How we Age

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Record female life expectancy 1840 to the present. Horizontal black lines show asserted ceilings on life expectancy, with a short vertical line indicating the year of publication (Vaupel et al 2002).
The Demography of the World Population from 1950 to 2100

Shown is the age distribution of the world population – by sex – from 1950 to 2018 and the UN Population Division’s projection until 2100.


The data visualization is available at OurWorldInData.org, where you find more research on how the world is changing and why.
Evolution of the Relative Levels of Mortality and Fertility Rates Over Time

Evolution of the relative levels of mortality and fertility rates over time is illustrated in the diagram. The three stages are:

1. **Pre-industrial Steady State**
   - High mortality and fertility rates

2. **Urbanization Growth**
   - Lower fertility rates
   - Cross-over point
   - Transition from high mortality to low mortality

3. **Post-urbanization Shrinking and Ageing**
   - Further decline in fertility rates
   - Low mortality rates

Countries with the highest projected population shrinking by 2050.

Note: The bars denote the projected fraction of population shrinking between 2020 and 2050 (in %)

Increases in Health and Longevity are not Random

What makes us age differently?

- Genetic inheritance
- Who we are
- Our health behaviour
- Our access to health care
- Where we live

and a lifetime of:
Changes in Life Expectancy at Birth Between 1958 and 2018 in Different States

Range in 1959 = 5.6 years

Range in 1984 = 4.9 years

Range in 2017 = 7.0 years

Connecticut
Oklahoma

The Increase in Lifespan is not Matched by Increases in Healthspan

Changes (1998-2006) in those over 60 years old

- Life Exp.
- CHD
- MI
- Stroke
- Cancer
- Diabetes
- Motility

% Change

Modified from Crimmins and Beltrán-Sánchez – J. Gerontol B-66:75
Increase over 20 years in the overall period of time that men over 65 in the U.S. lived with disease, HRS (E. Crimmins, PAA Presidential Address 2021)
The Decline of Mortality is Mostly Attributable to Cardiovascular Diseases and (to a lesser extent) Cancer. Chronic Complex Multimorbidity is on the Rise

Death rates among people age 65 and over, by selected leading causes of death, 2000-2018.

Rates are age adjusted using the 2000 U.S. standard resident population.
SOURCE: National Center for Health Statistics, National Vital Statistics System
Aging is the Strongest Risk Factors for All major Age-Related Chronic Diseases

Severity of Underline Damage

Disease-Free Life Expectancy

OA
CHD
COPD
Cancer

Clinical Threshold

Severity of Underline Damage
Aging and Multimorbidity

A Model of Intrinsic Aging

A

- Resilience reserve
- Damage
- Compensated Stress

Robustness → Damage accumulation that overcomes resiliency potential → Frailty

B

Robustness → Accelerated aging by excess damage accumulation → Early Mortality

C

Robustness → Accelerated aging by rapidly shrinking resilience → Early Mortality
Functional Status After 4 Years (%)

Mobility Disability
ADL Disability

Short Physical Performance Battery Score at Baseline

Walking Speed is a Powerful Predictor of Mortality

InCHIANTI 1998-2005

Walking Speed

Second-to-Fifth Quintiles

Lowest Quintile (<0.8 m/sec)

Cancer

Follow-up (years)

Percent Survivors

Long rank test p<0.0001
Age-Adjusted Hazard Ratio for Death per 0.1-m/s Higher Gait Speed

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Deaths</th>
<th>Total Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Health Study, 1991</td>
<td>3851</td>
<td>5801</td>
</tr>
<tr>
<td>Established Populations for the Epidemiologies Study of the Elderly, 1985</td>
<td>1955</td>
<td>2128</td>
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<tr>
<td>Health, Aging, and Body Composition Study, 2009, 2005</td>
<td>848</td>
<td>3048</td>
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<tr>
<td>Hispanic Established Populations for Epidemiological Study of the Elderly, 1999</td>
<td>972</td>
<td>1905</td>
</tr>
<tr>
<td>Invecchiare in Chianti, 2000</td>
<td>187</td>
<td>972</td>
</tr>
<tr>
<td>Osteoporotic Fractures in Men, 2005</td>
<td>1073</td>
<td>5833</td>
</tr>
<tr>
<td>Third National Health and Nutrition Examination Study, 2004</td>
<td>2837</td>
<td>3958</td>
</tr>
<tr>
<td>Predicting Elderly Performance, 2003</td>
<td>293</td>
<td>491</td>
</tr>
<tr>
<td>Study of Osteoporotic Fractures, 1990</td>
<td>5512</td>
<td>10349</td>
</tr>
</tbody>
</table>

