# Lifespan & Healthspan

# Summer School Vienna

June, 2016

**Eileen M. Crimmins**

Davis School of Gerontology

University of Southern California

## Questions?

- Life Expectancy - Can it keep increasing?

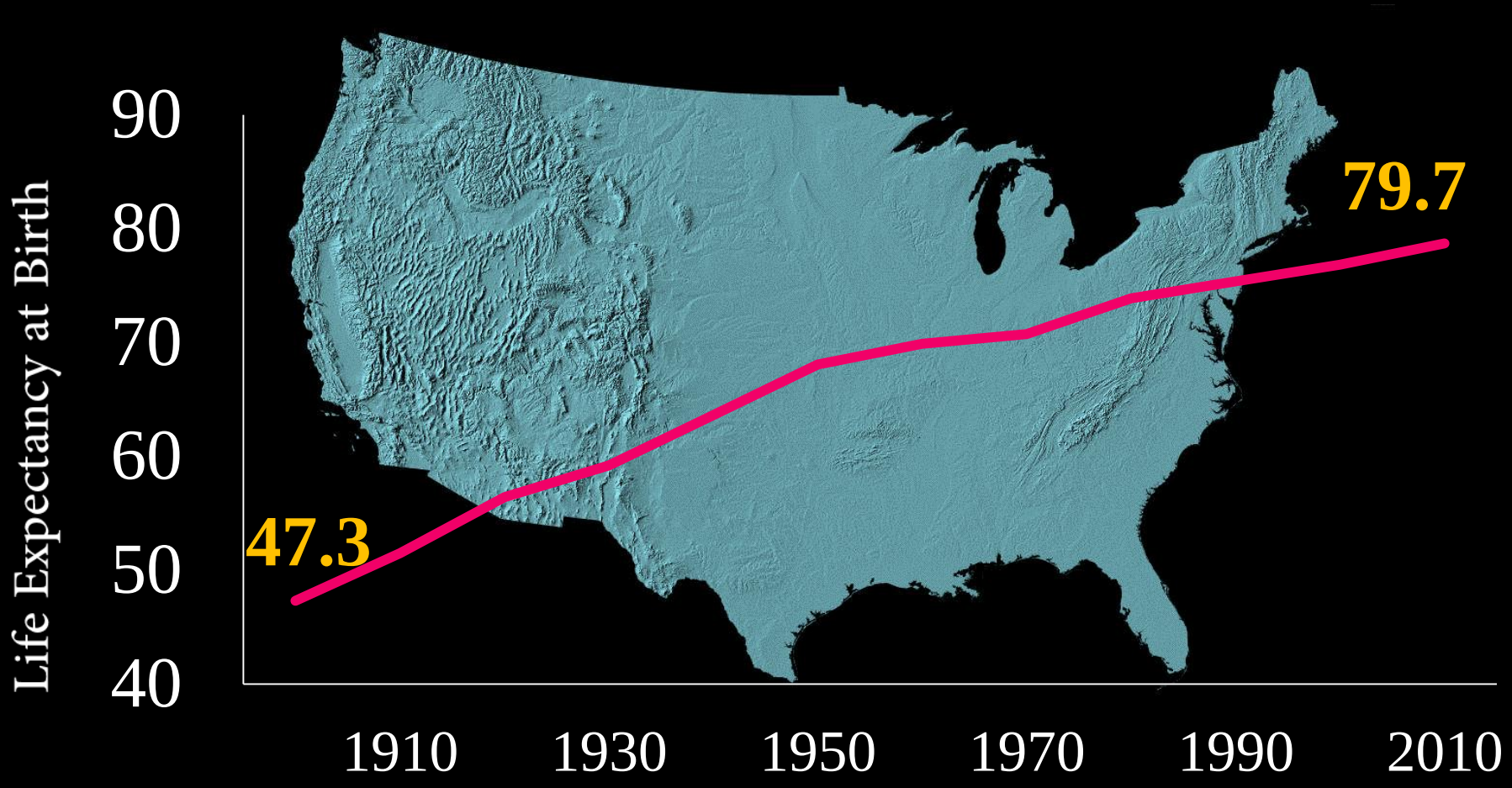
- Healthy life - Has it increased? Will it increase?
- Source for this section is “Lifespan and Healthspan: Past, Present and Promise.” 2015. E.M. Crimmins. The Gerontologist. 55(6):901-11. PMID: 26561272.

## Frontiers of health science research

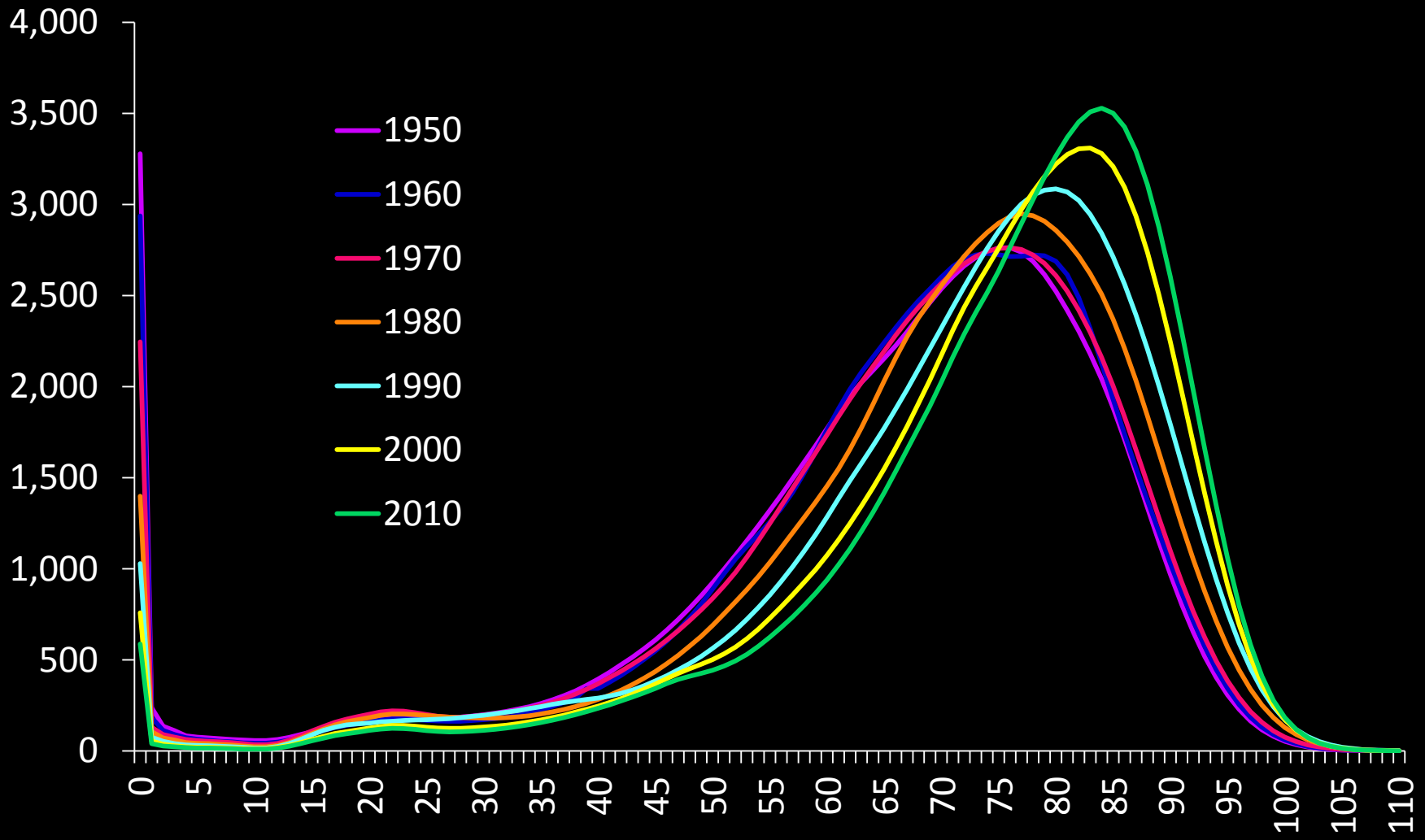
- We can improve understanding of healthspan in the future by increasing understanding of the process of aging

# Increasing Life Expectancy

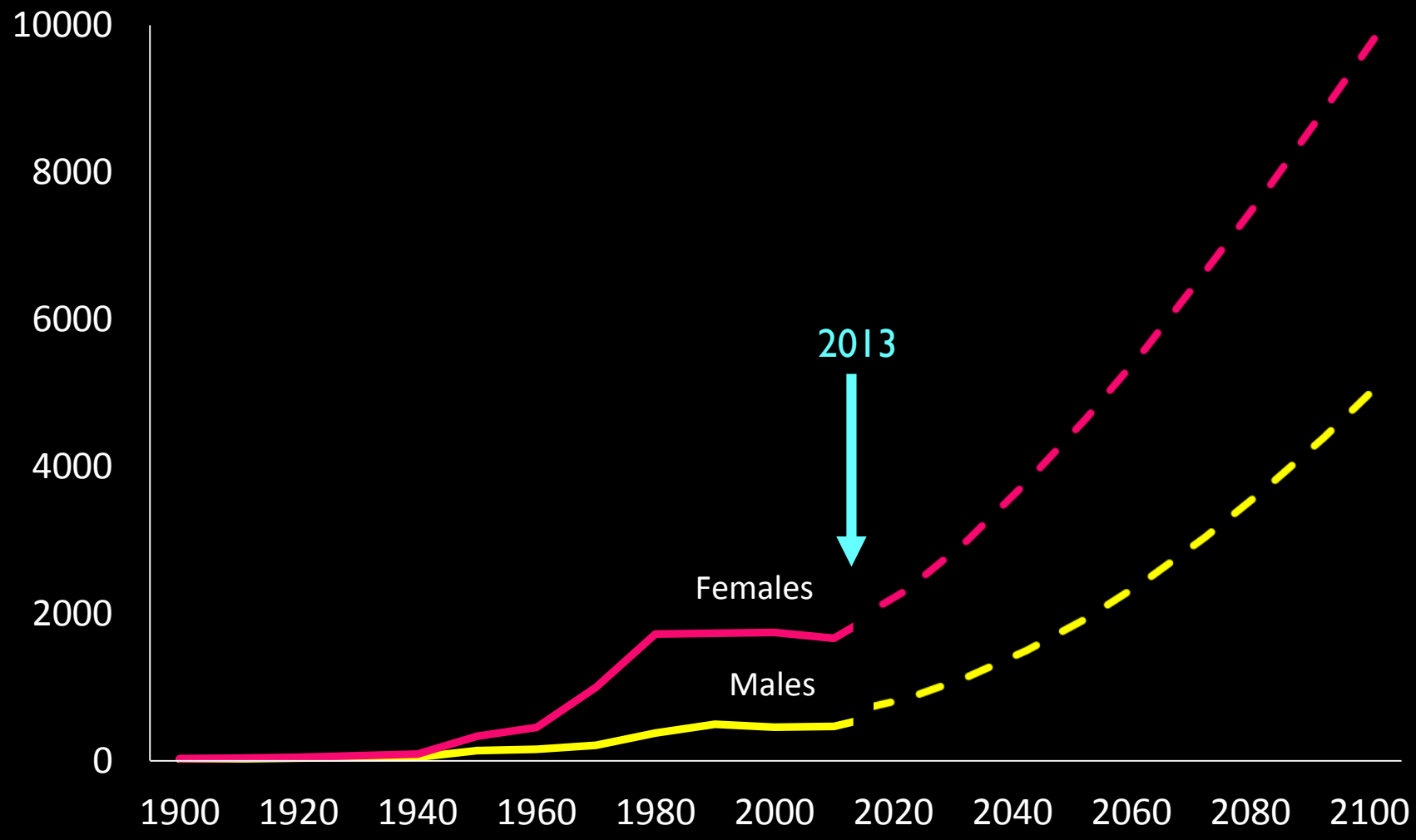
## The greatest accomplishment of the 20th century



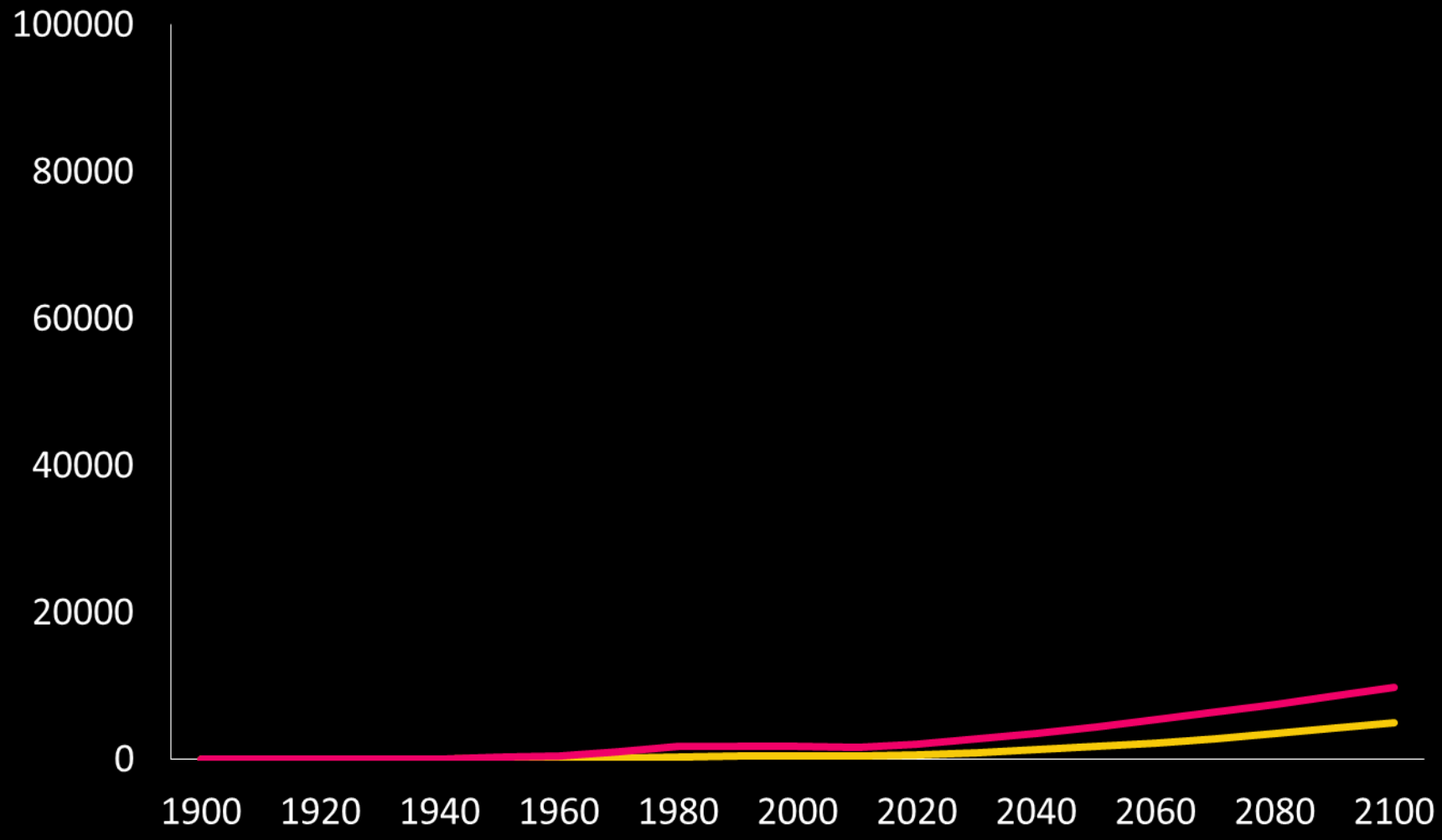
# Death occurs at increasingly older ages and deaths are more concentrated about the mode



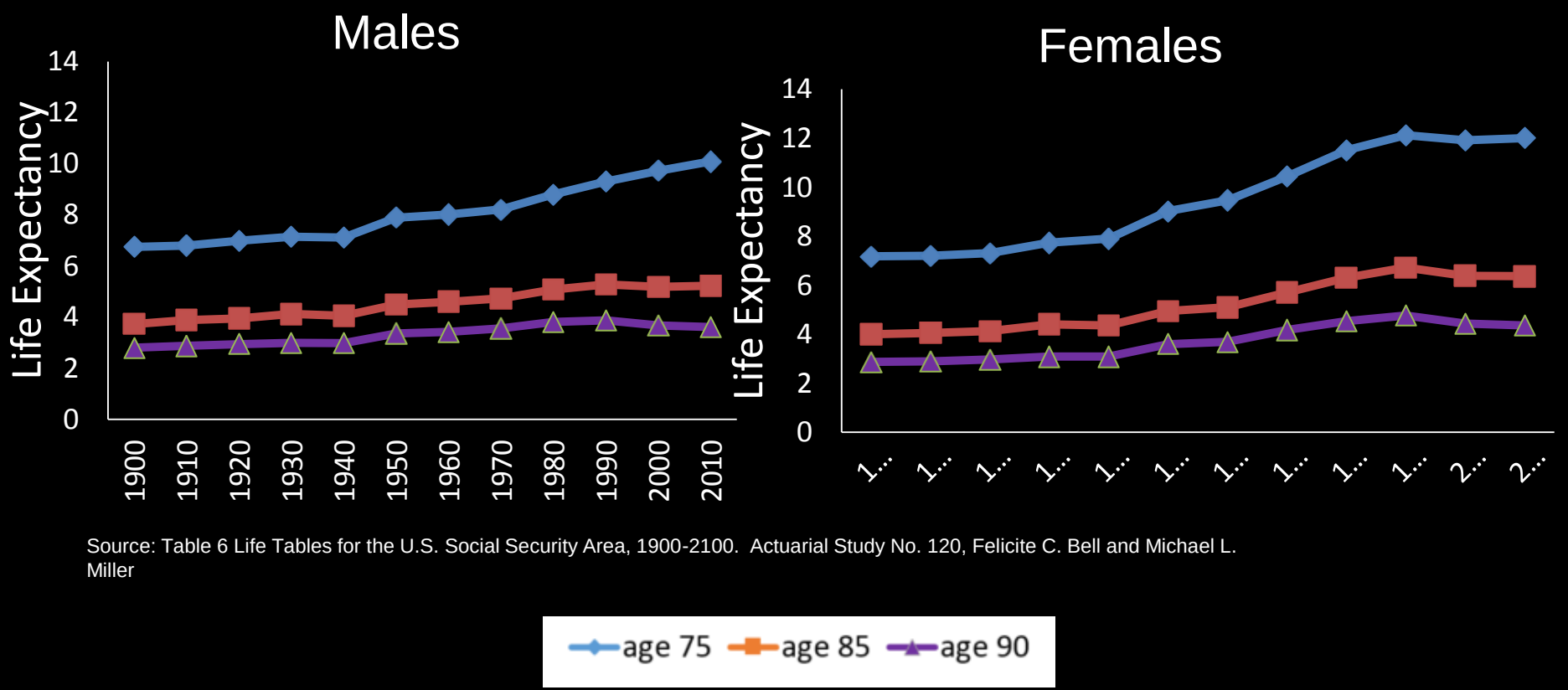
# Increasing Number of People Reaching Age 100
# But the probability is low and projected to remain low



