From Synergy to Impact: A Vision for An OHDSI-CISNET Partnership

Ruth Etzioni

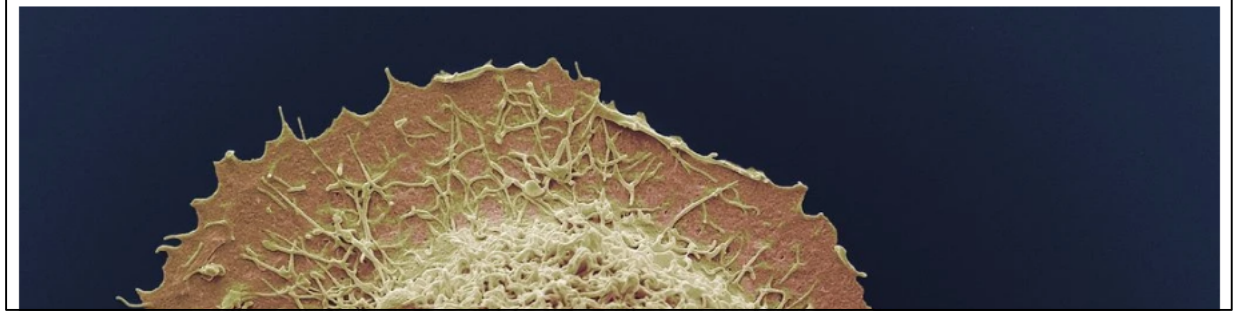
Fred Hutch Cancer Center

Knight Cancer Institute

The New York Times

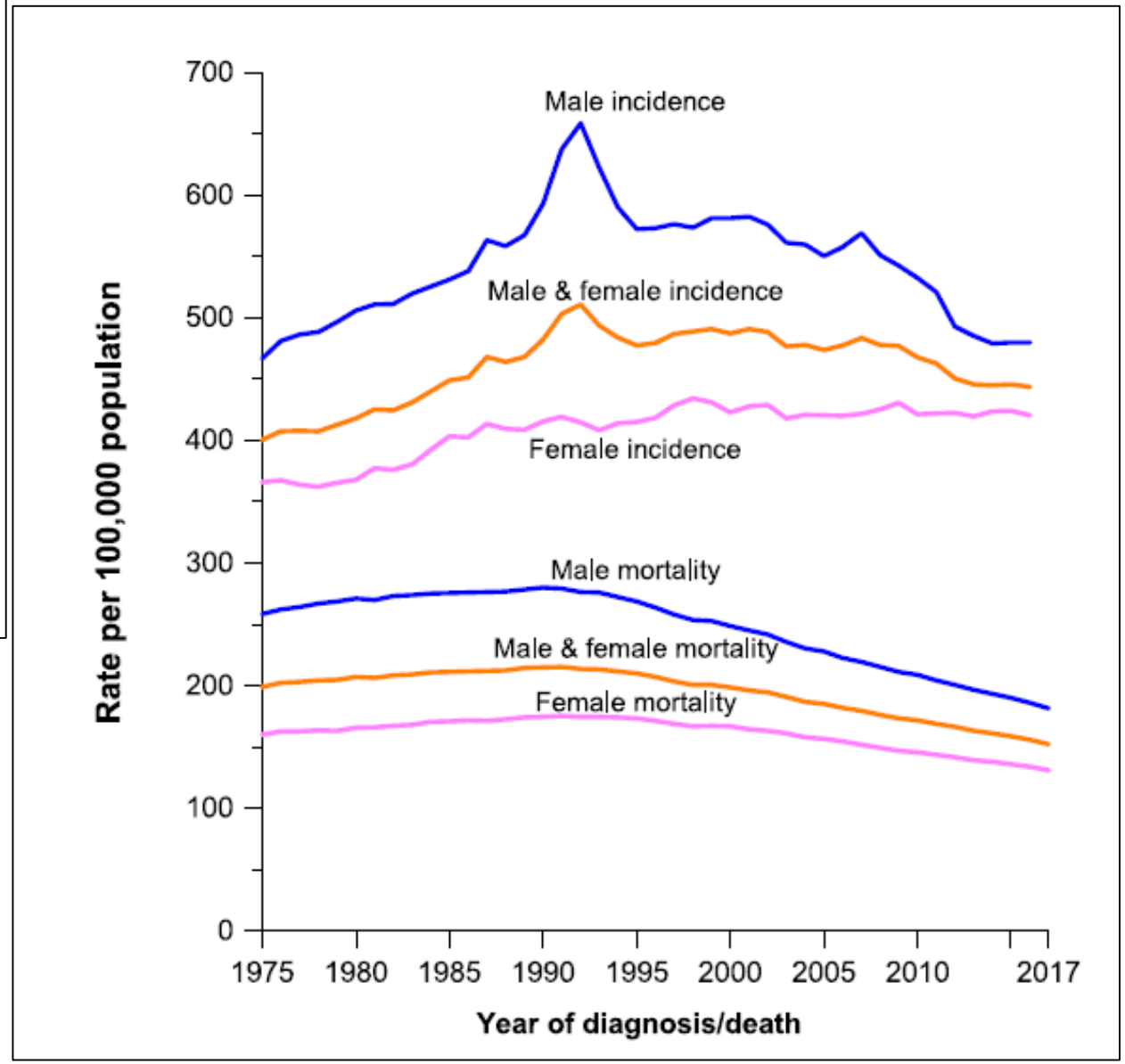
Cancer Death Rate in U.S. Sees Sharpest One-Year Drop

