



SOCIETY OF
ACTUARIES®

2019 **ANNUAL
MEETING**
& EXHIBIT

October 27-30
Toronto, Canada

Session 171: Developments in Mortality Improvement Around the Globe

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Developments in Mortality Improvement Around the Globe:

Medical “Game-Changers”

Dave Rengachary, MD

SVP and Chief Medical Director, US Mortality Markets

30.10.19

RGGA

- PSCK-9 inhibitors
- Universal Flu Vaccine
- All Things Genomic
- Senolytics
- Alzheimer's Cure



PCSK-9 Inhibitors – How *Low* Can You Go?

Familial Hypercholesterolemia

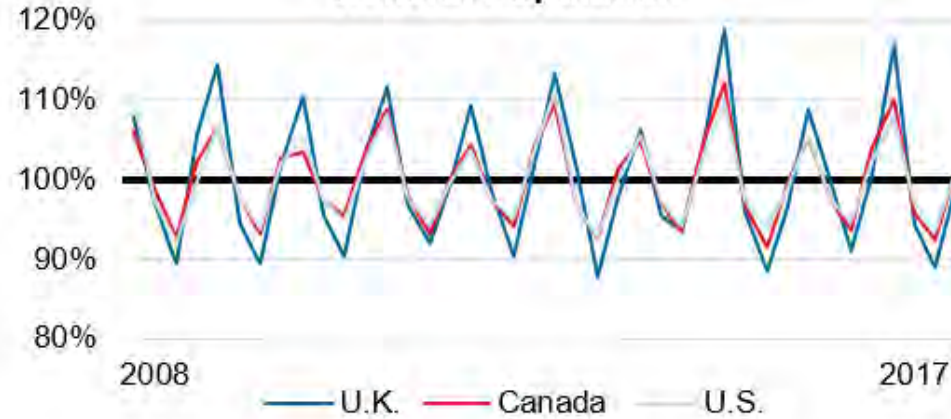
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graph TD; A[Familial Hypercholesterolemia] --> B[Prior cardiovascular events]; B --> C[Prevention?];
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Prior cardiovascular events

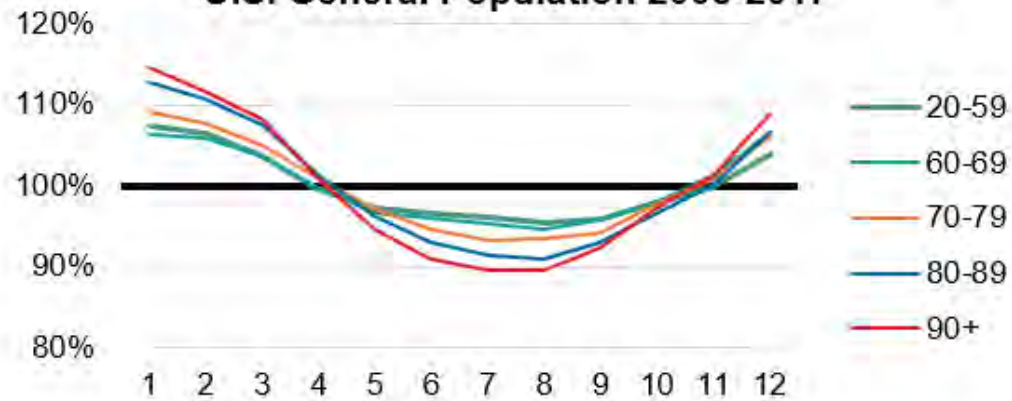
Prevention?

Influenza

Relative Mortality by Calendar Quarter, General Population



Relative Medical Cause Mortality by Month and Age, U.S. General Population 2008-2017



Spanish Influenza (1918)

“The Mother of All Pandemics”



- Mortality estimates vary widely between 30-100 million
- 2.5% case fatality rate but infected 28% of all Americans
- Caused by H1N1 family of viruses
- Especially high relative virulence among those 15-34, enhanced by WWI living conditions



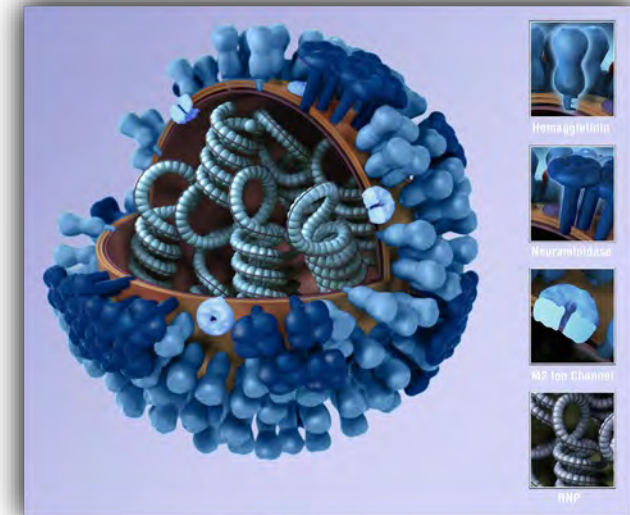
Influenza

Why so deadly?

- High levels of “antigenic drift” – virus lacks adequate error-checking capabilities
 - Mutation rates 300 x similar viruses
 - Allows to escape environmental pressures through rapid evolutionary selection
 - Allows evasion from host immunity
 - 2009 – a new strain for humans emerged; a subtype of H1N1 (“swine flu”)
- Antigenic “shift” – exchange of genetic material between two different strains of influenza (during coinfection of a host)
 - While these occur less often they can be quite virulent (responsible for the three major pandemic outbreaks)
- Infects as a population of viruses with minor variants (not a single virus)
- “If you have seen one influenza season, you have seen one influenza season”

Universal Flu Vaccine

- **February 2018**
NIAID (part of NIH) deems development of universal influenza vaccine as a priority
- **April 2018**
Gates foundation launch “Universal Influenza Vaccine Development Grand Challenge”
- **April 2018**
First NIH human trial (Phase 1 trial of H1ssF_3928)
- **October 2018**
BiondVax launches first phase3 trial of M-001



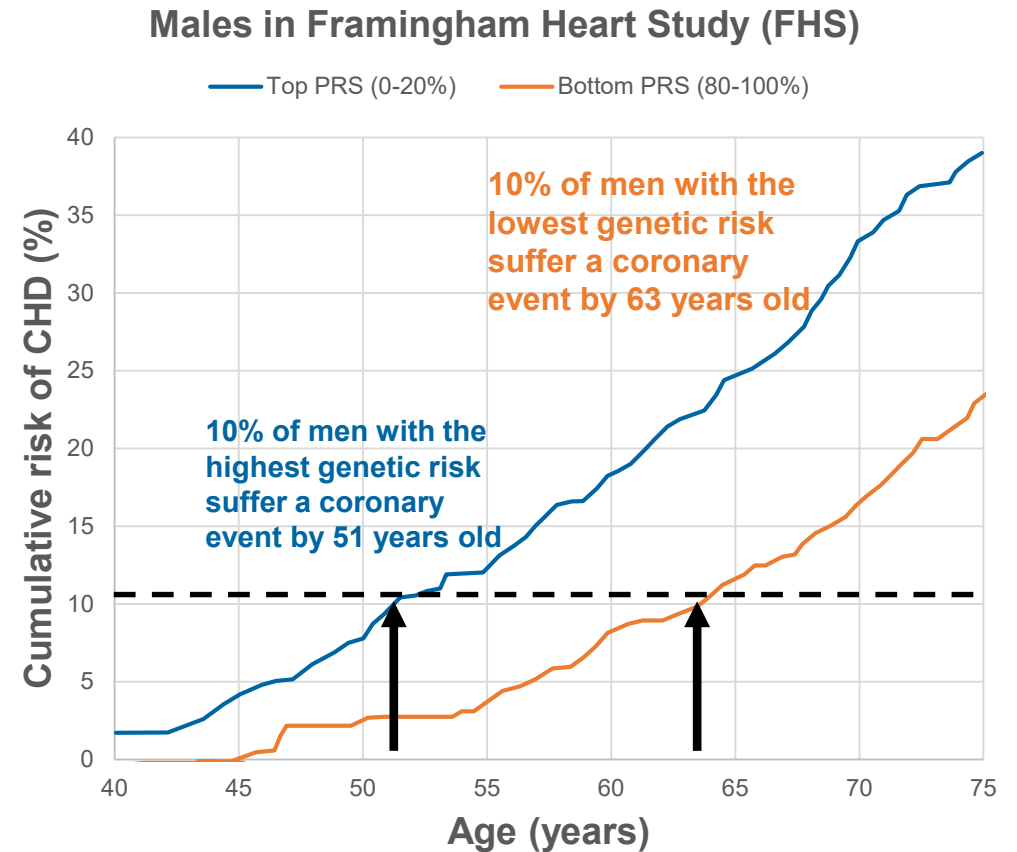
Conditions Included in CIA and SOA Modeling

Condition	Prevalence	Penetrance
Hypertrophic cardiomyopathy	1/500	69%
Hereditary nonpolyposis colorectal cancer	1/500	50%
Breast cancer (BRCA1 and 2)	1/900	75%
Polycystic kidney disease	1/1,000	100%
Brugada syndrome	1/2,000	75%
Long QT syndrome	1/2,000	25%
Arrhythmogenic right ventricular cardiomyopathy	1/2,500	75%
Dilated cardiomyopathy	1/2,700	75%
Marfan syndrome	1/5,000	50%
Myotonic dystrophy (Types 1 and 2)	1/8,000	75%
Catecholaminergic polymorphic ventricular tachycardia	1/10,000	75%
Early onset (AD) Alzheimer's disease early onset	1/19,000	100%
Huntington's disease	1/20,000	95%

PRS for Coronary Heart Disease Increases Predictive Power

Even after adjustment for clinical risk factors

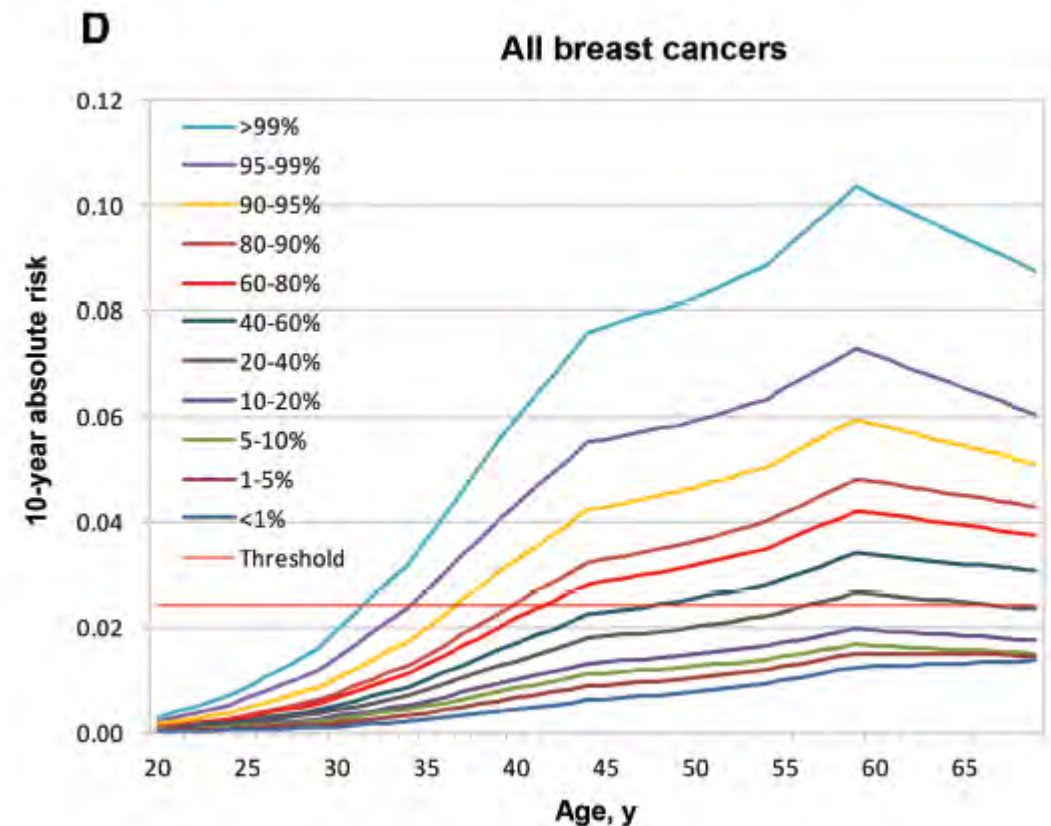
- A study by Abraham and colleagues* tested the clinical utility of a PRS for coronary heart disease (CHD), in terms of lifetime CHD risk and relative to traditional clinical risk
- PRS tested in independent cohorts (FINRISK and Framingham Heart Study [FHS]; combined $n = 16,802$ with 1,344 incident CHD events)
- **The PRS was tested alongside the best clinical risk factors as well as family history. After controlling for these risk factors, the PRS still proved to be a very powerful differentiator of CHD risk.**



How PRS Could be Adopted into Clinical Medicine

Cancer screening

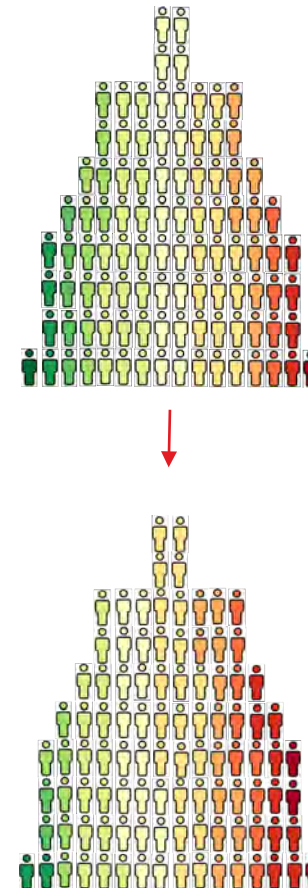
- Individuals with the highest 1% or 5% of PRS values could be offered:
 - Regular screening
 - Encouraged to participate in lifestyle modifications
 - Prescribed therapeutic interventions
- For example, the USPTF generally recommends mammogram screening at age 50, based on a 10-year risk of breast cancer in the average woman, but:
 - Women in the top 5% of PRS-risk reach the average level at age 37
 - Women in the lowest 20% of PRS-risk will never reach the average level



Potential for Anti-Selection – Example in Breast Cancer

Percentile	% in general population	Hazard ratio for breast cancer	Probability of purchasing insurance *	% in new risk pool
0-1	1%	0.44	0.44x	0.4%
1-5	4%	0.68	0.68x	2.4%
5-10	5%	0.66	0.66x	3.0%
10-20	10%	0.69	0.69x	6.2%
20-40	20%	0.9	0.9x	16.1%
40-60	20%	1	1x	17.9%
60-80	20%	1.25	1.25x	22.4%
80-90	10%	1.58	1.58x	14.1%
90-95	5%	1.74	1.74x	7.8%
95-99	4%	2.04	2.04x	7.3%
99-100	1%	2.71	2.71x	2.4%

* Note: We make no assumptions for preventative measures



- **+12.6%** increase in incidence
- **Further +2.2%** if include **BRCA1/2 mutations** (assuming 0.2% prevalence and 5x odds ratio)

State of Liquid Biopsy

A crowded landscape ...



- 70-gene screen in *known* cancer patients
- 5,000+ ordering physicians
- High tissue biopsy concordance (90%) in lung cancer



- Tests for 8 different cancers
- 69-98% sensitive** for five cancers (ovarian, liver, stomach, pancreas, and esophageal)
- 99% specific

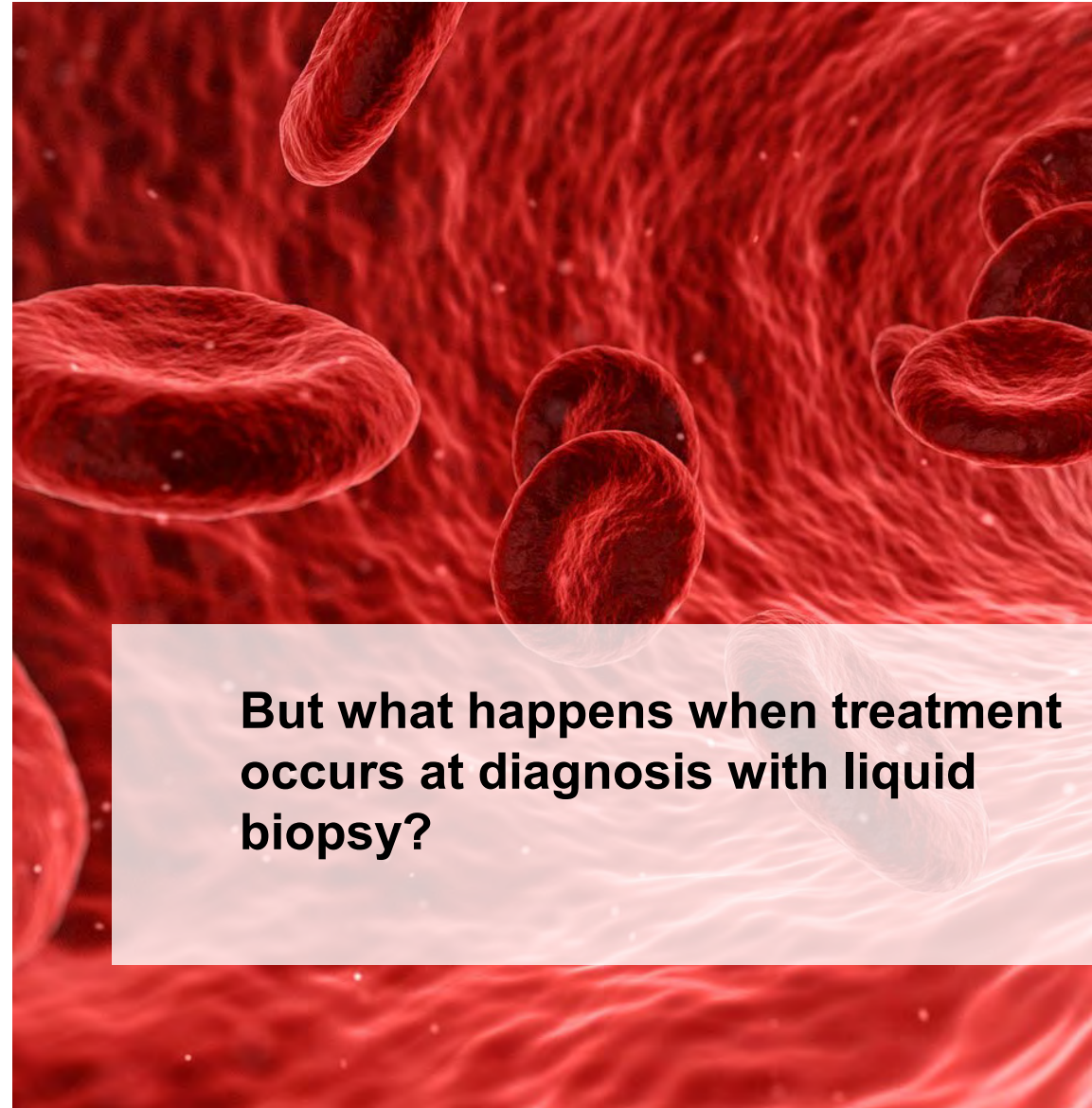


- 1.5 billion raised since 2016 (Bezos, Illumina, Gates)
- ASCO 2019 abstract: identified tumor of origin in 90% of samples for 12 cancer types
- Identified more aggressive tumors more frequently

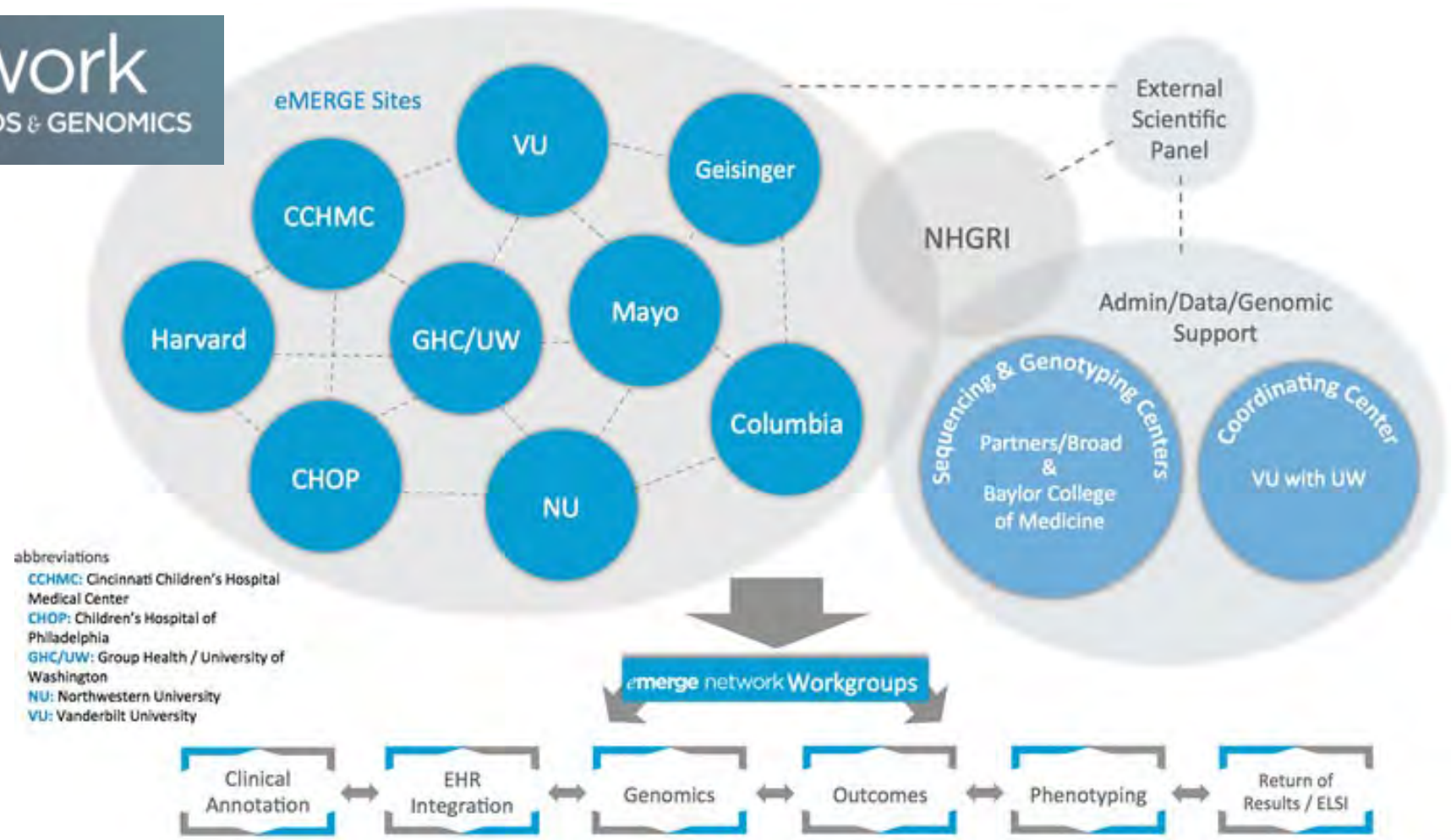
Eye on Living Benefits

RGA critical illness implications

- For the above definition, the following are not covered:
 - All cancers *only* identified from tumor cells, pieces of DNA, or any other biomarkers, any of which may be present in the blood, saliva, urine, or other bodily fluids, including, but not limited to, tests known as “liquid biopsies”



Genomic Medicine – in the Next 5-10 Years ...

