahead For Today's Younger Americans

ABSTRACT Traditional methods of projecting population health statistics, such as estimating future death rates, can give inaccurate results and lead to inferior or even poor policy decisions. A new “three-dimensional” method of forecasting vital health statistics is more accurate because it takes into account the delayed effects of the health risks being accumulated by today's younger generations. Applying this forecasting technique to the US obesity epidemic suggests that future death rates and health care expenditures could be far worse than currently anticipated. We suggest that public policy makers adopt this more robust forecasting tool and redouble efforts to develop and implement effective obesity-related prevention programs and interventions.

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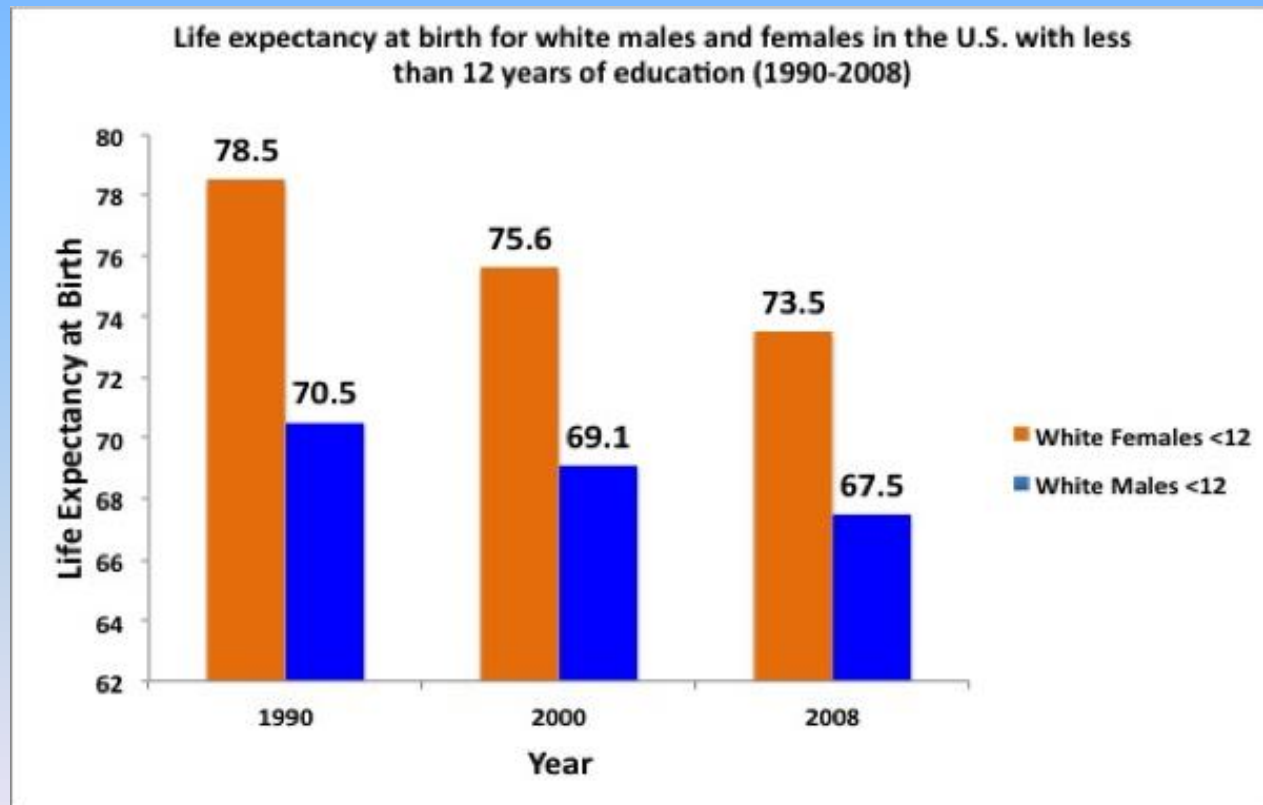
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S. Jay Olshansky is a professor in the School of Public Health at the University of Illinois, in Chicago.

Yang Yang is an associate professor in the Department of Sociology and the Lineberger Comprehensive Cancer Center at the University of North Carolina, in Chapel Hill.

By S. Jay Olshansky, Toni Antonucci, Lisa Berkman, Robert H. Binstock, Axel Boersch-Supan, John T. Cacioppo, Bruce A. Carnes, Laura L. Carstensen, Linda P. Fried, Dana P. Goldman, James Jackson, Martin Kohli, John Rother, Yuhui Zheng, and John Rowe

Differences In Life Expectancy Due To Race And Educational Differences Are Widening, And Many May Not Catch Up



Olshansky SJ et al. 2012. *Health Affairs*.



ABOUT
mission & people

SCIENCE & TECHNOLOGY
advanced products

PARTNERS
strategic collaborations

MEDIA
resources & news


CAREERS
we're hiring

Aging is the single biggest risk factor for virtually every significant human disease...

...our goal is to extend and enhance the healthy, high-performance lifespan and change the face of aging. For the first time, the power of human genomics, informatics, next generation DNA sequencing technologies, and stem cell advances are being harnessed in one company, Human Longevity Inc., with the leading pioneers in these fields. Our goal is to solve the diseases of aging by changing the way medicine is practiced.

It's not just a long life we're striving for, but one which is worth living.

Human Longevity Inc. (HLI) Launched to Promote Healthy Aging Using Advances in Genomics and Stem Cell Therapies

 [@JCVenter](#) on CBS Morning Show <http://t.co/RPaInhQpGm>
[#genomics](#)
[2 days ago]

Part IV: What does Brown Think?

- I think there is a maximum Lifespan of around 120 years which will not be exceeded
- We can get closer to 120, but population life expectancy of 100 will be difficult

Part IV: What does Brown Think?

- We know that Life Expectancy is a function of Education and Income
- I also think a causal factor is the robustness of that income
- For example, a person with a Defined Benefit pension will live longer than a person with a bank account
- Financial Income Security drives longevity!

Part IV: What does Brown Think?

- This is exciting because it means the actuarial profession has a causal role to play in enhancement of Life Expectancy
- I have research ongoing to try to support this hypothesis
- Look for the movie in your local cinema