Lifespan & Healthspan

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Davis School of Gerontology
University of Southern California
Questions?

• Life Expectancy - Can it keep increasing?

• Healthy life - Has it increased? Will it increase?

Frontiers of health science research

• We can improve understanding of healthspan in the future by increasing understanding of the process of aging
Increasing Life Expectancy

The greatest accomplishment of the 20th century
Death occurs at increasingly older ages and deaths are more concentrated about the mode.
Increasing Number of People Reaching Age 100
But the probability is low and projected to remain low
Future Projected Increases in Number Reaching Age 100 out of 100,000 Born
Modest Life Expectancy Increase over more than a century, 1900 – 2010 at Age 75, 85, 90

Source: Table 6 Life Tables for the U.S. Social Security Area, 1900-2100. Actuarial Study No. 120, Felicite C. Bell and Michael L. Miller
Years of Increase in Life Expectancy between 1900 and 2010 at age 75, 85, 90

Bar chart showing years of increase in life expectancy for males and females at ages 75, 85, and 90.
Estimates of U.S. Life Expectancy for 2050

<table>
<thead>
<tr>
<th>Method</th>
<th>Females</th>
<th>Males</th>
</tr>
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<tbody>
<tr>
<td>Social Security</td>
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Estimates of U.S. Life Expectancy for 2050

- Social Security
- Bongaarts
- Oeppen-Vaupel
- observed 2000

Females
Males
Reasons why the potential for large increase in life expectancy in very old age is limited

- Much gain has been because of early life changes and this is over (Crimmins and Finch 2006; Finch and Crimmins 2004; Hayward and Gorman 2004).
Similar historical trends over 150 years for cohort death rates at age 1 yr and 70 yr

Swedish Mortality at Age 1 and Age 70 by Birth Cohort (1751-1899)

Source: Berkeley Mortality Database

France: Cohort (1806-1899) Mortality at age 1 and at age 70 and Mean Difference from maximum height at age 20-21

Source: 1. tables de mortalite francaises pour les XIX siecles et projections pour le XXI siecle-Jaques Vallin and France Mesle, tableau-II-C-2
Reasons why the potential for large increase in life expectancy in very old age is limited

• Much gain has been because of early life changes and this is over (Crimmins and Finch 2006; Finch and Crimmins 2004).

• The rate of mortality increase in old age, the rate of aging, seems to be increasing (Beltran-Sanchez, Finch and Crimmins, 2012)
Early cohort mortality predicts the cohort rate of aging - Low childhood mortality linked to higher rate of aging

Strong association between early life mortality \( (q_{0-10}) \) and cohort Gompertz parameters across many countries and 150 years:

- Low childhood mortality linked to lower level of mortality at the beginning of old age - Positive association with Gompertz intercept but Inverse association with Gompertz slope

Association between $q_{0-10}$ and Gompertz parameters

Beltran-Sanchez et al. 2012.
Reasons why the potential for large increase in life expectancy in very old age is limited

- Much gain in life expectancy at older ages has been because of early life changes and this is over (Crimmins and Finch 2006; Finch and Crimmins 2004).
- Currently, the rate of aging - mortality increase with age - in old age seems to be increasing (Beltran-Sanchez, Finch and Crimmins, 2012)
- Specific to US - Recent poor relative change in life expectancy vis à vis other countries in the U.S. and poor performance, even decrease in life expectancy, among some groups
U.S. Life Expectancy is relatively low and our rank is declining - 22 OECD Countries

Crimmins, Preston and Cohen, 2011, NAS>
In the US Life Expectancy is declining for some Lower than 30 years age for women in Red Counties

Change in years of life Expectancy in US counties from 1987 to 2007

First Rise in U.S. Death Rate in Years Surprises Experts

By SABRINA TAVERNISE  JUNE 1, 2016

WASHINGTON — The death rate in the United States rose last year for the first time in a decade, preliminary federal data show, a rare increase that was driven in part by more people dying from drug overdoses, suicide and Alzheimer’s disease. The death rate from heart disease, long in decline, edged up slightly.
Reasons why the potential for large increase in life expectancy in very old age is limited

• Much gain has been because of early life changes and this is over (Crimmins and Finch 2006; Finch and Crimmins 2004).