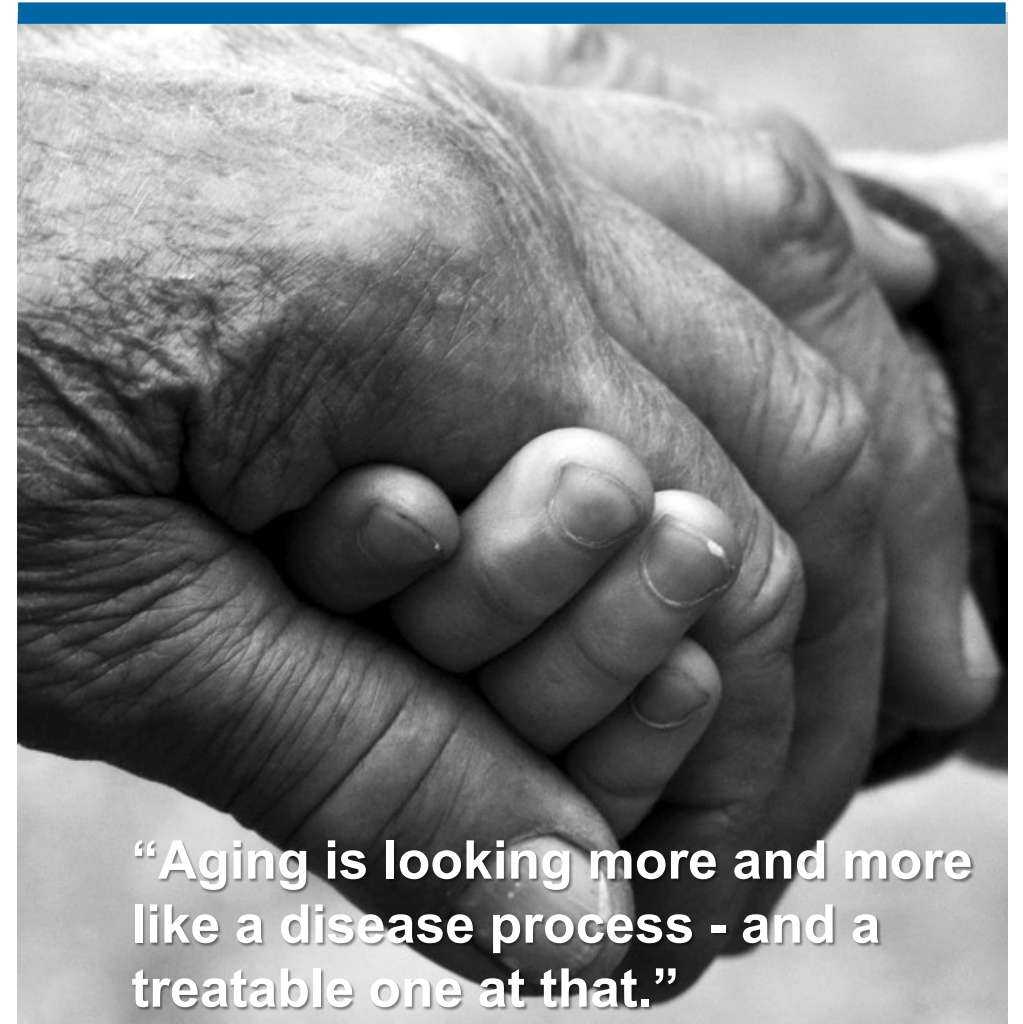


abbreviations
CCHMC: Cincinnati Children's Hospital Medical Center
CHOP: Children's Hospital of Philadelphia
GHC/UW: Group Health / University of Washington
NU: Northwestern University
VU: Vanderbilt University

Senolytics

Targeting aging as a process

- As cells age, they become *senescent* and stop dividing
- Worse yet, they become toxic to those cells around them by releasing pro-inflammatory signals and protein-degrading enzymes
- Senolytic drugs selectively target these senescent cells
- 2018 – Trial in mice extended life by an average of 36%



Senolytic Trials

Unity Biotechnology

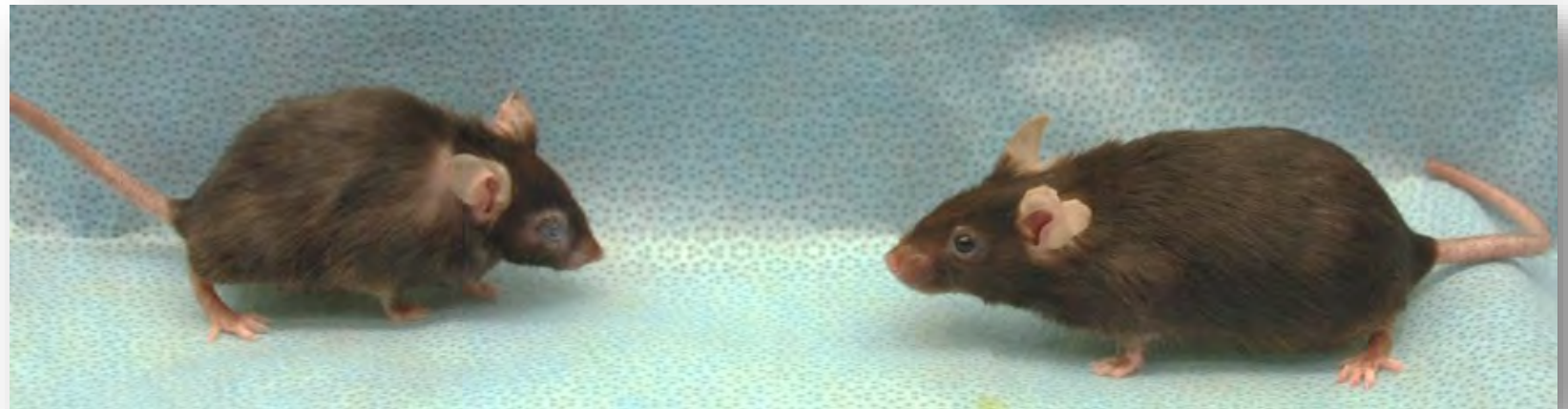
- Osteoarthritis*
- Glaucoma
- Kidney Disease
- COPD
- Systemic Sclerosis

Senolytic Therapeutics

- Idiopathic pulmonary fibrosis
- Several cancers
- Anti-aging

Scripps Institute/Mayo

- Idiopathic pulmonary fibrosis*



Results of Phase III, Randomized Placebo-Controlled, Double-Blinded Studies

Modified from: Update on Alzheimer's Disease Clinical Trials, Laurie Ryan, PhD Program Director, Alzheimer's Disease Clinical Trials, National Institute on Aging, National Institutes of Health⁵

Agent	Mechanism	Outcome
Atorvastatin	HMG CoA reductase	NEGATIVE
Dimebon	Mitochondrial function	NEGATIVE
LY450139 (Semagacestat)	Gamma secretase modulator	NEGATIVE
NSAIDs	Anti-inflammatory	NEGATIVE
Phenserine	Cholinesterase inhibitor	NEGATIVE
Rosiglitazone	PPAR gamma agonist	NEGATIVE
Simvastatin	HMG CoA reductase	NEGATIVE
Crenezumab	Monoclonal antibody	NEGATIVE
Aducanumab	Monoclonal antibody	NEGATIVE
Solanezumab	Monoclonal antibody	NEGATIVE
Verubecestat	BACE inhibitor	NEGATIVE

August 01, 2019 **ARTICLE**

High-precision plasma β -amyloid 42/40 predicts current and future brain amyloidosis

Suzanne E. Schindler, James G. Bollinger, Vitaliy Ovod, Kwasi G. Mawuenyega, Yan Li, Brian A. Gordon, David M. Holtzman, John C. Morris, Tammie L.S. Benzinger, Chengjie Xiong, Anne M. Fagan,  Randall J. Bateman

First published August 1, 2019, DOI: <https://doi.org/10.1212/WNL.00000000000008081>

- 94% accurate in the detection of Alzheimer's (as compared to CSF and amyloid PET imaging)
- Those with positive blood test (and negative PET) had 15x chance of developing later positive PET imaging
- Positive easily 20 years in advance of symptoms
- Game-changer in recruitment and outcome metrics for Alzheimer's trials

Alzheimer's Research

What's on the horizon ...

DIAN and API

- Dominantly Inherited Alzheimer's Network
- Alzheimer's Prevention Initiative
- Gantenerumab, crenezumab, solanezumab, (CAD106)

Big Data Strategies

- Global Alzheimer's Association Interactive Network (GAAIN)
- Predictions from EHR, wearable data
- Human Brain Project (failure!)

Prevention

- FINGER study
 - Diet
 - Physical activity
 - Cognitive training
 - Social activities
 - Vascular risk-factor control

Rethinking Amyloid Hypothesis

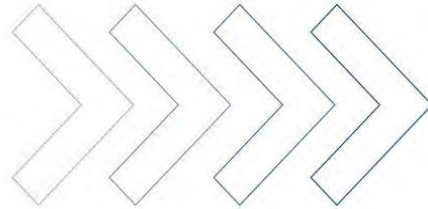
- Vascular hypoperfusion
- Oxidative stress
- Inflammatory immune process
- Infectious?

Session 171: Developments in Mortality Improvement Around the Globe

Dennis Yang, Actuary, Biometric Research

Munich Reinsurance Company Canada Branch (Life)

Mortality Improvement – Recent Analysis



U.S. Population Mortality Observations
Updated with 2017 Experience



Actuarial
Research Centre
Institute and Faculty
of Actuaries

Canadian
Institute of
Actuaries  Institut
canadien
des actuaires



Trends in Canadian Mortality By
Pension Level: Evidence From the CPP
and QPP

 Office for
National Statistics



Article

Socioeconomic inequalities in avoidable mortality, England and Wales: 2001 to 2017

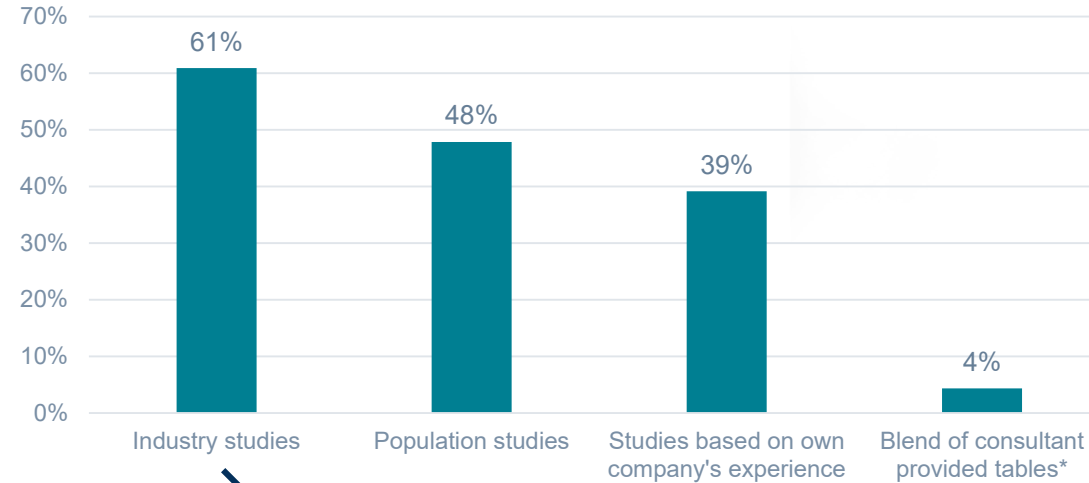
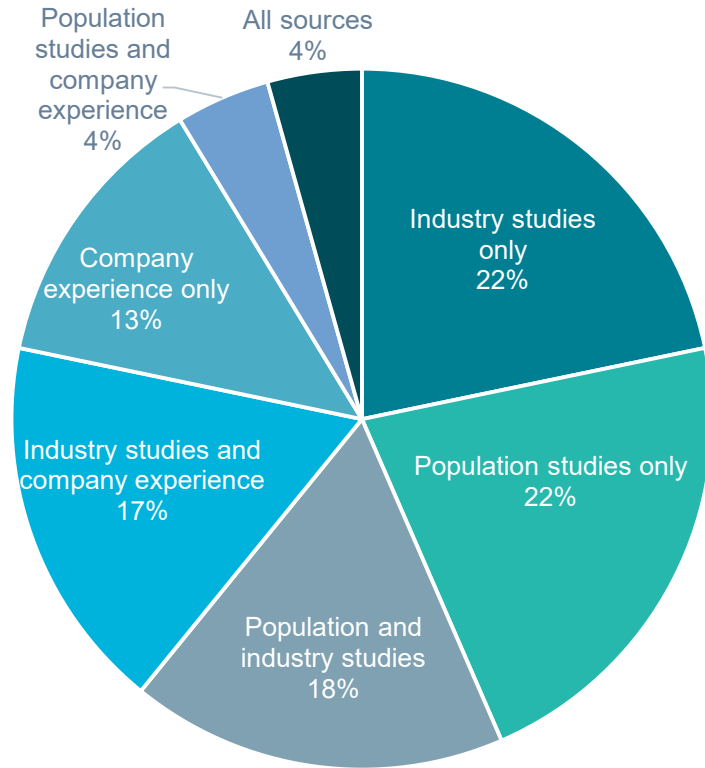
Avoidable mortality in England and Wales, using measures of multiple deprivation to
measure socioeconomic inequalities.

Mortality Improvement Around the Globe

- **Population = Insured?**
- **How closely are they related?**
- **What data to use?**

Munich Re US – Mortality Improvement Pulse Survey

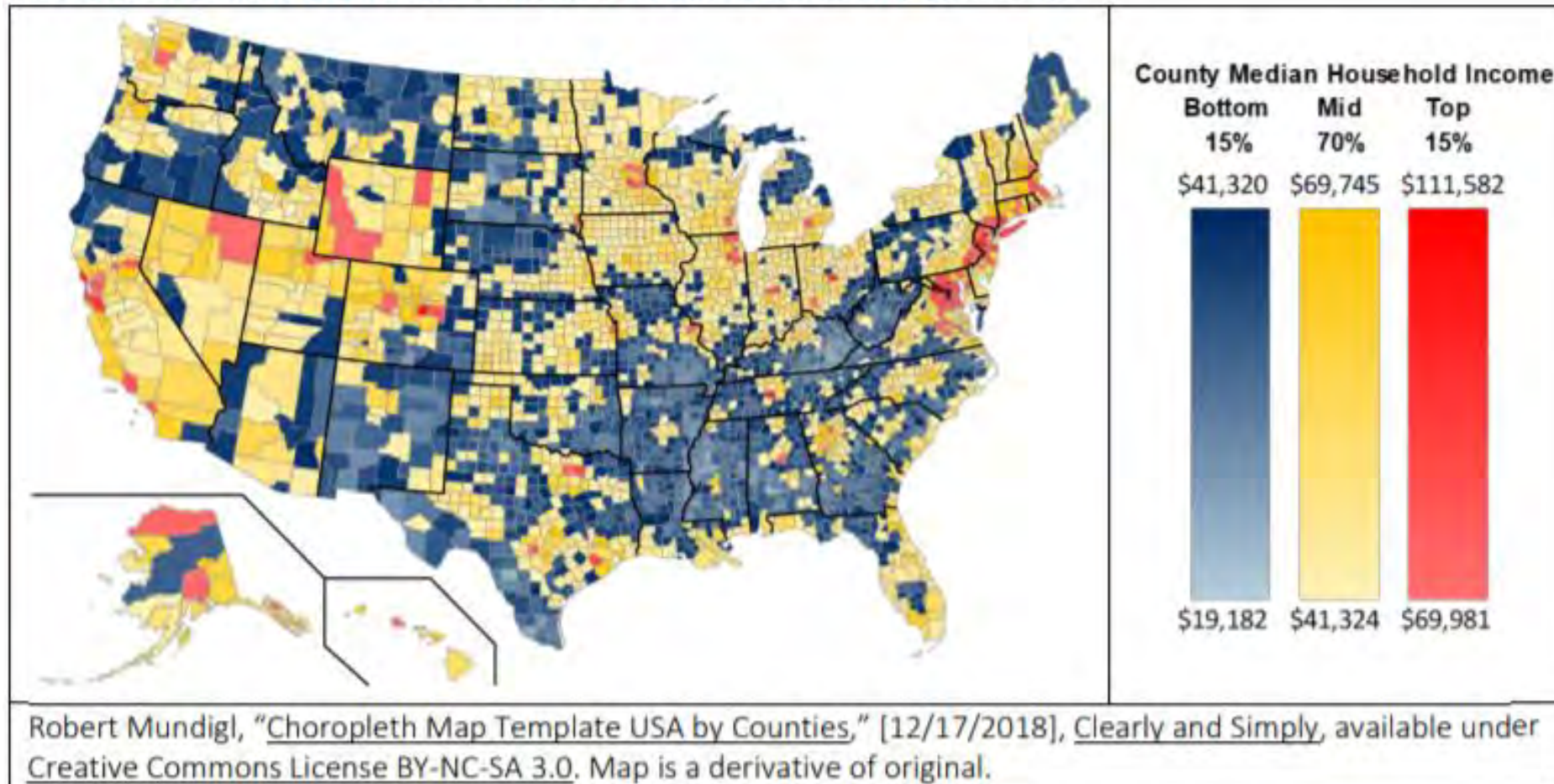
Q: What is/are the source(s) of data used to derive your company's mortality improvement assumption?



Industry study	% of User
SOA MI Scale Recommendation	53%
Consultant/Reinsurer's Study	20%
SOA RPEC MP Model	13%
Other SOA/CIA Study	13%

US Population – County Level Income

U.S. CENSUS BUREAU 2008 COUNTY MEDIAN HOUSEHOLD INCOME ESTIMATES



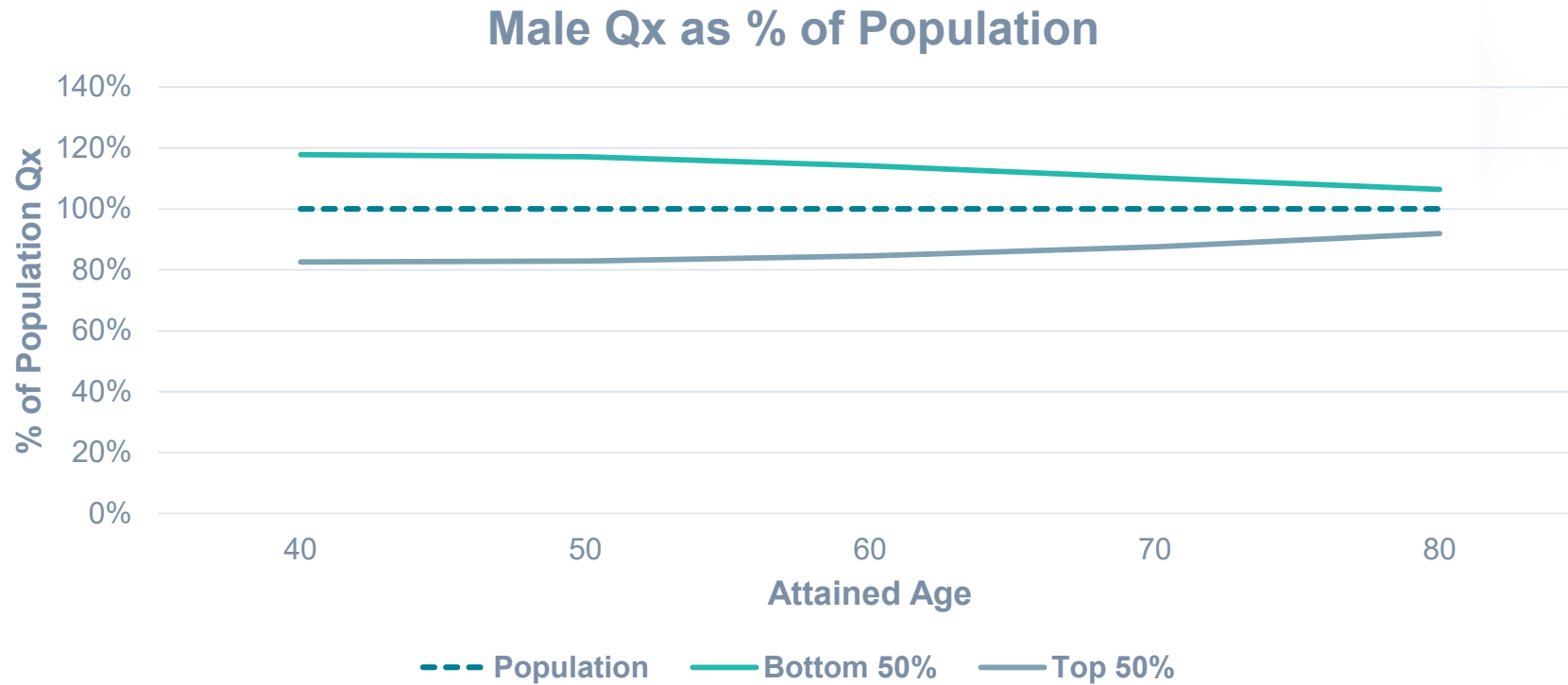
US Population – County Level Income

Census Bureau Median Household Income

CDC Segments	# of Counties	Median HH Income (2008)
Bottom 15%	1,435	\$35,339
Bottom 35%	2,170	\$38,286
Bottom 50%	2,580	\$40,070
Bottom 85%	3,005	\$42,645
General Population	3,124	\$44,064
Top 65%	954	\$57,205
Top 50%	544	\$63,005
Top 15%	119	\$79,897