Pooled (random effects)
Pooled (shared frailty model)

Studenski, S. et al. JAMA 2011;305:50-58
Changes in Energy Regulation with Aging

- Lower Peak VO₂
- Lower Resting Metabolic Rate
- Greater energetic cost of walking

Energy Reserves Expressed as:
- Cost of walking (ml/kg/min)
- Peak VO₂ (ml/kg/min)
• Younger, healthier persons tend to walk at < 50% of their peak VO$_2$
• Older adults with a higher costs and lower capacity tend walk with an energetic cost that is close to peak VO$_2$
Assessing the Rate of Aging

- Interfering with the fundamental basic mechanisms of aging may reduce the age-related global susceptibility to age-related chronic diseases (Seals & Melov, 2014, left figure).
- But... can we slow down aging? ... And, before that, can we measure aging?

Specific Disease Prevention

Coronary Heart Disease
Cerebrovascular Disease
Hypertension
Cancer
Alzheimer
Parkinson’s Disease
Osteoarthritis
Diabetes
Chronic Kidney Disease

Why Longitudinal Studies?
1. To deal with different lifetime exposures

- Age 90
  - 1990
  - WW2 1939-1945
  - Baby Boom 1946-1964
  - The Green Revolution 1965-1975
  - The Fall of the Berlin Wall Nov 9th, 1989
  - Unemployment rate drops to 3.8% 2000

- Age 50
  - 1970
  - Baby Boom 1946-1964
  - The Green Revolution 1965-1975
  - The Fall of the Berlin Wall Nov 9th, 1989
  - Unemployment rate drops to 3.8% 2000

- Age 20
  - 1930
  - Great Depression 1929-1940
  - WW2 1939-1945
  - Baby Boom 1946-1964
  - The Green Revolution 1965-1975
  - The Fall of the Berlin Wall Nov 9th, 1989
  - Unemployment rate drops to 3.8% 2000

- Now
  - 1900
  - WW1 1914-1918
  - The Great Train Robbery ES Porter, 1903
  - WW1 1914-1918
  - The Great Depression 1929-1940
  - The Green Revolution 1965-1975
  - The Fall of the Berlin Wall Nov 9th, 1989
  - Unemployment rate drops to 3.8% 2000
Why Longitudinal Studies?

2. To deal with selective mortality or loss to follow-up (real data from BLSA)
Accelerated Aging Comes in Many Flavors

Studying longitudinal relationships between chronological and biological age is fundamental to understand mechanisms of accelerated aging and develop strategies aimed at slowing down the pace of aging, thereby preventing chronic diseases and functional decline.

- Older biological age at birth and "normal" pace afterward.
- Normal biological age at birth and "accelerated" pace afterwards.
- Both older biological age at birth and "accelerated" pace afterwards.
Distribution of slopes of percent methylation per year across clocks
Biomarkers for Aging Identified in Cross-sectional Studies Tend to Be Non-causative

Individuals with lower intrinsic mortality rates are likely to survive to older ages than their peers with high mortality rates and are more likely to be observed at older ages. This bias, known as “cohort selection”, complicates the search for biomarkers of aging.

The deviation between an individual’s chronological age and predicted age informs the rate of aging, as measured by the slope of the Gompertz mortality curve (A), but not the intercept of the Gompertz mortality curve (B).
A Word of Caution: Resilience affects the Temporal Relationships Between Metrics of Aging

Can we assess the rate of decline in this period?
"It would be so nice if something made sense for a change."

(Alice's Adventures in Wonderland; July 4, 1865 - Charles L. Dodgson)