# Future Projected Increases in Number Reaching Age 100 out of 100,000 Born

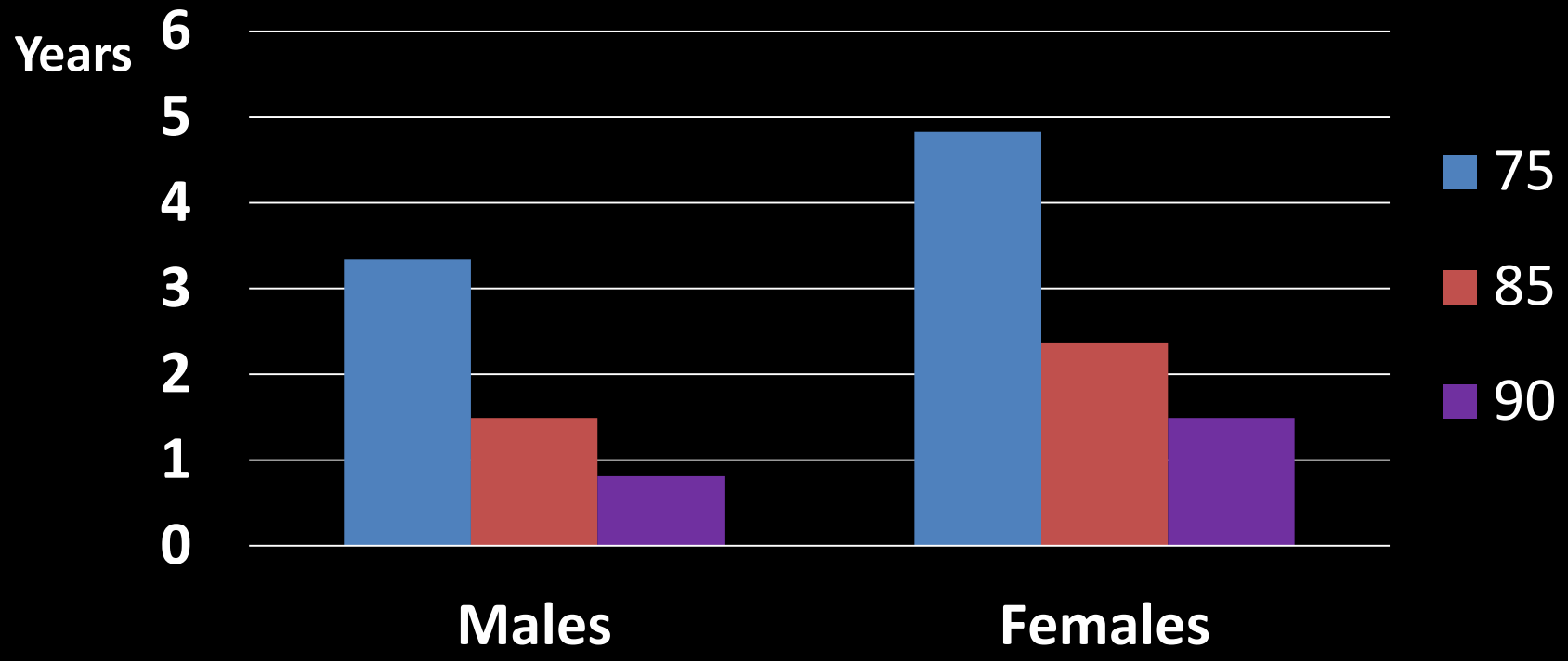


# Modest Life Expectancy Increase over more than a century, 1900 – 2010 at Age 75, 85, 90

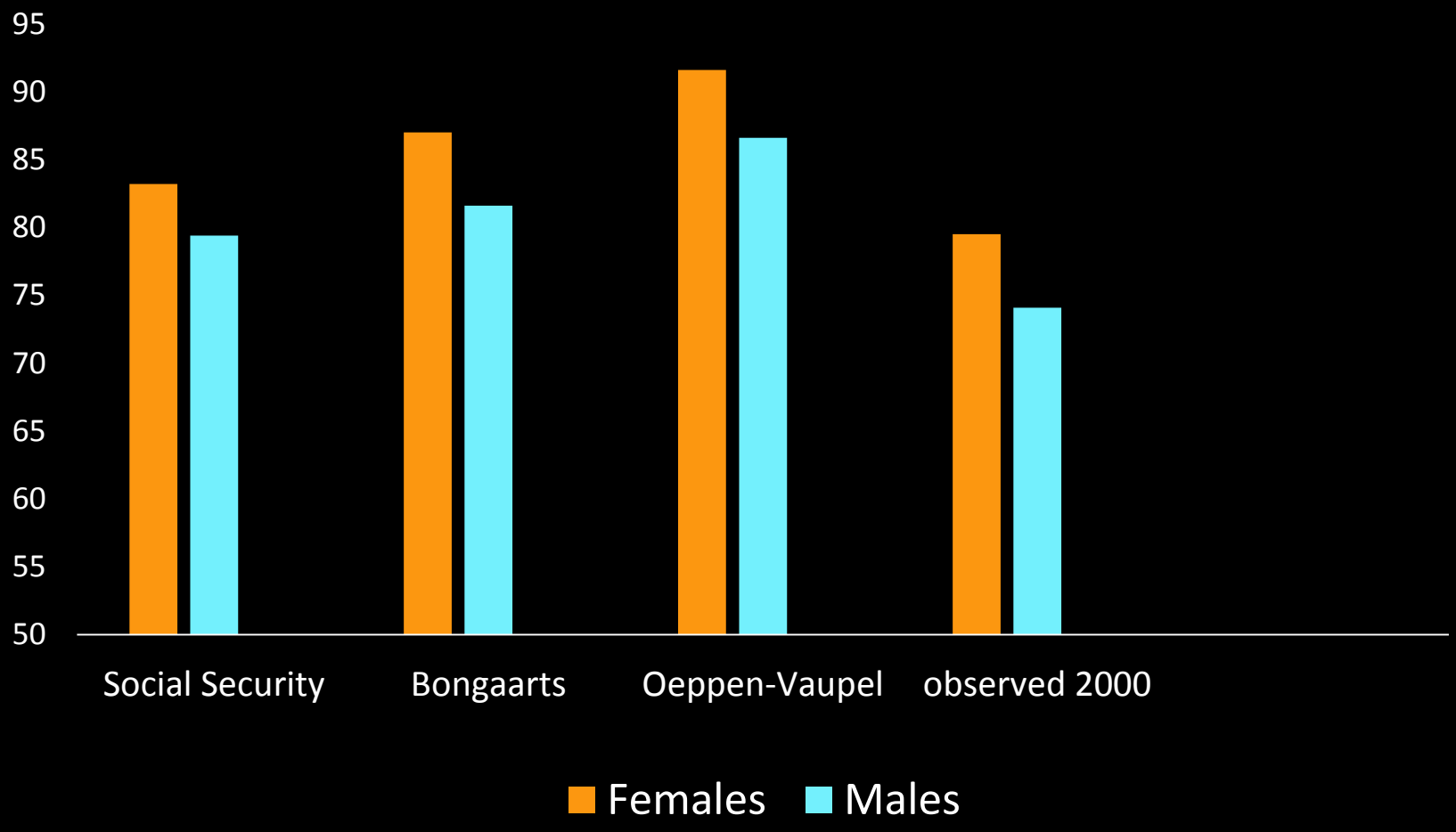



Source: Table 6 Life Tables for the U.S. Social Security Area, 1900-2100. Actuarial Study No. 120, Felicite C. Bell and Michael L. Miller

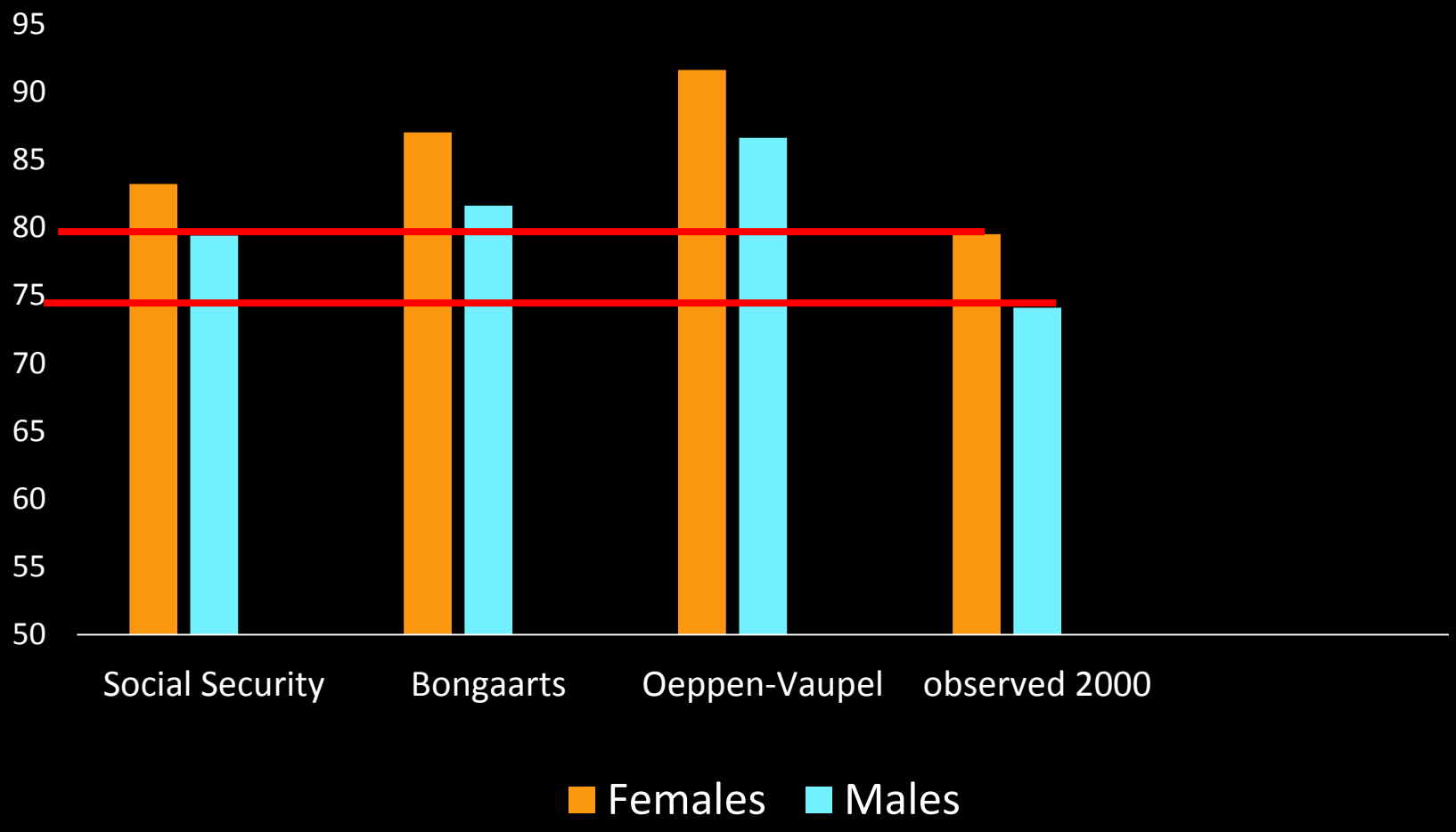
## Years of Increase in Life Expectancy between 1900 and 2010 at age 75, 85, 90



# Estimates of U.S. Life Expectancy for 2050



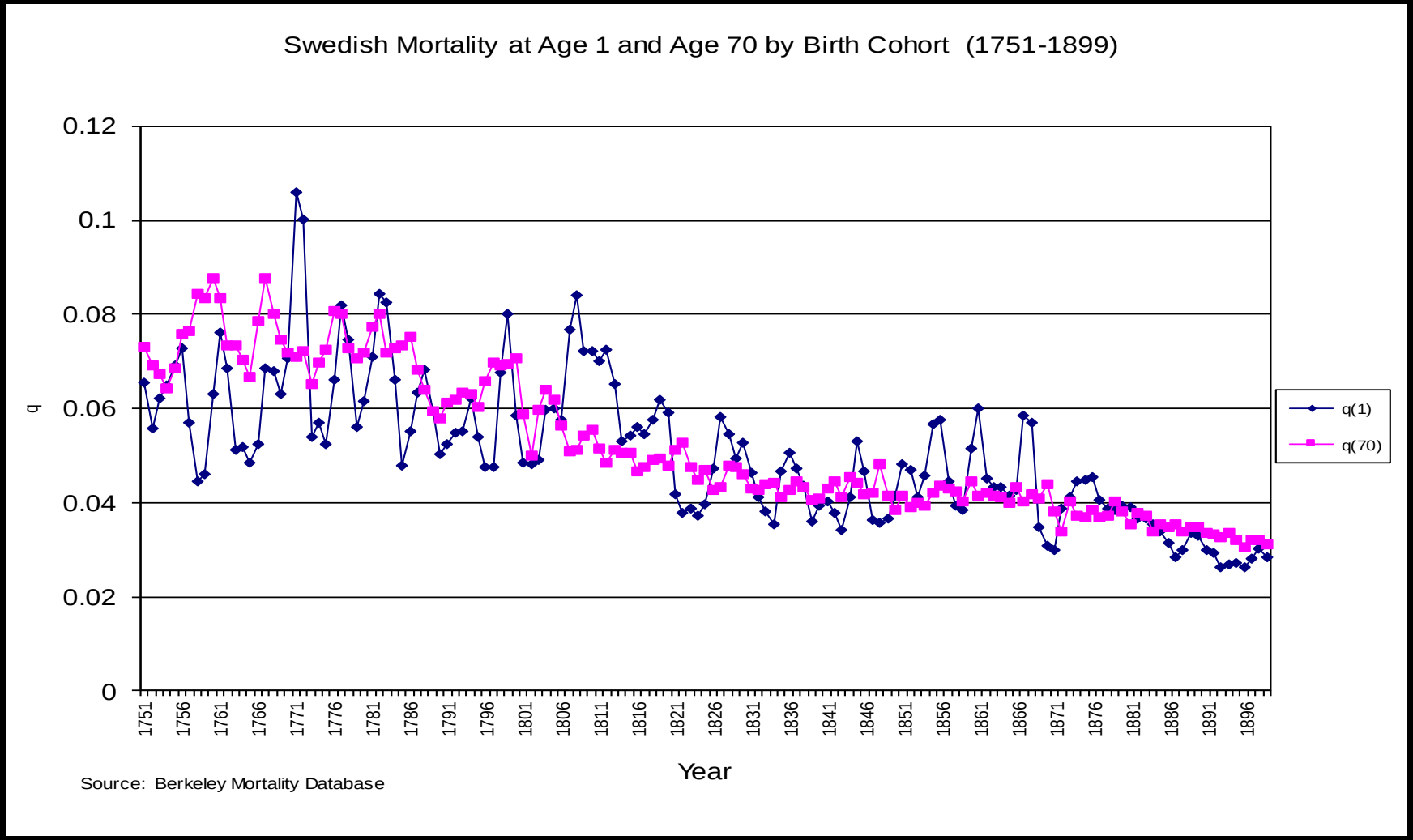
# Estimates of U.S. Life Expectancy for 2050



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

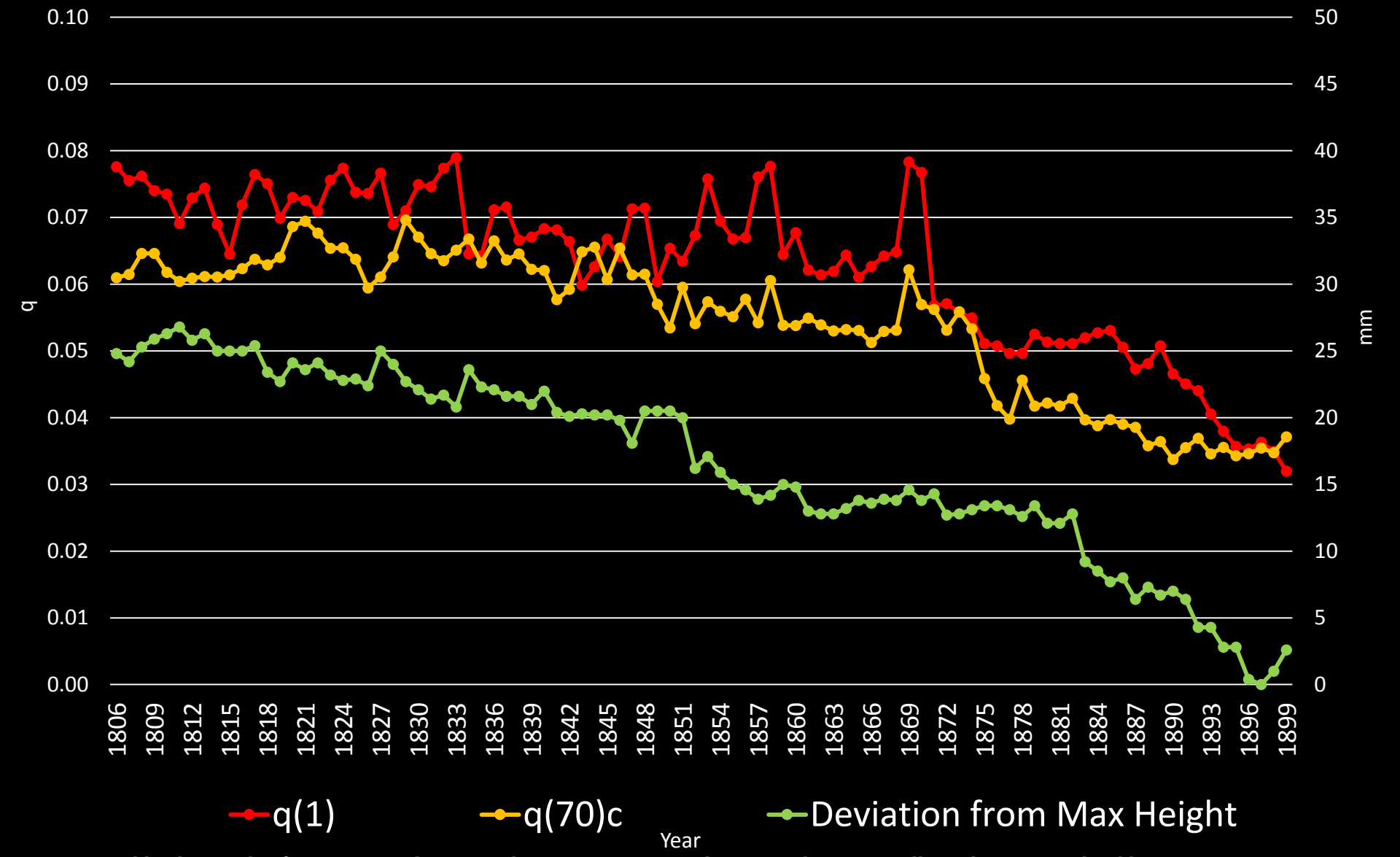
- Much gain has been because of early life changes and this is over (Crimmins and Finch 2006; Finch and Crimmins 2004; Hayward and Gorman 2004 ).