Munich Re US HH Income by FA Bands				
Face Amount	<100K	100K-499K	500K+	Total
Avg. Income	\$89,000	\$116,000	\$160,000	\$150,000

US Population – County Level Income



Source: CDC Wonder and Bureau of Economic Analysis

US Population – County Level Income

Male 10-Year MI – Population by Income Level

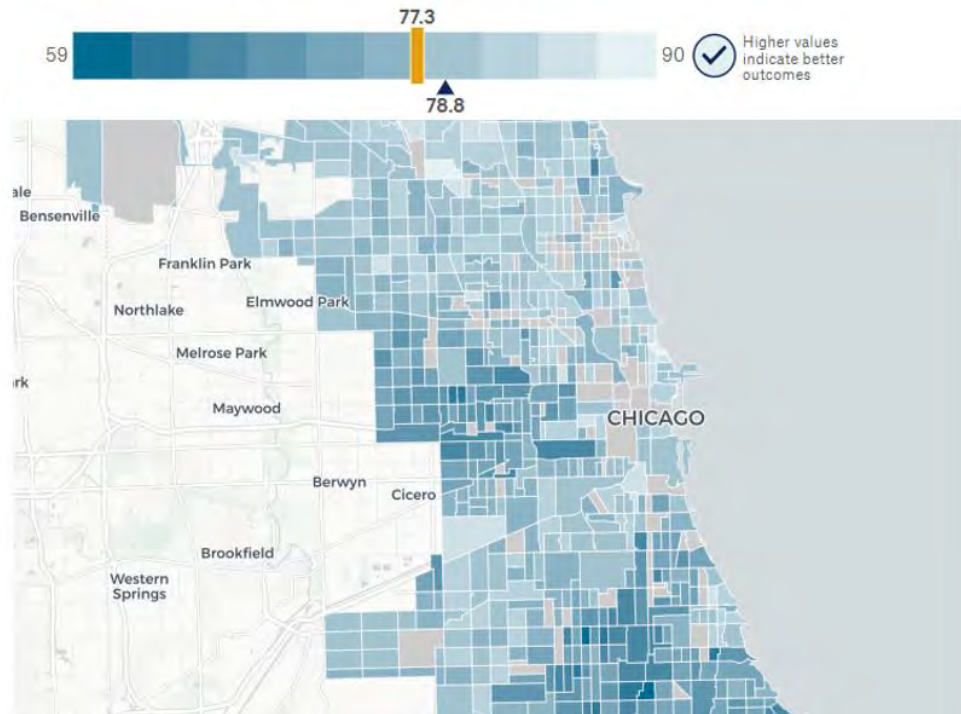


Source: CDC Wonder and Bureau of Economic Analysis

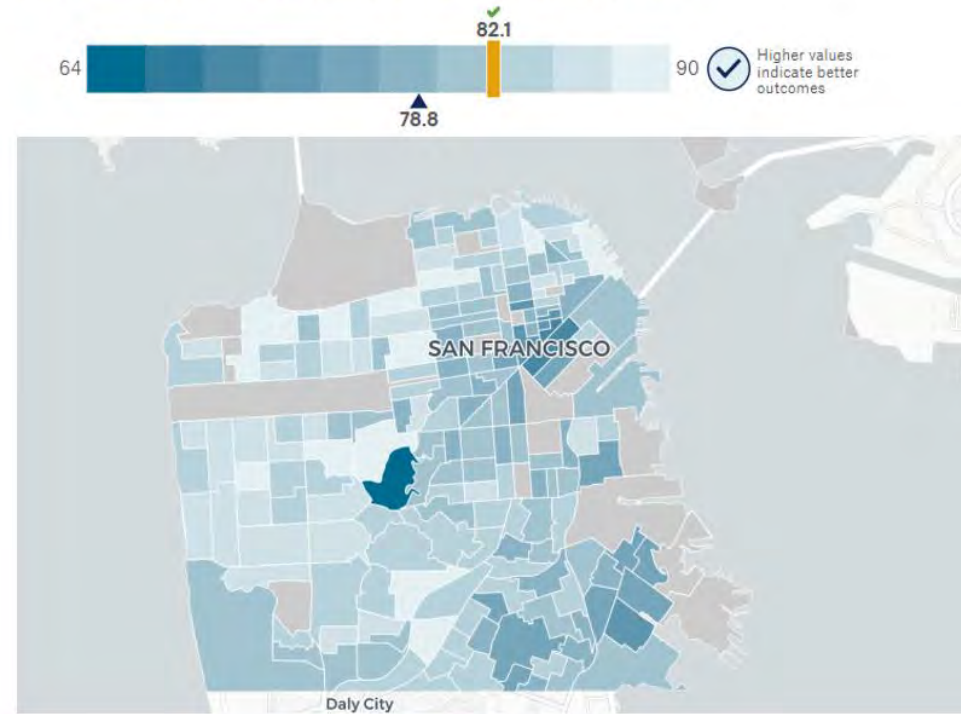
US Population – City Life Expectancy

City Health Dashboard

City Value for Life Expectancy in Chicago, IL



City Value for Life Expectancy in San Francisco, CA



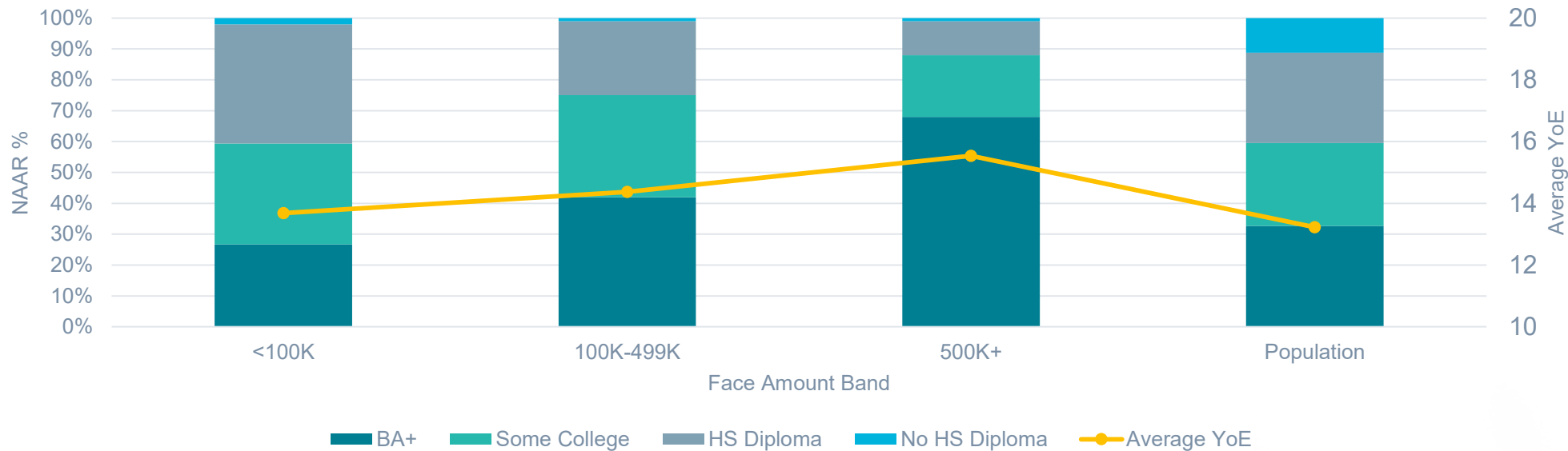
- Chicago (Cook County, IL) – Bottom 15%
- San Francisco (San Francisco County, CA) – Top 15%

US Population – Educational Level

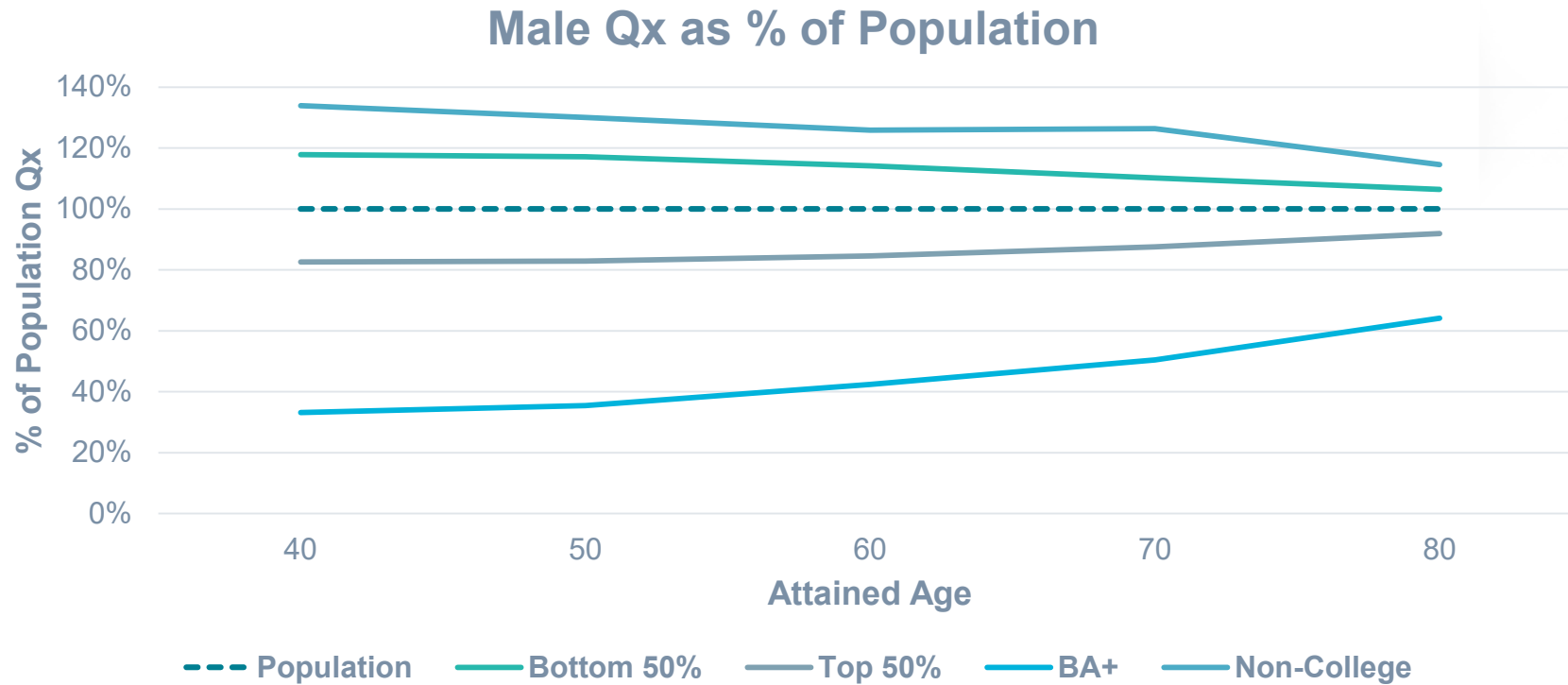
CDC 2012-2017 Data by Educational Level

Level of Education	Years of Education* (YoE)	Distribution
BA+	17	32.7%
Some College	13	26.8%
HS Diploma	12	29.3%
No HS Diploma	6	11.2%
Average YoE	13.2	100.0%

Munich Re US Business Distribution by Educational Level



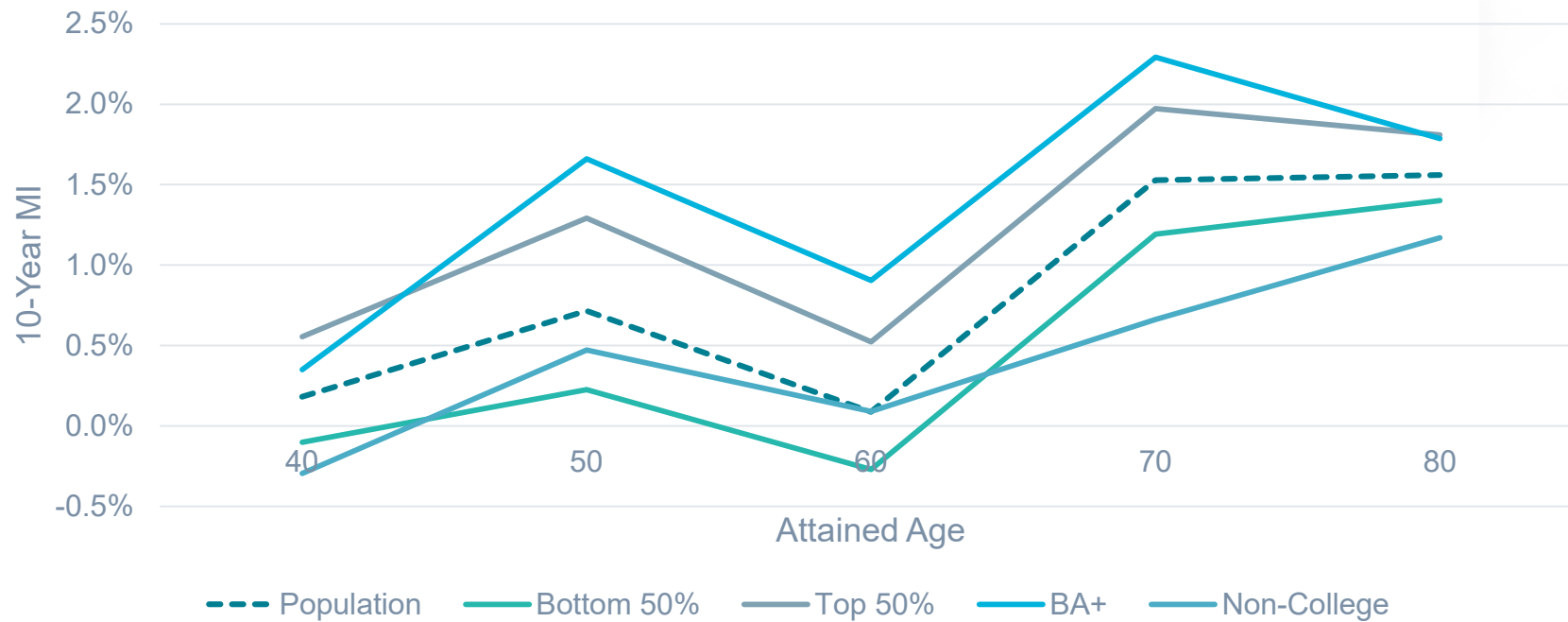
US Population Mortality – Income vs. Education



Source: CDC Wonder and Bureau of Economic Analysis

US Population Mortality Improvement – Income vs. Education

Male 10-Year MI – Education vs. Income Level



Source: CDC Wonder and Bureau of Economic Analysis

Canadian Mortality Gap Between Income & Educational Level

Canadian Trends in Mortality Inequalities, using the CanCHEC

- Emma Marshall-Catlin, Tracey Bushnik, Michael Tjepkema Statistic Canada

- **CanCHEC – Canadian Census Health Environment Cohort**
- **CanCHEC data: 1991, 1996, 2001, 2006 and 2011**
- **Mortality gap between individual-level socioeconomics**
- **Age standardized to 2011 Canadian Population**
- **Access to full report: <http://ph2019.isilive.ca/files/321/Emma%20Marshall-Catlin%20-%20Canadian%20trends%20in%20mortality%20inequalities,%20using%20the%20CanCHEC.pdf>**

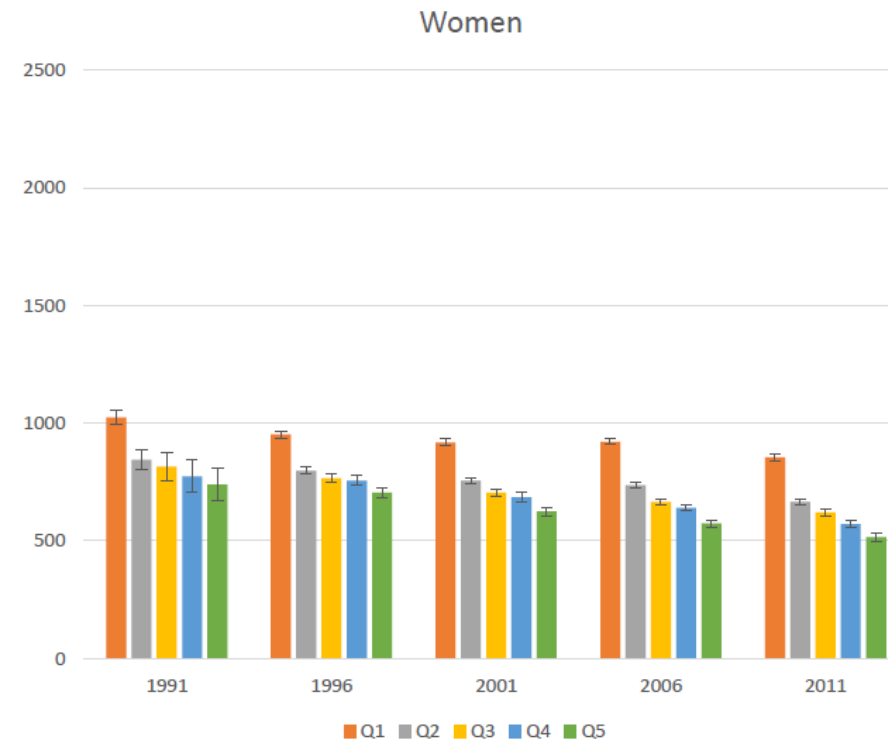
Source: [Emma Marshall-Catlin - Canadian trends in mortality inequalities, using the CanCHEC](#)

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- Mortality Rate / 100,000 by Income Level



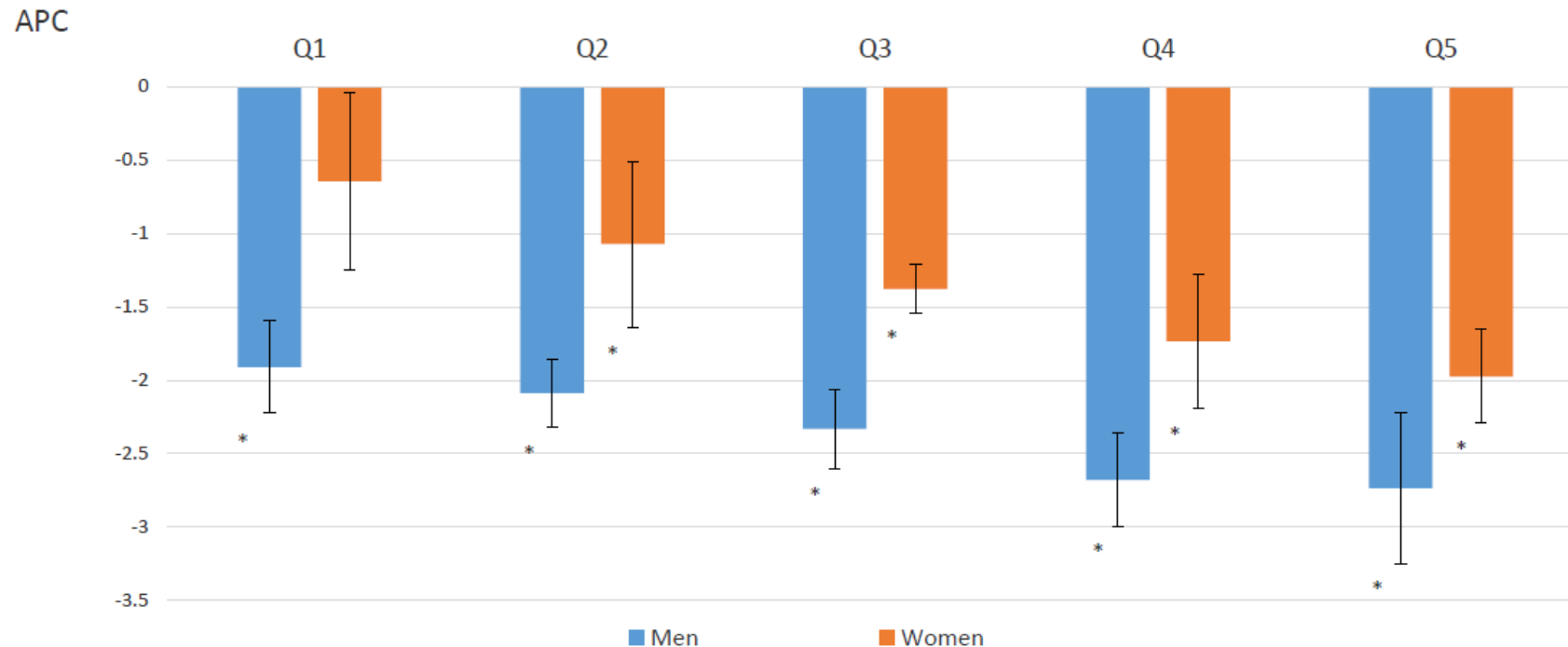
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- Average Percentage Change in Mortality Rate by Income Level