• Currently, the rate of mortality increase in old age seems to be increasing (Beltran-Sanchez, Finch and Crimmins, 2012)

• Recent lack of increase in life expectancy in the U.S. and decreases among some groups

• There is great potential in improving life expectancy for those with low social status and at younger ages
US Ranks as worst or second to worst in mortality at most ages up to older age
— 17 Peer Countries, 2006-2008 —

Healthspan: There is potential for increasing healthspan and delaying the Morbidity Process

Total Cholesterol Declines over 50 years

--- After 1960 ---

Males

<table>
<thead>
<tr>
<th>Year</th>
<th>40-49</th>
<th>50-59</th>
<th>60-74</th>
<th>75+</th>
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<td>1961</td>
<td>250</td>
<td>230</td>
<td>210</td>
<td>190</td>
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<td>1973</td>
<td>240</td>
<td>220</td>
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<td>180</td>
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<tr>
<td>1978</td>
<td>230</td>
<td>210</td>
<td>190</td>
<td>170</td>
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<tr>
<td>1991</td>
<td>220</td>
<td>200</td>
<td>180</td>
<td>160</td>
</tr>
<tr>
<td>2001</td>
<td>210</td>
<td>190</td>
<td>170</td>
<td>150</td>
</tr>
<tr>
<td>2009</td>
<td>200</td>
<td>180</td>
<td>160</td>
<td>140</td>
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Females

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Measured High Cholesterol Declines; Use of Medications Increases; Overall Diagnosed High Cholesterol Increases: 65+

Update of Crimmins, Kim, and Vasunilashorn, Demography, 2010.
Mean Systolic Blood Pressure Declines over 50 years

**Males**

- 1961: 150
- 1973: 145
- 1978: 140
- 1991: 135
- 2001: 130
- 2009: 125

**Females**

- 1961: 140
- 1973: 135
- 1978: 130
- 1991: 125
- 2001: 120
- 2009: 115

After 1960

55-64

65-74

45-54
Measured High Blood Pressure Declines; Medication use Increases; Overall Diagnosed High Blood Pressure Stays Constant: 65+

Update of Crimmins, Kim, and Vasunilashorn, Demography, 2010.
Mean C-reactive Protein Levels Decrease over about 10 years after 2000.
Worsening Physiological Status: Prevalence of Obesity Increases After 1960

Uses participants’ measured biomarker values ($x_j$), as well as the slope ($k_j$), intercept ($q_j$), root mean squared error ($s_j$) from equations of chronological age regressed on each biomarker, and the variance ($s_{BA}^2$) of the random variable, $R_{BA}$, which represents the difference between participants’ biological and chronological ages.
Biological age has declined over time (1988-2010): More for older people and men

Changes in behavior and medication use explain substantial part of improvement in biological age

Increases in medication use benefitted older and middle-aged more than younger adults.

Decreases in smoking especially benefited older persons, especially older men.

Adverse effects resulted from increases in obesity.
On the other hand!

• Some health indicators not trending in a good direction
• Prevalence of many diseases and length of life with disease has increased
Increase over time in Diabetes


Percentage

Increase over time in Diabetes

Other Diseases with Increasing Prevalence

— 1970s-1990s —

Cancer
Heart Disease
Stroke
Modest decreases in disability –

Especially among the old -

Increase in life with and without disability that is fairly similar -
Improvement in Less Severe Disability:
Percent With Any Activity Limitation (1963 - 2010)
Life Expectancy at birth: 40 year increases in life expectancy Disability-Free and Community Disabled

Table 4. Life Expectancy, Life Expectancy With and Without Cardiovascular Disease, Cancer, or Diabetes, Life Expectancy With and Without Mobility Functioning Ability, 1998–2006 (years)

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<thead>
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<tr>
<td>Age 20 years</td>
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</tr>
<tr>
<td>Life expectancy</td>
<td>55.0</td>
<td>56.1</td>
</tr>
<tr>
<td>With at least one disease</td>
<td>10.0</td>
<td>12.3</td>
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<td>Without disease</td>
<td>45.0</td>
<td>43.8</td>
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<td>3.8</td>
<td>5.8</td>
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<td>Able to function</td>
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<tr>
<td>Age 65 years</td>
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<tr>
<td>Life expectancy</td>
<td>16.0</td>
<td>17.0</td>
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<tr>
<td>With at least one disease</td>
<td>7.2</td>
<td>8.9</td>
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<tr>
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<td>8.8</td>
<td>8.1</td>
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<td>8.9</td>
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Cognitive disability is a different story –

Reduction in dementia and
Increase in life free of dementia

Decrease in life with dementia
% With Good Cognition Increases in last ten years

- Male 2000
- Male 2010
- Female 2000
- Female 2010
Increases in Cognitively Intact Life Expectancy Decreases in Life expectancy with dementia At age 65, US Males.