# Similar historical trends over 150 years for cohort death rates at age 1 yr and 70 yr




Finch and Crimmins. 2004. Science, 305, 1736-1739.

# 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 sieles et projections pour le XXI siecle-Jaques Vallin and France Mesle,tableau-II-C-2

2.Economic Welfare and Physical Well-Being in France, 1750-1990

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)

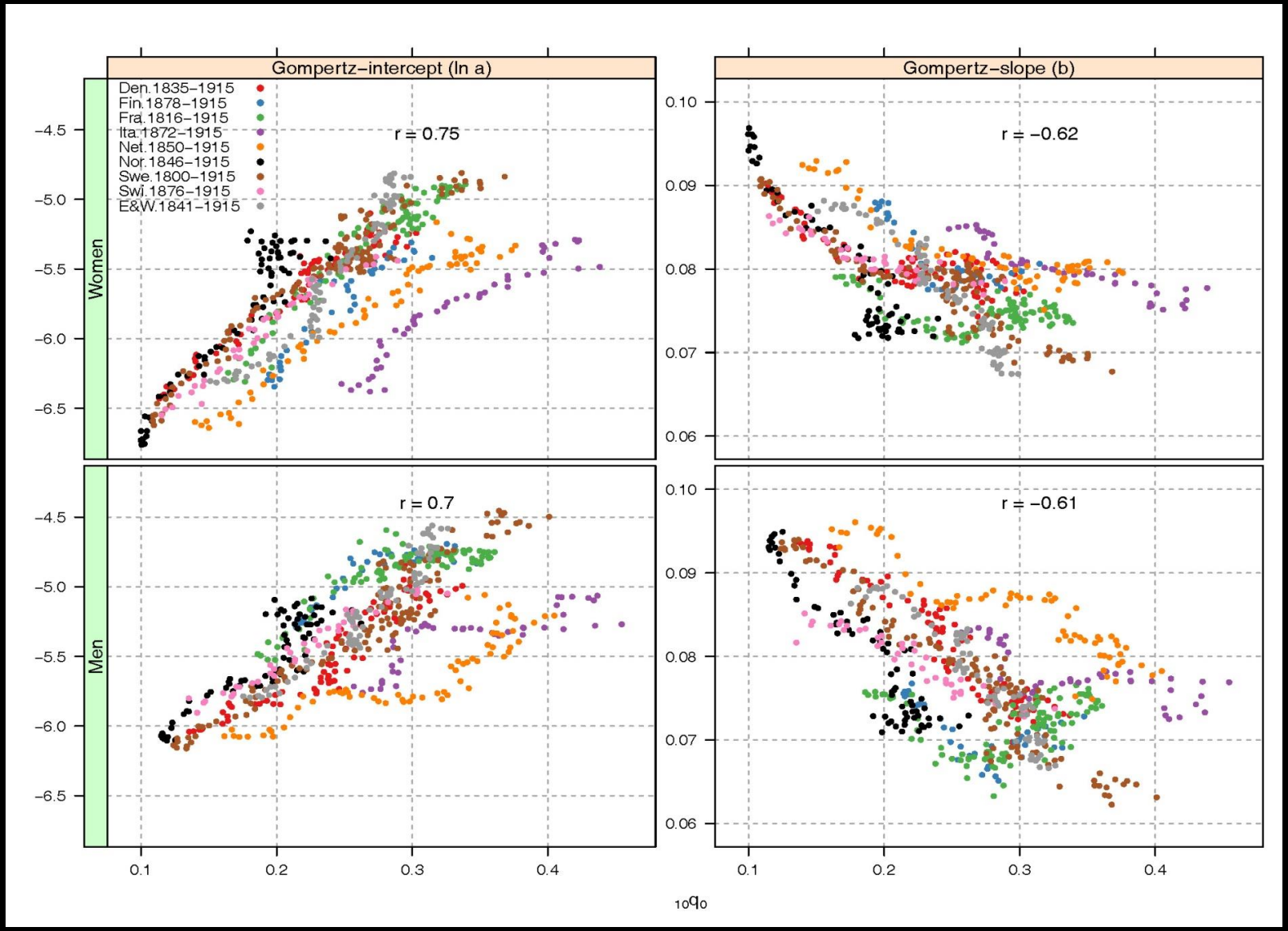
# Early cohort mortality predicts the cohort rate of aging - Low childhood mortality linked to higher rate of aging

Strong association between early life mortality ($q_{0\text{-}10}$) 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

Early Cohort Mortality Predicts the Cohort Rate of Aging: an Historical Analysis." 2012. H. Beltrán-Sánchez, E.M. Crimmins, and C.E. Finch. Journal of Developmental Origins of Health and Disease, 3(5); 380-386.

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

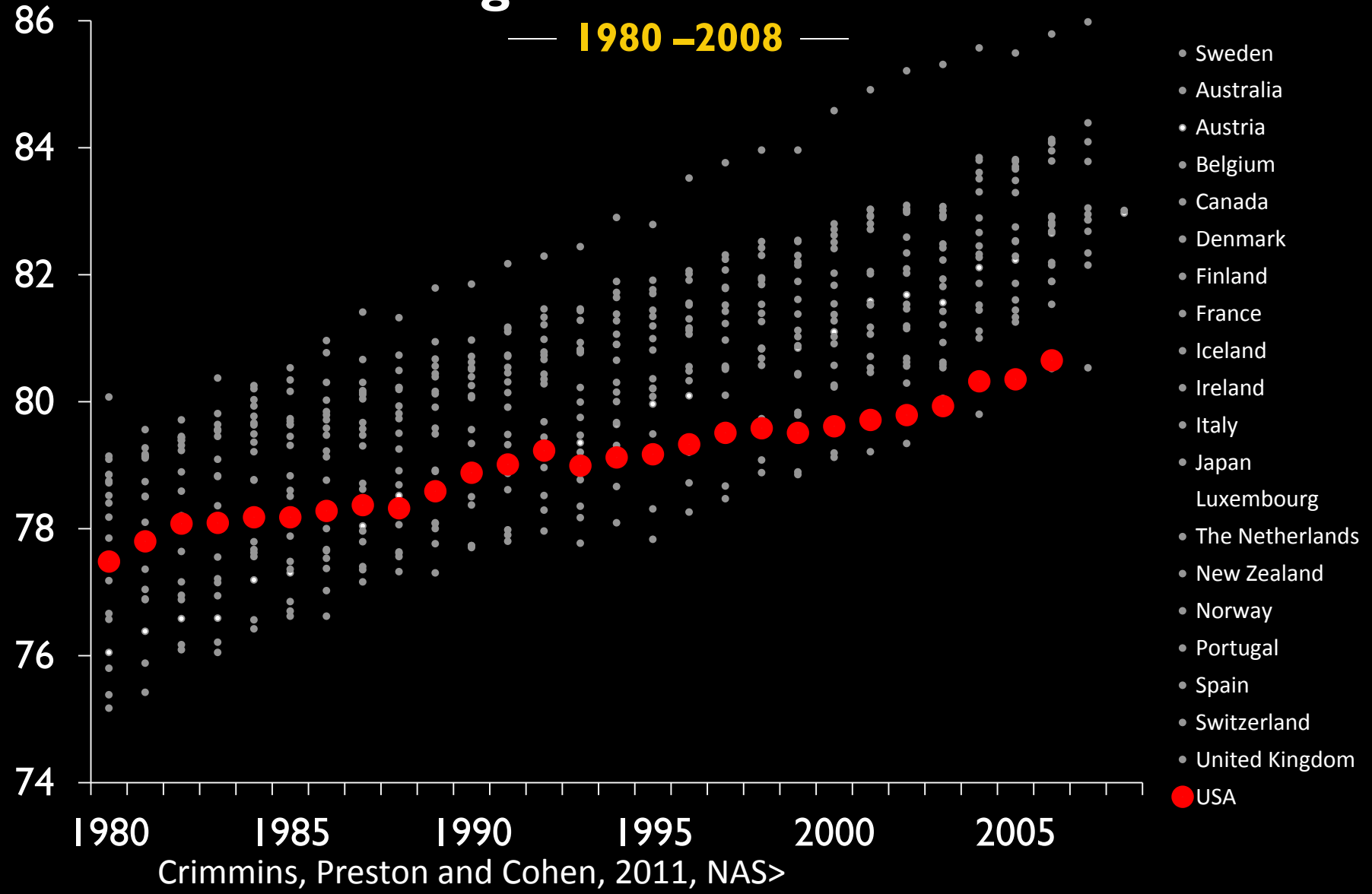



Beltran-Sanchez et al. 2012.

# 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 a vis other countries in the U.S. and poor performance, even decrease in life expectancy, among some groups

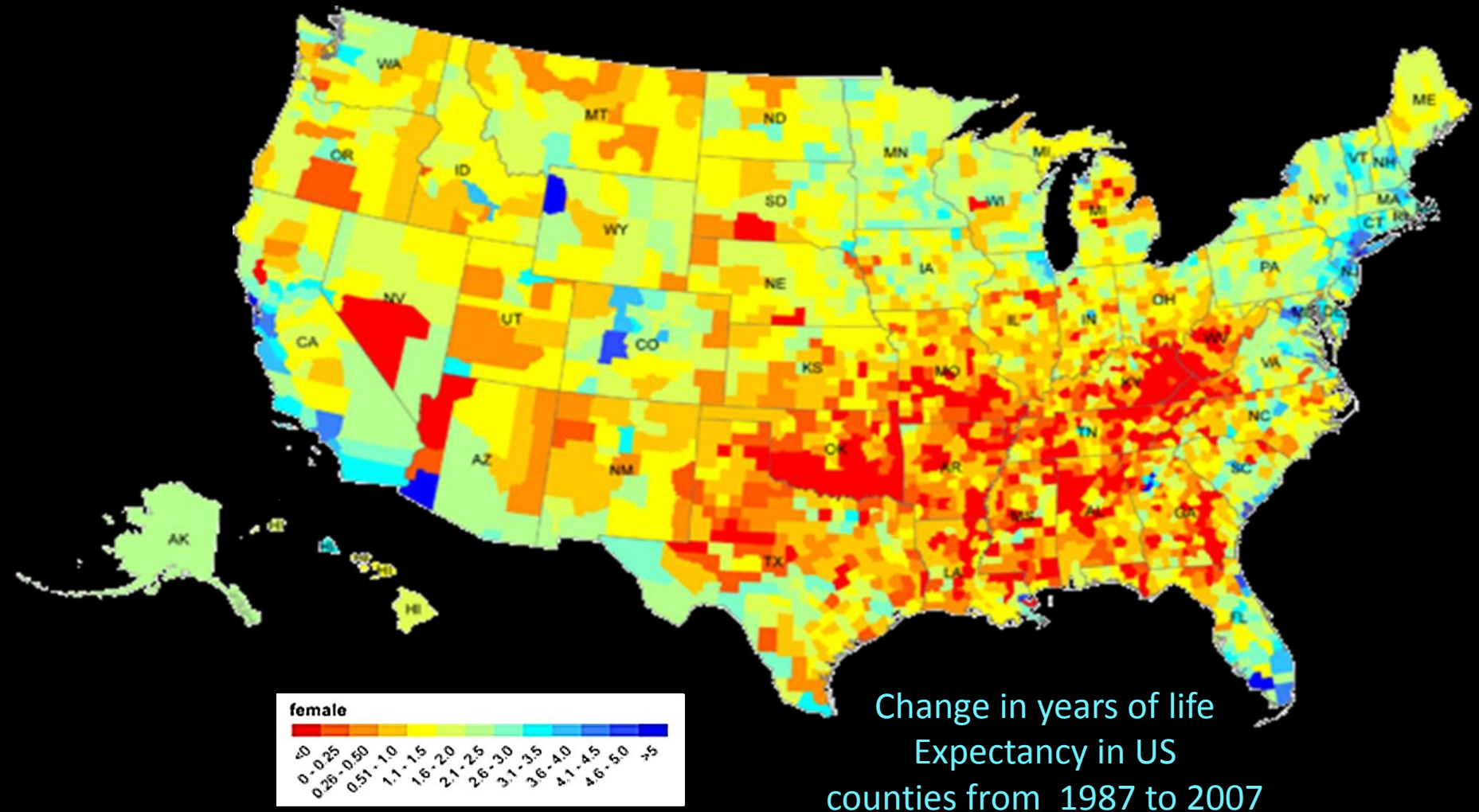
# U.S. Life Expectancy Is Relatively Low and our rank is Declining - 22 OECD Countries




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

Source: Institute for Health Metrics, 2011. John Goodman's Health Policy Blog

The New York Times | http://nyti.ms/1RLkJyx

HEALTH

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

By SABRINA TAVERNISE JUNE 1, 2016

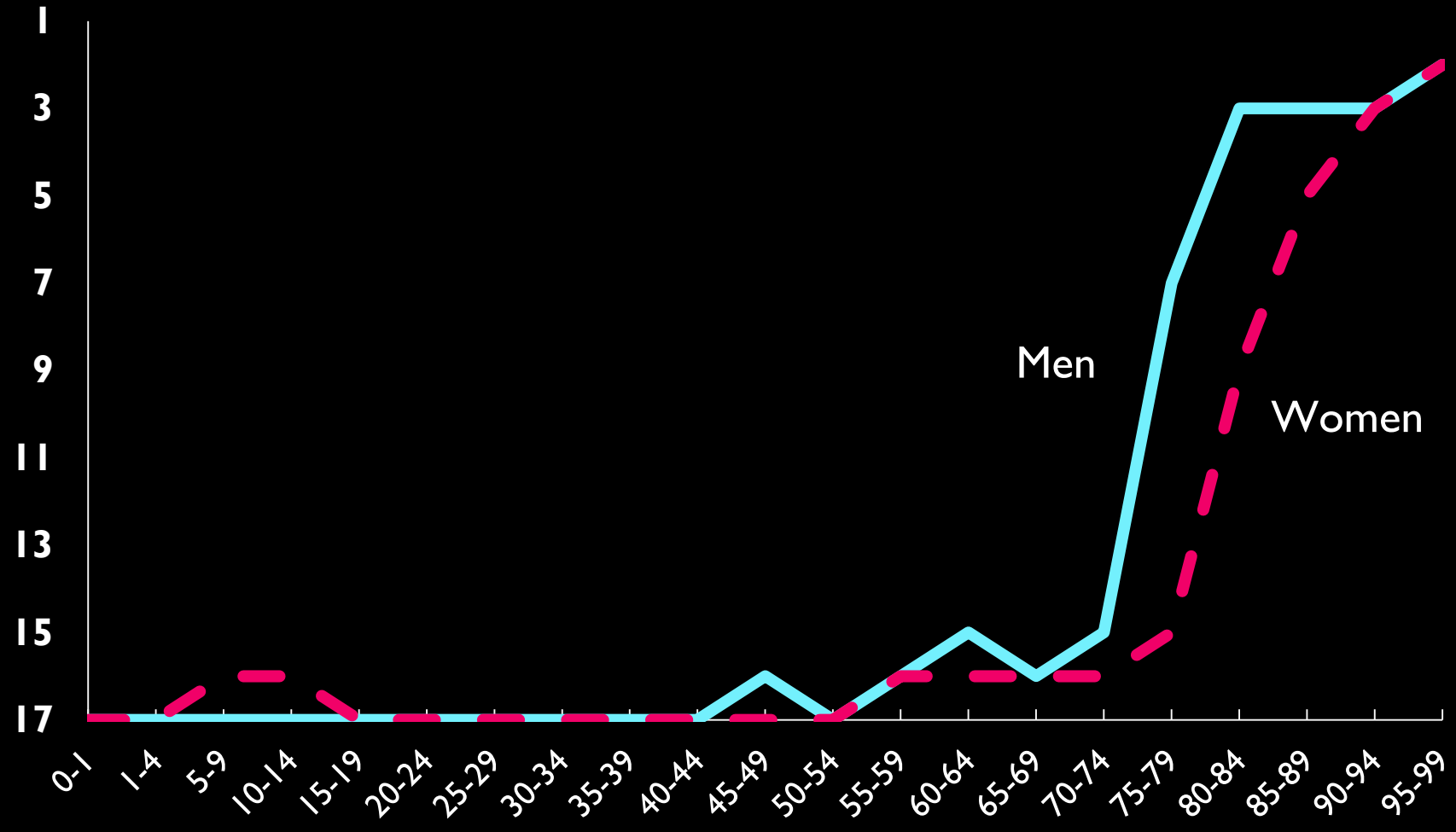
WASHINGTON — The death rate in the United States rose last year for the first time in a decade, preliminary federal data show, a rare increase that was driven in part by more people dying from drug overdoses, suicide and Alzheimer's disease. The death rate from heart disease, long in decline, edged up 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