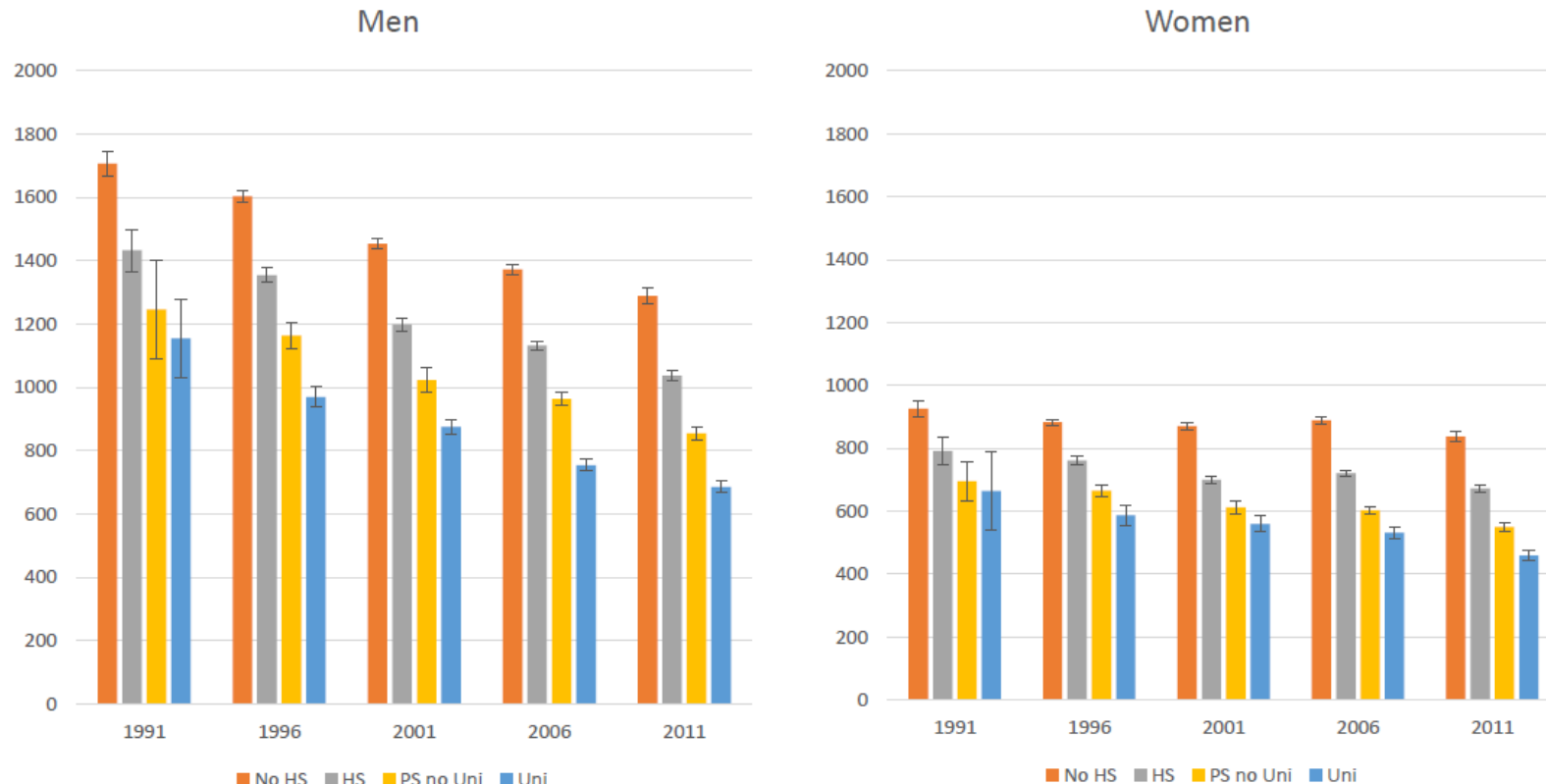
Source: [Emma Marshall-Catlin - Canadian trends in mortality inequalities, using the CanCHEC](#)

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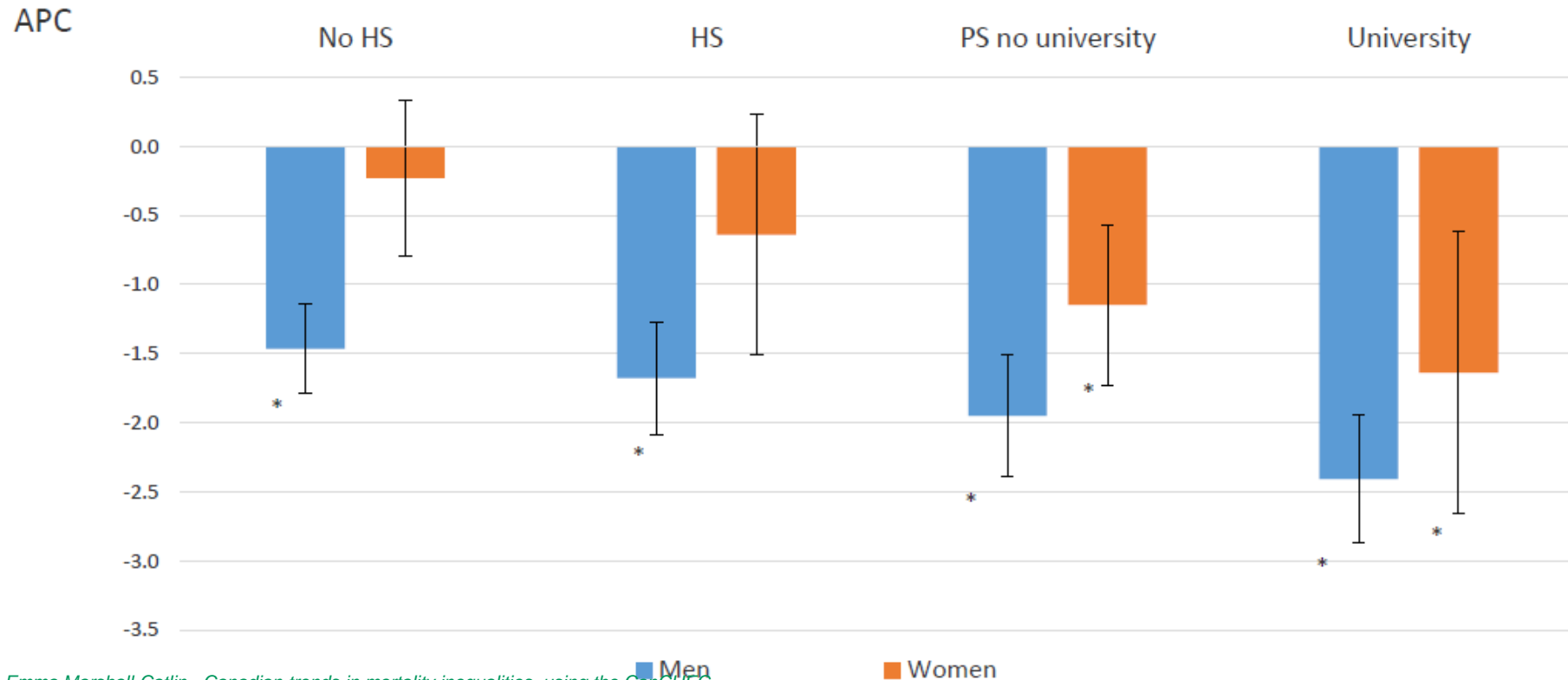
Source: [Emma Marshall-Catlin - Canadian trends in mortality inequalities, using the CanCHEC](#)
 Session 171: Developments in Mortality Improvement Around the Globe

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Conclusion

- **Clear differentiation in mortality trend between socioeconomic classes**
- **“Gap between university education and without high school has grown”**
- **“Gap between high and low income has decreased for male and increased for female”**

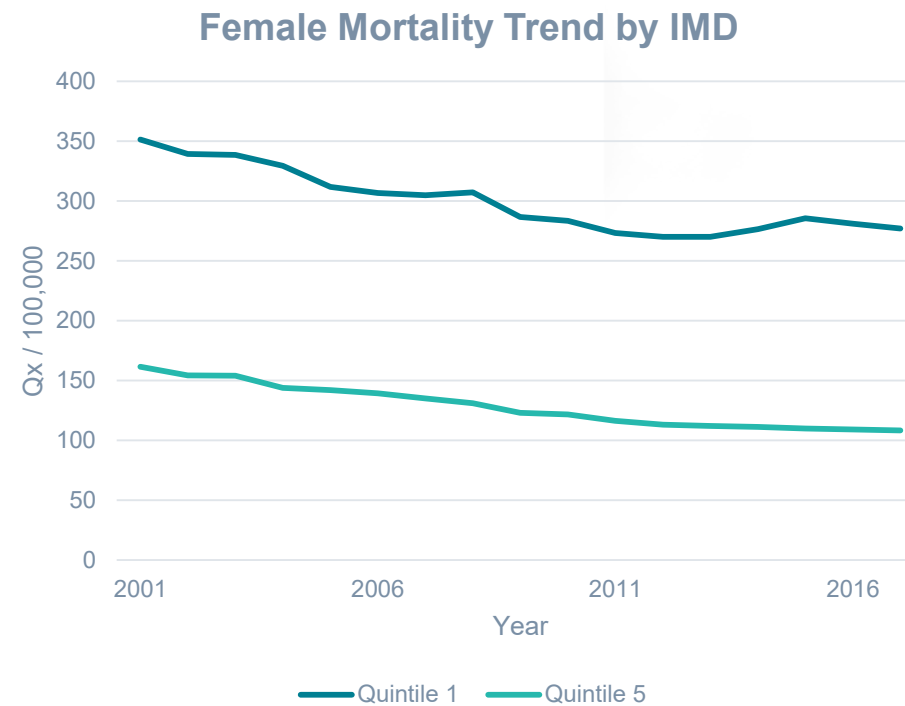
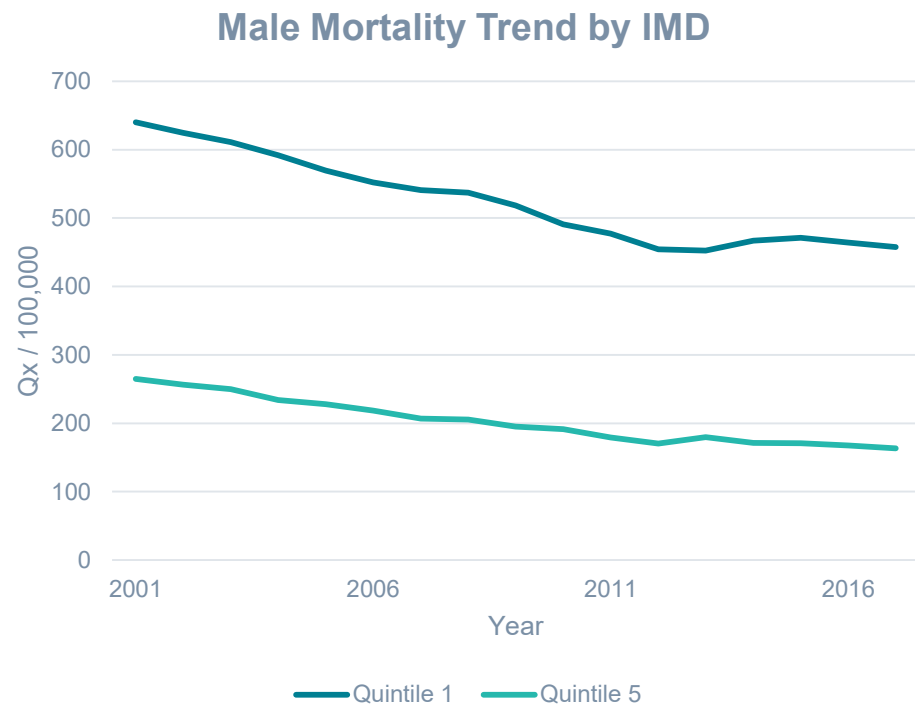
UK – Mortality Improvement by IMD

- **Mortality trend by Index of Multiple Deprivation (IMD)**
 - **Index of Multiple Deprivation**
 - **Income**
 - **Employment**
 - **Education/ skills and training**
 - **Health and disability**
 - **Crime**
 - **Barriers to housing and service**
 - **Living environment**
- **IMD segment to neighborhood level**
- **Avoidable Mortality Trend – Amendable and Preventable**

Source: Office for National Statistics,
data:<https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/causesofdeath/datasets/measuring socioeconomic inequalities in avoidable mortality england analysis>

UK – Mortality Improvement by IMD

- Mortality trend by Index of Multiple Deprivation (IMD)**

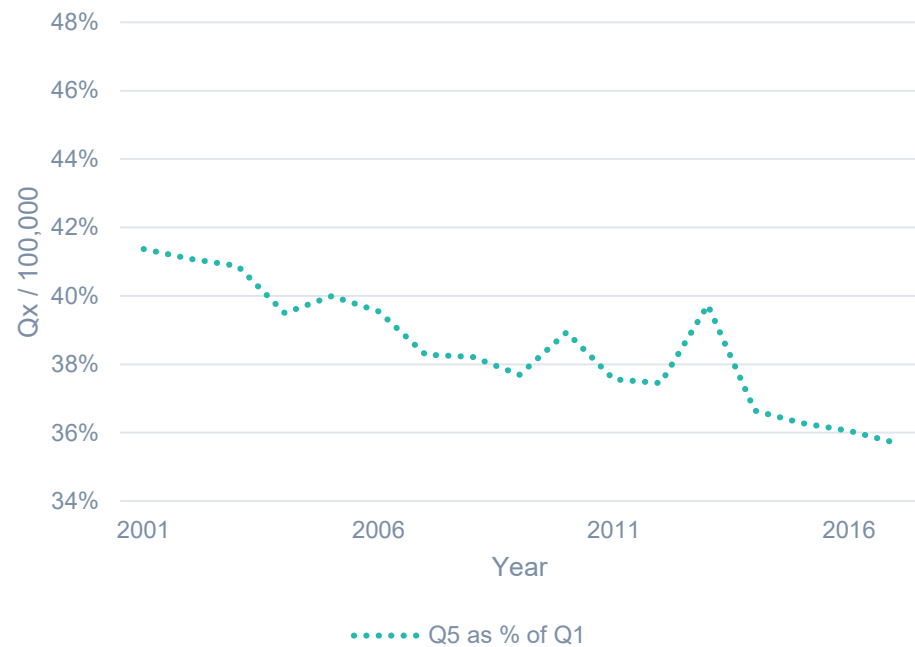


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UK – Mortality Improvement by IMD

- Mortality trend by Index of Multiple Deprivation (IMD)**

Male Mortality Trend by IMD



Female Mortality Trend by IMD



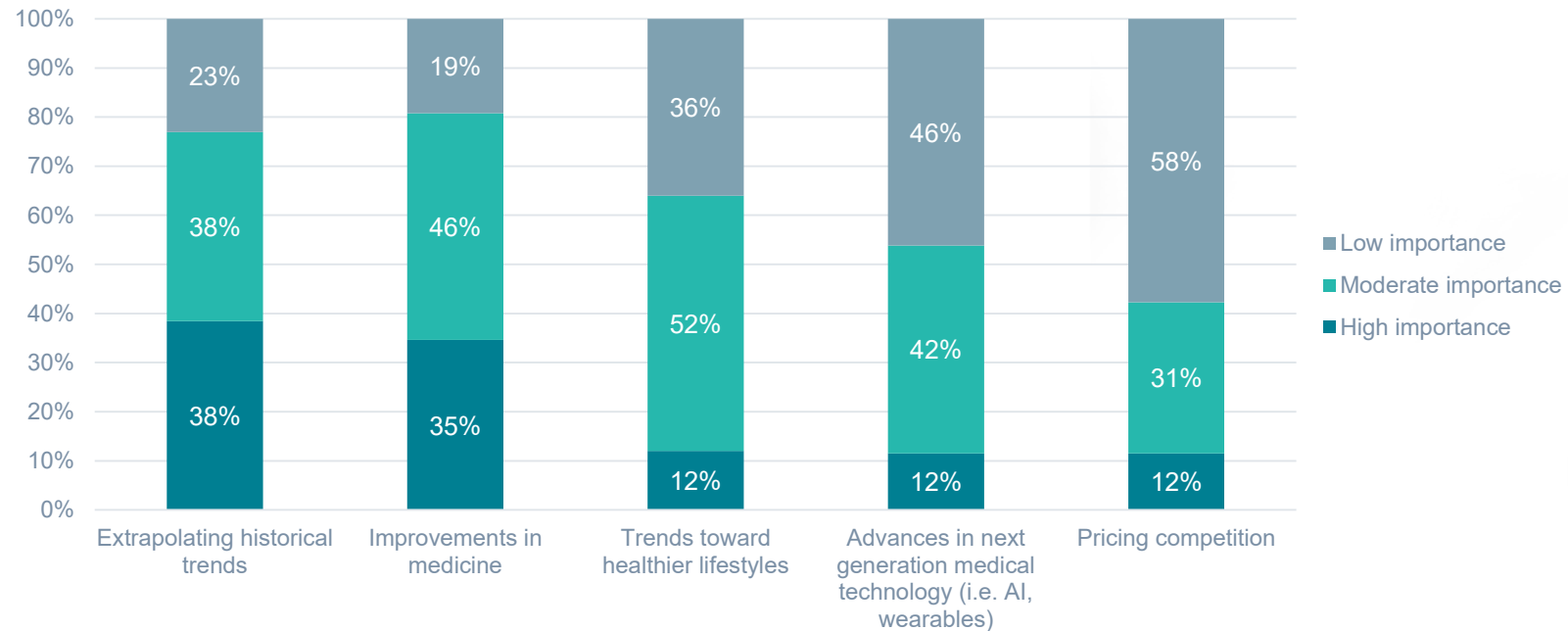
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Key Takeaways

- General population data may not relate to insured business directly
- Mortality gap between socioeconomic classes exists in US, Canada and UK
- Application of socioeconomic segmentation should relate to business mixture

Munich Re US – Mortality Improvement Pulse Survey

Q: Please rate the importance of the following justifications for using future MI assumptions.



Top Selections:

- Extrapolating historical trends
- Improvements in medicine
- Trends toward healthier lifestyle
- Advances in next generation technology
- Pricing competition

Thank you



International perspectives on US mortality trends

Magali Barbieri

Associate Director, Human Mortality Database

University of California, Berkeley, and French Institute for Demographic Research

and

The Human Mortality Database team at the University of California, Berkeley

Annual meeting of the SOA, Toronto, International Section, Session #171, Wednesday, October 30, 2019

Goal of study

- To provide some international context for US mortality trends
- To better understand the reversal in US mortality
- To identify the ages at which mortality has deteriorated
- To identify the causes of death responsible for the reversal
- To identify the states with the most serious problems

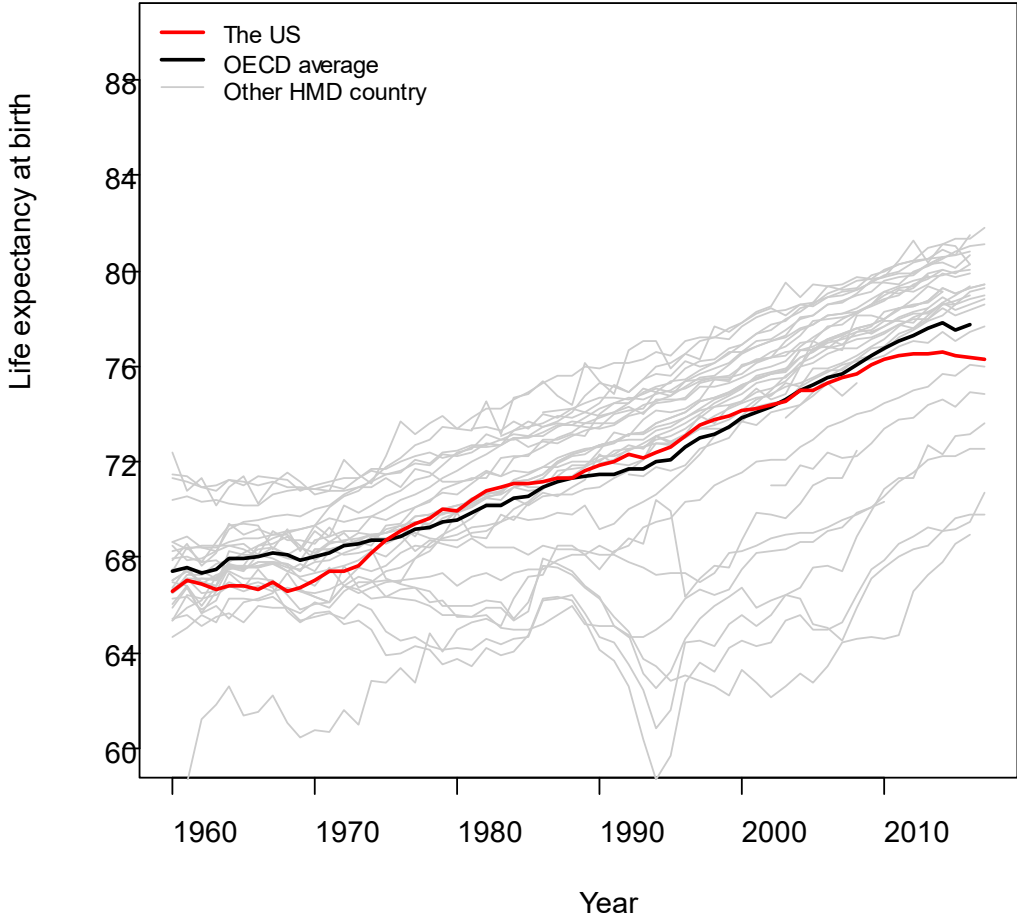
Data and methods

Combining two datasets

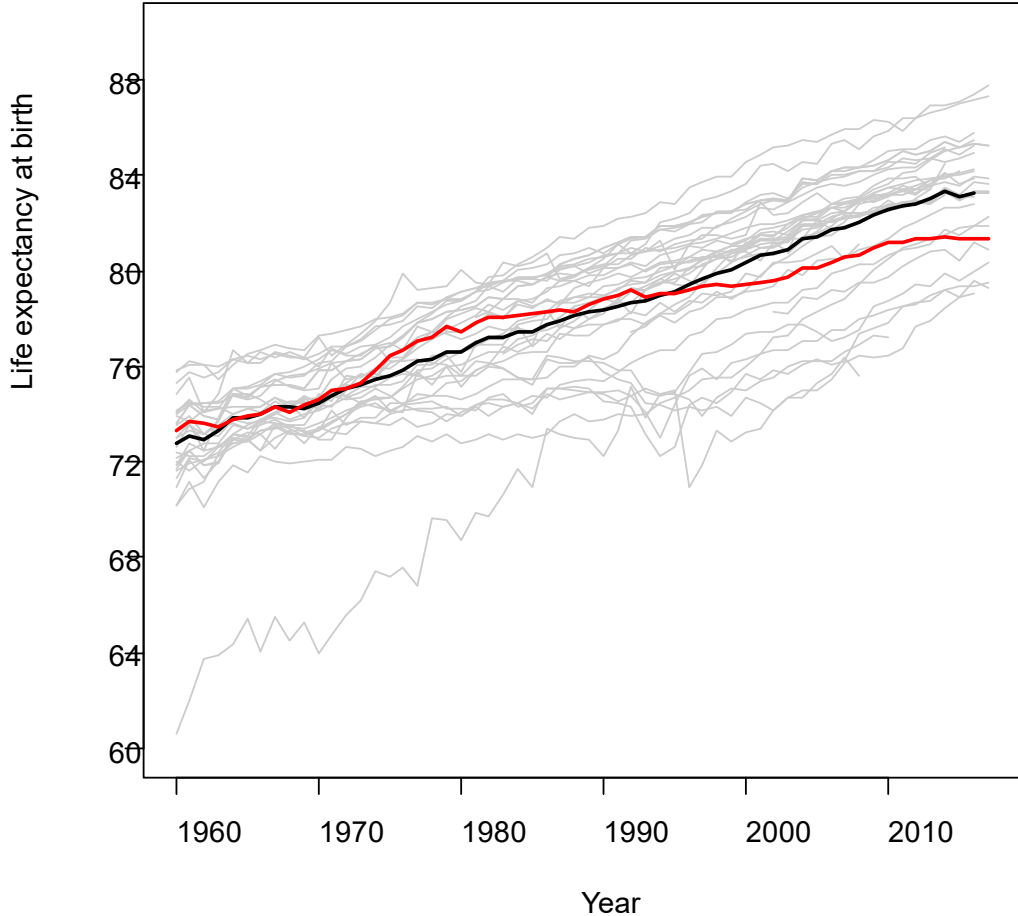
- Life tables from the Human Mortality Database (www.mortality.org)
 - US Cause-of-death data from the National Center for Health Statistics
 - Cause-of-death data from the World Health Organization mortality database (https://www.who.int/healthinfo/mortality_data/en/) for countries in the comparison
1. To compare lifetable values between the US and other countries
 2. To measure the contribution of age groups and causes of death to recent change in life expectancy at birth in the US
 3. To compare trends in age-standardized cause-specific mortality rates between the US and other countries

