Will precision medicine improve population health?

Sandro Galea

Boston University School of Public Health

The loyal opposition

to the aspirations of science

The loyal opposition

to compelling ideas that do not advance health

The loyal opposition

There is one question that matters. Will precision approaches improve population health?

No, unless.

Three reasons why not.

1. The challenges of complexity in biology

Genes matter relatively little

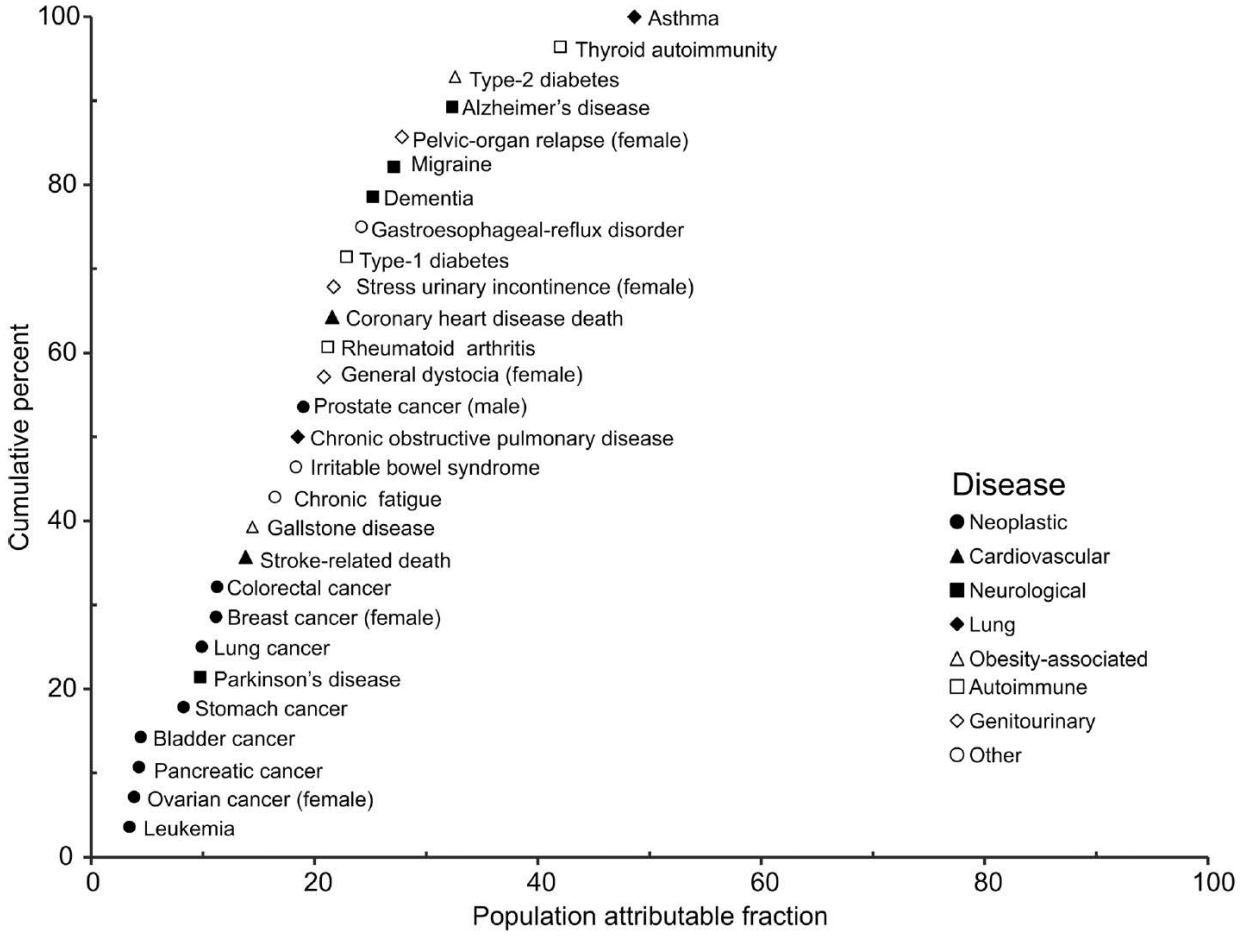
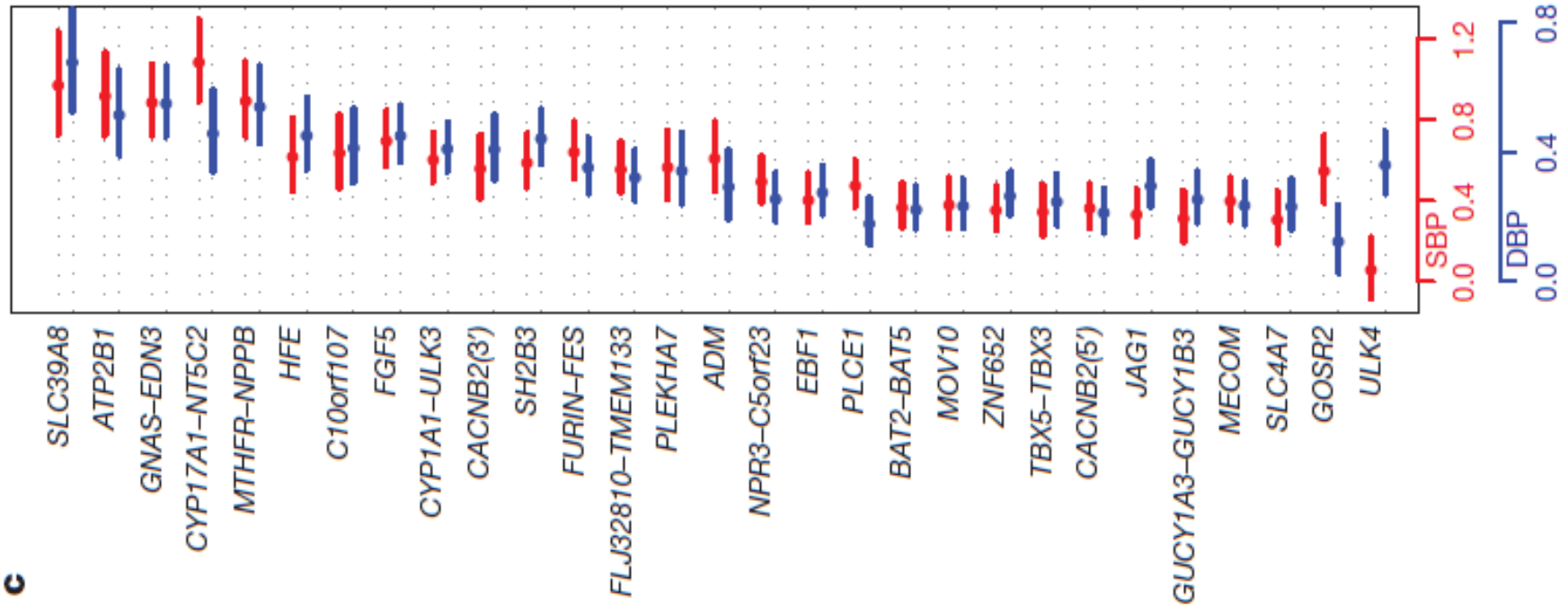


Fig 1. Population attributable fractions (PAFs) for 28 disease phenotypes estimated from studies of monozygotic twins. Sources of data and statistics are summarized in Table 2.