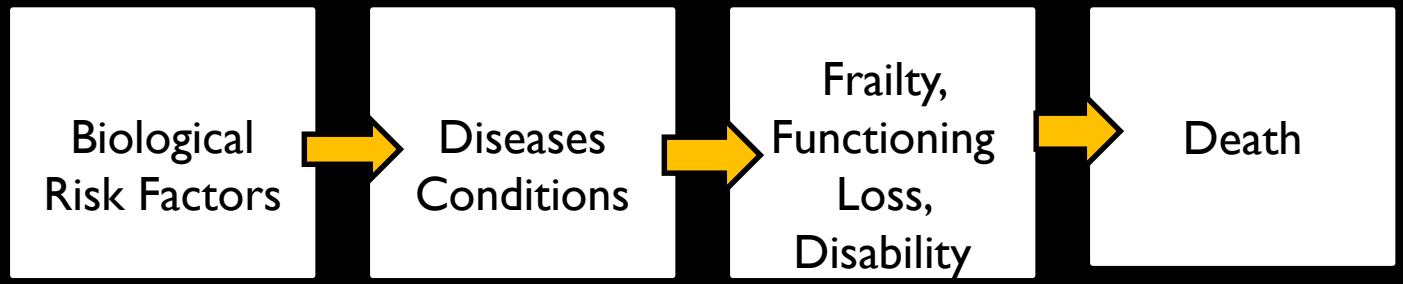
# US Ranks as worst or second to worst in mortality at most ages up to older age

## 17 Peer Countries, 2006-2008




NAS: US Health in International Perspcective: Shorter Lives, Poorer Health, 2013

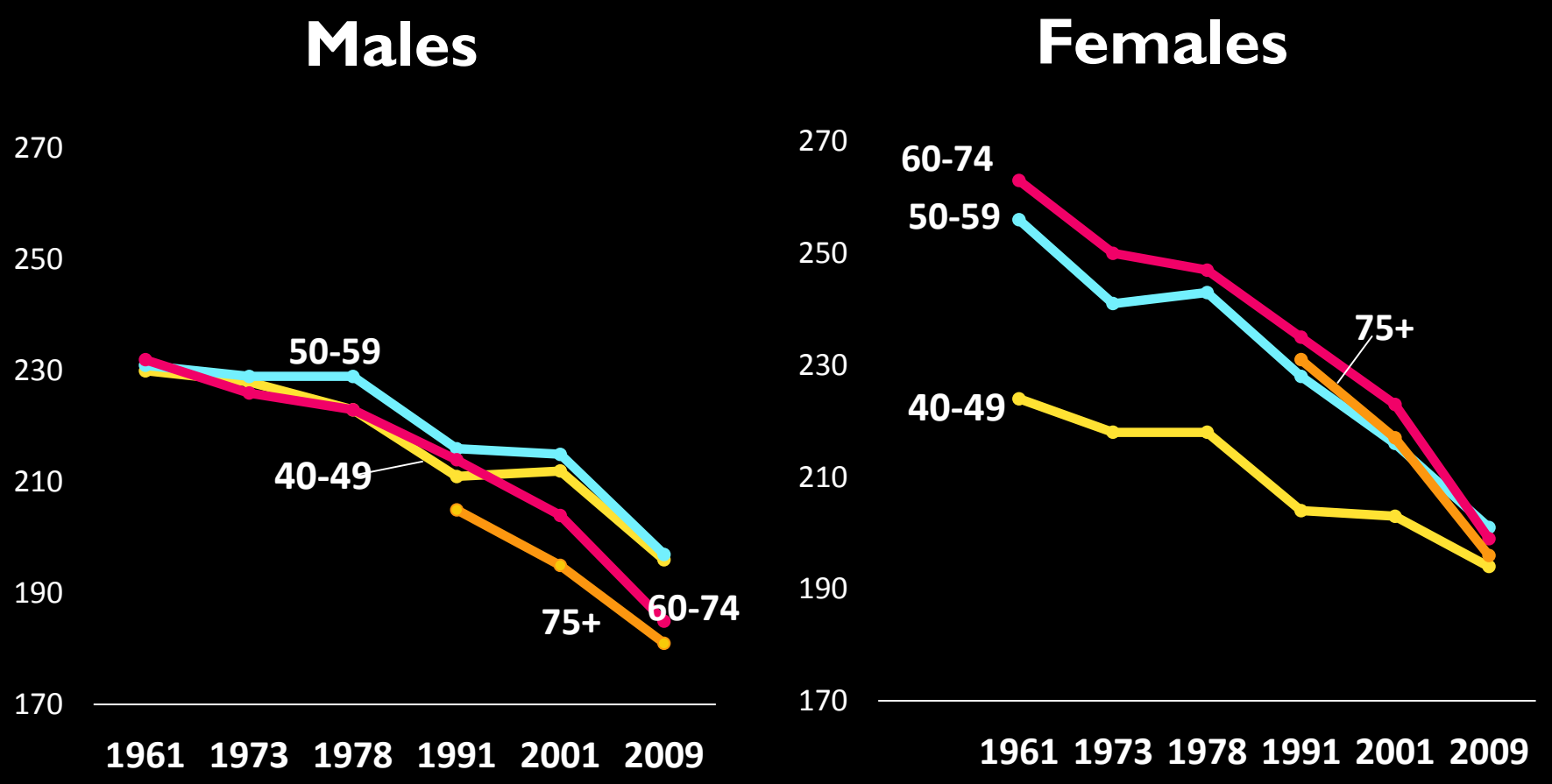
## Healthspan:
## There is potential for increasing healthspan and delaying the Morbidity Process



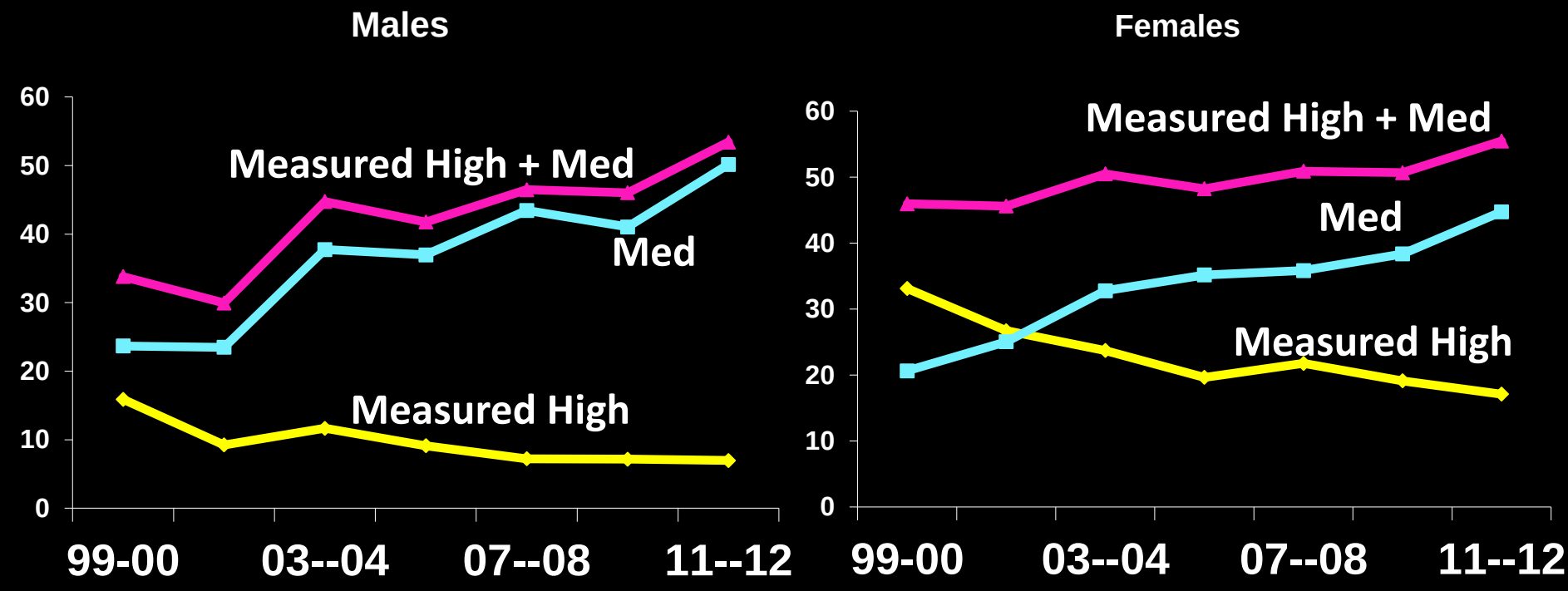

Crimmins et al. 2010. Biodemography: New Approaches to Understanding Trends and Differences in Population Health and Mortality. Demography, 47S: S41-S64.

# Total Cholesterol Declines over 50 years

**After 1960**



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

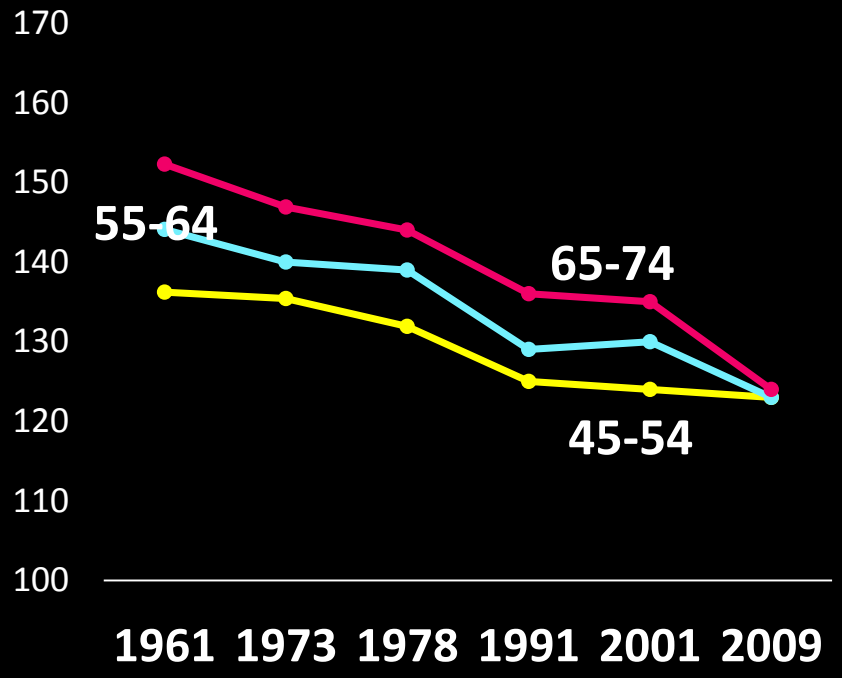



Update of Crimmins, Kim, and Vasunilashorn, Demography, 2010.

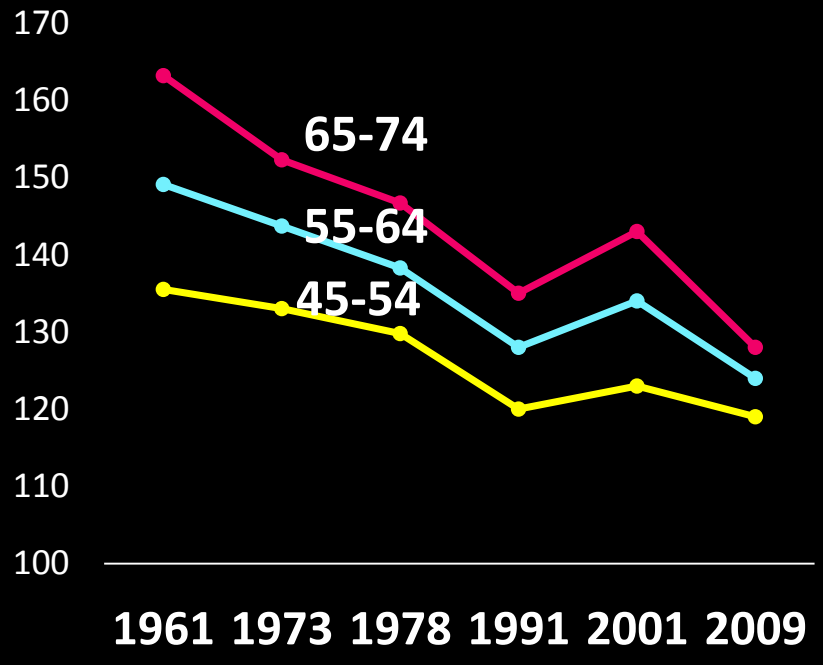
# Mean Systolic Blood Pressure Declines over 50 years