- **2000**
  - Cognitively Intact: 10.7 years
  - CIND: 3.7 years
  - Dementia: 1.8 years

- **2010**
  - Cognitively Intact: 12.5 years
  - CIND: 3.7 years
  - Dementia: 1.4 years
Lengthening the Morbidity Process
Reducing the Associations Between the Dimensions

In recent years
Reduction in biological risk
Less Disease among those with risk factors
Less Disability among those with Disease
Less Death among those with Disability
How to improve healthspan?

1. Delay the Morbidity Process with focus on the beginning of the process

2. Add a focus on conditions and diseases that are causes of disability but not mortality

3. Focus on maintaining health and returning to health rather than delaying death

4. Promote scientific advances to clarify how to slow the aging process
Understanding the Process: Model of Demographic, Socioeconomic, Behavioral and Biological Influences on Human Health Outcomes

Demographic Factors
- Age
- Sex
- Race/Ethnicity

Socioeconomic Status
- Childhood conditions

Genes

Health Behaviors
- Exercise
- Drinking
- Diet
- Smoking

Social Psychological Factors
- Social support
- Personality

Health Care
- Access
- Insurance Coverage
- Medication Use

Biological Risk
- Cardiovascular Risk
- Metabolic Factors
- HPA and SNS
- Organ functioning
- Antioxidant status
- Cognitive Risk
- Inflammation and Infection Markers
- Mitochondrial DNA
- Gene Expression and Methylation

Health Outcomes
- Mortality
- Chronic Diseases and Conditions
- Physical functioning
- Frailty
- Cognitive Functioning
Current and Future integration of risk factors and pathways –

Improve on current measure of biological age by looking at basic mechanisms of aging

- Gene X Environment interactions
- DNA Methylation
- Change in mitochondrial DNA
- Change in the transcriptome
- Inflammatory profiles
Genetics: Aim – Fill in the unknown box in predicting longevity and chronic disease. First approach, using GWAS results from HRS

Are long-lived smokers “resilient” or are they just lucky?
GWAS results for long-lived smokers used to define a Genetic Functional Interaction Network

215 genes in the network
Mapped to 784 Entrez genes
5,184 SNPs with $P < 5 \times 10^{-03}$

Top Enriched Pathways
- PI3K-Akt signaling (FDR$<1.0e^{-3}$)
- Pathways in Cancer (FDR$<5.0e^{-4}$)
- RAS Signaling (FDR$<2.0e^{-4}$)
- Signaling by PDGF (FDR$<3.3e^{-4}$)
- RAP1 Signaling (FDR$<1.7e^{-4}$)

Levine and Crimmins, JOG: Medical Sciences, 2015.
Polygenic Risk Score based on Network is related to likelihood of being very old among Non-Smokers

Levine and Crimmins, JOG: Medical Sciences, 2015.
PRS is related to lower likelihood of cancer among Non-Smokers

Levine and Crimmins, JOG: Medical Sciences, 2015.
ROC curves for 80+ population – HRS model of mortality with many variables
ROC curves for 50-79 population – HRS model of mortality with many variables.
Gene Expression:
Childhood trauma linked to expression of Inflammatory markers in late life: Early life stress may sensitize the body and brain to be hypersensitive to subsequent activity. HRS pilot sample N=113.
Psychosocial conditions linked to Conserved Transcriptional Response to Adversity: gene expression of proinflammatory markers up-regulated with loneliness and down-regulated with eudaimonia.

Data represent strength of association (b ± SE) between indicated predictor variables and the 53-gene CTRA indicator contrast in (A) separate analyses of loneliness and eudaimonia and (B) analyses in which each was adjusted for covariance with the other.

Conclusions

Life expectancy will continue to increase but modestly.

More people will get older and more (but not most) will become centenarians.

Healthspan and Lifespan are likely to increase in tandem.

We are beginning to better understand the pathways from life circumstances to health. These are the frontiers of population health science.

Intervention will follow which should improve healthspan.
Collaborators and Support

- Morgan Levine
- Jennifer Ailshire
- Caleb Finch
- Hiram Beltran-Sanchez
- Mark Hayward
- Yasuhiko Saito
- Jung Ki Kim
- Steve Cole
- Teresa Seeman

- National Institute on Aging