doi:10.1371/journal.pone.0154387.g001

Many variants, with very small effect



Little evidence for efficacy of molecular targeting

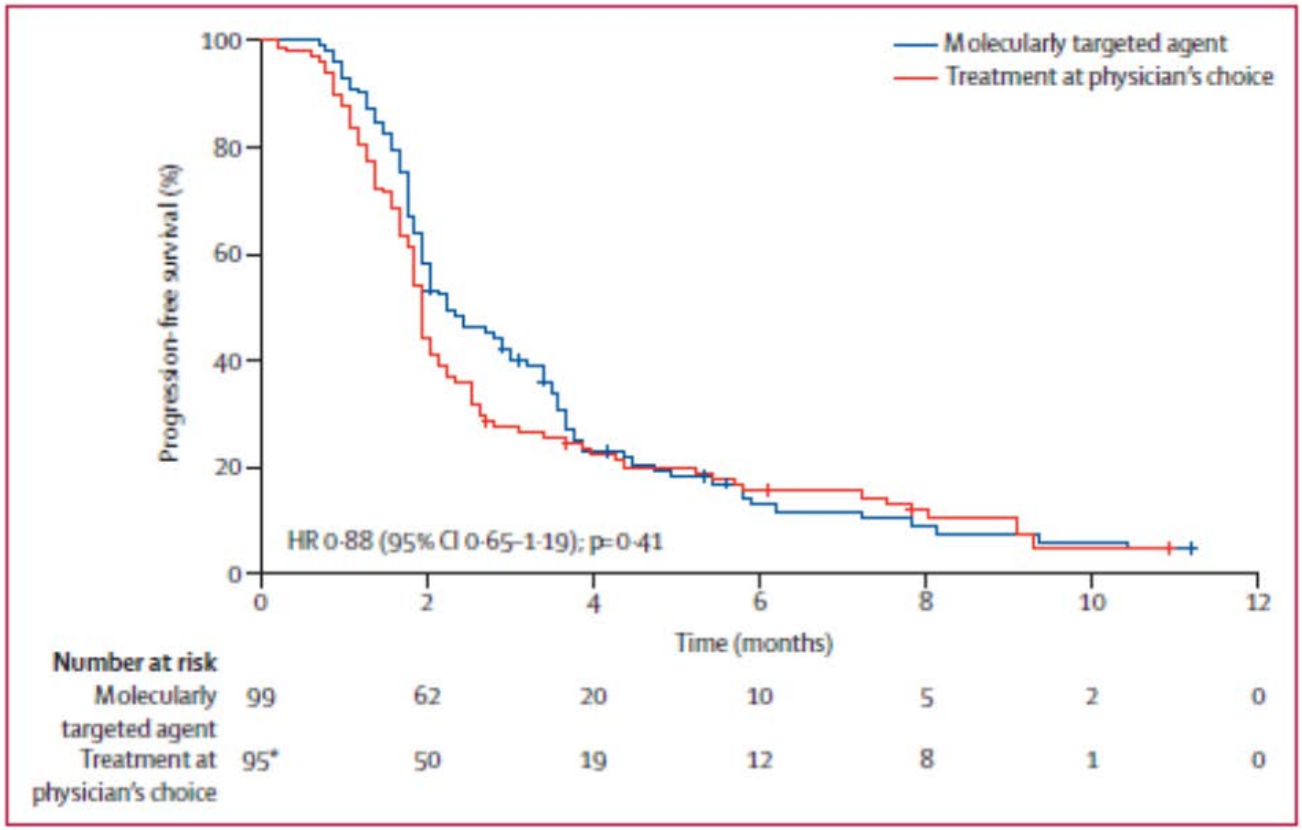
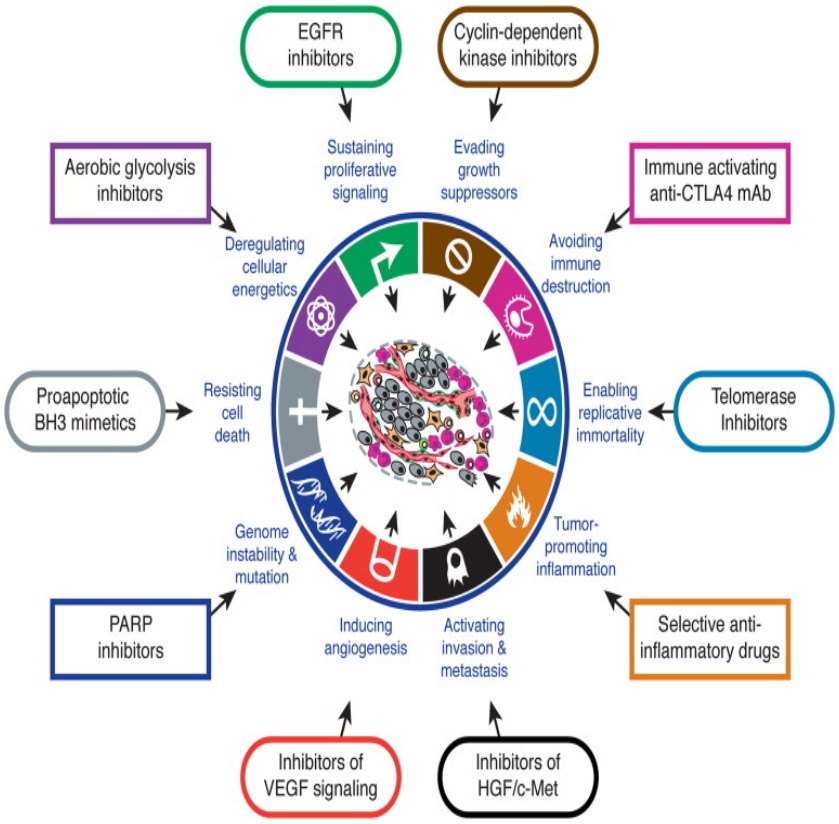


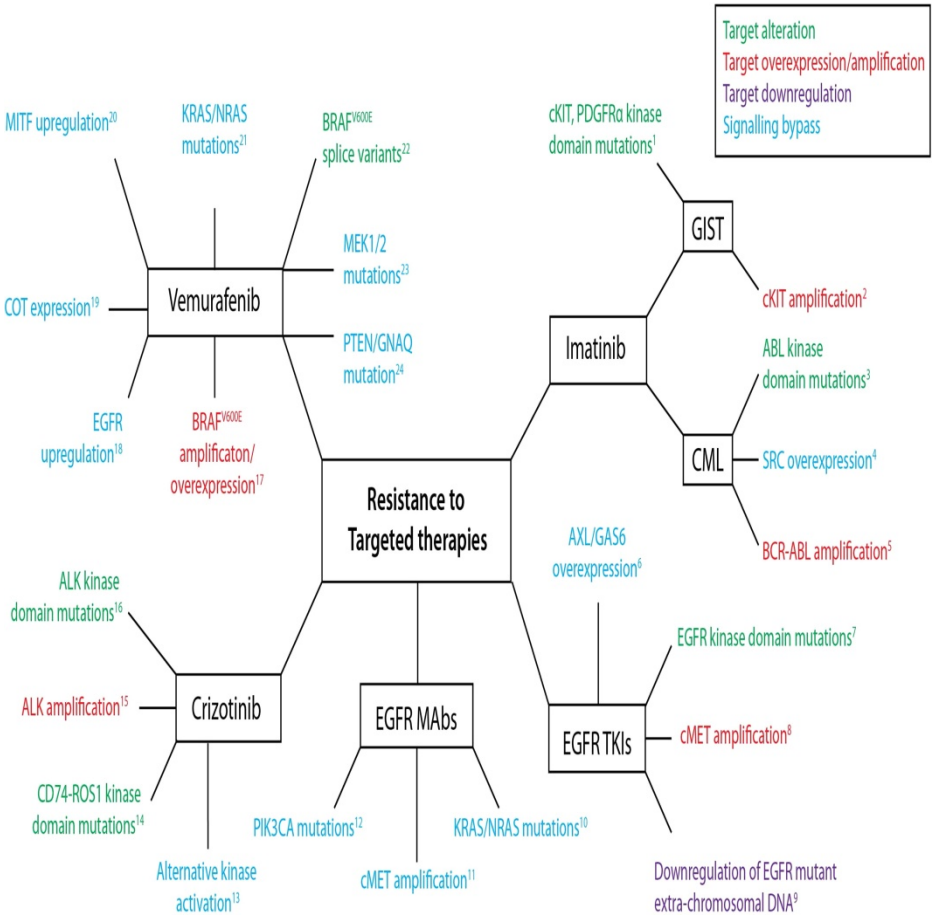
***Figure 3*: Progression-free survival**

*One patient had a follow-up of zero days so is not shown here.