Comparing the US with other OECD countries

Men

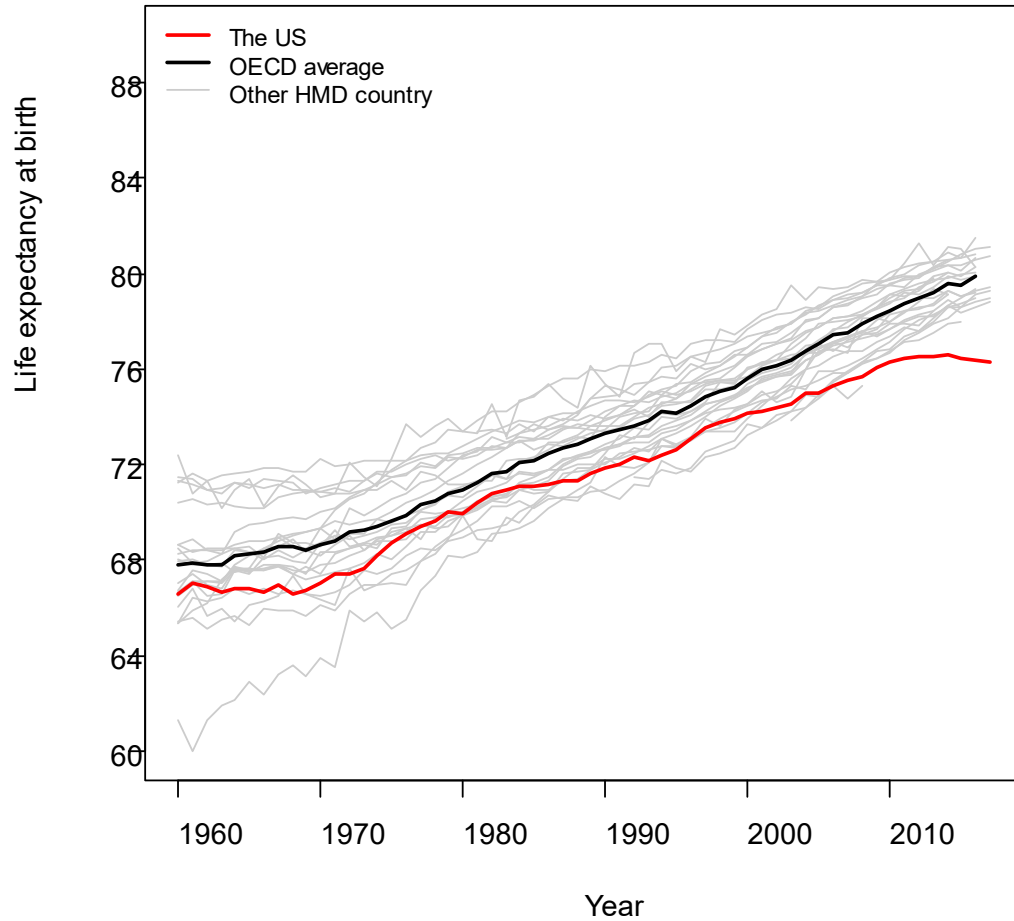


Women

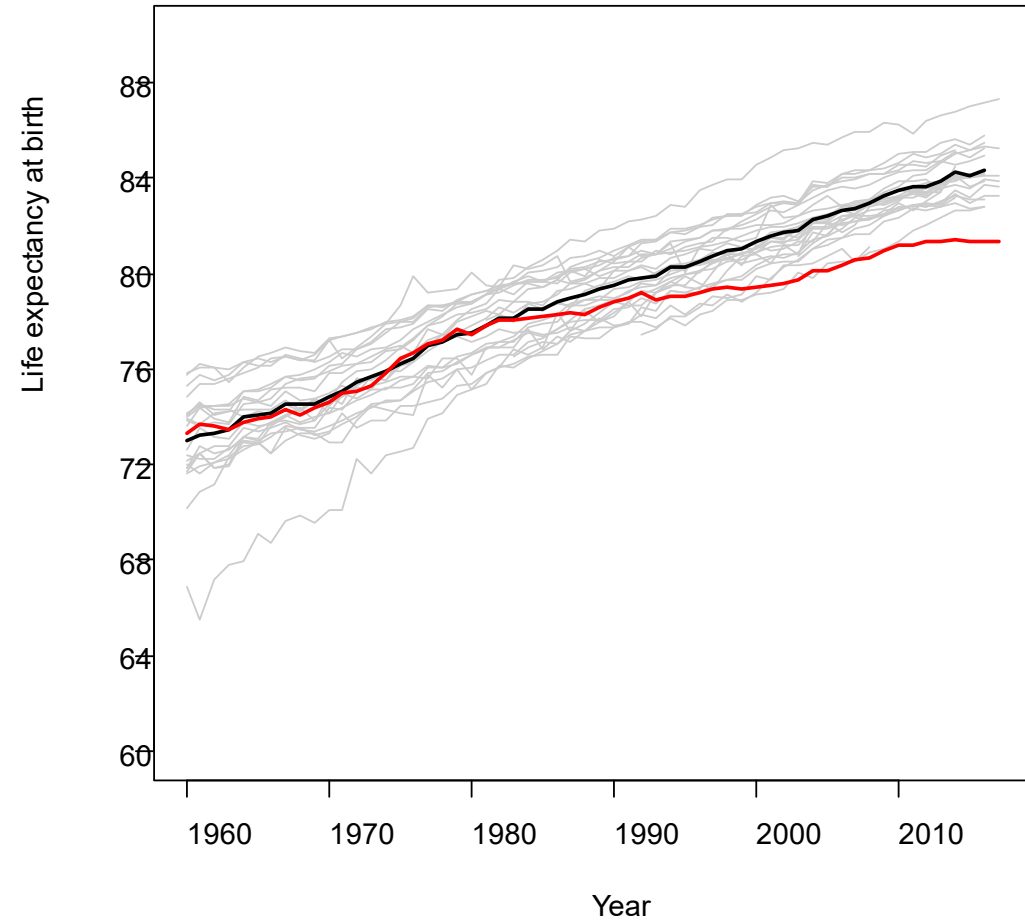


Excluding Eastern Europe

Men

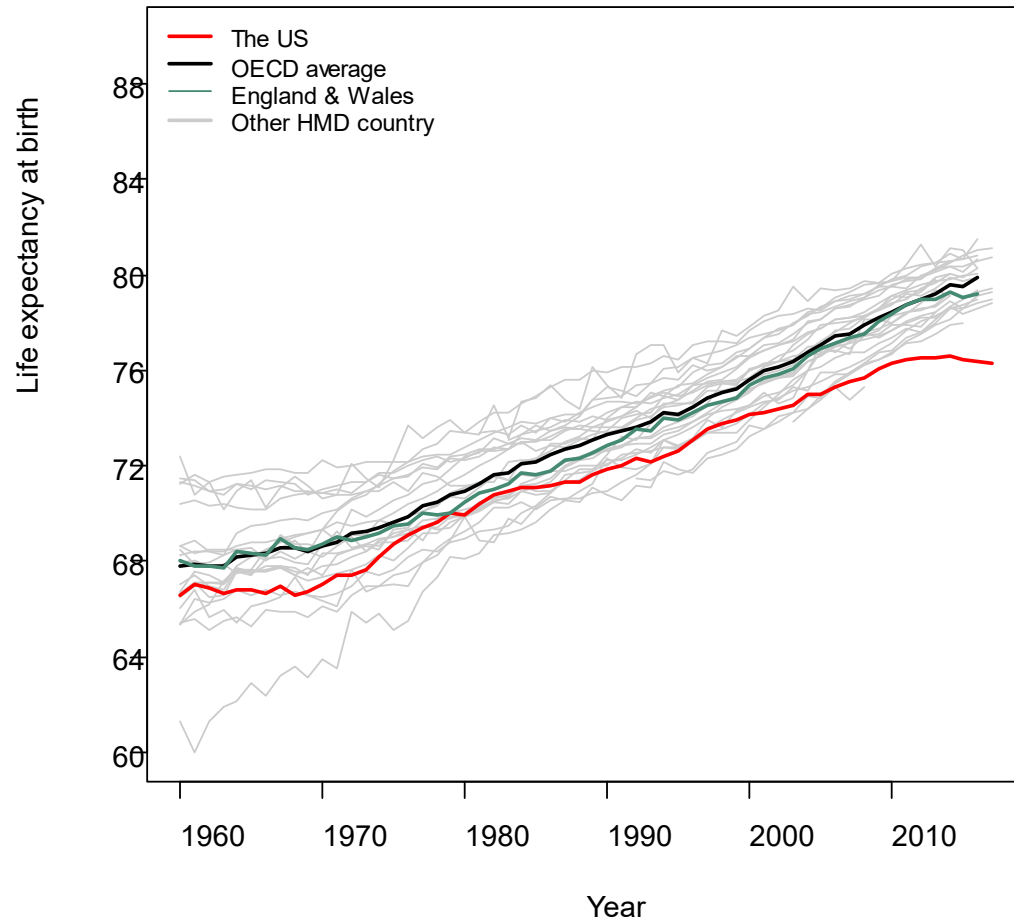


Women

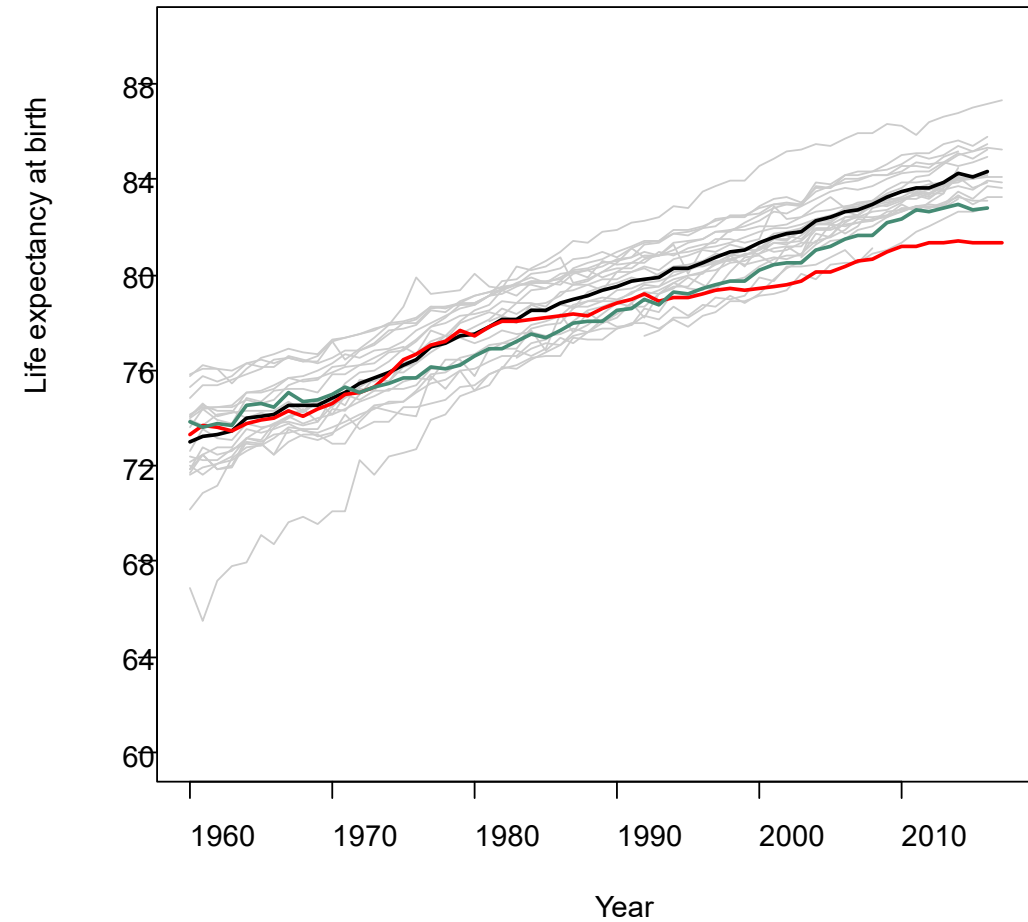


With a special emphasis on England and Wales

Men

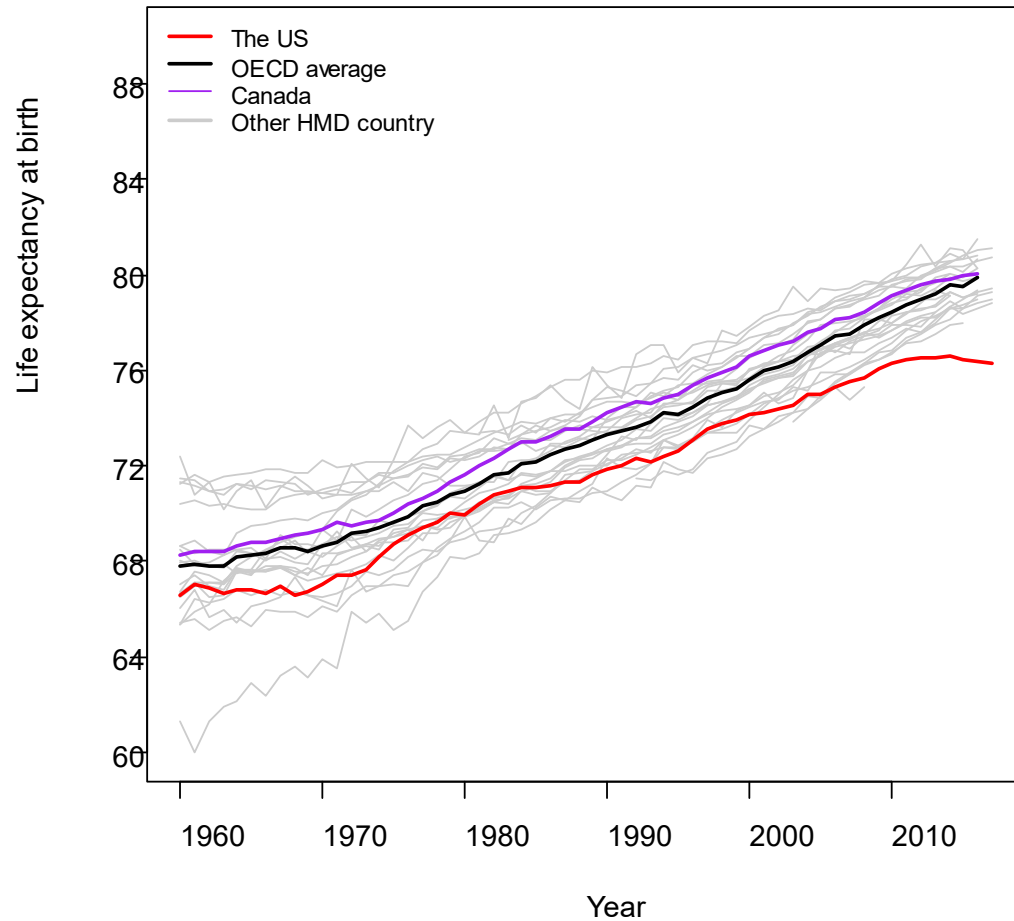


Women

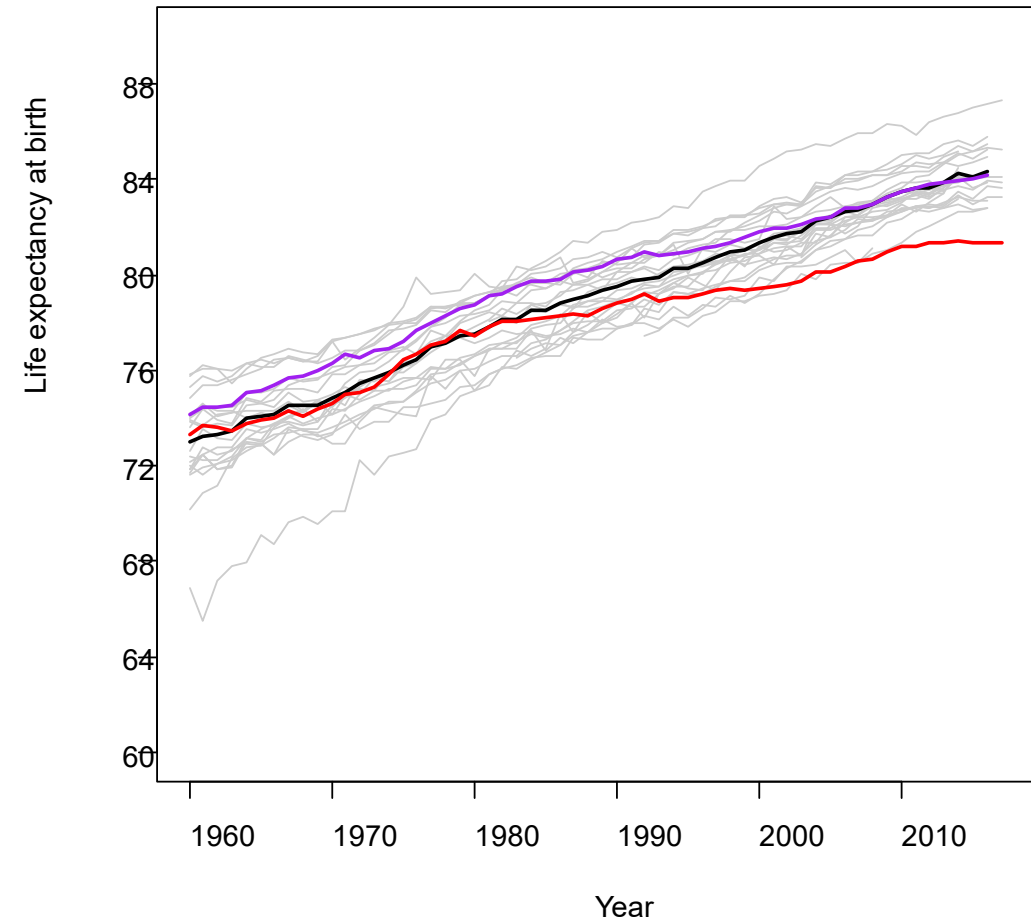


With a special emphasis on Canada

Men