## After 1960

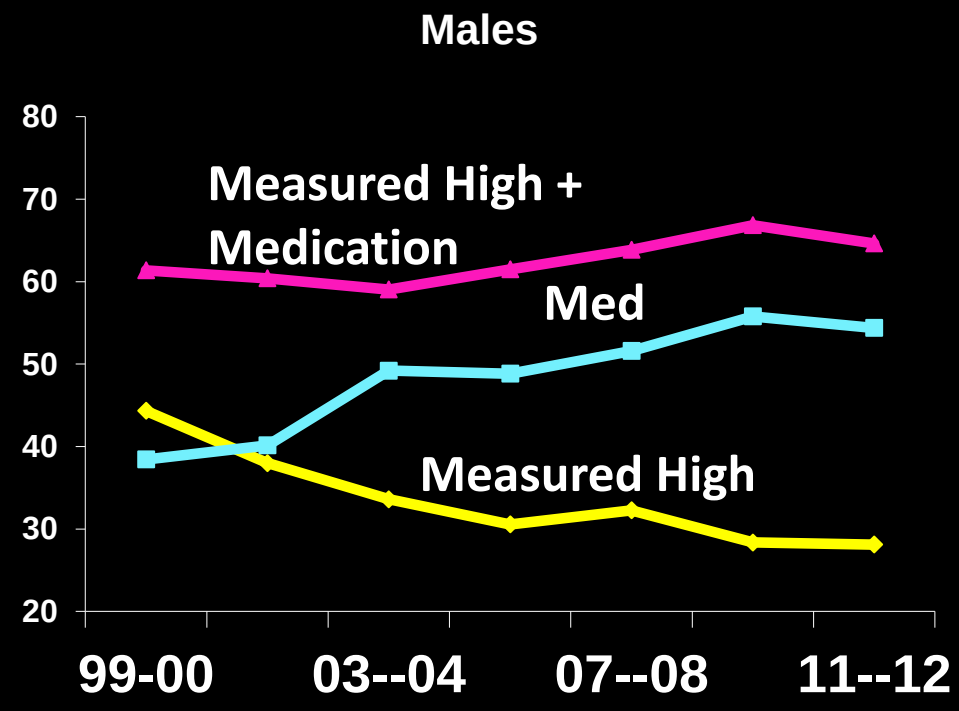
### Males

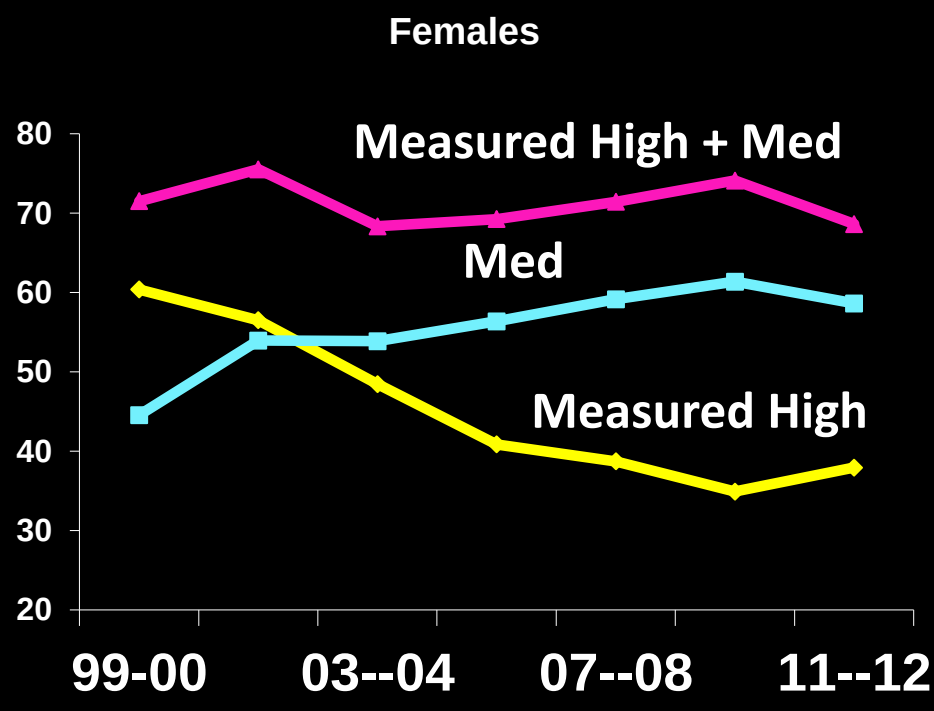



### Females



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

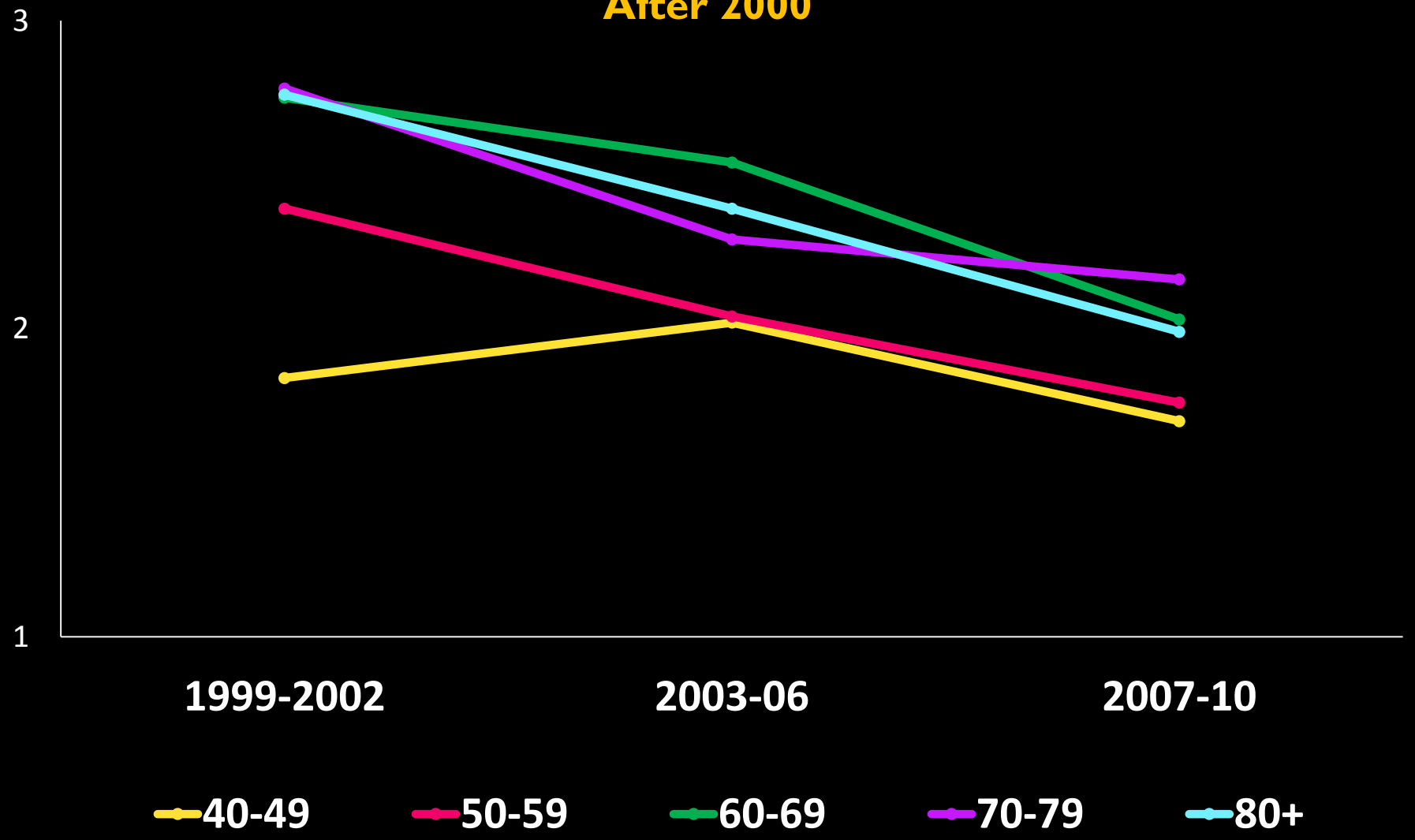



Update of Crimmins, Kim, and Vasunilashorn, Demography, 2010.

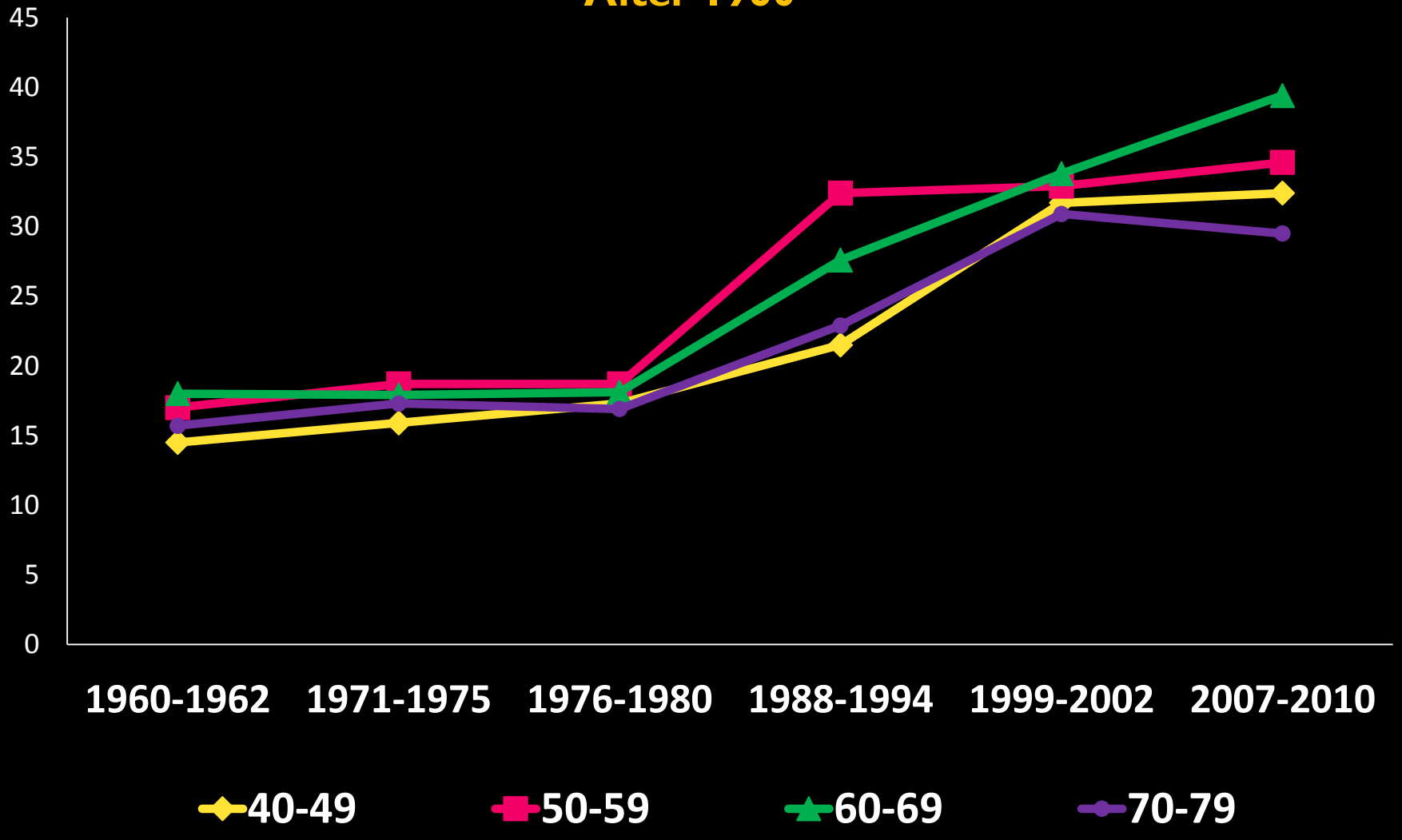
# Mean C-reactive Protein Levels Decrease over about 10 years

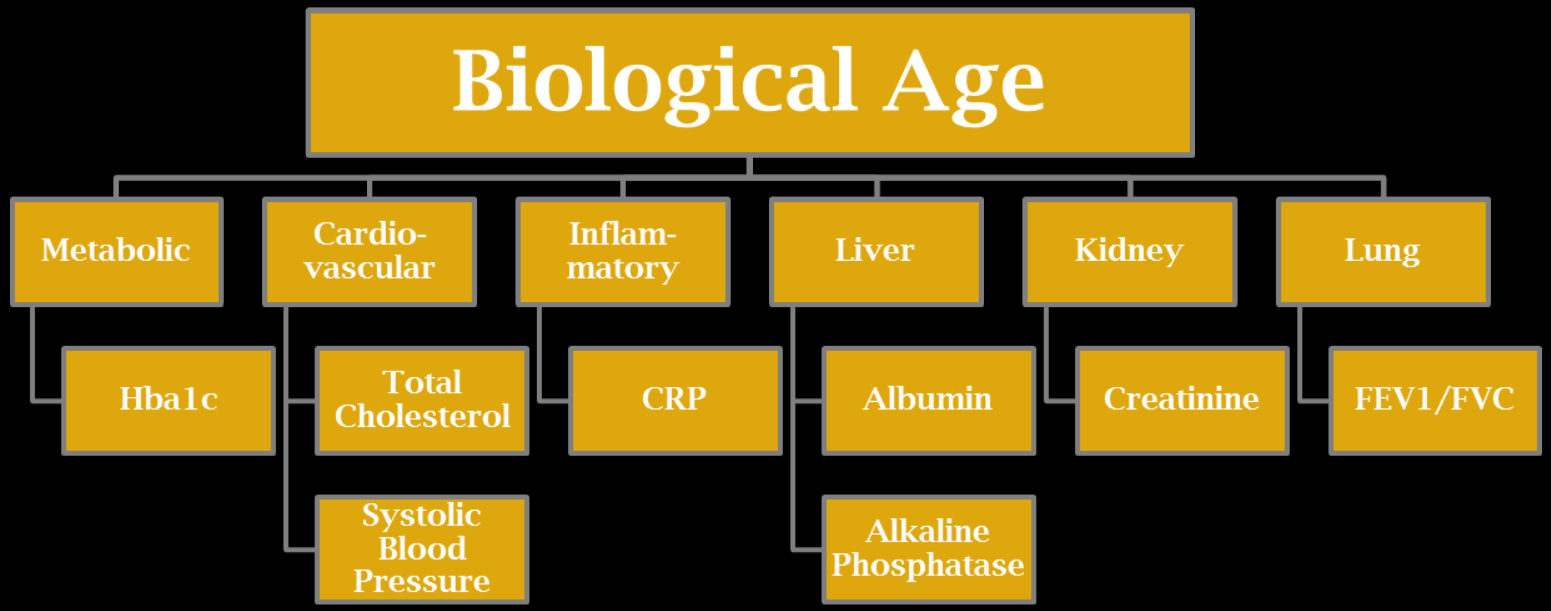
**After 2000**



# Worsening Physiological Status: Prevalence of Obesity Increases

## After 1960

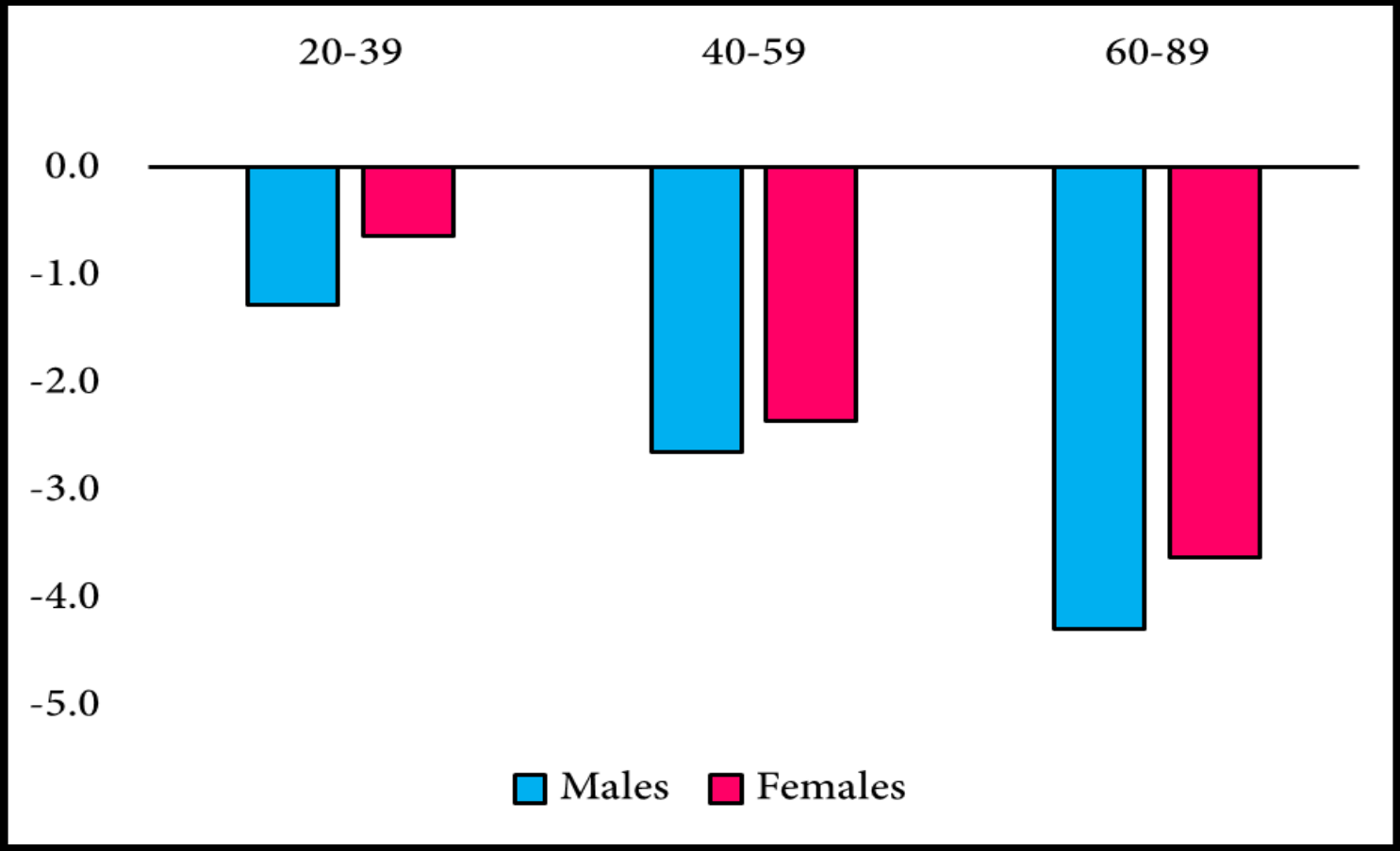





Levine, 2013, Journal of Gerontology Med Sciences.

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 ($s^2_{BA}$)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




Levine and Crimmins. Demography. Forthcoming.

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

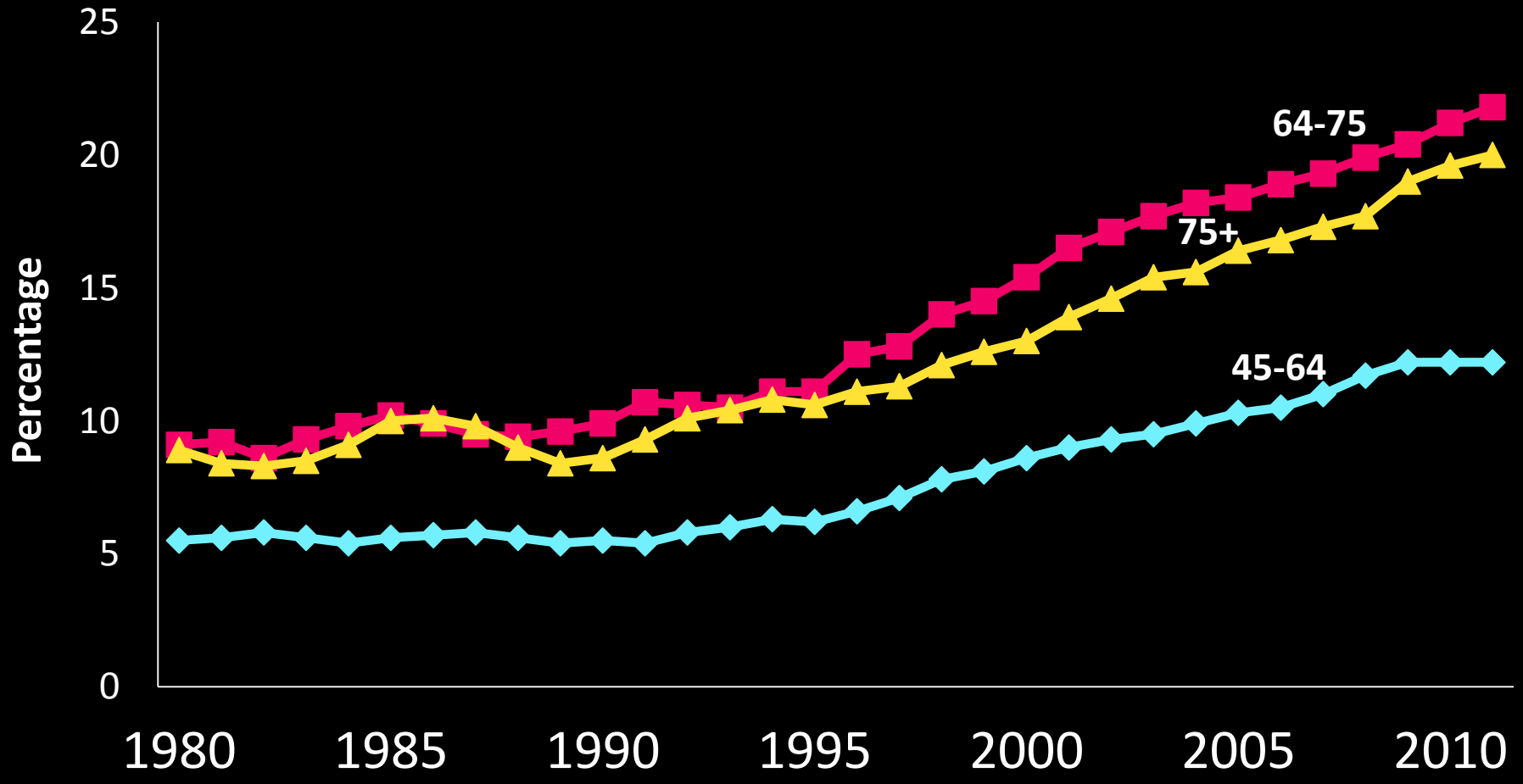
- Increases in medication use benefitted older and middle-aged more than younger adults.
- Decreases in smoking especially benefited older persons, especially older men.
- Adverse effects resulted from increases in obesity.