Le Tourneau et al, Lancet Onc 2015

Multimechanism diseases with predictable resistance



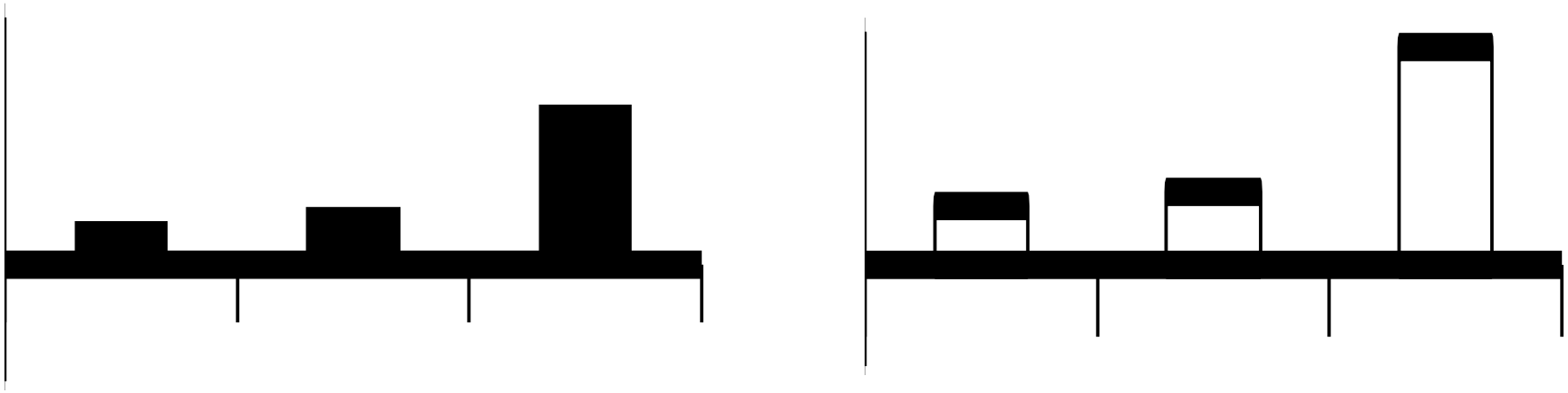


Hanahan D, Weinberg R. Cell 2011; 144: 646-774

Burrell RA, Swanton C. Mol Oncol 2014; 8: 1095-1111

Slide courtesy of Michael Fernandes

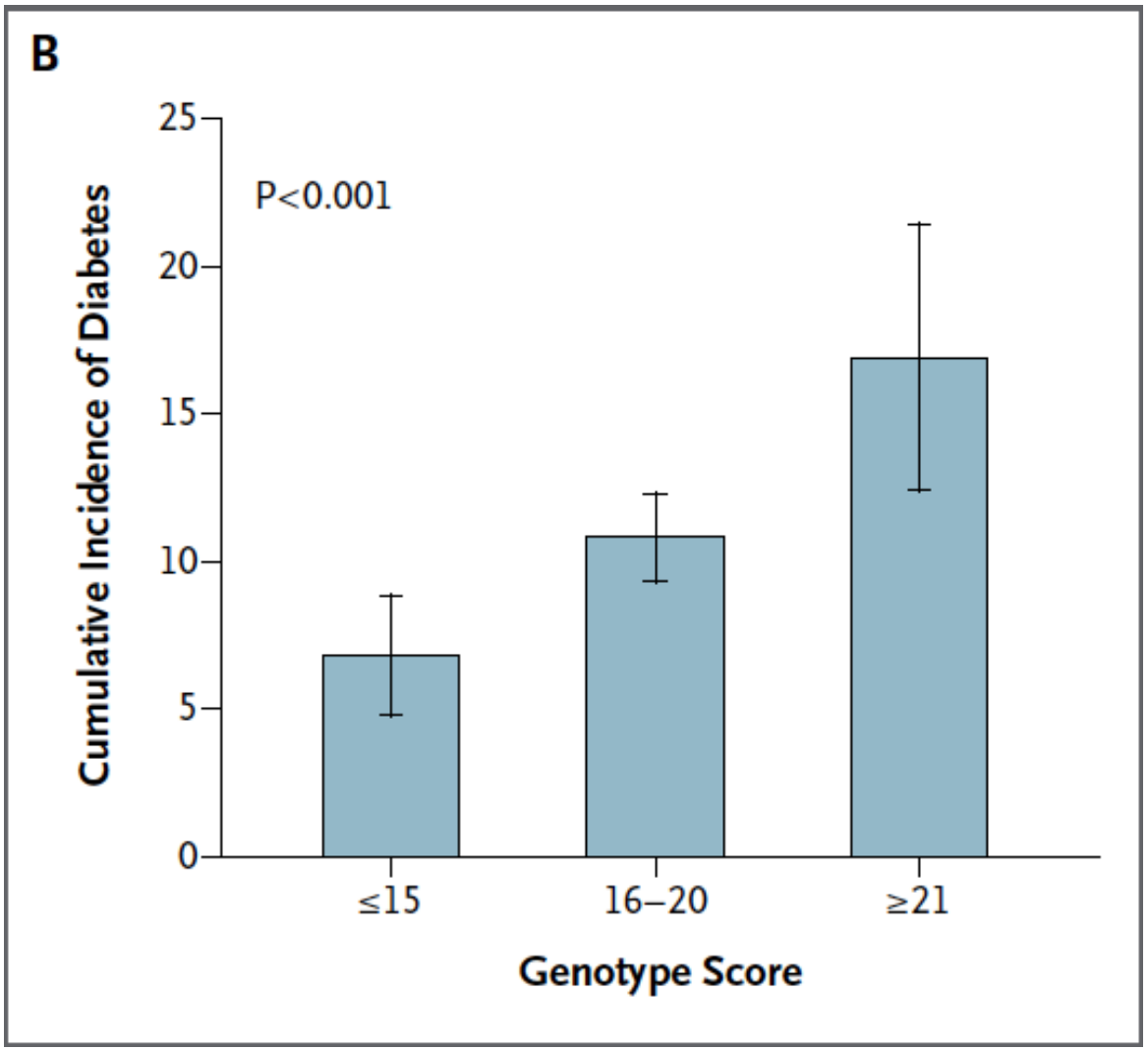
The inevitable overwhelming role of behavior



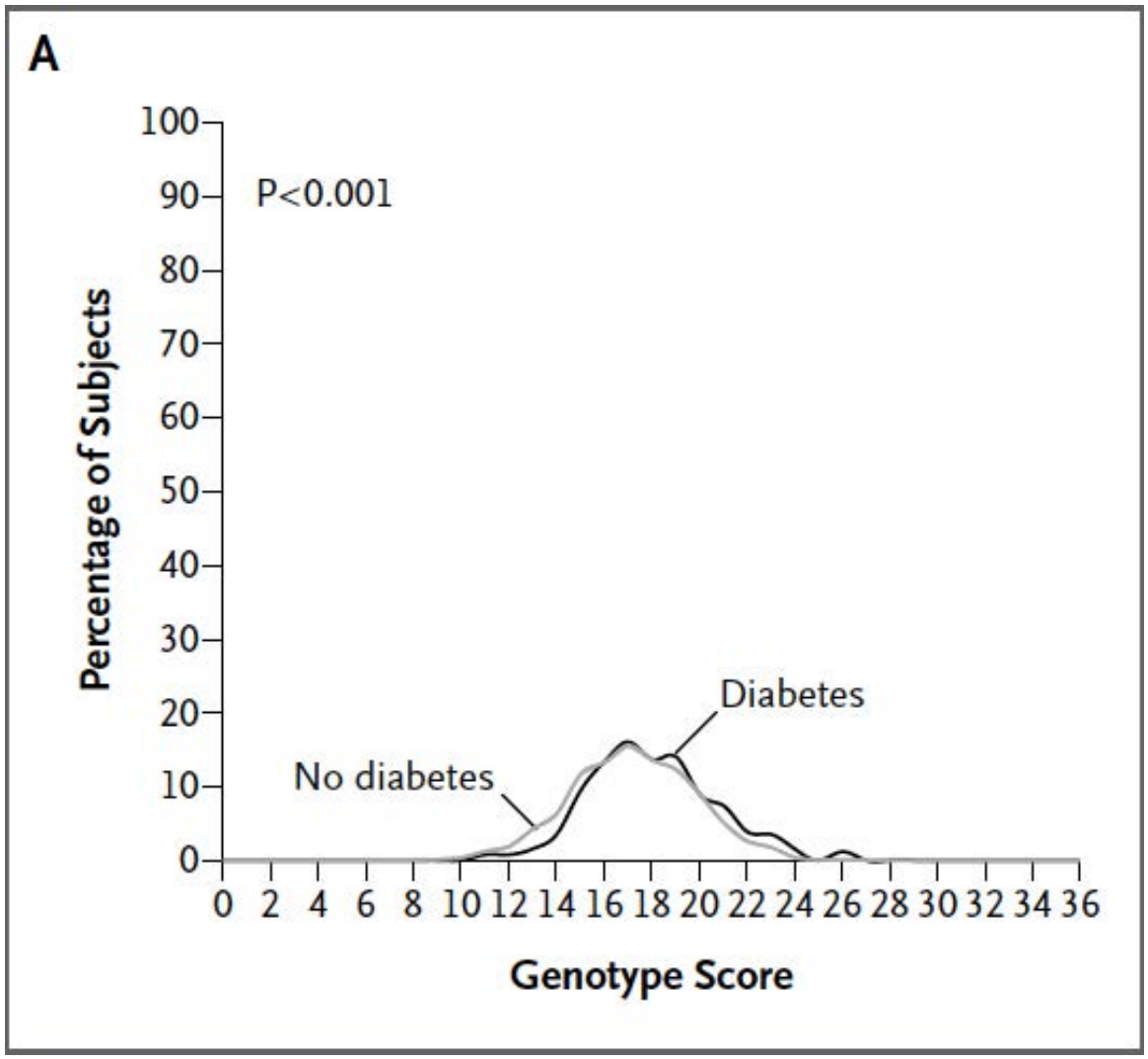
Calle et al. N. Engl. J. Med. 2003; 348: 1625-1638

Slide courtesy of Michael Joyner

2. The conflation of the individual and population



Meigs JB, Shrader P, Sullivan LM, McAteer JB, Fox CS, Dupuis J, Manning AK, Florez JC, Wilson PW, D'Agostino RB Sr, Cupples LA. Genotype score in addition to common risk factors for prediction of type 2 diabetes. N Engl J Med. 2008 Nov 20;359(21):2208-19



Meigs JB, Shrader P, Sullivan LM, McAteer JB, Fox CS, Dupuis J, Manning AK, Florez JC, Wilson PW, D'Agostino RB Sr, Cupples LA. Genotype score in addition to common risk factors for prediction of type 2 diabetes. N Engl J Med. 2008 Nov 20;359(21):2208-19