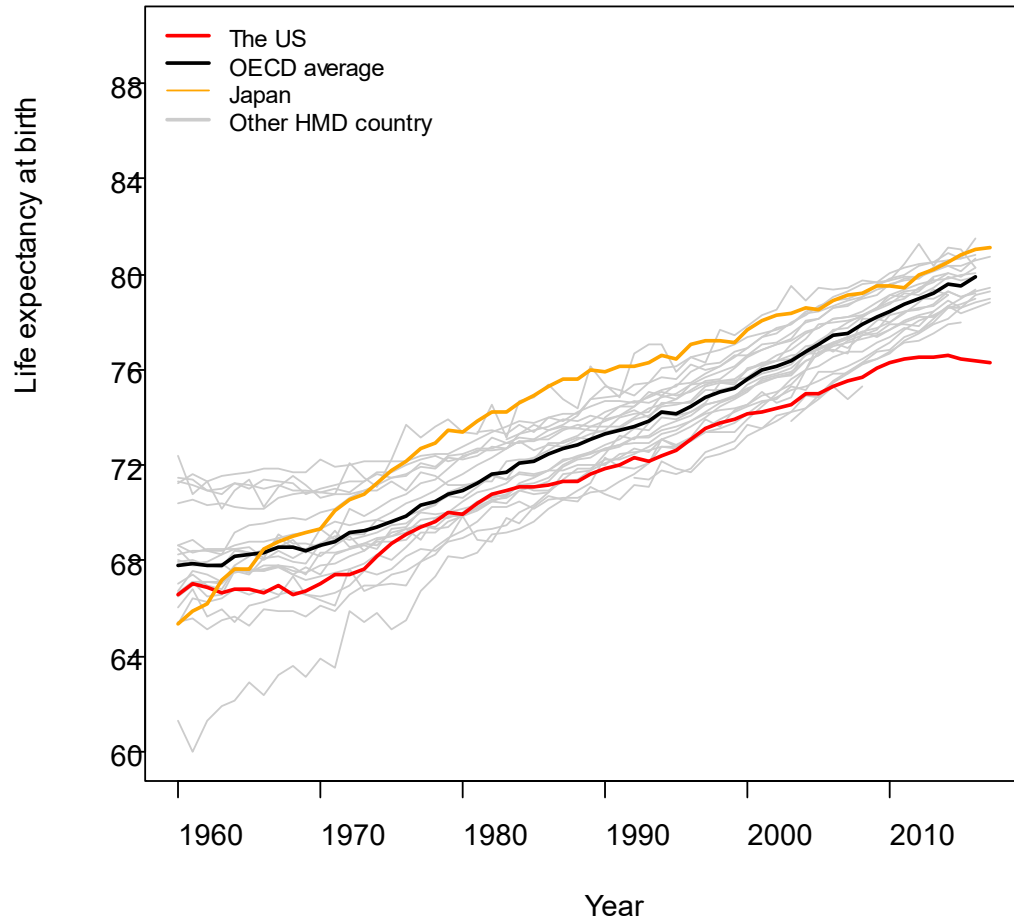


Women

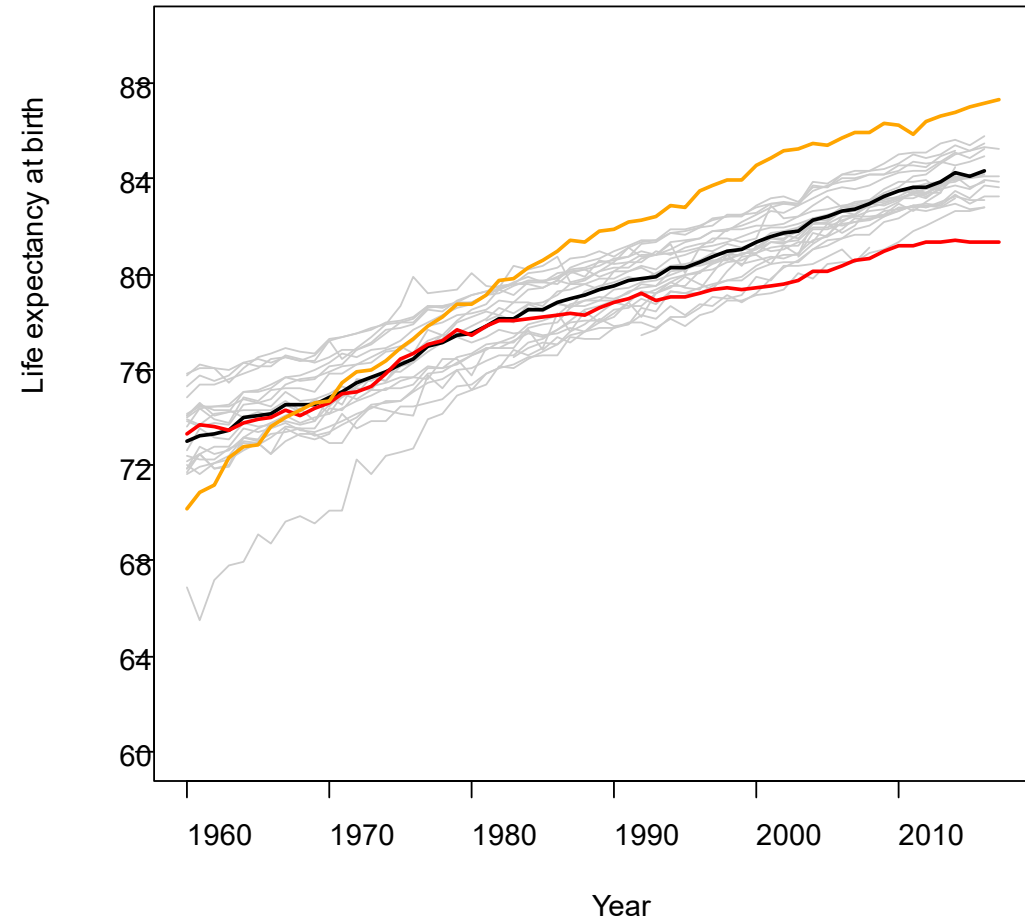


With a special emphasis on Japan

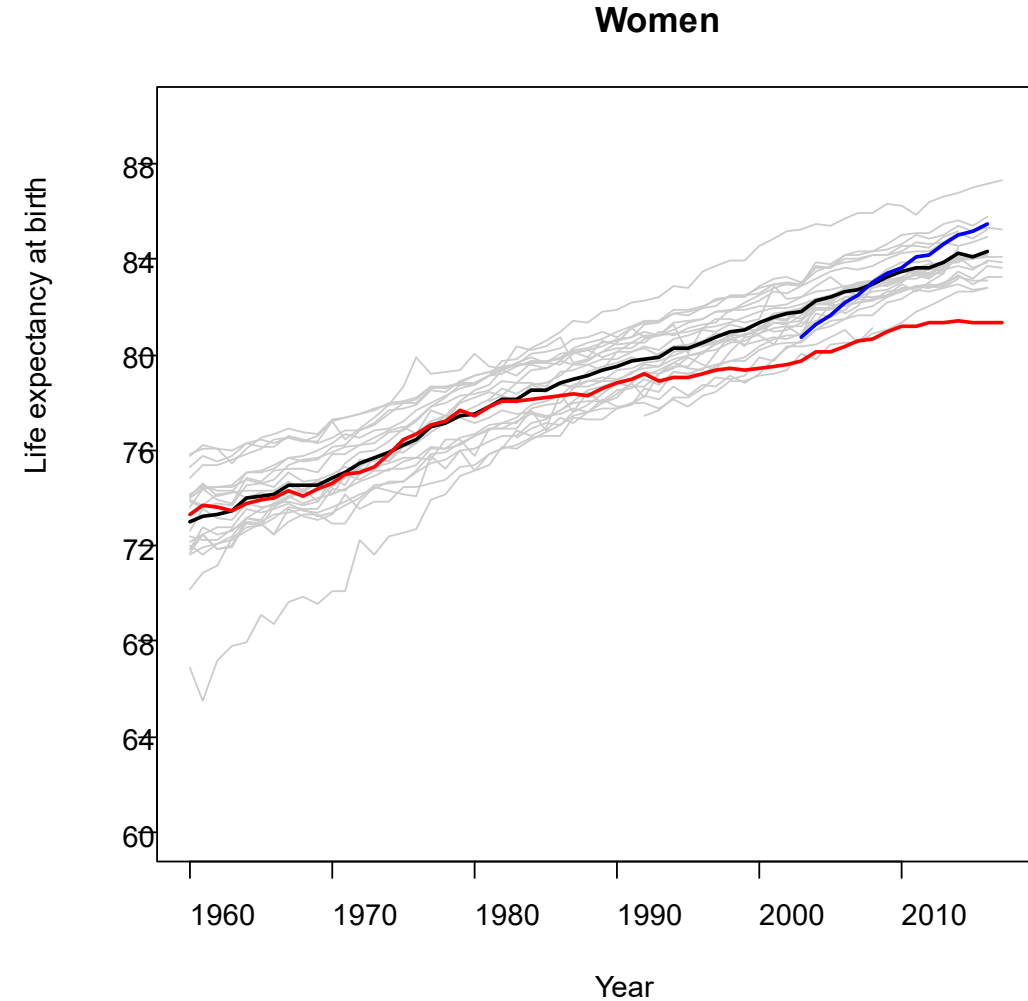
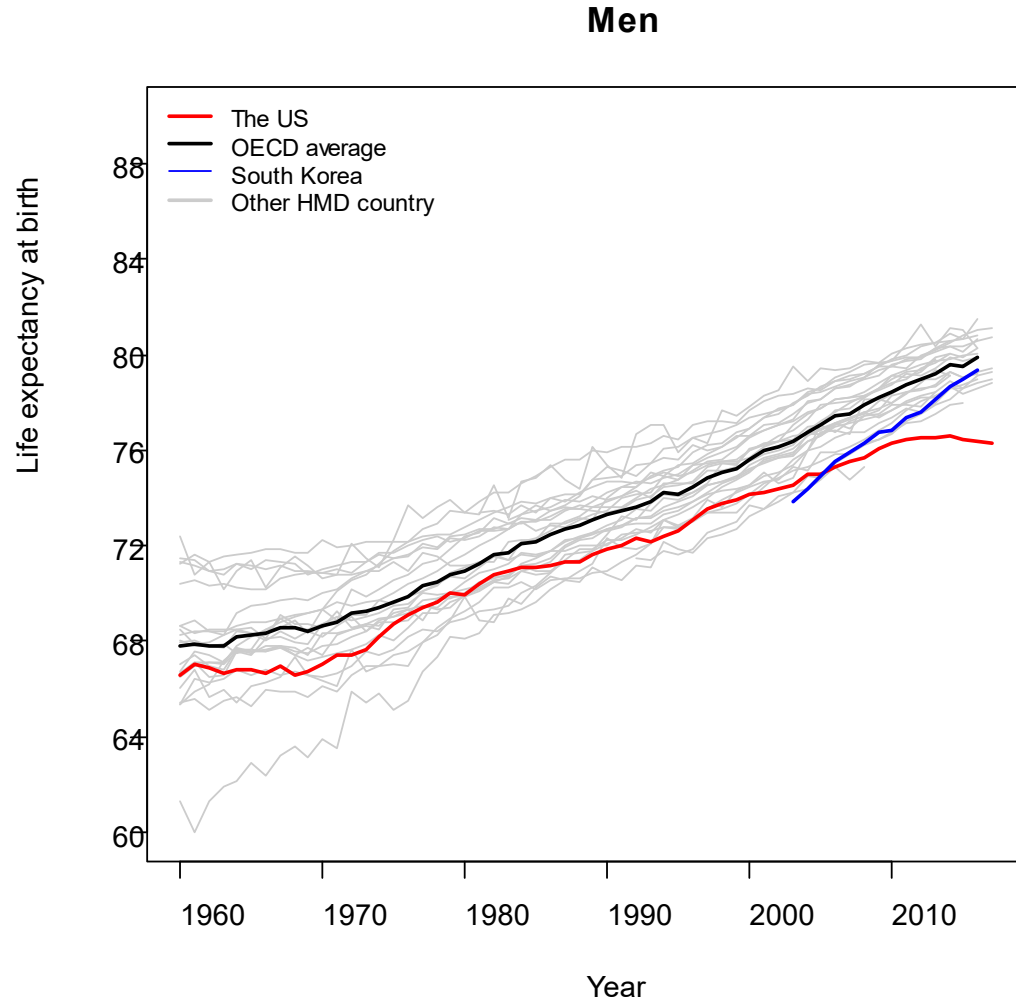
Men



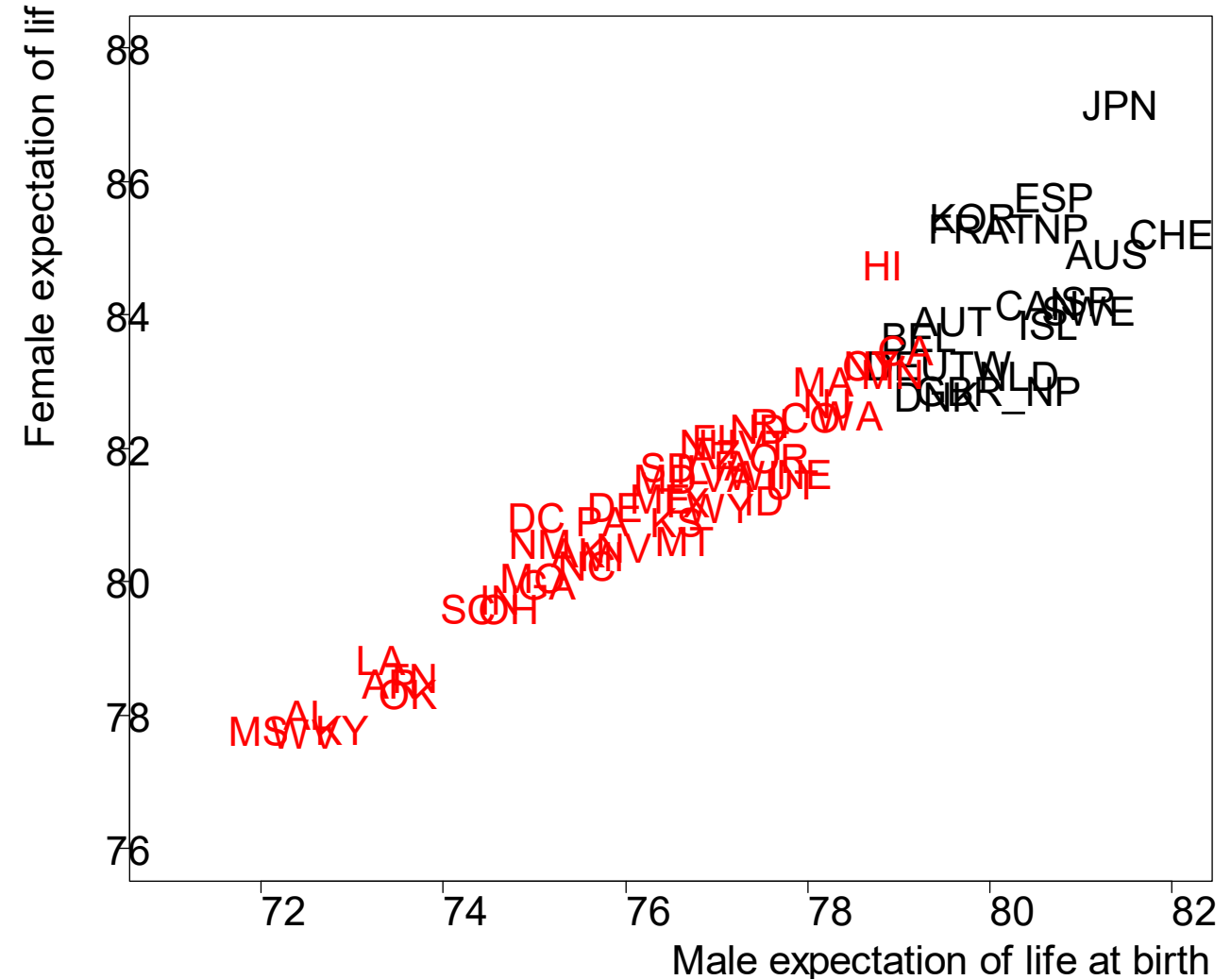
Women



With a special emphasis on South Korea

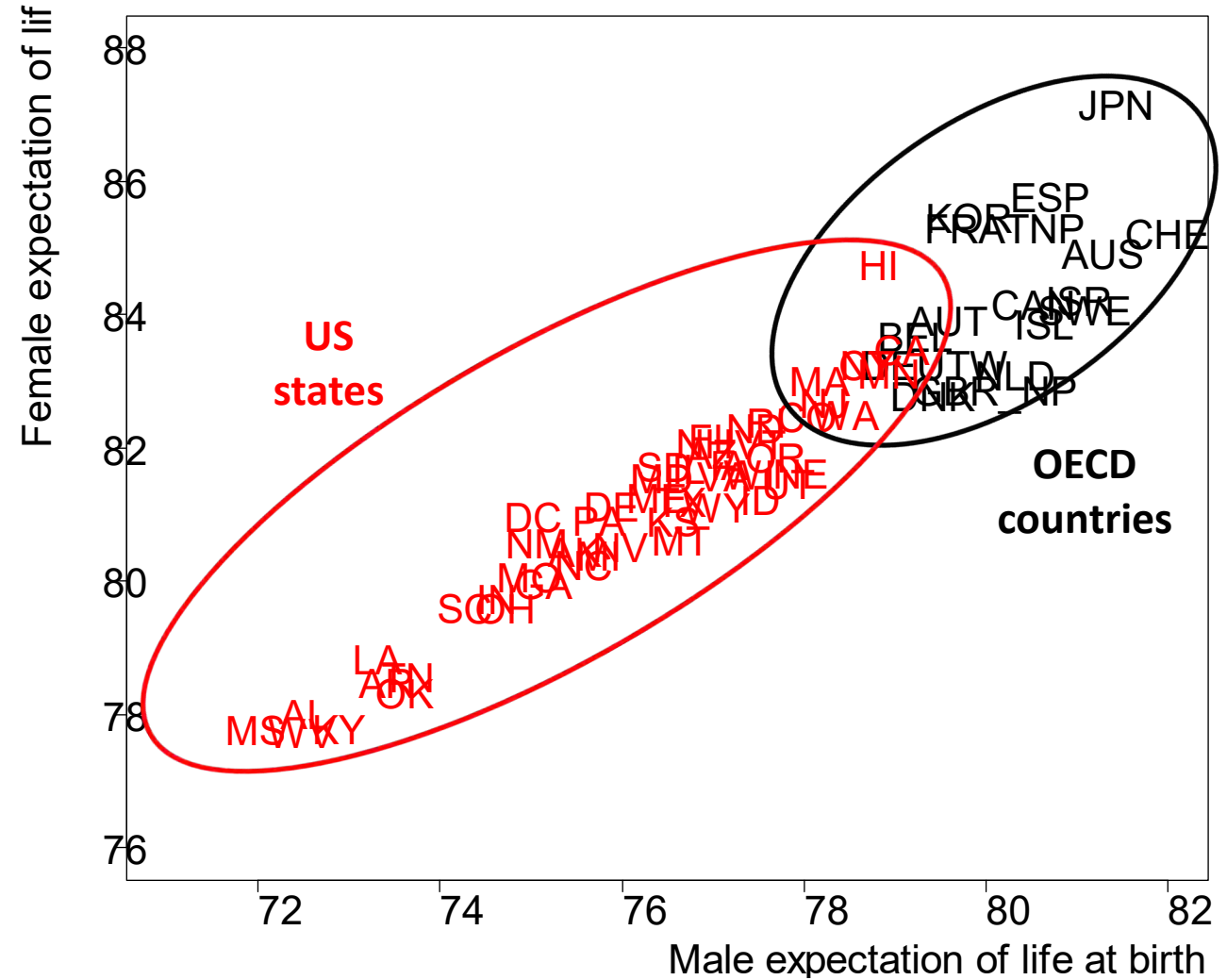


Nearly all states are behind the OECD countries in 2016



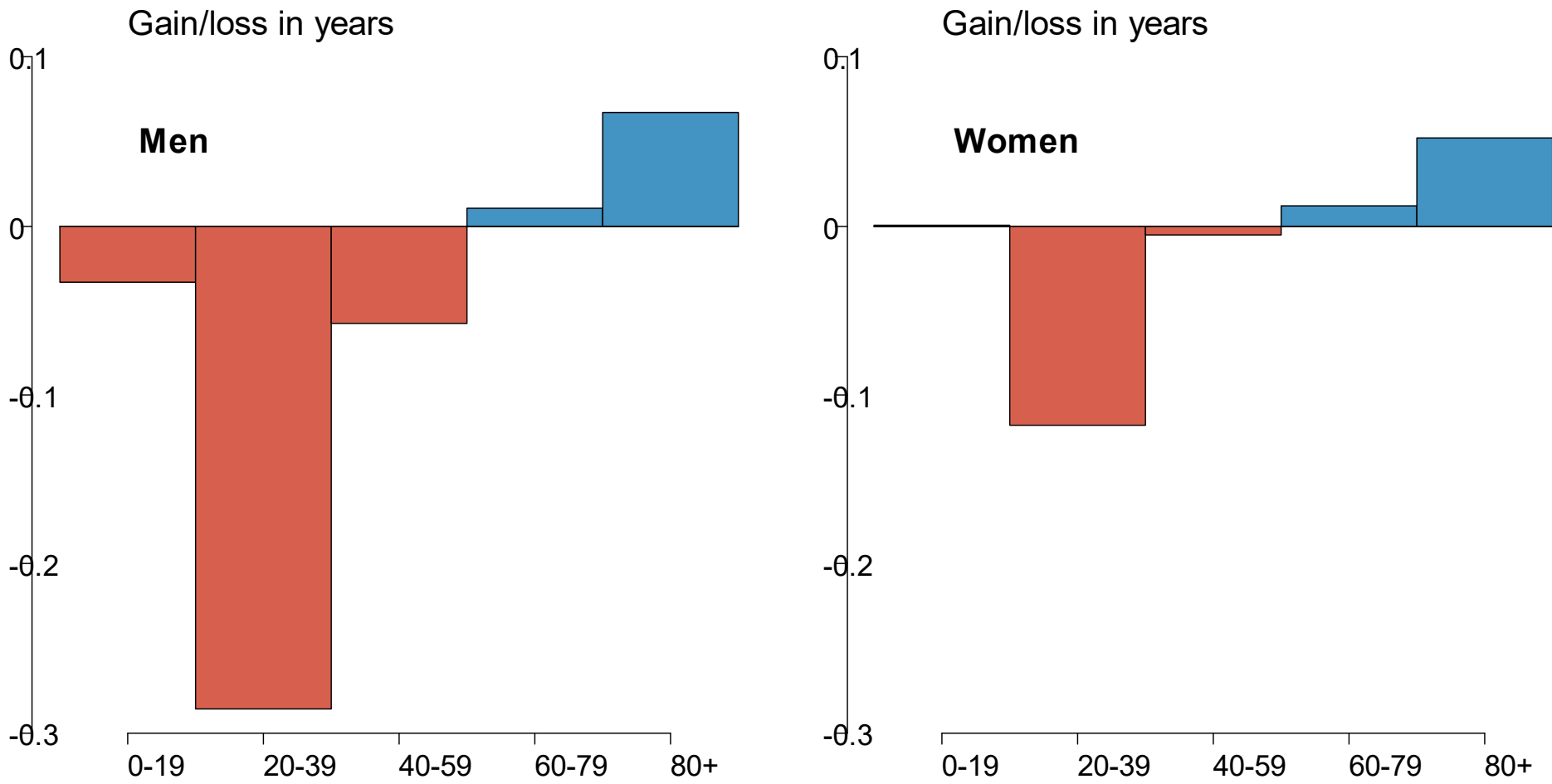
* Excluding Eastern Europe.