# 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

## Prevalence of Diagnosed Diabetes US (1980-2010)



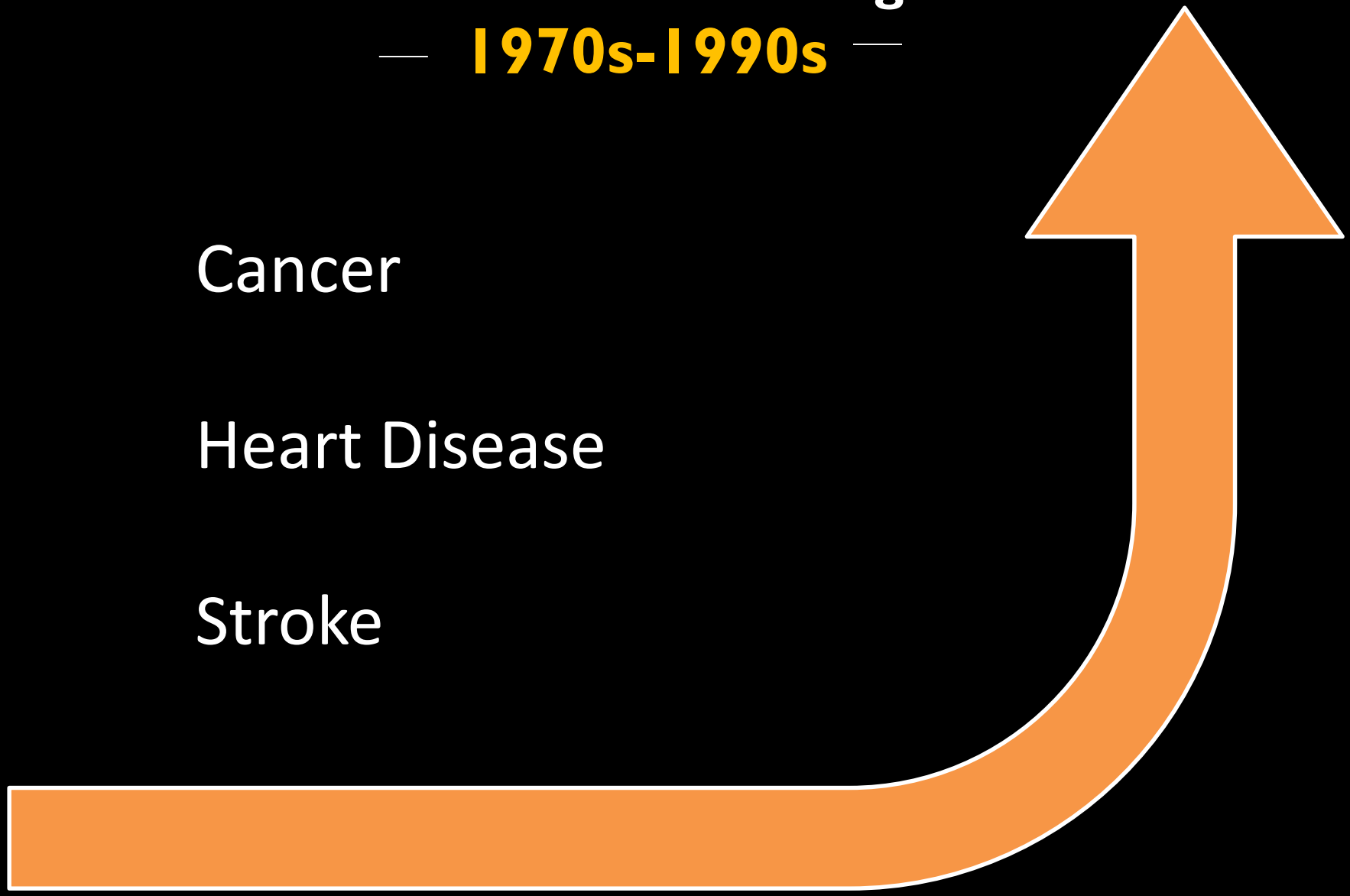
# Other Diseases with Increasing Prevalence

## 1970s-1990s

Cancer

Heart Disease

Stroke

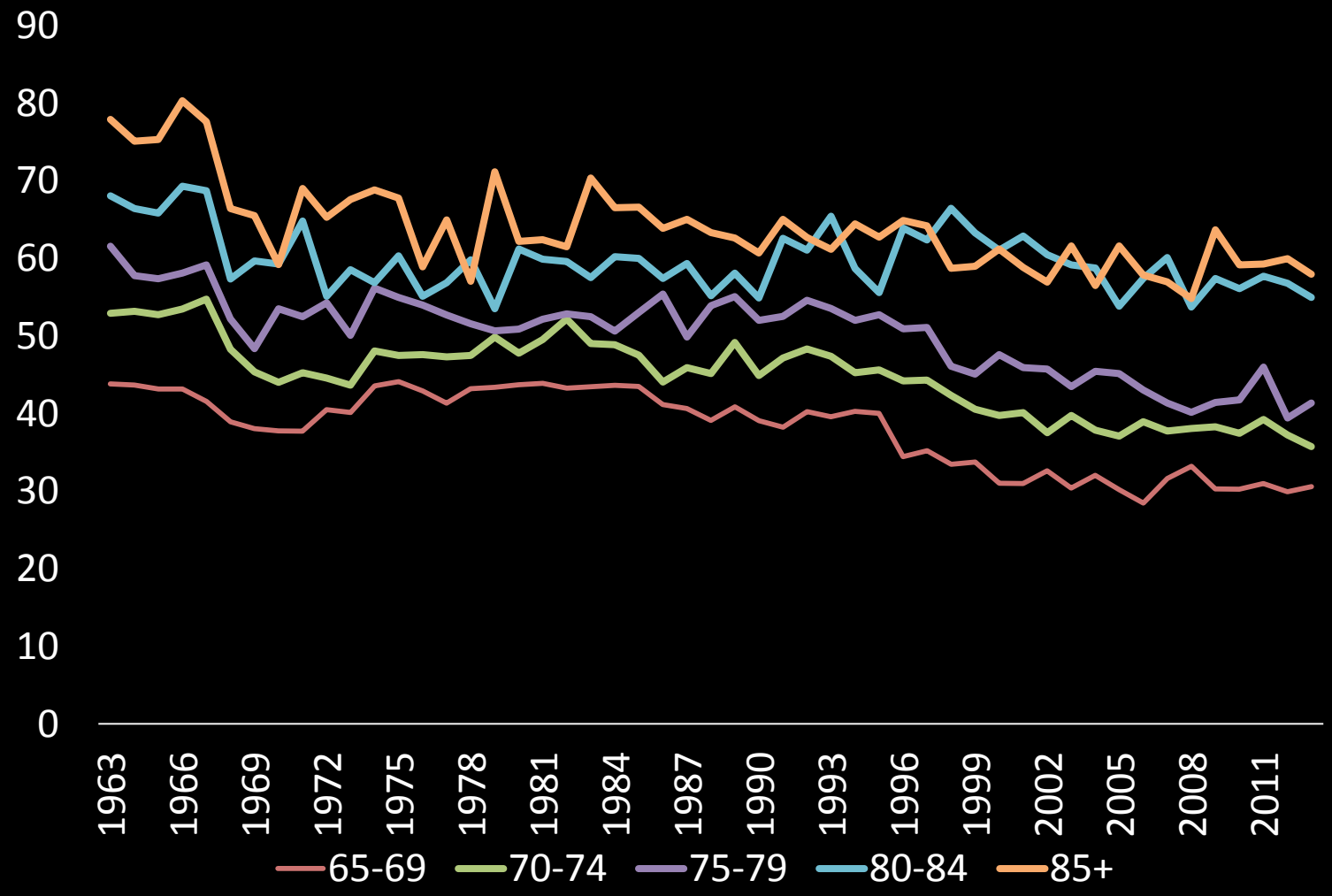


**Modest decreases in disability –**

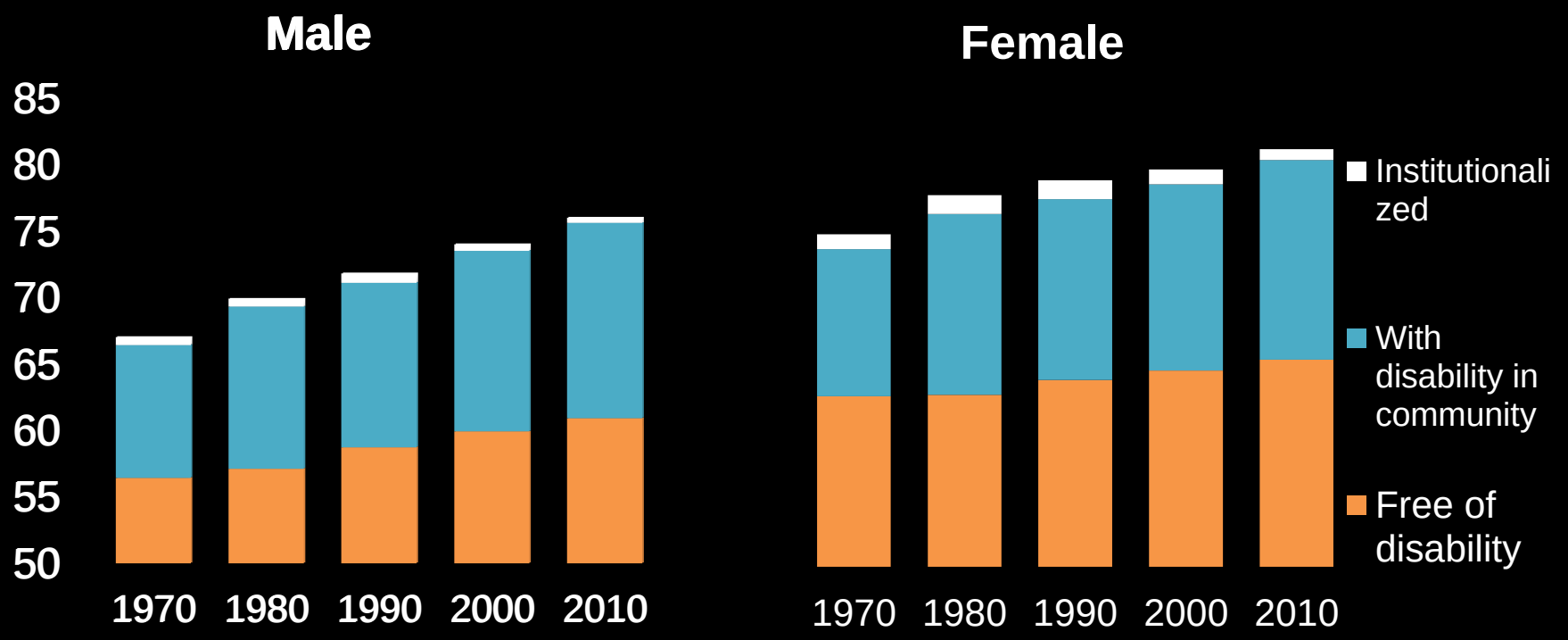
**Especially among the old -**

**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




Crimmins, Zhang, Saito. 2016. Trends over Four Decades in Disability-Free Life Expectancy in the United States. American Journal of Public Health. Forthcoming.

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)

| | Men | | Women | |
|---|---|---|---|---|
| | 1998 | 2006 | 1998 | 2006 |
| Age 20 years | | | | |
| Life expectancy | 55.0 | 56.1 | 60.3 | 61.0 |
| With at least one disease | 10.0 | 12.3 | 11.1 | 13.0 |
| Without disease | 45.0 | 43.8 | 49.2 | 48.0 |
| Unable to function | 3.8 | 5.8 | 7.3 | 9.8 |
| Able to function | 51.2 | 50.3 | 53.0 | 51.2 |
| Age 65 years | | | | |
| Life expectancy | 16.0 | 17.0 | 19.2 | 19.7 |
| With at least one disease | 7.2 | 8.9 | 7.4 | 8.4 |
| Without disease | 8.8 | 8.1 | 11.8 | 11.3 |
| Unable to function | 2.9 | 4.5 | 5.8 | 7.3 |
| Able to function | 13.1 | 12.5 | 13.4 | 12.4 |

"Trends in Mortality and Morbidity: Is there a compression of morbidity?" 2011. E. Crimmins and H. Beltran-Sanchez. Journal of Gerontology: Social Sciences, 66: 75-86. PMID: 20948986 PMCID:

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)

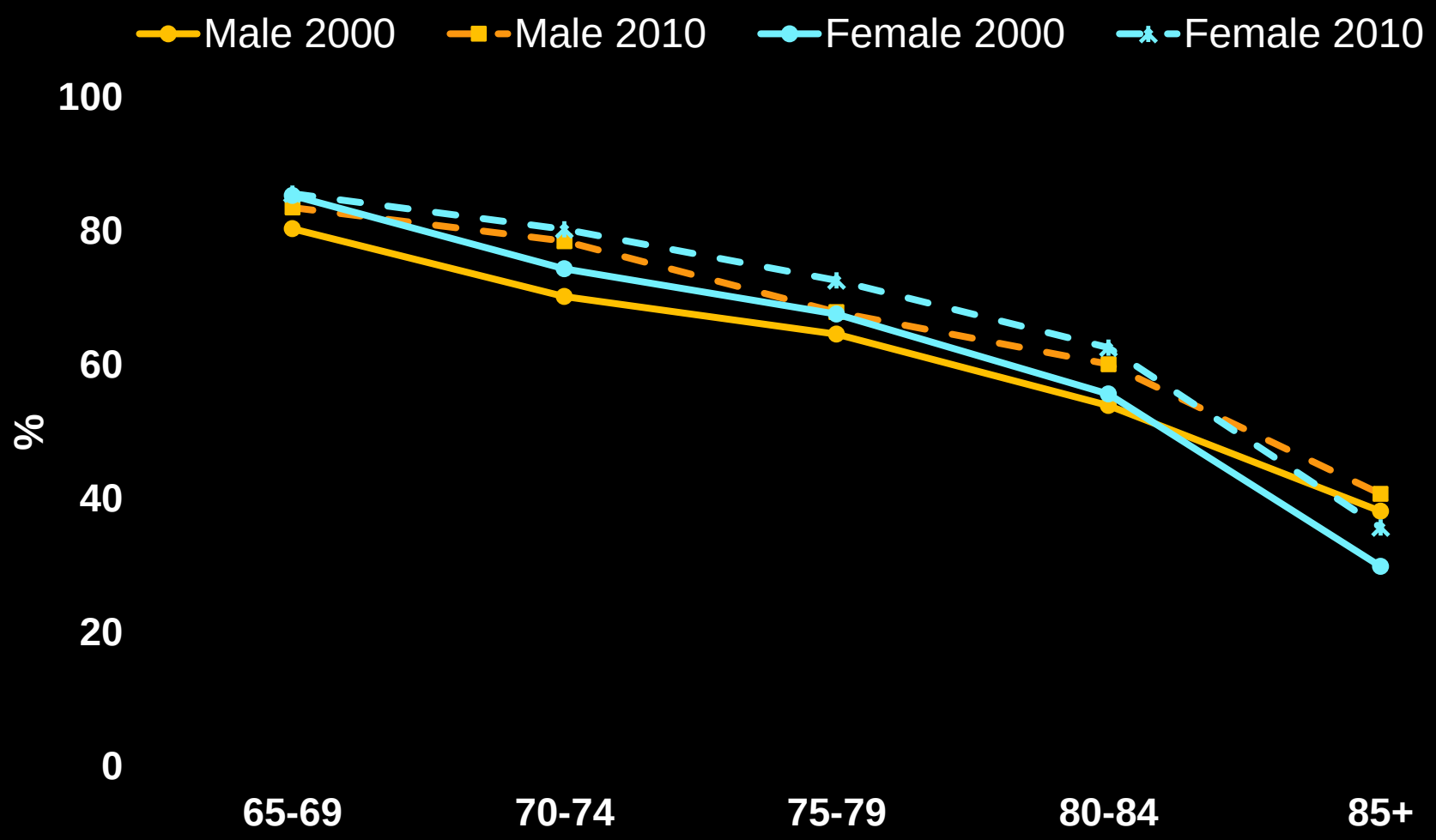
| | Men | | Women | |
|---|---|---|---|---|
| | 1998 | 2006 | 1998 | 2006 |
| Age 20 years | | | | |
| Life expectancy | 55.0 | 56.1 | 60.3 | 61.0 |
| With at least one disease | 10.0 | 12.3 | 11.1 | 13.0 |
| Without disease | 45.0 | 43.8 | 49.2 | 48.0 |
| Unable to function | 3.8 | 5.8 | 7.3 | 9.8 |
| Able to function | 51.2 | 50.3 | 53.0 | 51.2 |
| Age 65 years | | | | |
| Life expectancy | 16.0 | 17.0 | 19.2 | 19.7 |
| With at least one disease | 7.2 | 8.9 | 7.4 | 8.4 |
| Without disease | 8.8 | 8.1 | 11.8 | 11.3 |
| Unable to function | 2.9 | 4.5 | 5.8 | 7.3 |
| Able to function | 13.1 | 12.5 | 13.4 | 12.4 |