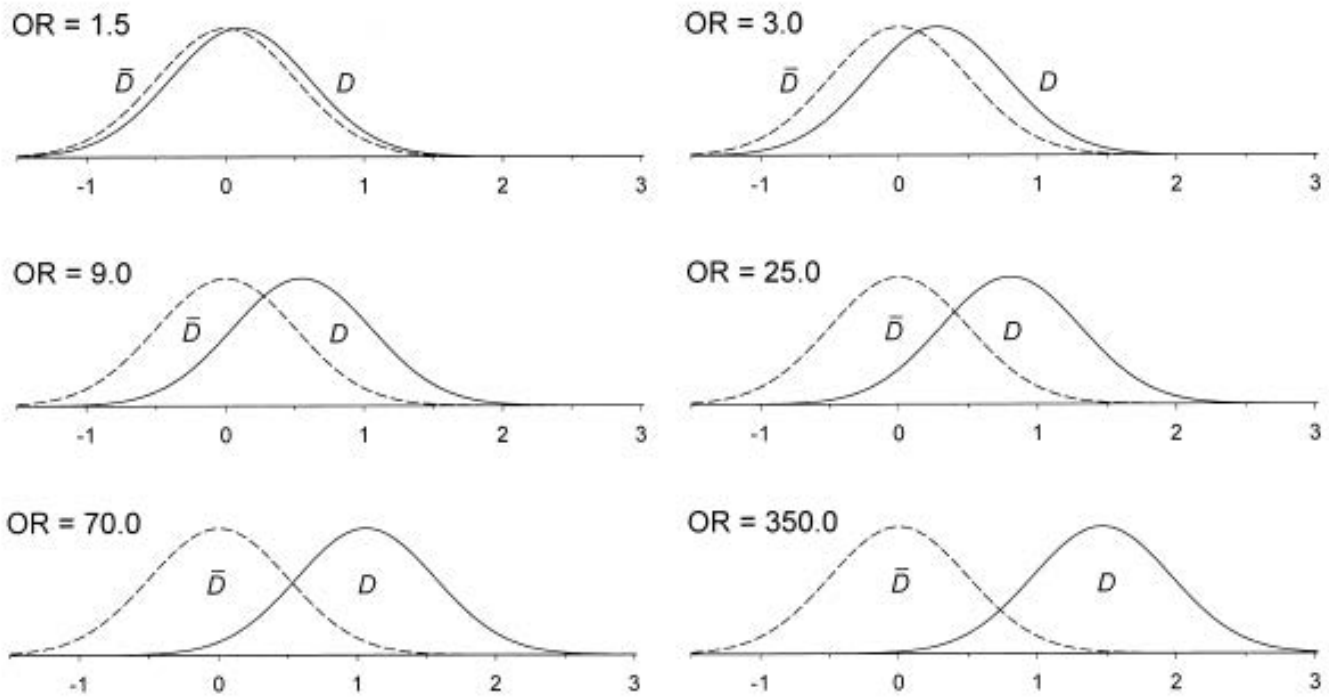
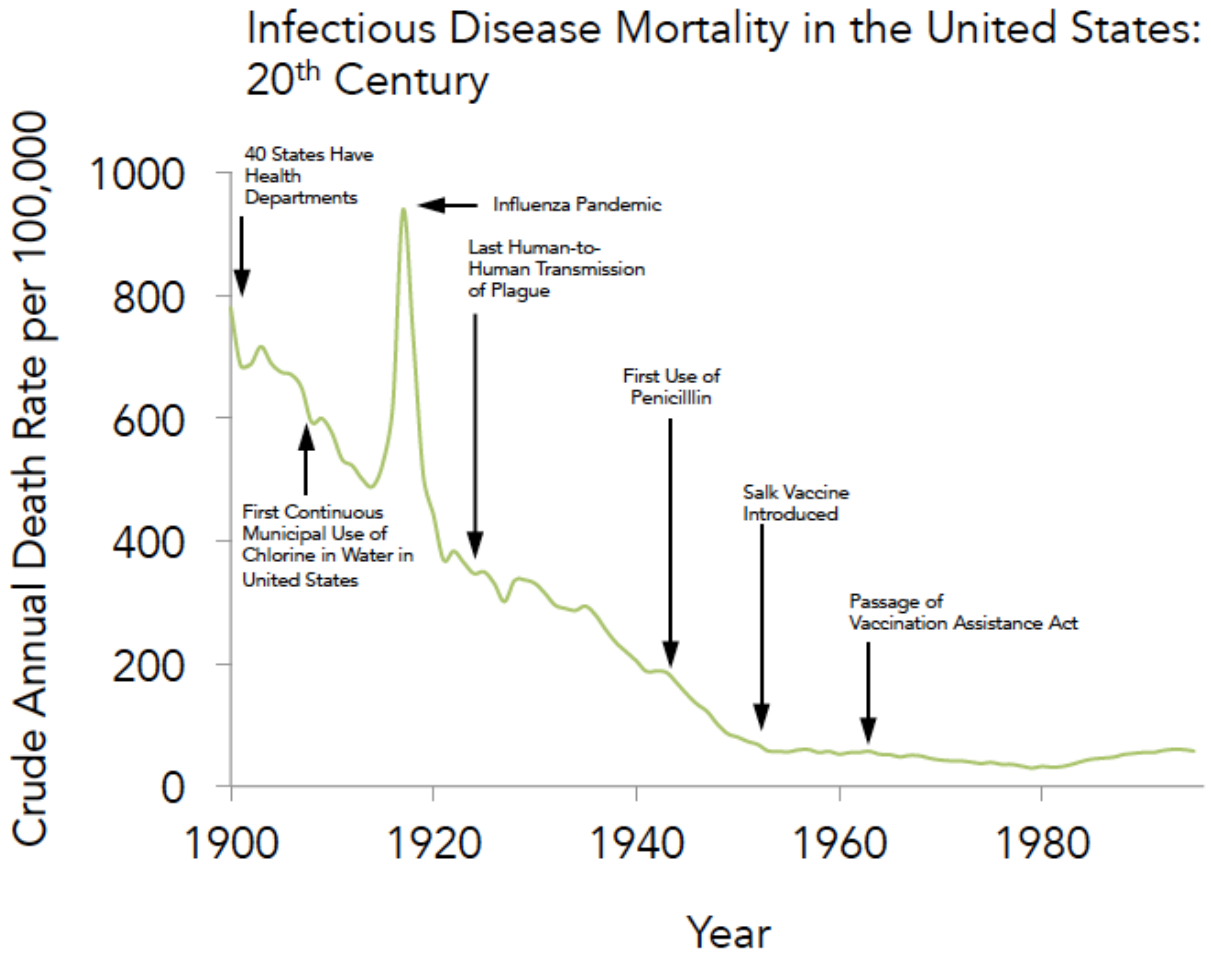
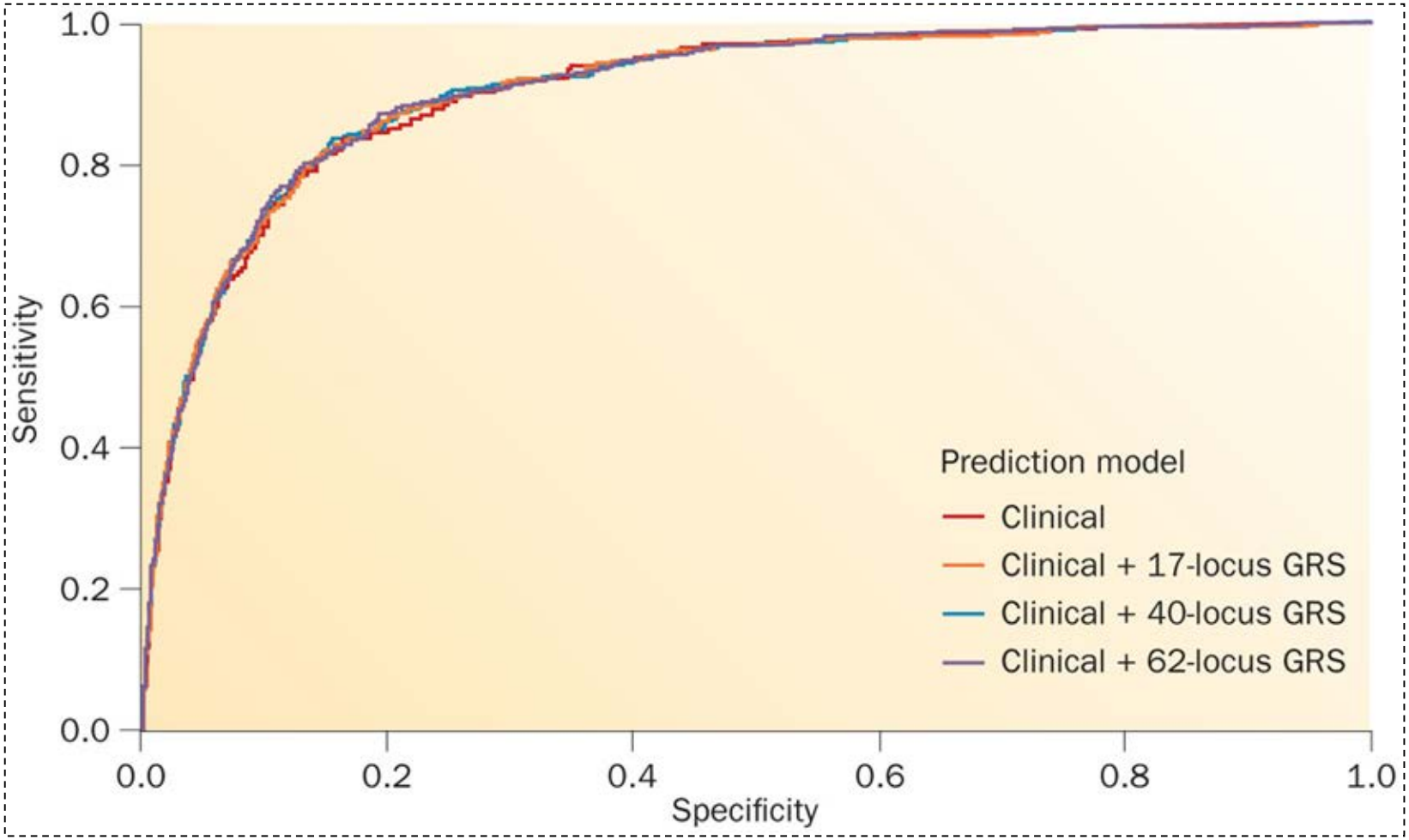


FIGURE 2. Probability distributions of a marker, X, in cases (solid curves) and controls (dashed curves) consistent with the logistic model $\text{logit}P(D = 1|X) = \alpha + \beta X$. It has been assumed that X has a mean of 0 and a standard deviation of 0.5 in controls so that a unit increase represents the difference between the 84th and 16th percentiles of X in controls. The marker is normally distributed, with the same variance in cases. The odds ratio (OR) per unit increase in X is shown.

Pepe MS, Janes H, Longton G, Leisenring W, Newcomb P. Limitations of the odds ratio in gauging the performance of a diagnostic, prognostic, or screening marker. American Journal of Epidemiology 2004; 159:882-890.


Infectious Disease Mortality in the United States: 20th Century
Crude Annual Death Rate per 100,000
1000
800
600
400
200
0
1900
1920
1940
1960
1980
Year
40 States Have Health Departments
Influenza Pandemic
Last Human-to-Human Transmission of Plague
First Use of Penicilllin
Salk Vaccine Introduced
Passage of Vaccination Assistance Act
First Continuous Municipal Use of Chlorine in Water in United States

Predicting diabetes



Hivert MF et al. Nat Rev Endocrinol, 2014; slide courtesy of Michael Joyner.

3. The fallacy of individual behavior change

ectations that such interventions could play a major role in motivating behaviour change to improve population health

Expectations that communicating DNA based risk estimates changes behaviour is not supported by existing evidence

ectations that such interventions could play a major role in motivating behaviour change to improve population health

This discussion is not academic. Three reasons why it matters.