Nearly all states are behind the OECD countries in 2016



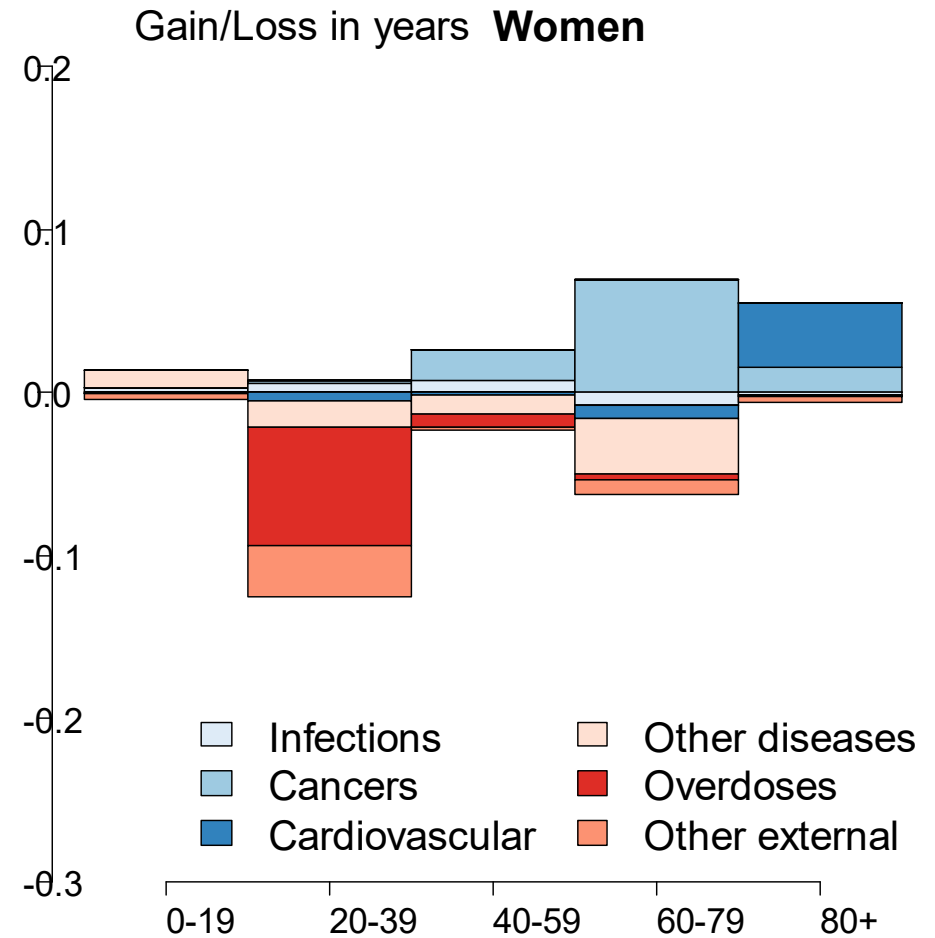
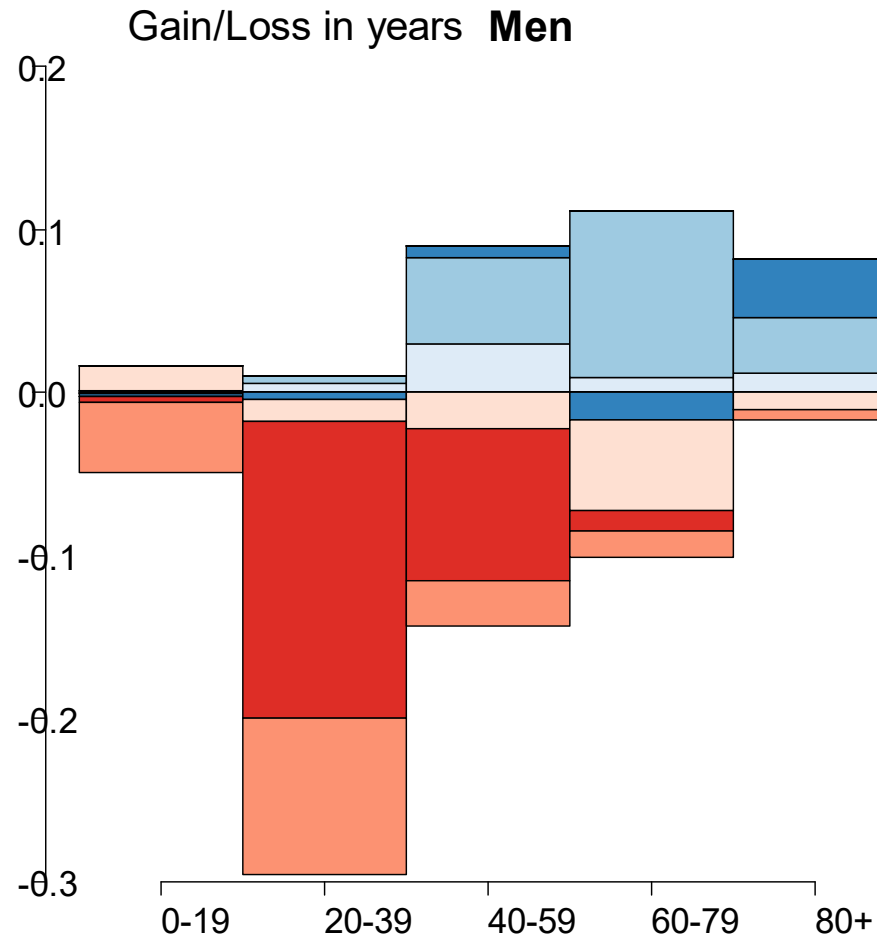
* Excluding Eastern Europe.

Contribution of age groups to the decline in life expectancy in the US between 2014 and 2017: Ages 20-40 yrs most affected

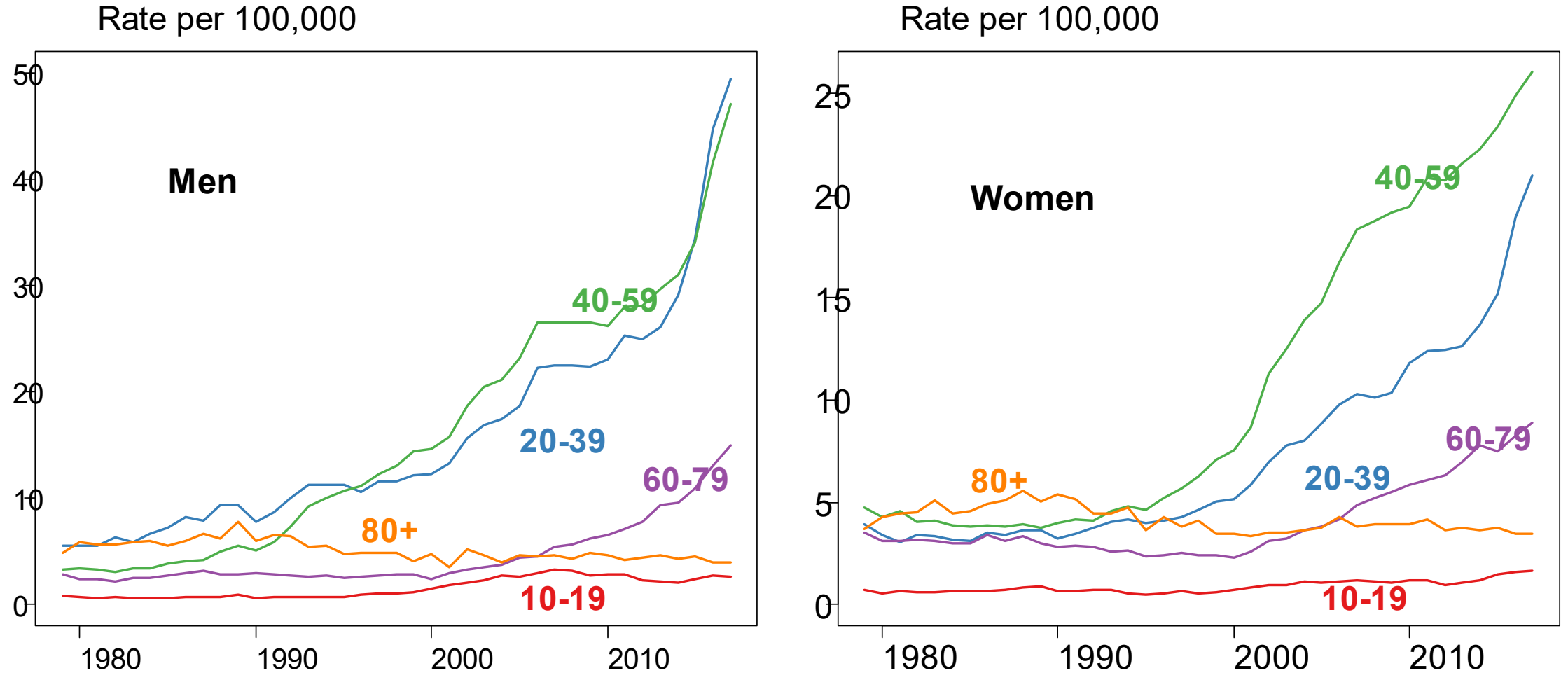


Total number of years of life lost between 2014 and 2017: 0.3 years for men, 0.06 years for women.

Major role of **drug overdoses** and, to a smaller extent, other external causes (suicide)



An exponential increase in mortality from drug overdoses since 1980

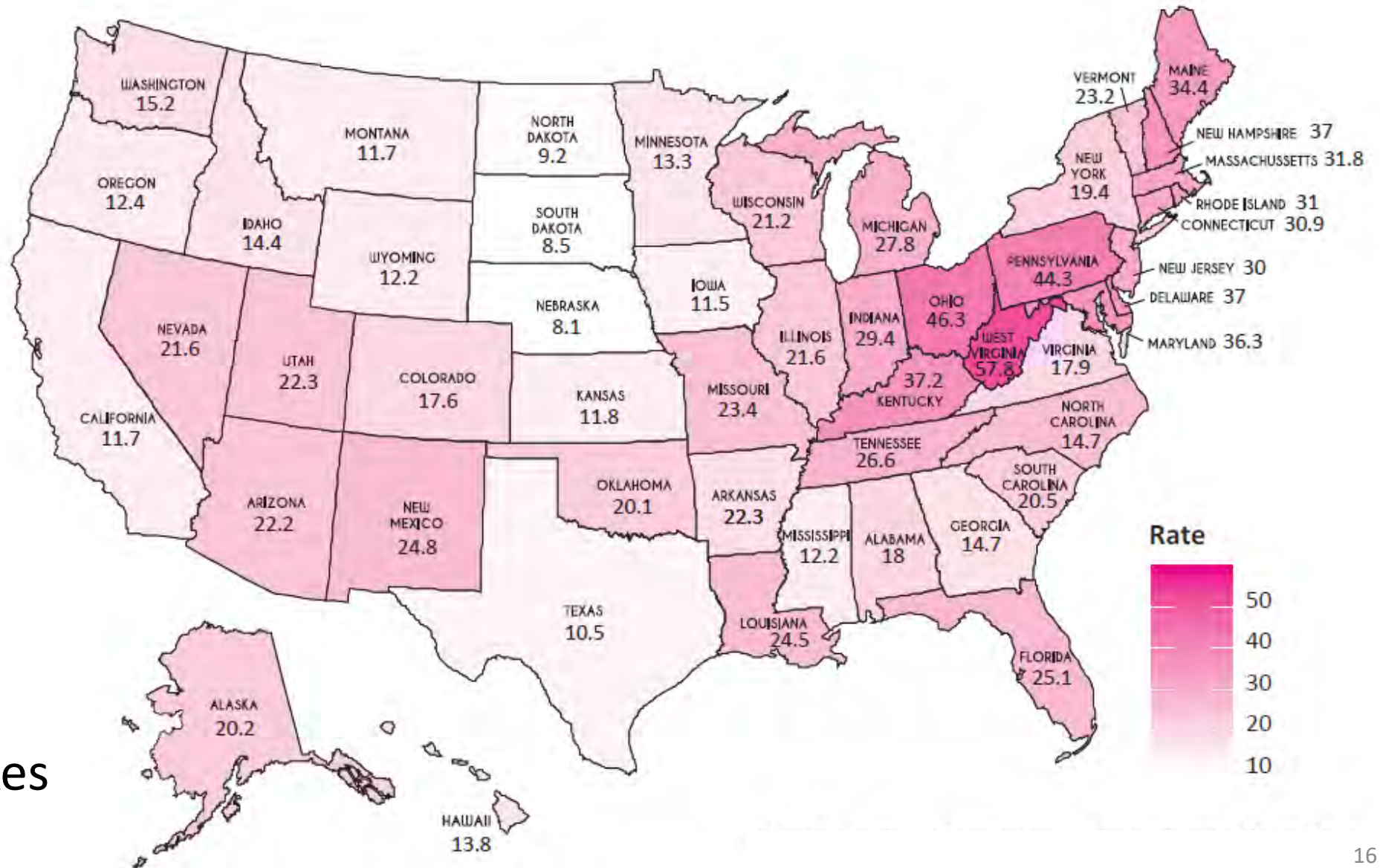


Age-specific mortality rate from drug overdose (p. 100,000), 1979-2017, men and women.

A short history of the overdose epidemic

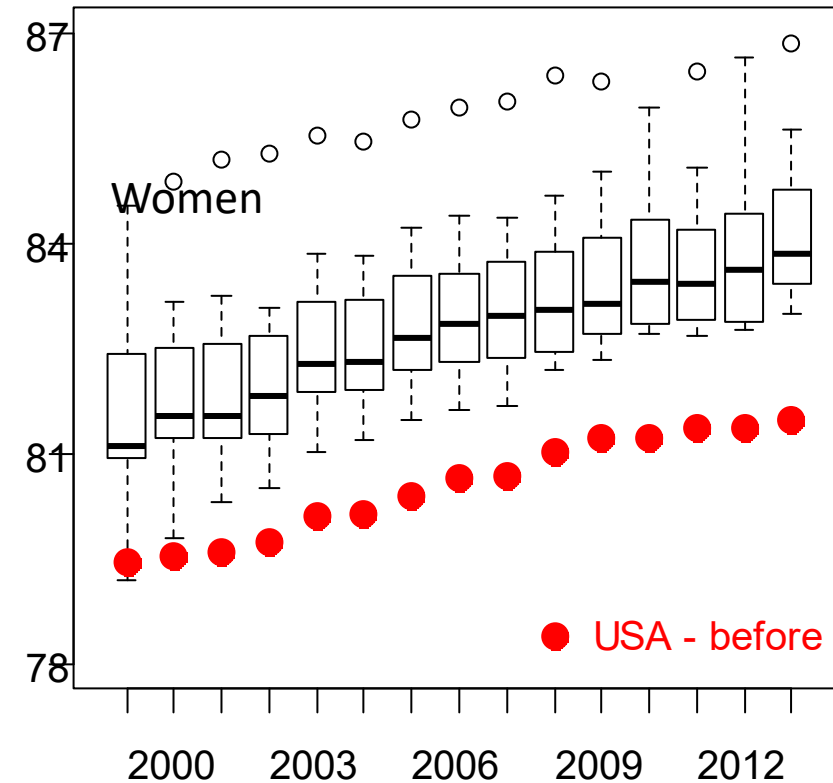
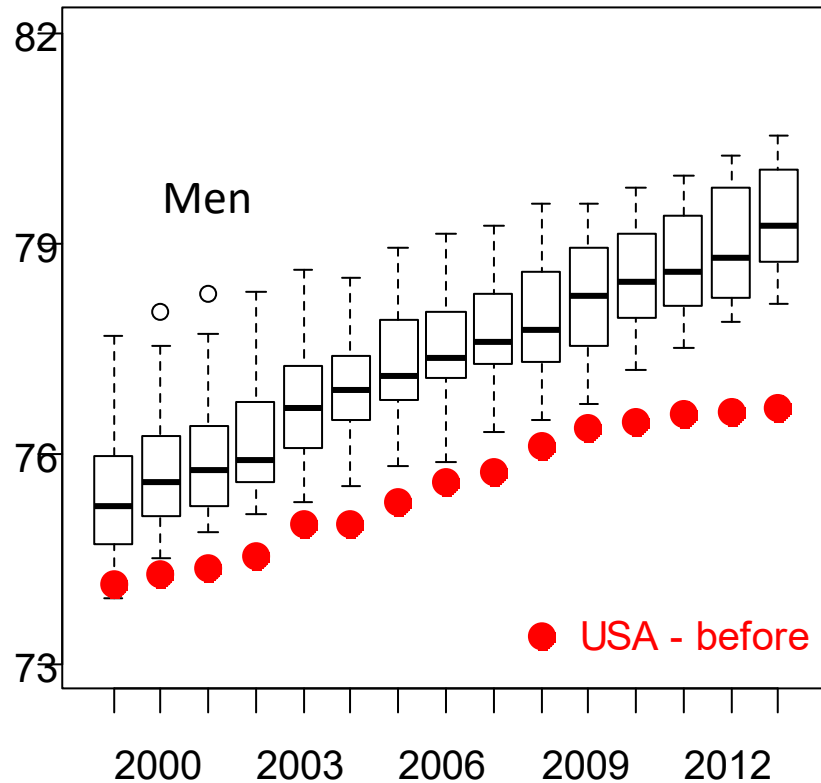
- 1996 Publication of an article on the low risk of addiction from medical prescription of opioid-based painkillers
- 1996-2000 The pharmaceutical industry develops aggressive campaigns to promote opioid-based painkillers (oxycodone, hydrocodone, meperidine, hydromorphone and propoxyphene)
- 2000 Government directive to reduce the prescription of opioid-based painkillers
- 2013 The black market is invaded by synthetic opioids (fentanyl, tramadol)
- 2017 Record-high number of deaths from drug overdoses (70,000)
- 2018 The monthly death count reached a peak in November and the increase appears to have stopped since then

Nearly all states are affected by the overdose epidemic



Mortality rate from overdose (p. 100,000) in 2017, both sexes combined.

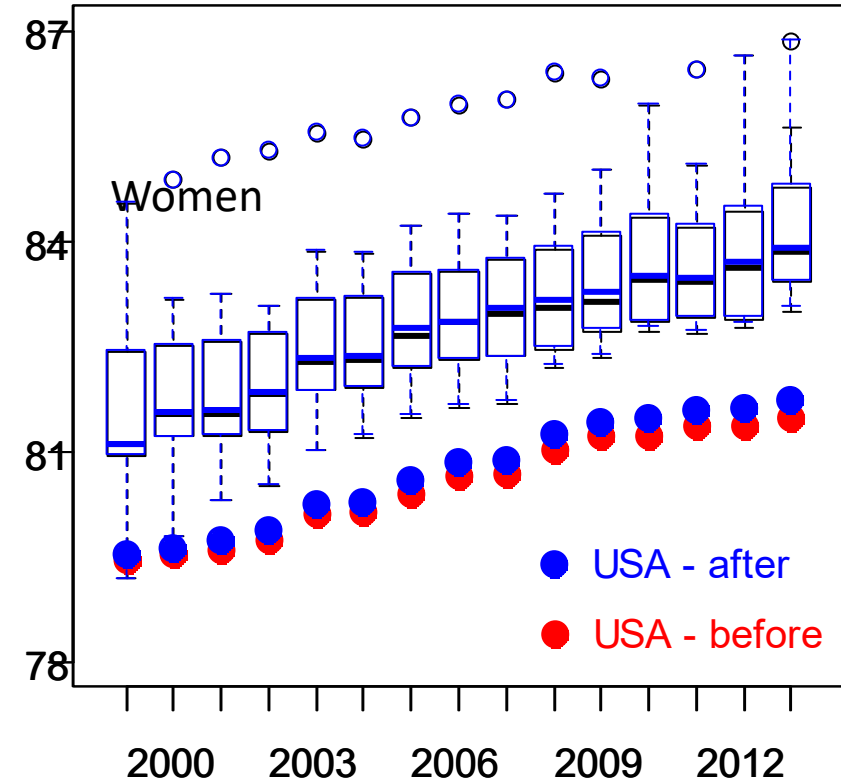
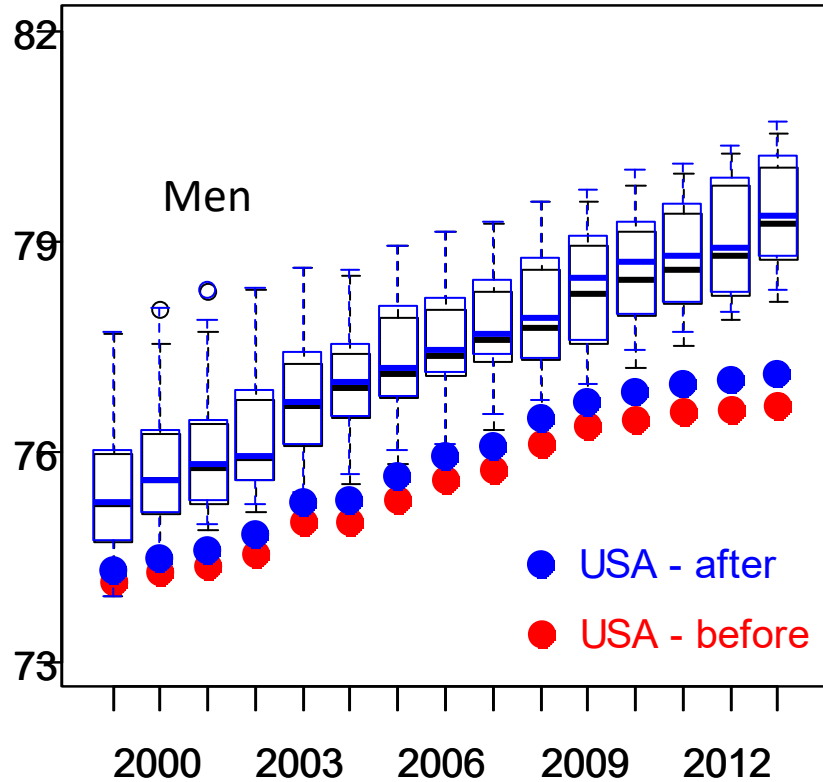
Life expectancy at birth in the US and 18 other high-income countries, 1980-2014



Source: HMD data for Australia, Austria, Belgium, Denmark, Finland, France, Iceland, Ireland, Japan, Luxembourg, New-Zealand, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom and West Germany.