Cognitive disability is a different story –

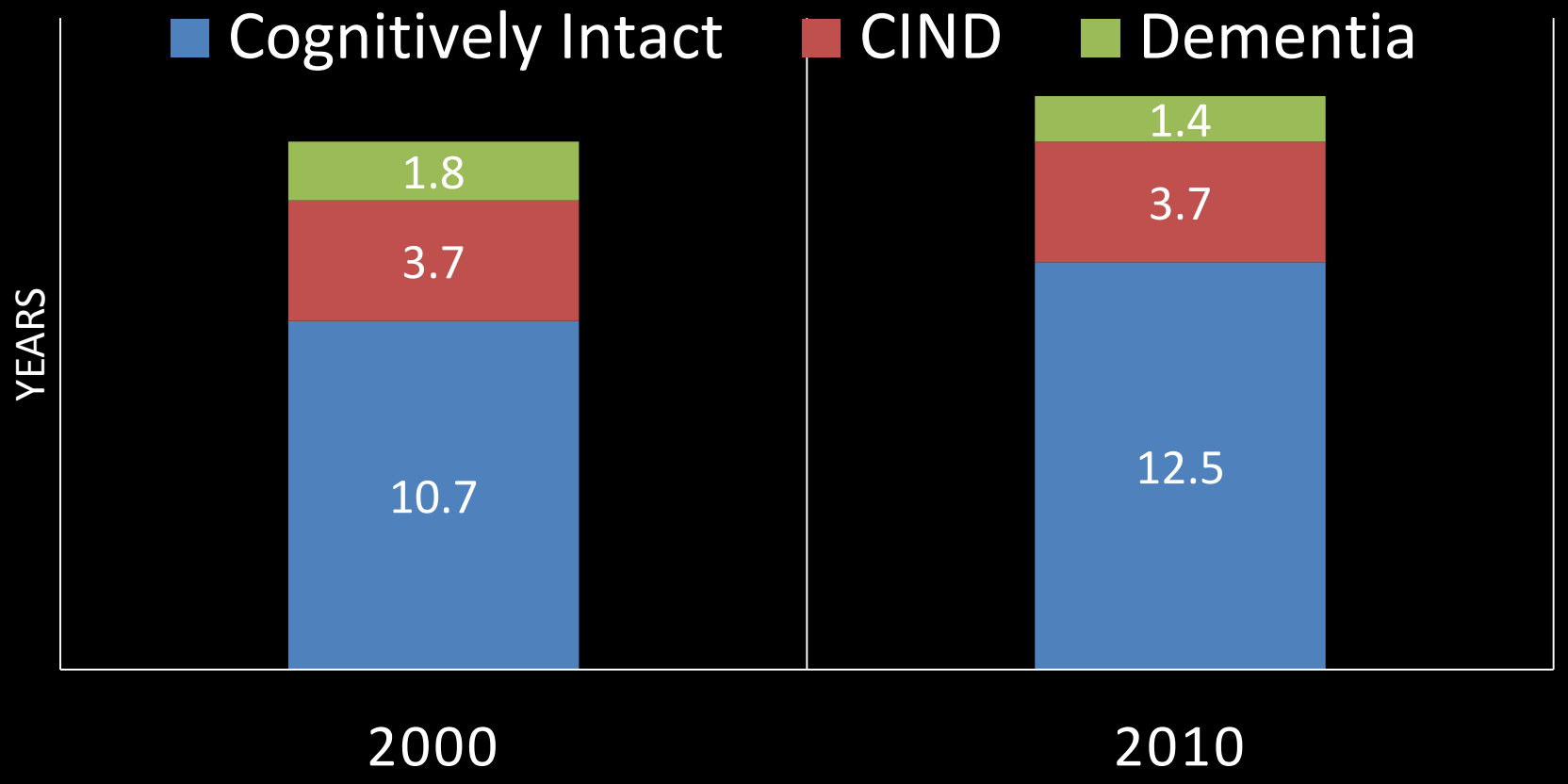
Reduction in dementia and
Increase in life free of dementia

Decrease in life with dementia

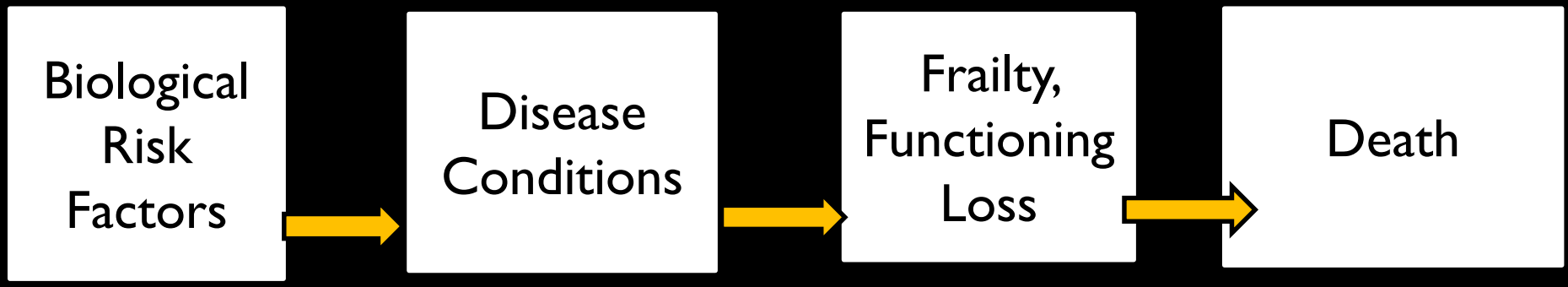
# % With Good Cognition Increases in last ten years



# Increases in Cognitively Intact Life Expectancy
# Decreases in Life expectancy with dementia
# At age 65, US Males.



# 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?

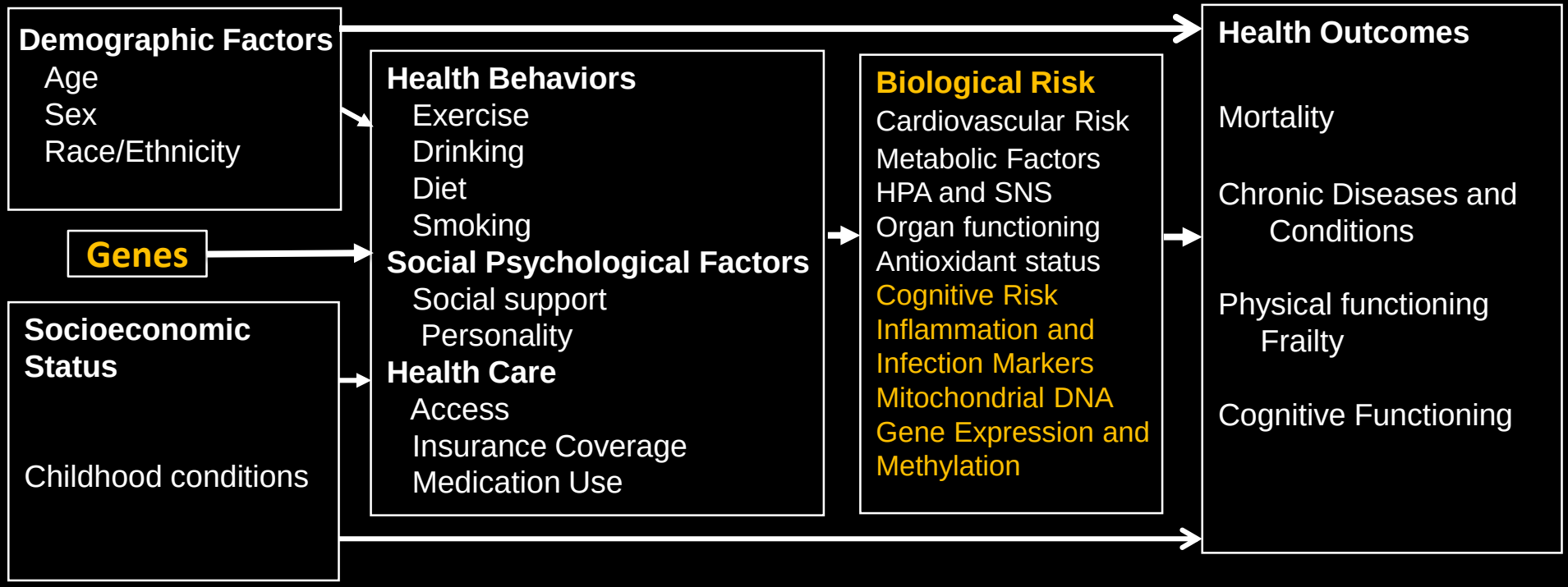
1. Delay the Morbidity Process with focus on the beginning of the process

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



Current and Future integration of risk factors and pathways –

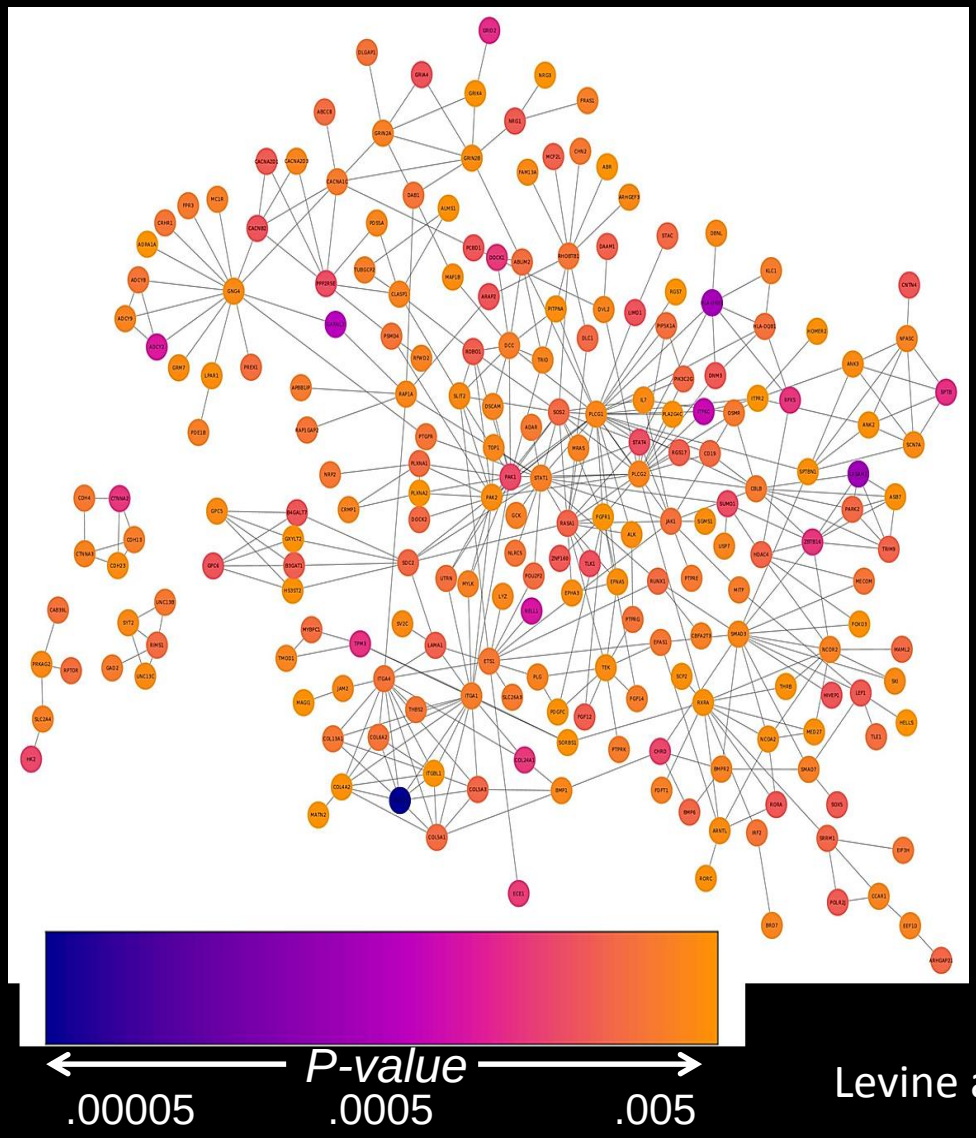
Improve on current measure of biological age by looking at basic mechanisms of aging

- 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

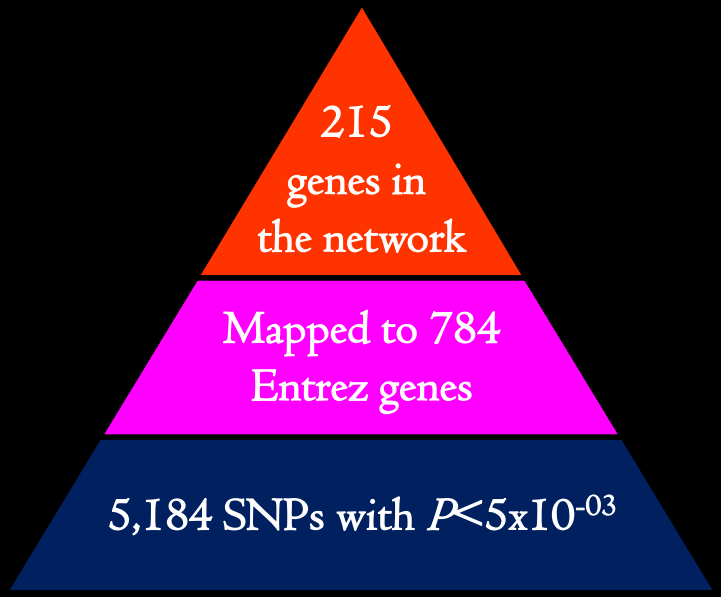
Are long-lived smokers “resilient” or are they just lucky?

# GWAS results for long-lived smokers used to define a Genetic Functional Interaction Network



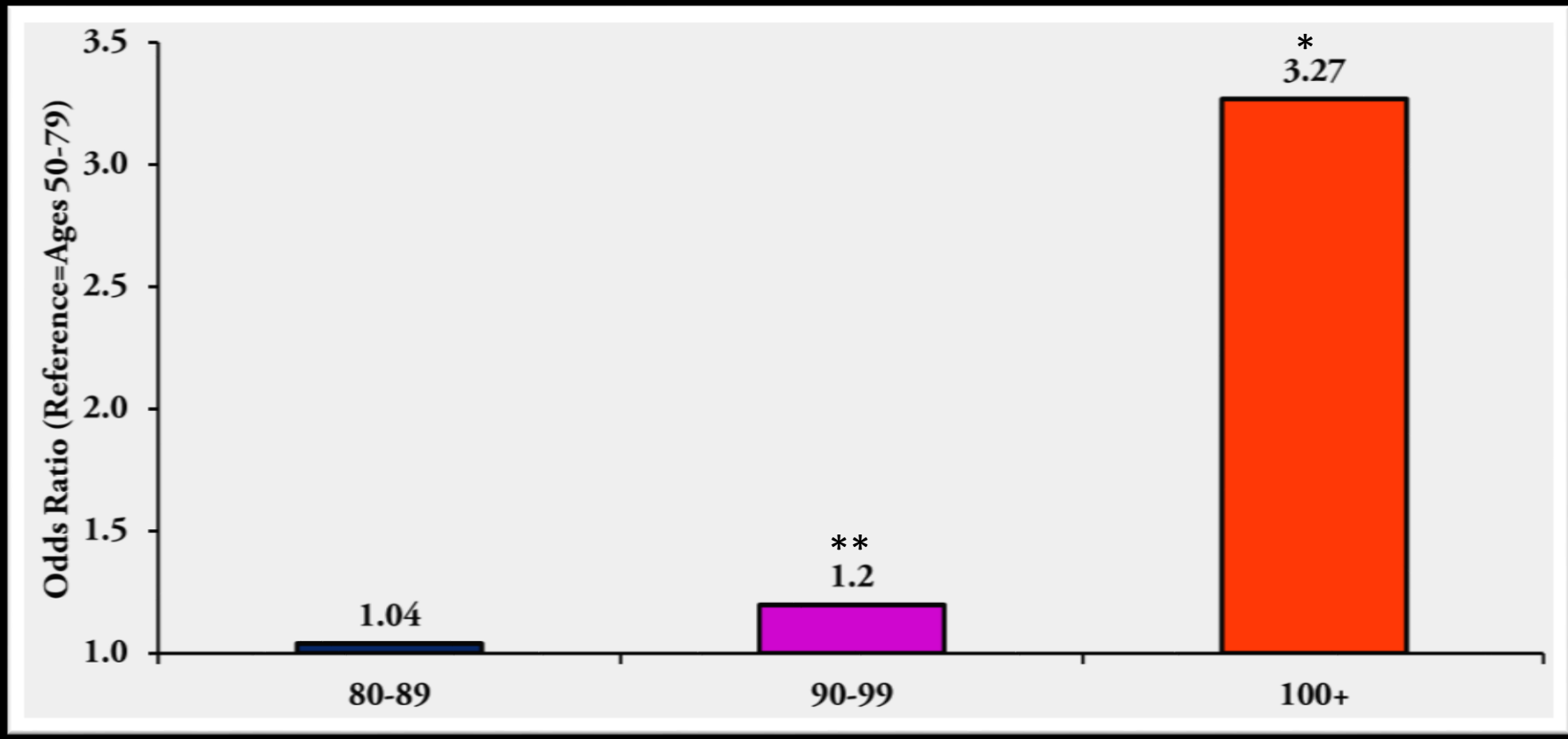

Top Enriched Pathways

**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$^{-4}$)**



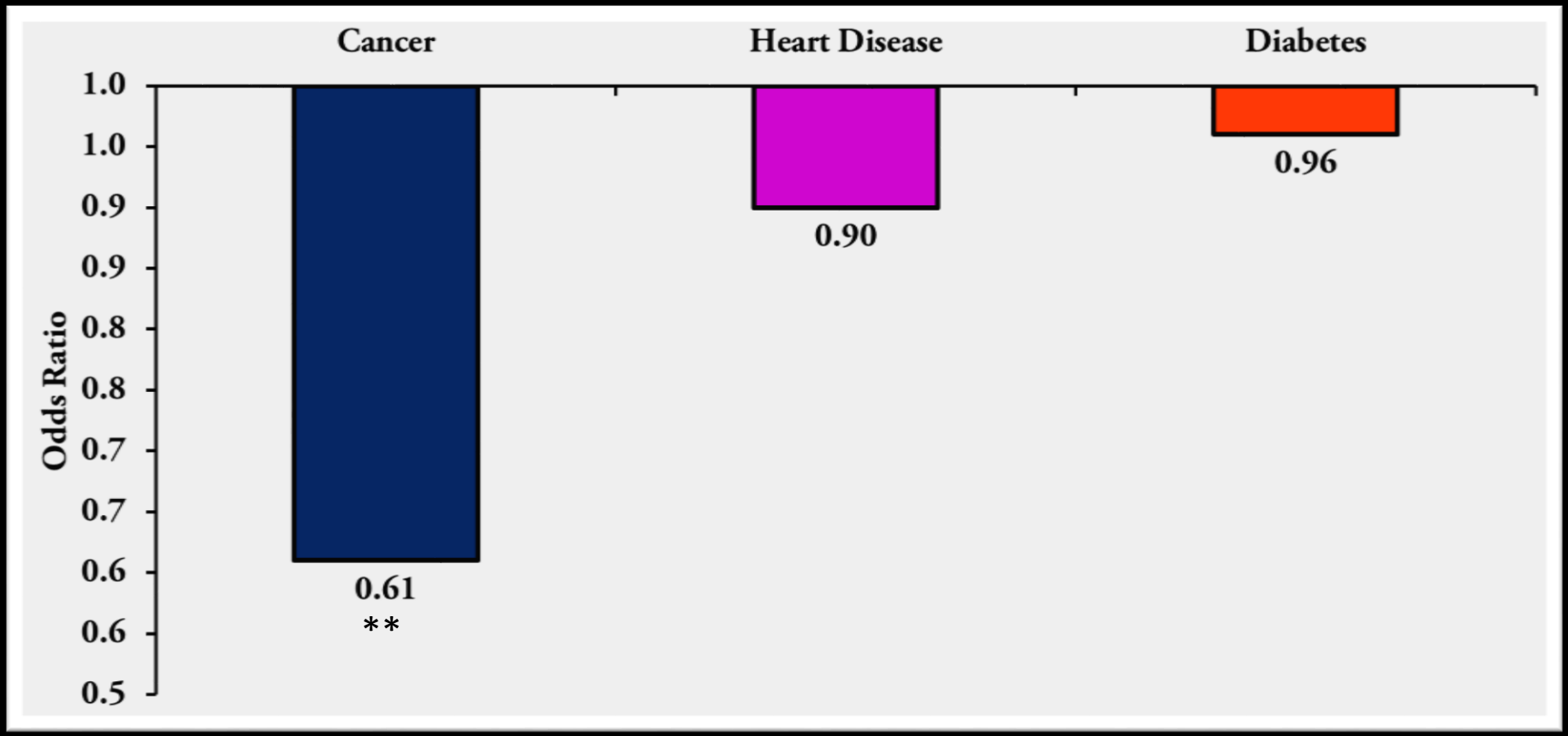

Levine and Crimmins, JOG: Medical Sciences, 2015.