1. Missing the important, on compelling distraction

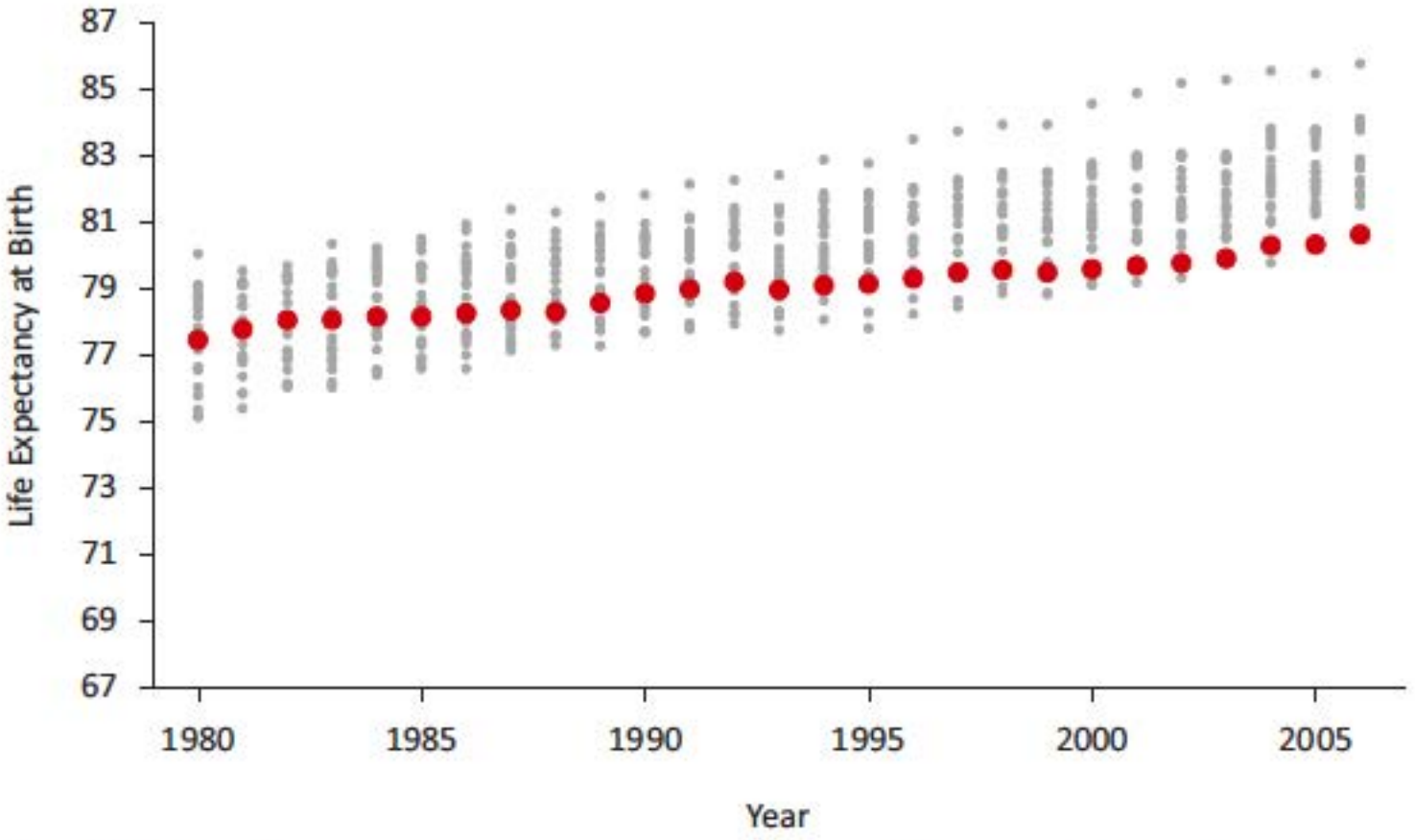


FIGURE 1-6 U.S. female life expectancy at birth relative to 21 other high-income countries, 1980-2006.

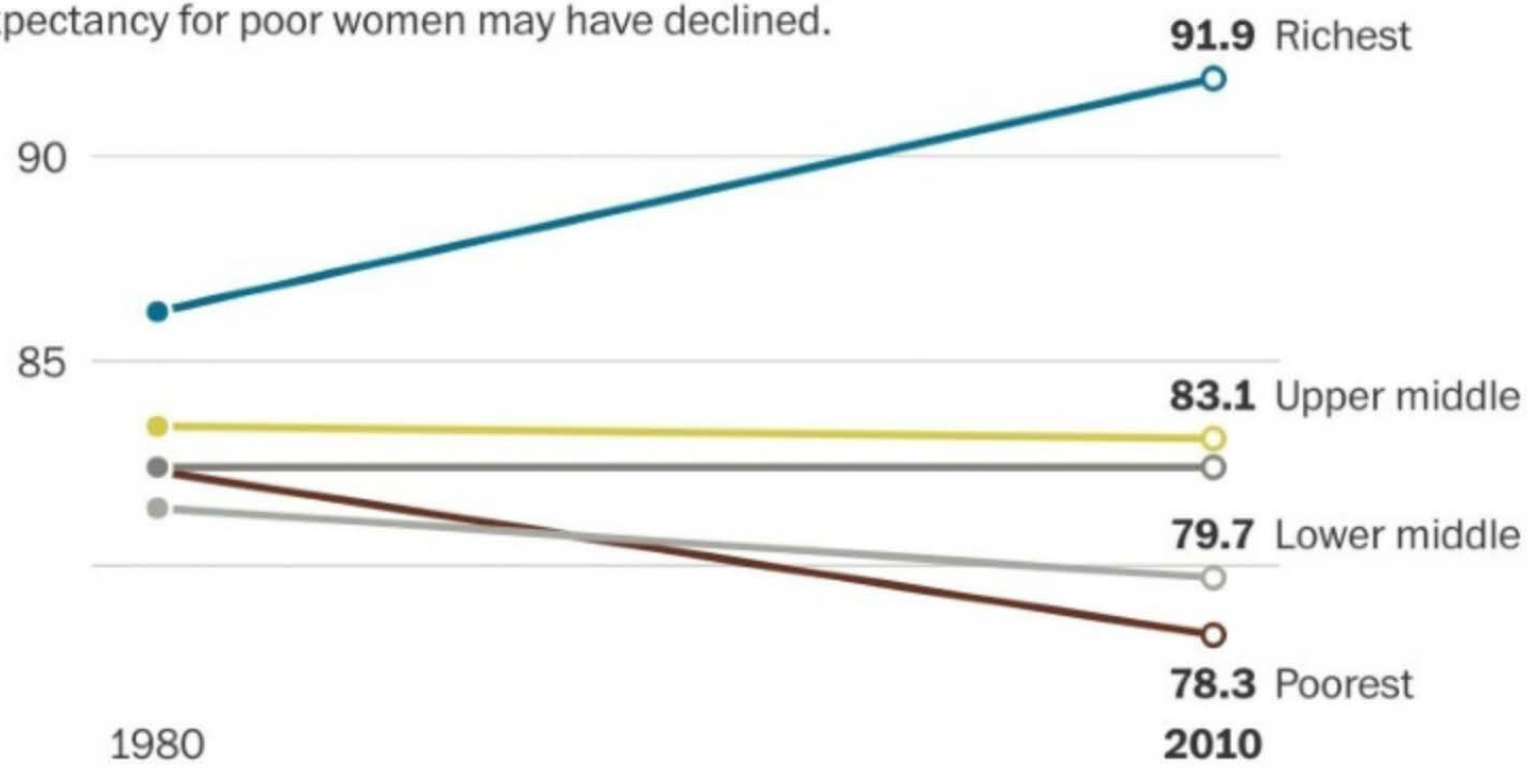
NOTES: Red circles depict newborn life expectancy in the United States. Grey circles depict life expectancy values for Australia, Austria, Belgium, Canada, Denmark, Finland, France, Iceland, Ireland, Italy, Japan, Luxembourg, the Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom, and West Germany.

SOURCE: National Research Council (2011, Figure 1-4).

US Health in International Perspective. Shorter lives, poorer health. S Woolf, L Aron, eds. NRC and IOM. 2012.

Inequality in life expectancy widens for women

Wealthier women can expect to live longer than their parents did, while life expectancy for poor women may have declined.

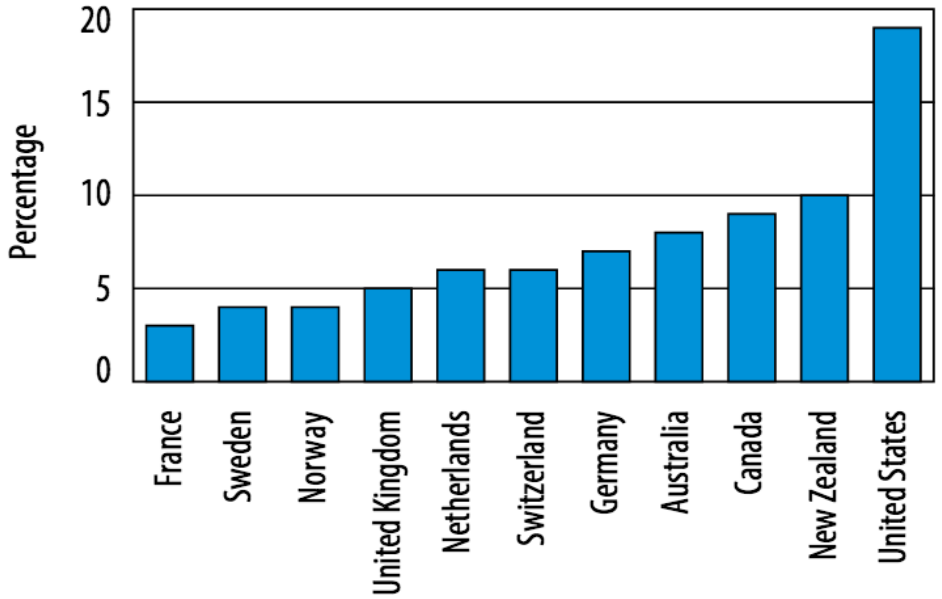


Life expectancy for 50-year-olds in a given year, by quintile of income over the previous 10 years