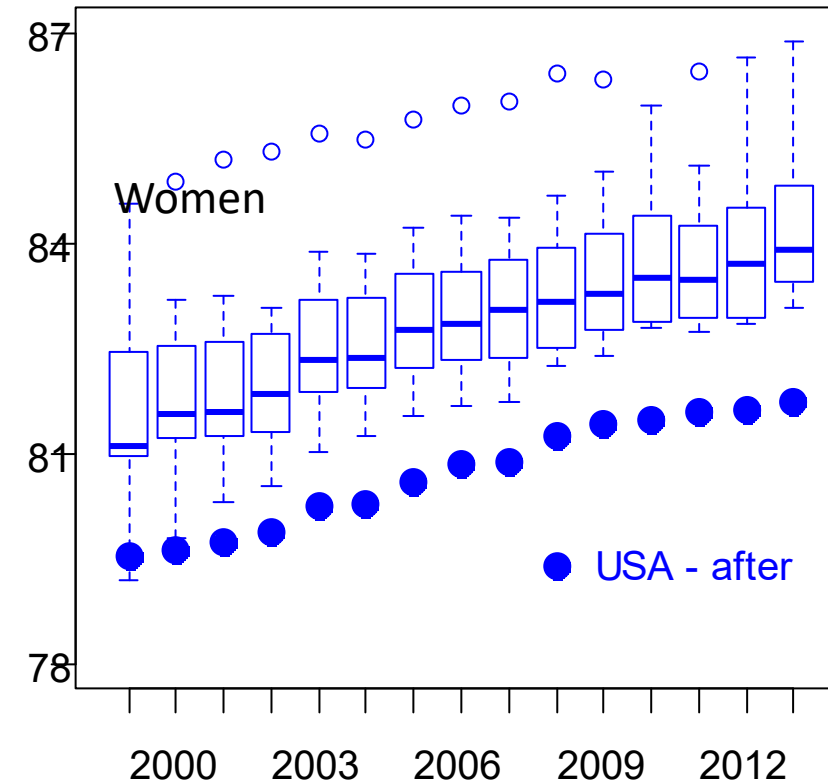
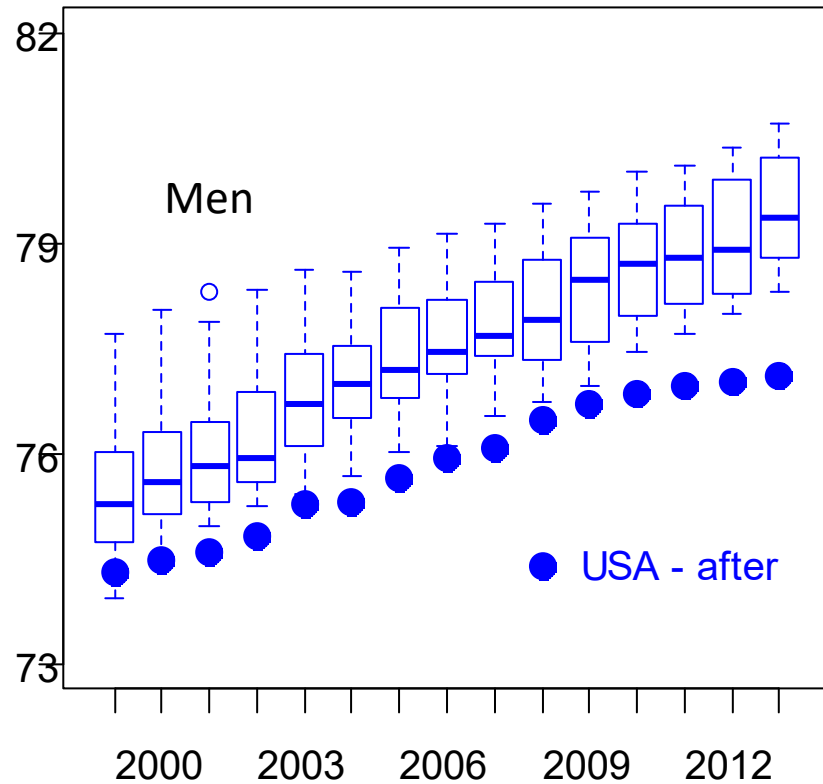
Before and after eliminating drug-related deaths

Life expectancy at birth

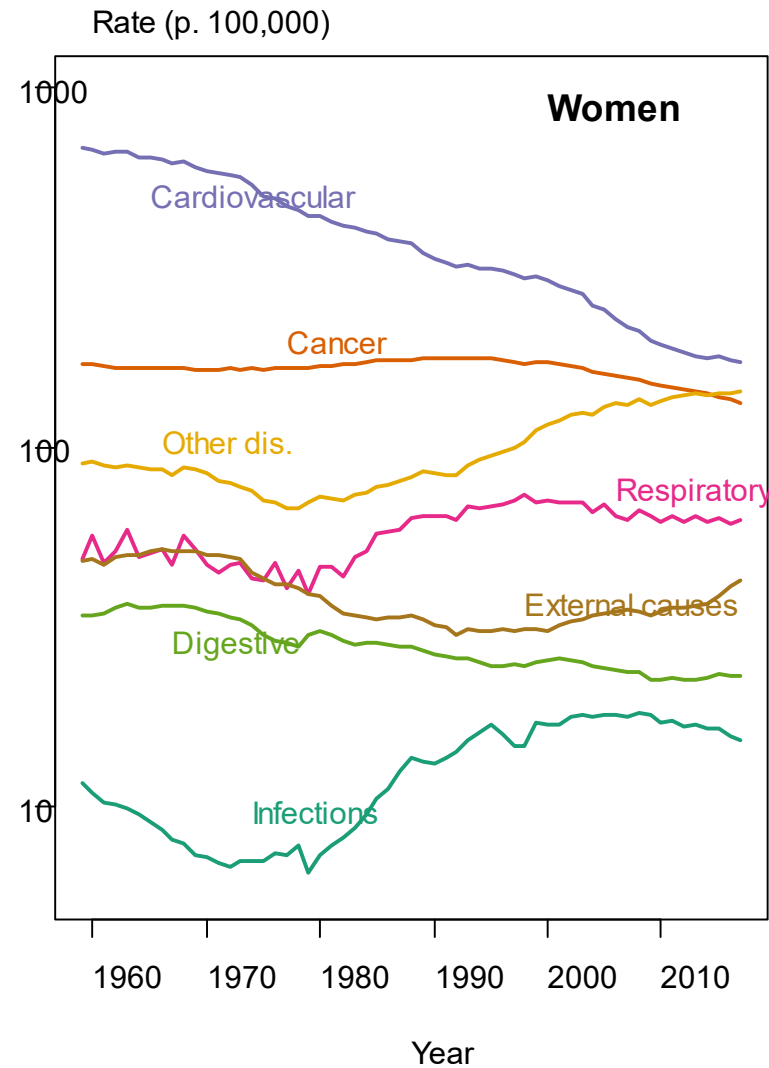
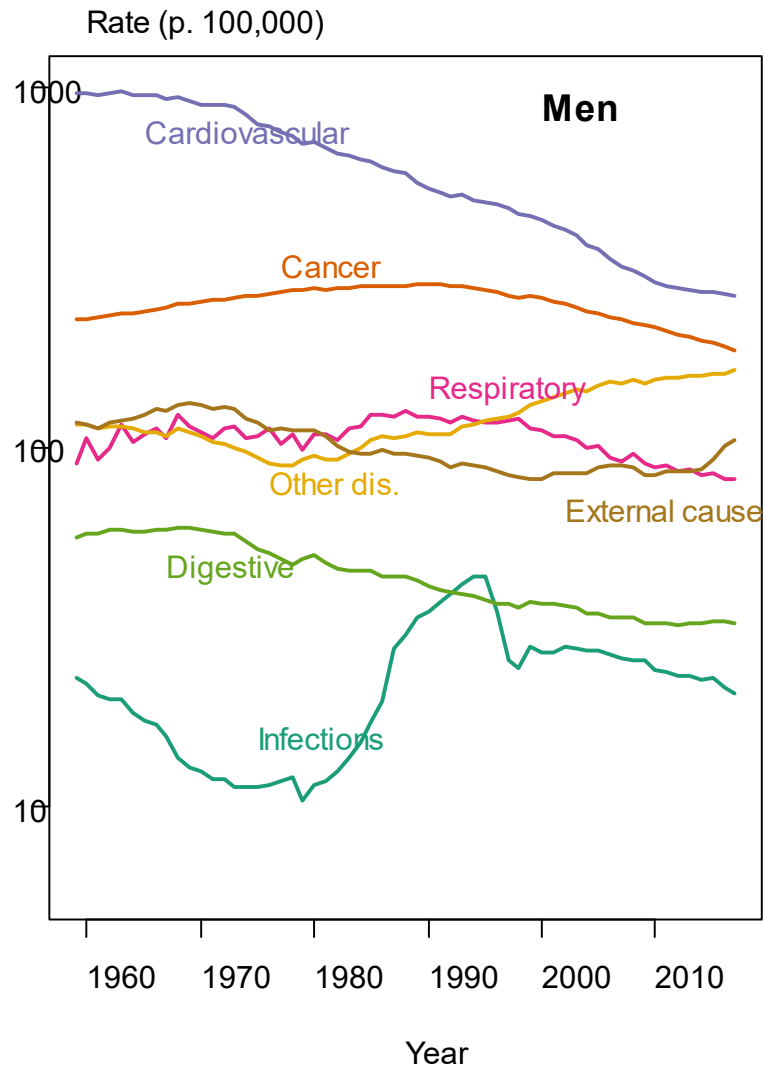


After eliminating drug-related deaths

Life expectancy at birth



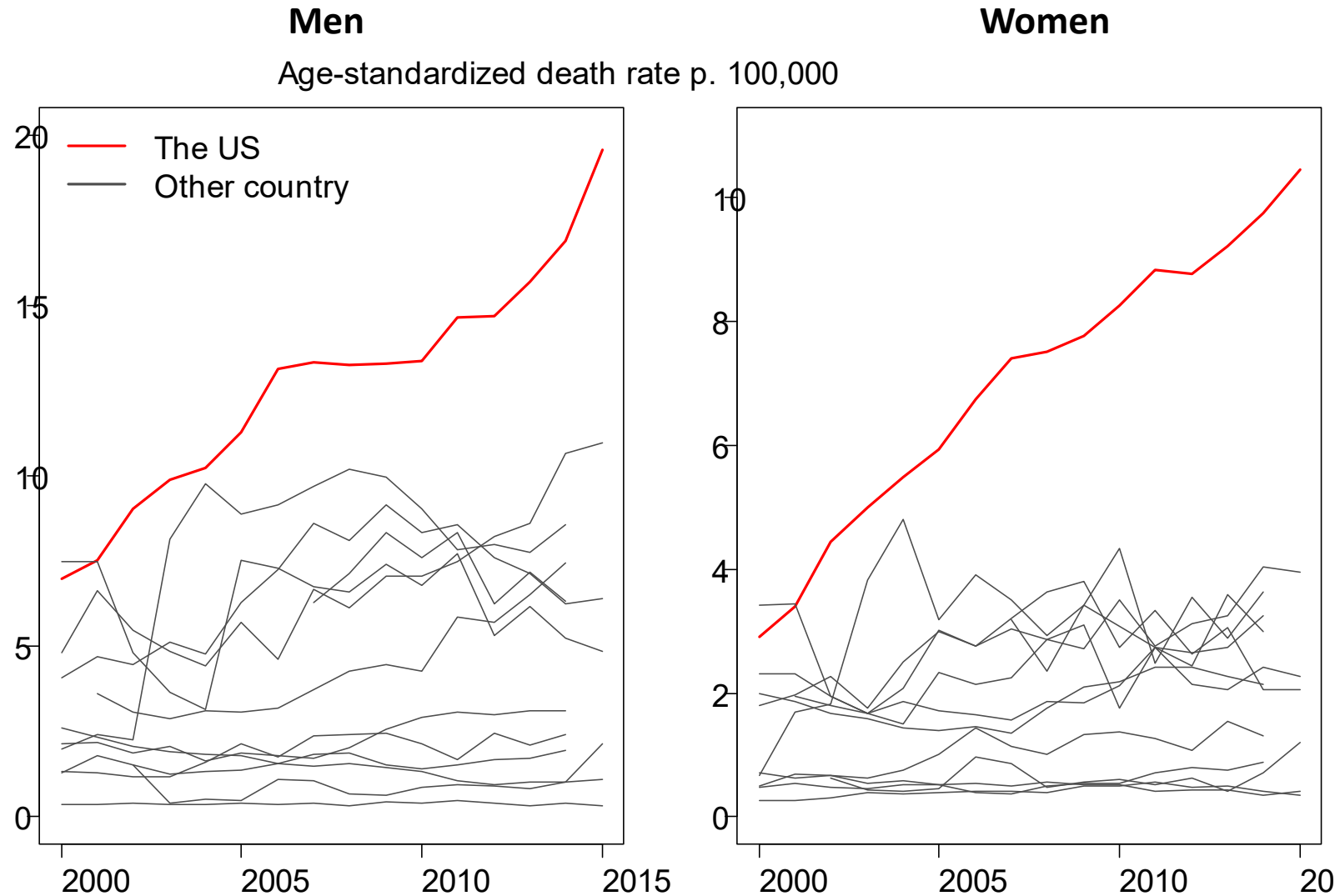
A slowing down of progress in cardiovascular mortality also contributed



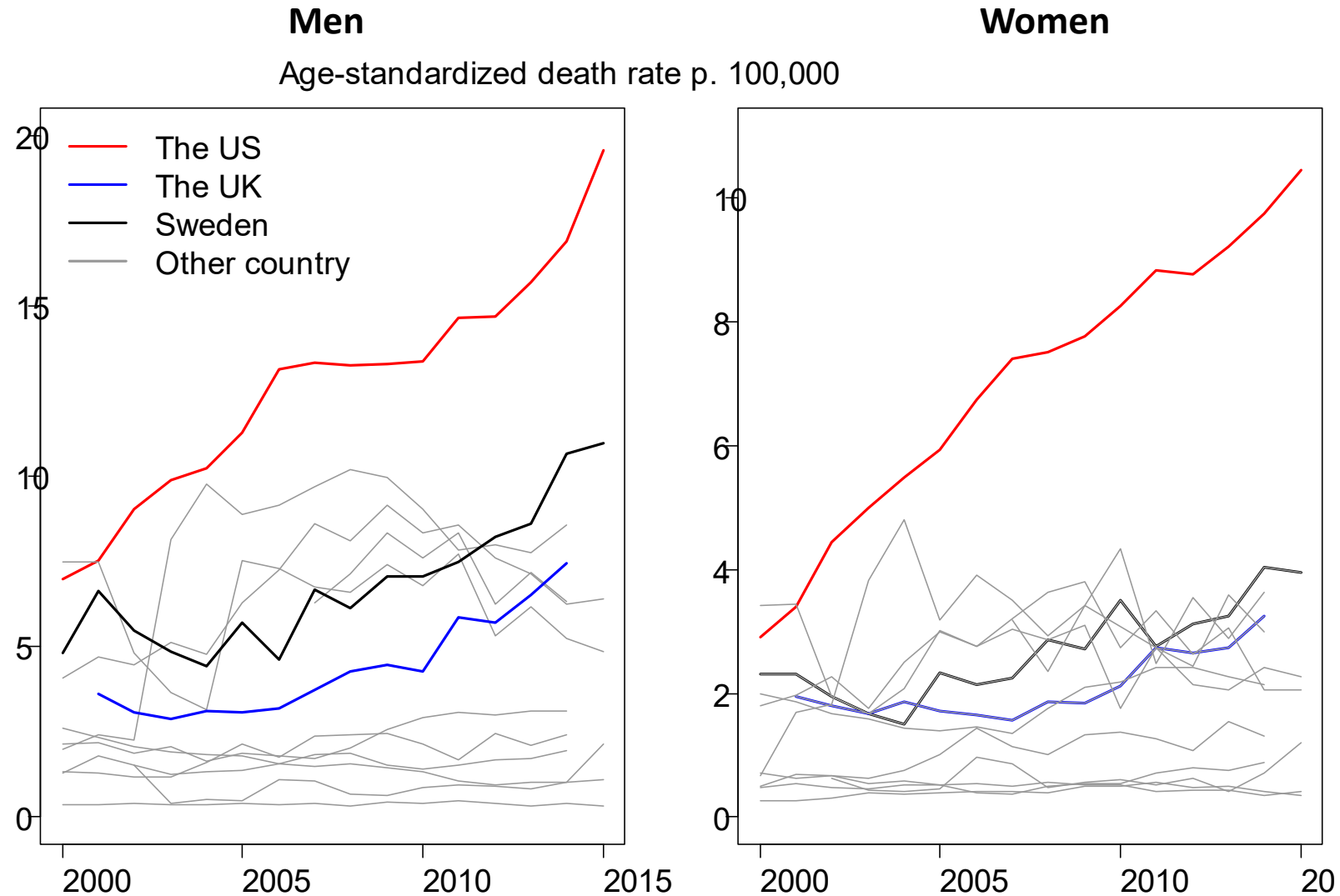
The US: A leader in a new international mortality trend?

- Unlikely as regards the drug epidemic => magnitude very specific to the US
- Maybe as regards cardiovascular diseases => discernible slow down in the control of mortality from such diseases

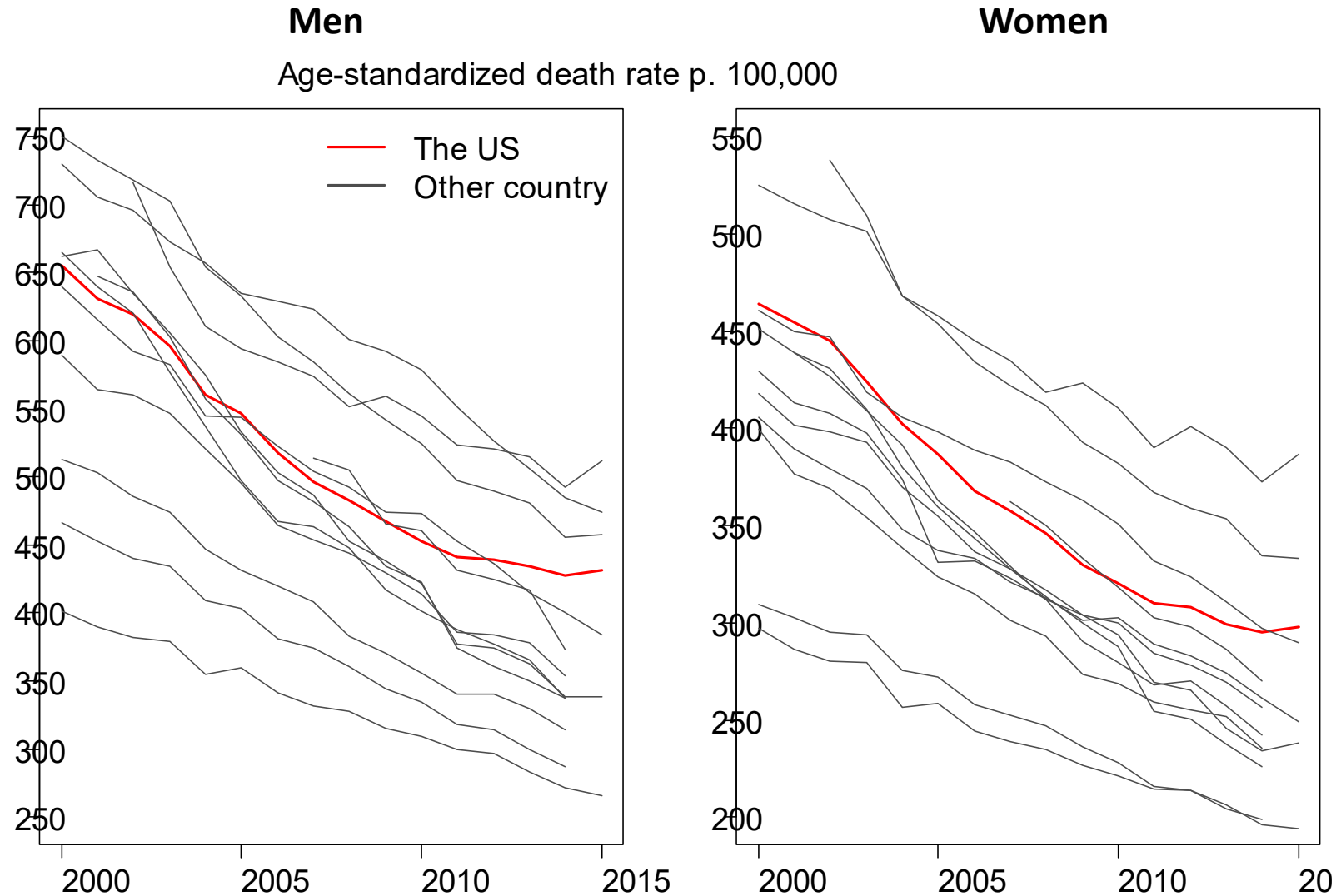
Drug-related age-standardized mortality rate in the US and 12 other high-income countries, 2000-2015



Drug-related age-standardized mortality rate in the US and 12 other high-income countries, 2000-2015



Age-standardized mortality rate from cardiovascular diseases in the US and 12 other high-income countries, 2000-2015



Conclusions

- Life expectancy in the US has been lagging behind that in other high-income democracies starting around 1980
- The US mortality increase (since 2014) is unique (in its magnitude, if not in its occurrence)
- The opioid epidemic has played a major role in the reversal, especially for working-age men
- Even without overdose deaths, the US would remain far behind other countries
- The slowdown of progress to control cardiovascular mortality is a major underlying factor in the US mortality pattern (maybe due to rising obesity and diabetes)

Acknowledgments



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