# Polygenic Risk Score based on Network is related to likelihood of being very old among Non-Smokers



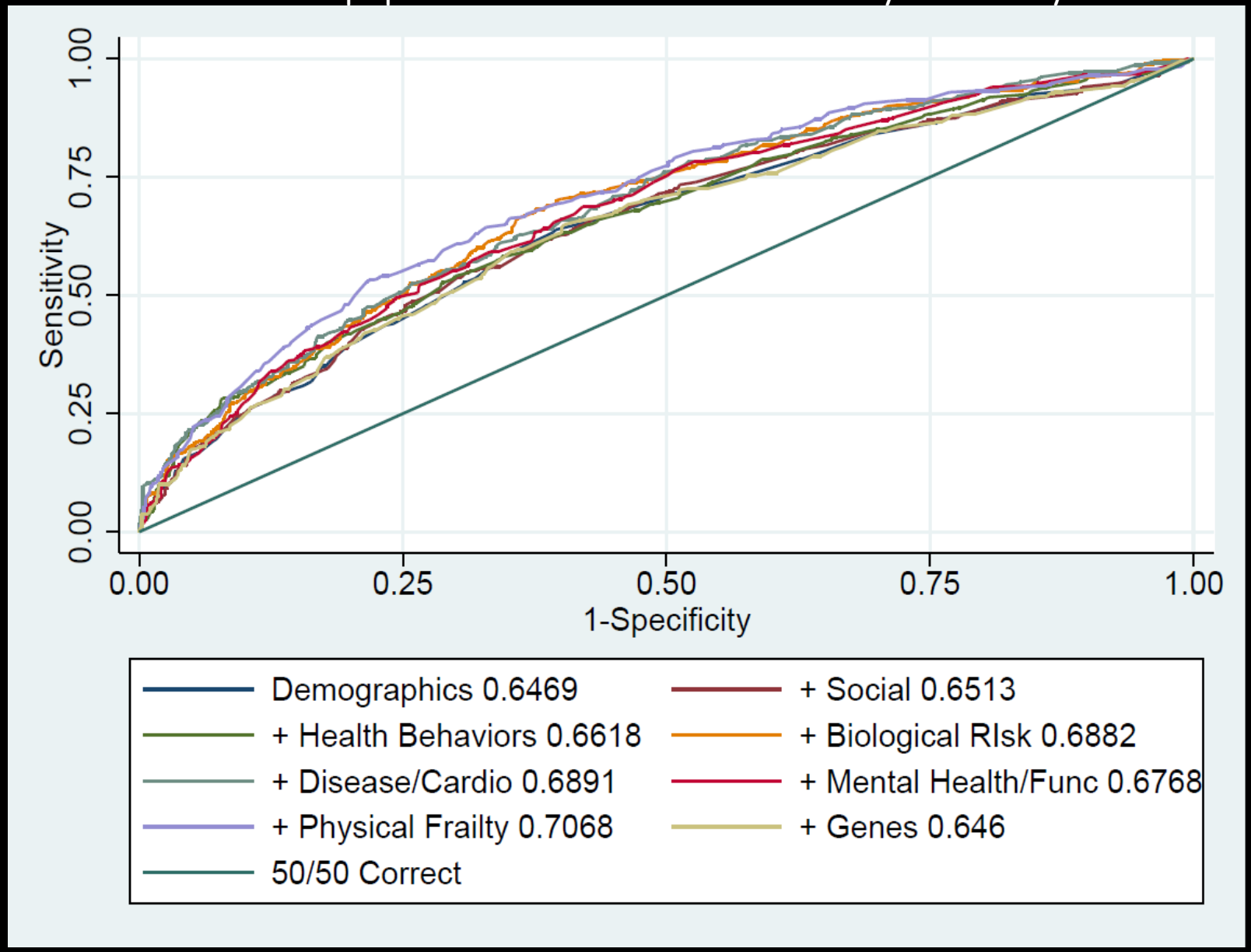

Levine and Crimmins, JOG: Medical Sciences, 2015.

# PRS is related to lower likelihood of cancer among Non-Smokers

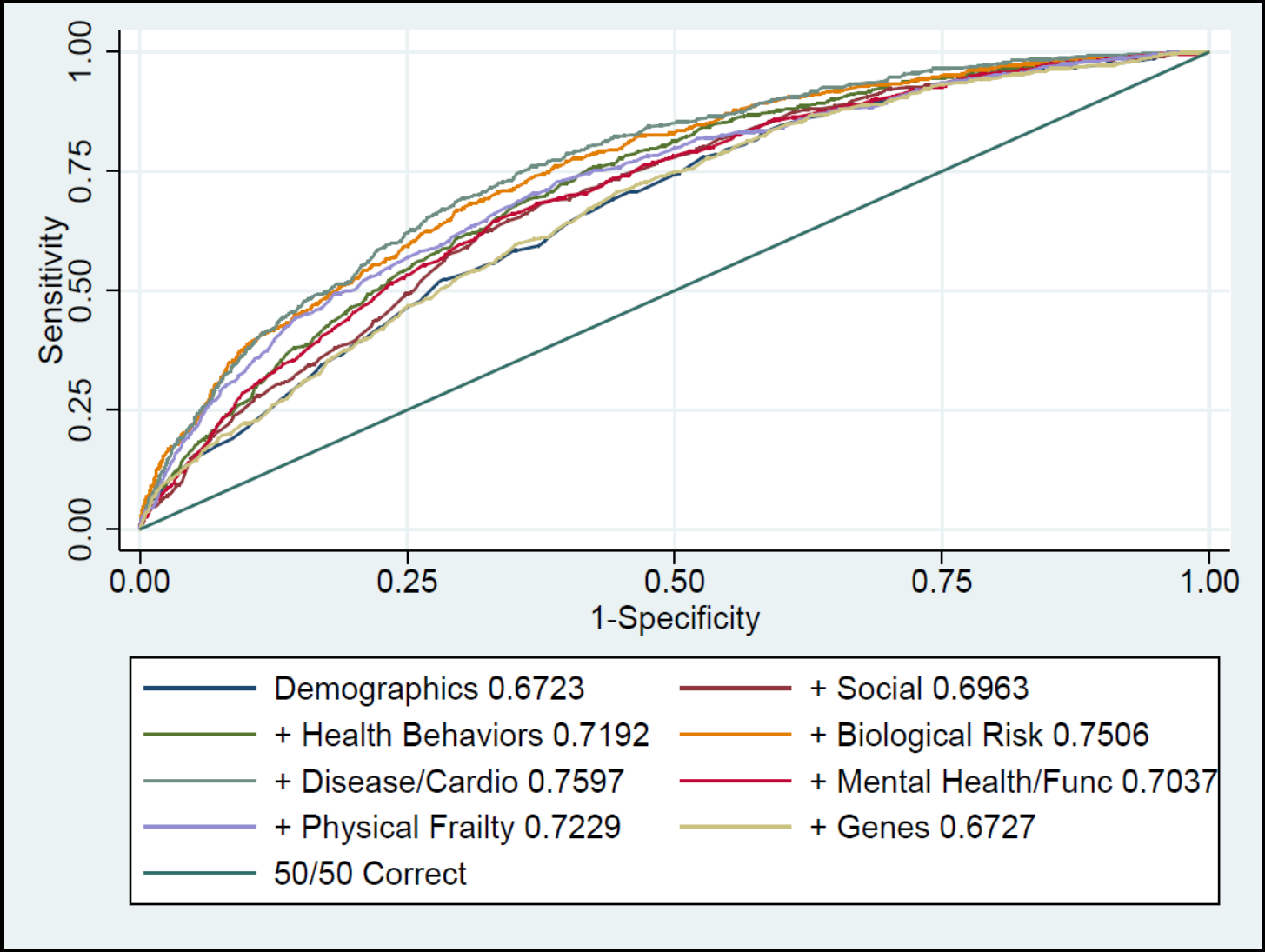



Levine and Crimmins, JOG: Medical Sciences, 2015.

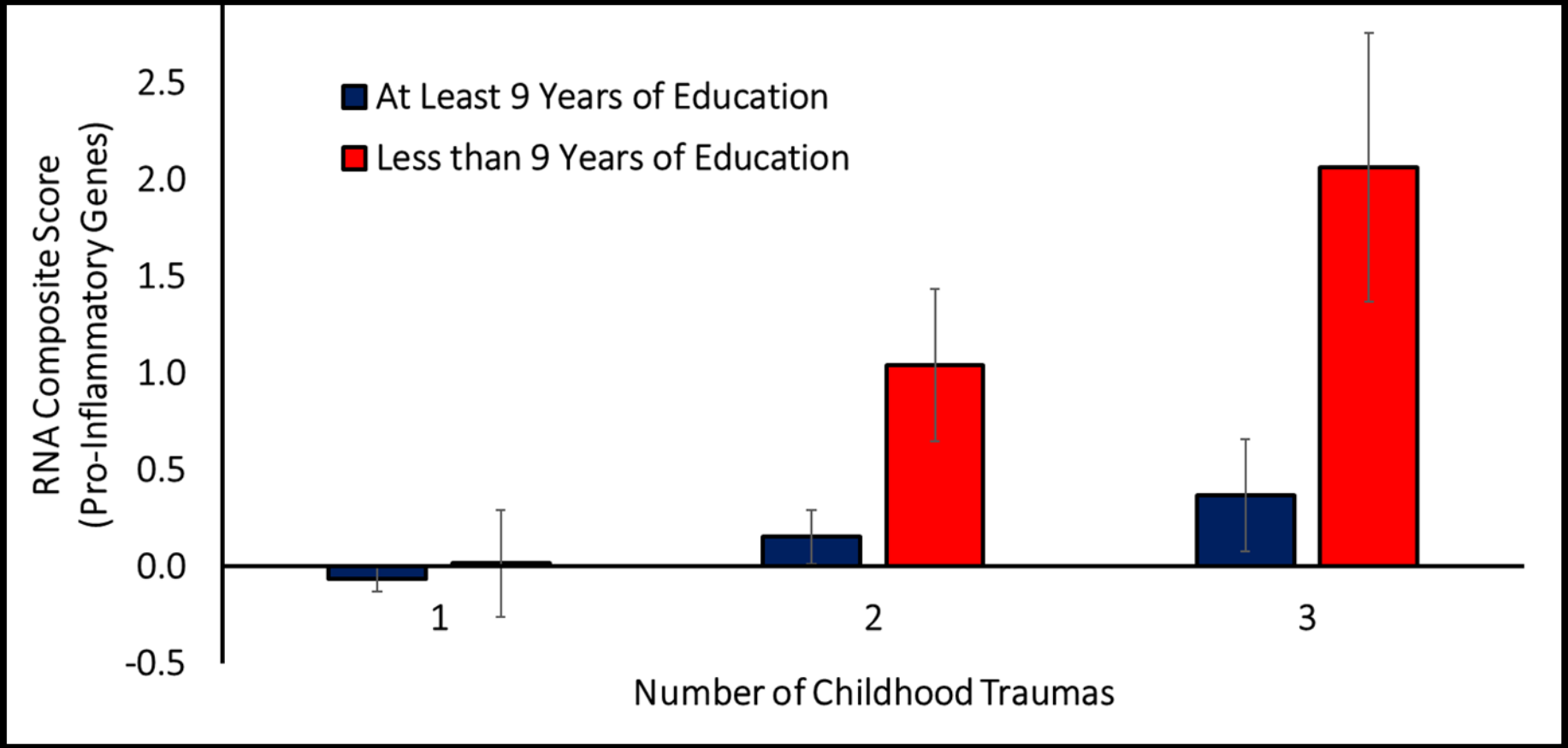
ROC curves for 80+ population – HRS model of mortality with many variables



ROC curves for 50- 79 population – HRS model of mortality with many variables

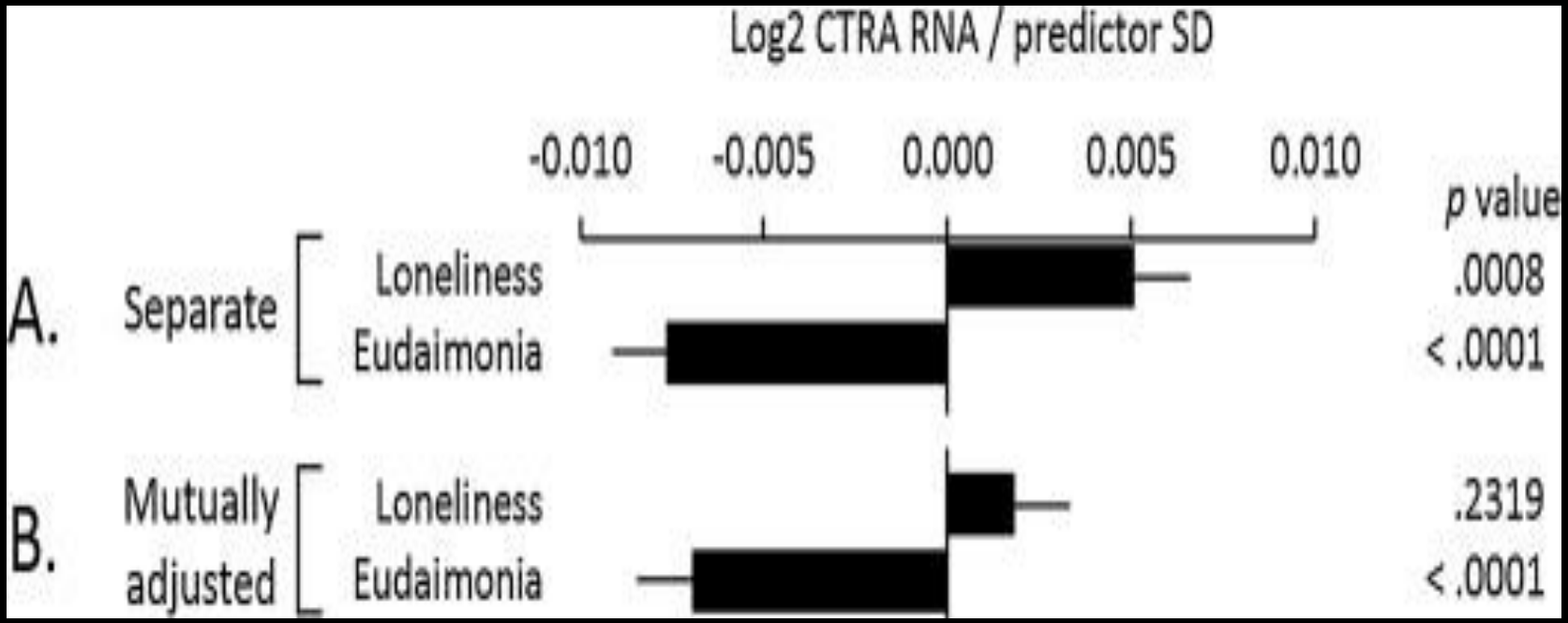


Gene Expression:
Childhood trauma linked to expression of Inflammatory markers in late life: Early life stress may sensitize the body and brain to be hypersensitive to subsequent activity. HRS pilot sample N=113.




Childhood and Later Life Stressors and Increased Inflammatory Gene Expression at Older Ages. 2015. Morgan Levine, Steven Cole, David Weir, Eileen Crimmins. Social Science and Medicine, 130:16-22.

# 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.

S. W. Cole, M.E.Levine, J. M.G. Arevalo, J. Ma, D.R. Weir, E.M. Crimmins. 2015. **Loneliness, eudaimonia, and the human conserved transcriptional response to adversity.** Psychoneuroendocrinology, Volume 62, 2015, 11–17

## 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