Source: National Academies of Science, Engineering and Medicine

National Academy of Medicine. The growing gap in life expectancy by income: Implications for federal programs and policy responses. 2015. http://www.nap.edu/download.php?record_id=19015#

Fig. 4.3. **Percentage of adults aged 65 years or older who had problems accessing health-care services during the past year due to their cost, 11 countries, 2014**

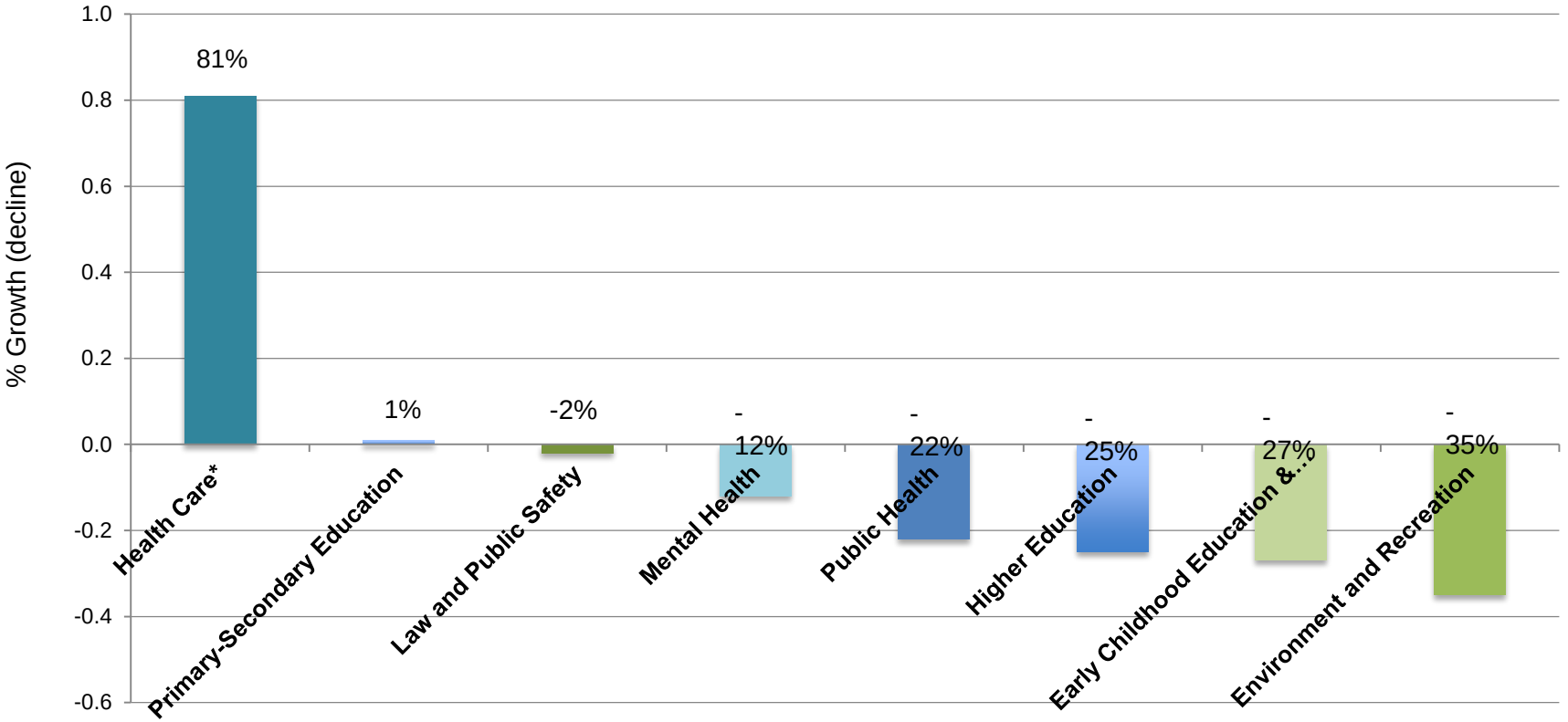


Note: Because of the cost, respondents with a medical problem did not visit a doctor, missed a medical test or treatment recommended by a doctor, did not fill out a prescription or missed a dose of medicine, or a combination of these.
Source: (*6*).

World Health Organization, "World Report on Ageing and Health."
<http://apps.who.int/iris/bitstream/10665/186463/1/9789240694811_eng.pdf?ua=1> Accessed March 25, 2016

2. Resource allocation, investing in the future

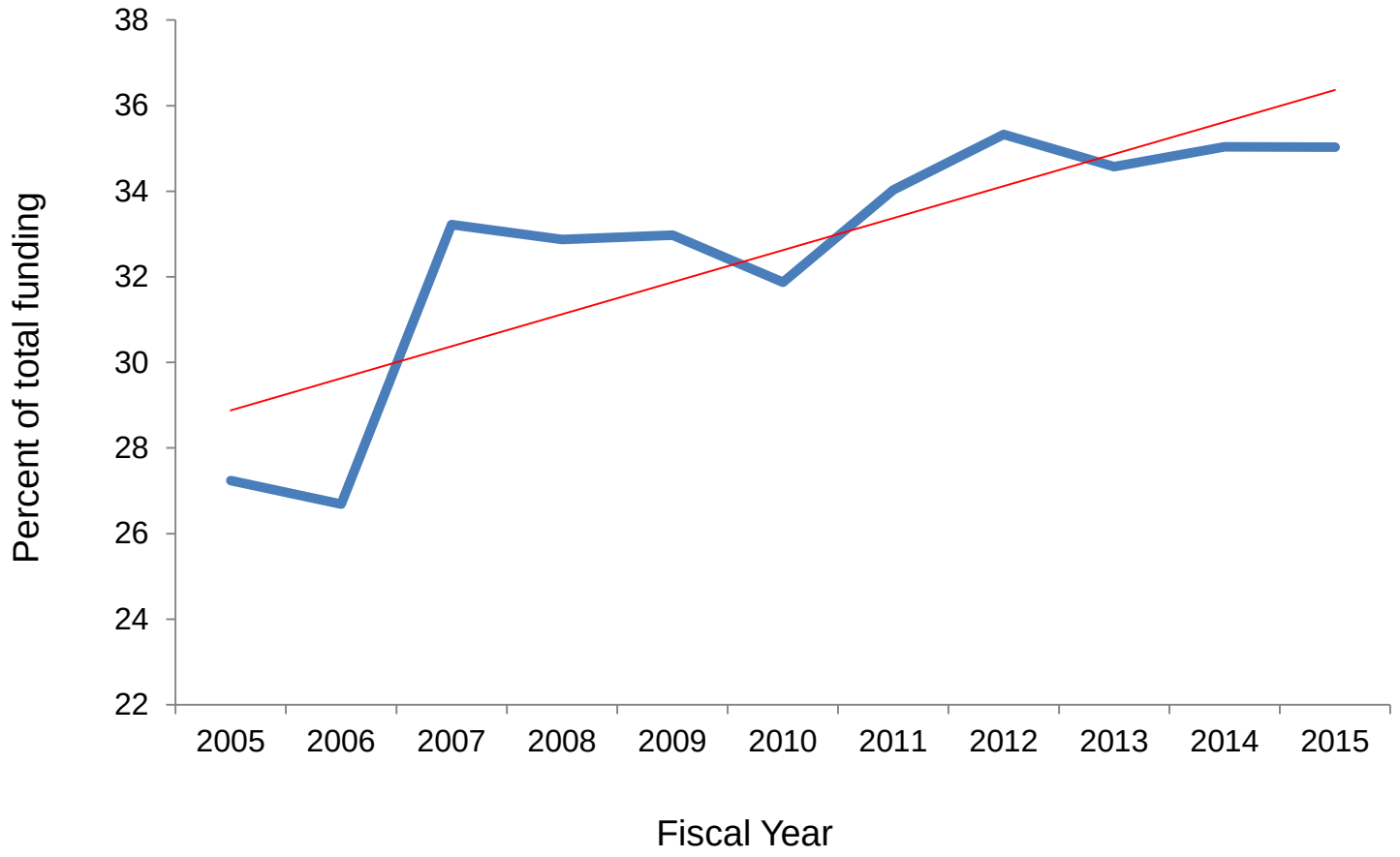
Change in Massachusetts State Government spending: 2001-14



* Health care expenditure is Group Insurance Commission spending plus MassHealth (Medicaid)

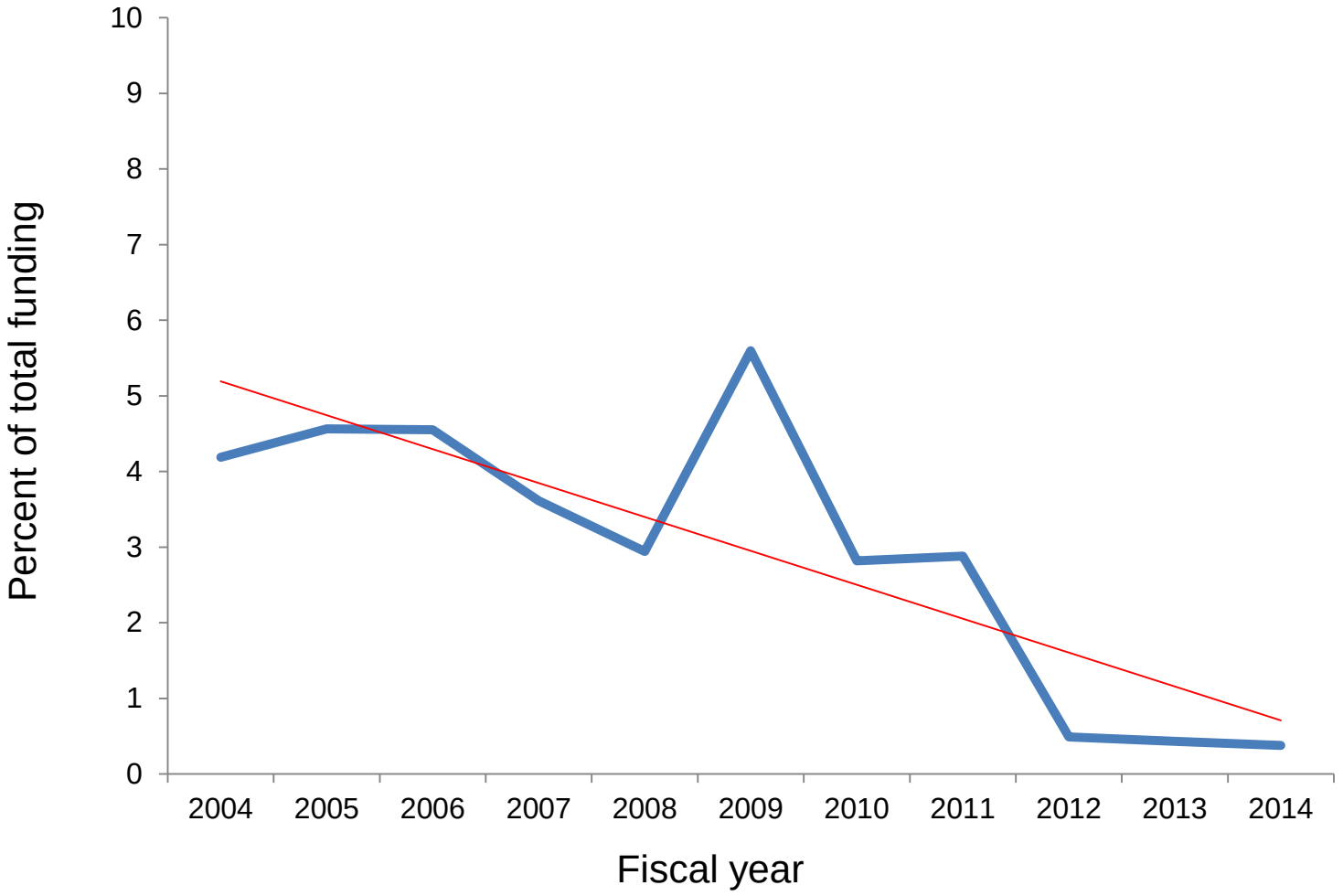
"Healthy People/Healthy Economy: An Initiative to Make Massachusetts the National Leader in Health and Wellness." 2015. Data from Massachusetts Budget and Policy Center Budget Browser. <http://www.tbf.org/tbf/56/hphe/Health-Crisis>

Proportion of NIH funding awarded to projects with the terms “genetic” or “genetics” in the title, abstract or terms



NIH RePORTER. Search results for projects for which funding data is available. <http://projectreporter.nih.gov/reporter.cfm> Accessed on November 20, 2014.

Proportion of NIH funding awarded to projects with the terms “population” or “public” in the title, abstract, or terms

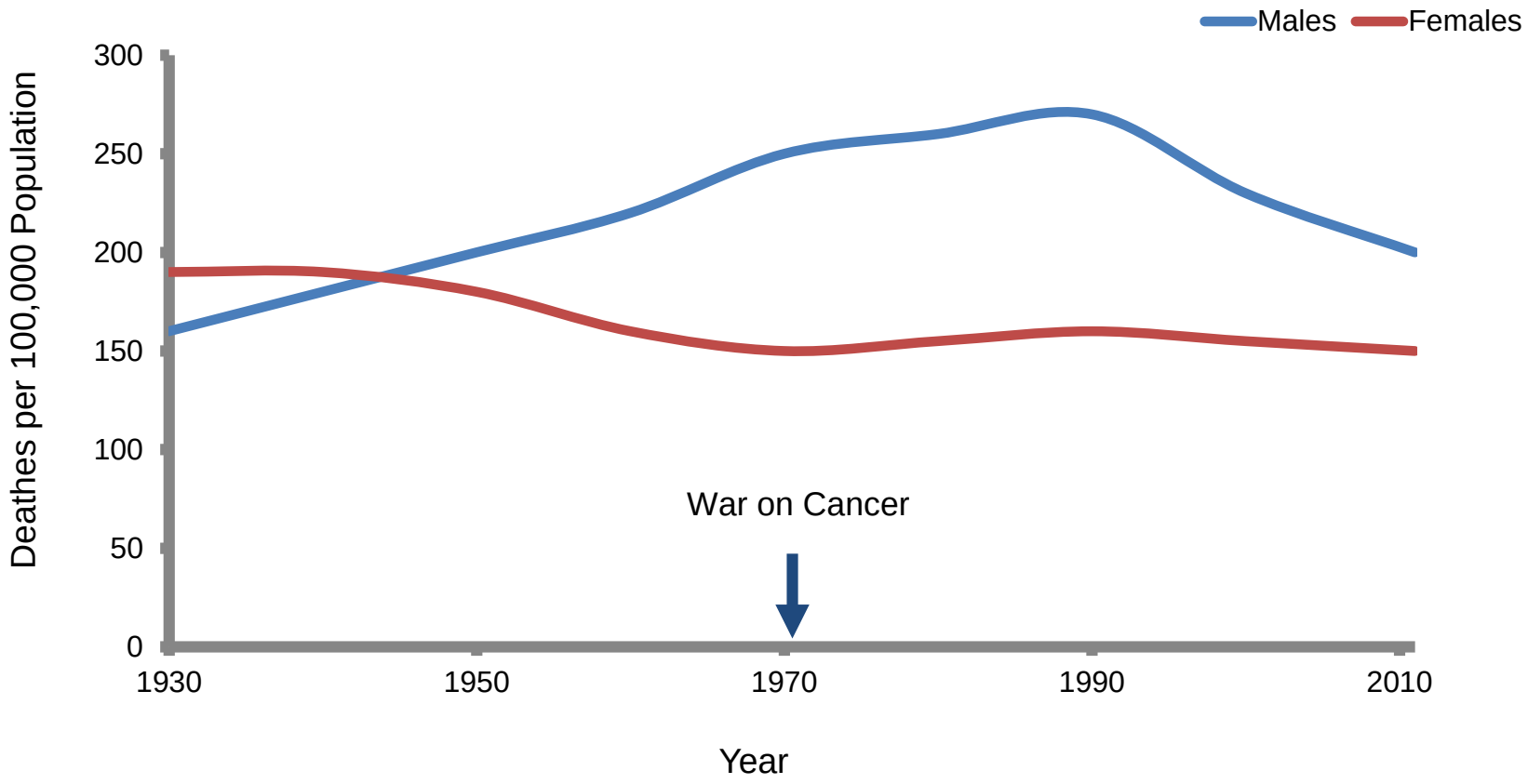


NIH RePORTER. Search results for projects for which funding data is available. <http://projectreporter.nih.gov/reporter.cfm> Accessed on November 20, 2014.

3. Hype over hope

“The time has come in America when the same kind of concentrated effort that split the atom and took man to the moon should be turned toward conquering this dread disease. Let us make a total national commitment to achieve this goal.”

President Richard Nixon, signing into law the National Cancer Act of 1971, December 1970



Siegel et al. Cancer statistics, 2014. CA Cancer J Clin (2014)

Slide courtesy of Michael Joyner

“Last year, Vice President Biden said that with a new moonshot, America can cure cancer . . . .Let’s make America the country that cures cancer once and for all.”

President Barak Obama, State of the Union address, January 2016

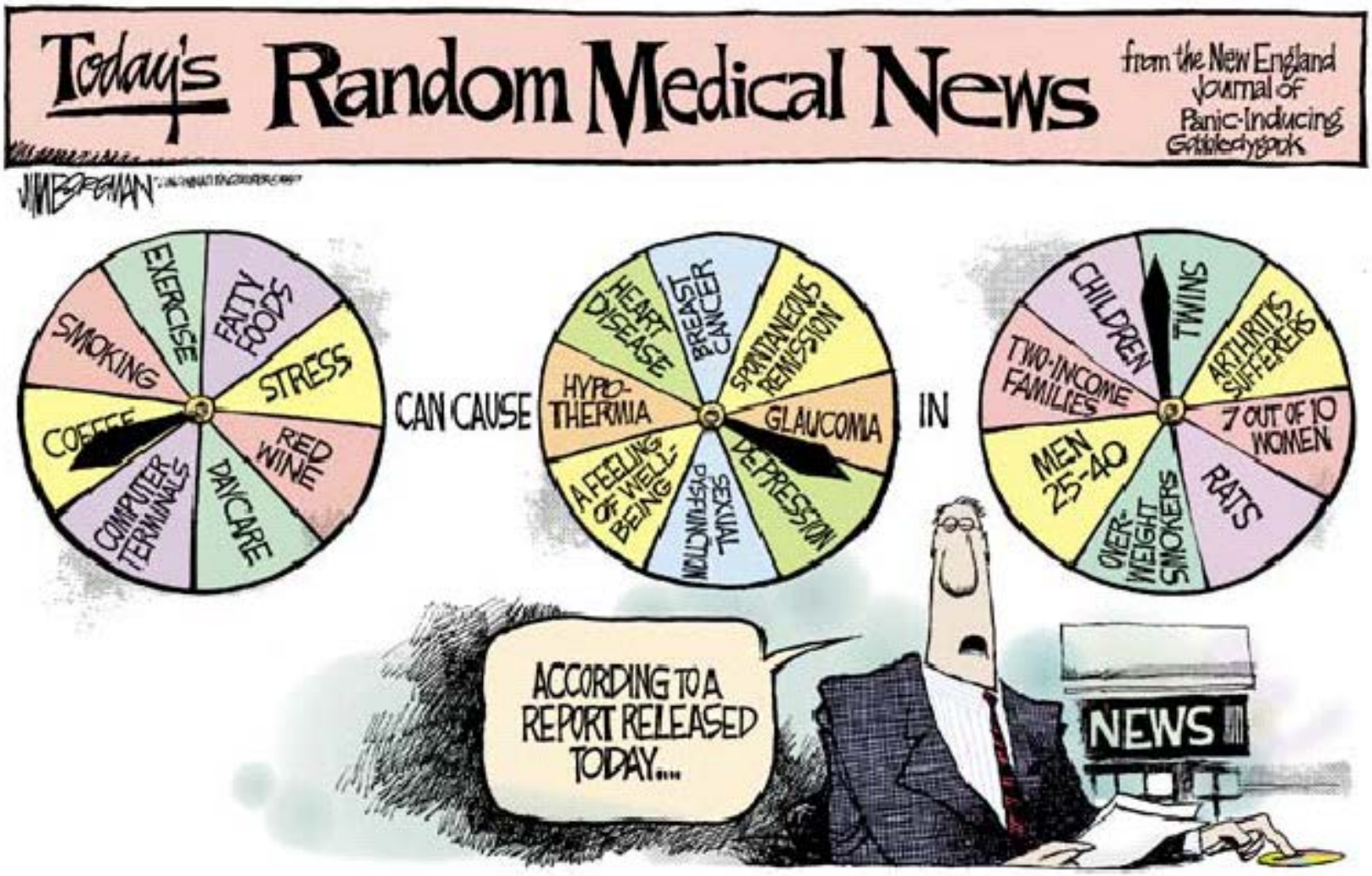
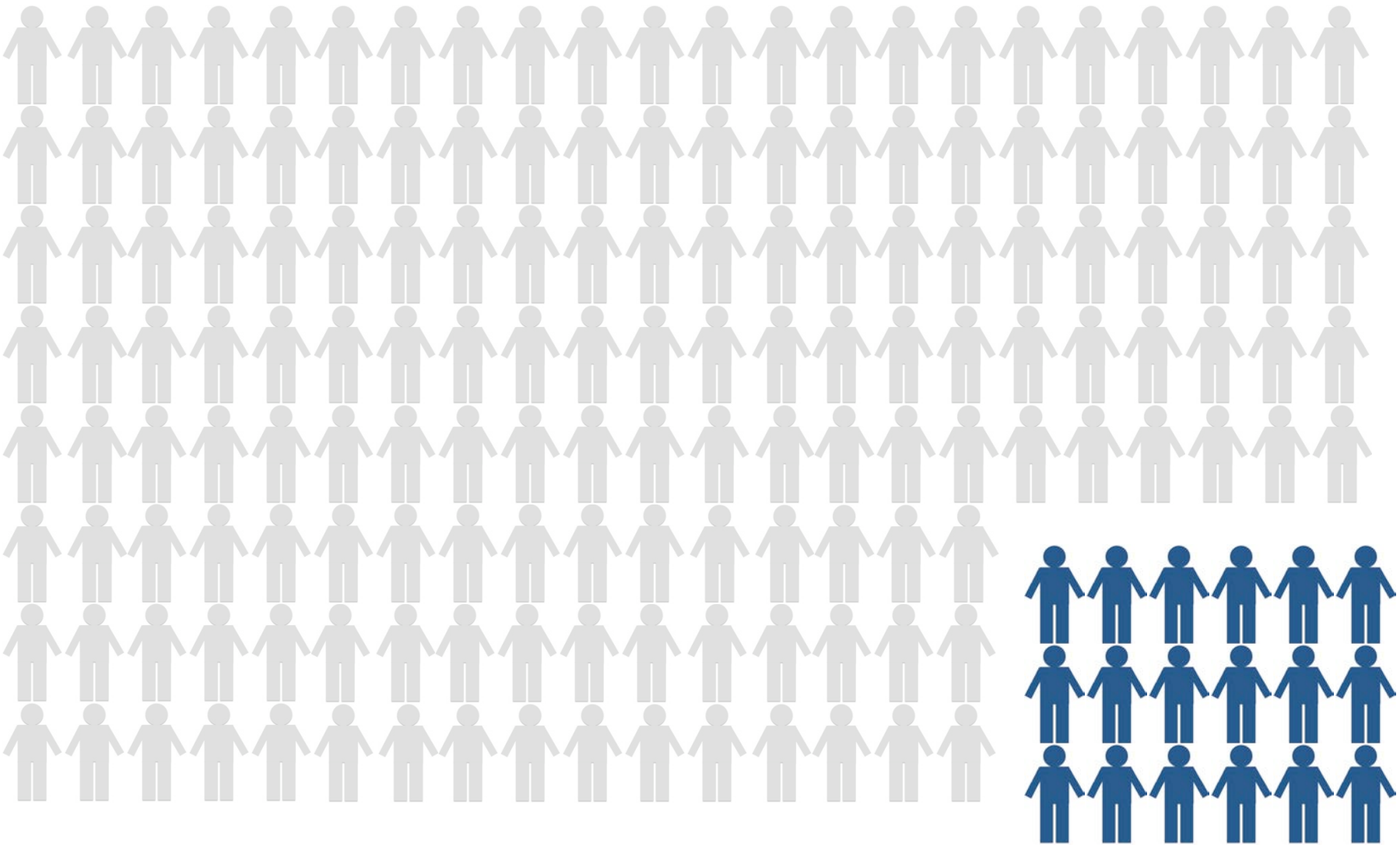


Figure 3: New England Journal of Panic-Inducing Gobbledygook.
Source: Jim Borgman, The Cincinnati Enquirer (27 April 1997, E4).

Unless.

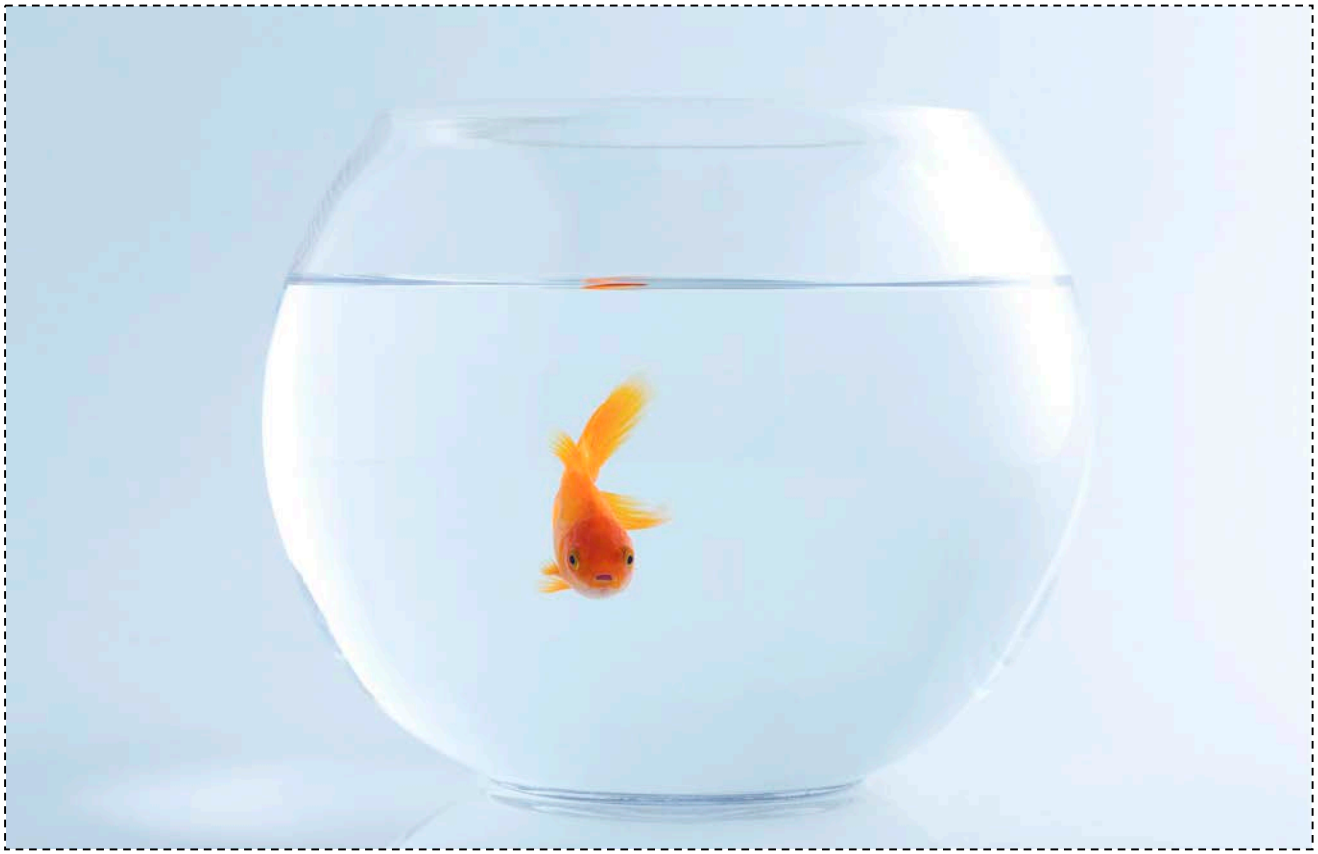
http://graphics8.nytimes.com/images/2009/03/11/opinion/13population.480.jpg



“I know this is a formidable technical task, one that may not be accomplished before the end of this century. Yet, current technology has attained a level of sophistication where it is reasonable for us to begin this effort. It will take years, probably decades, of effort on many fronts. There will be failures and setbacks just as there will be successes and breakthroughs. And as we proceed we must remain constant ….but isn't it worth every investment necessary….We know it is! ”

President Ronald Reagan announcing the launch of Star Wars, 1980.

"My loyal opposition wasn't loyal enough."



twitter/@sandrogalea

sgalea@bu.edu