Breakthrough treatments for lung cancer and melanoma have driven down cancer mortality overall — and from 2016 to 2017 spurred the largest-ever decline.

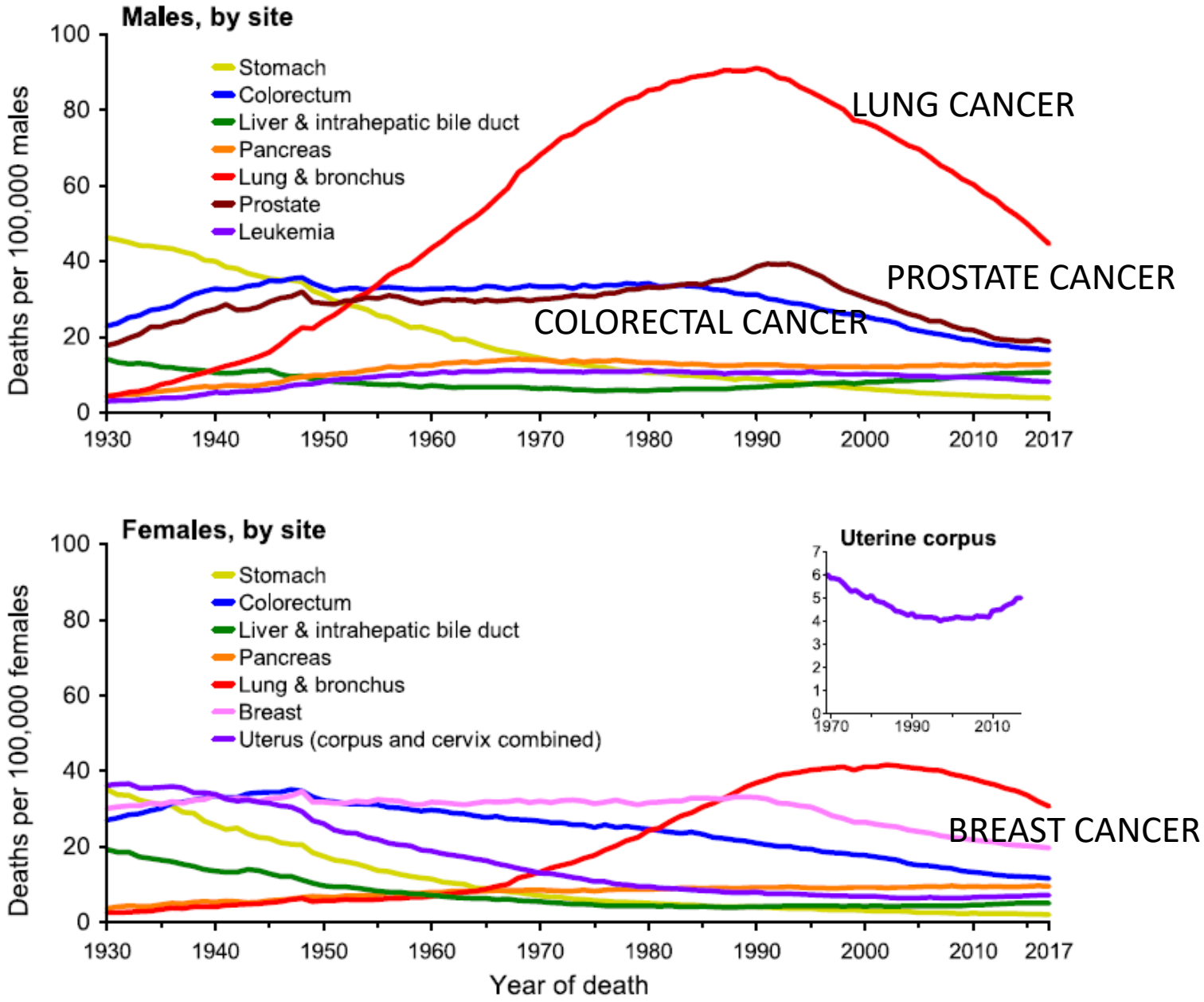


Cancer Statistics, 2020

Rebecca L. Siegel, MPH [1]; Kimberly D. Miller, MPH [1]; Ahmedin Jemal, DVM, PhD [1]



Mortality by site



Cancer Statistics, 2020

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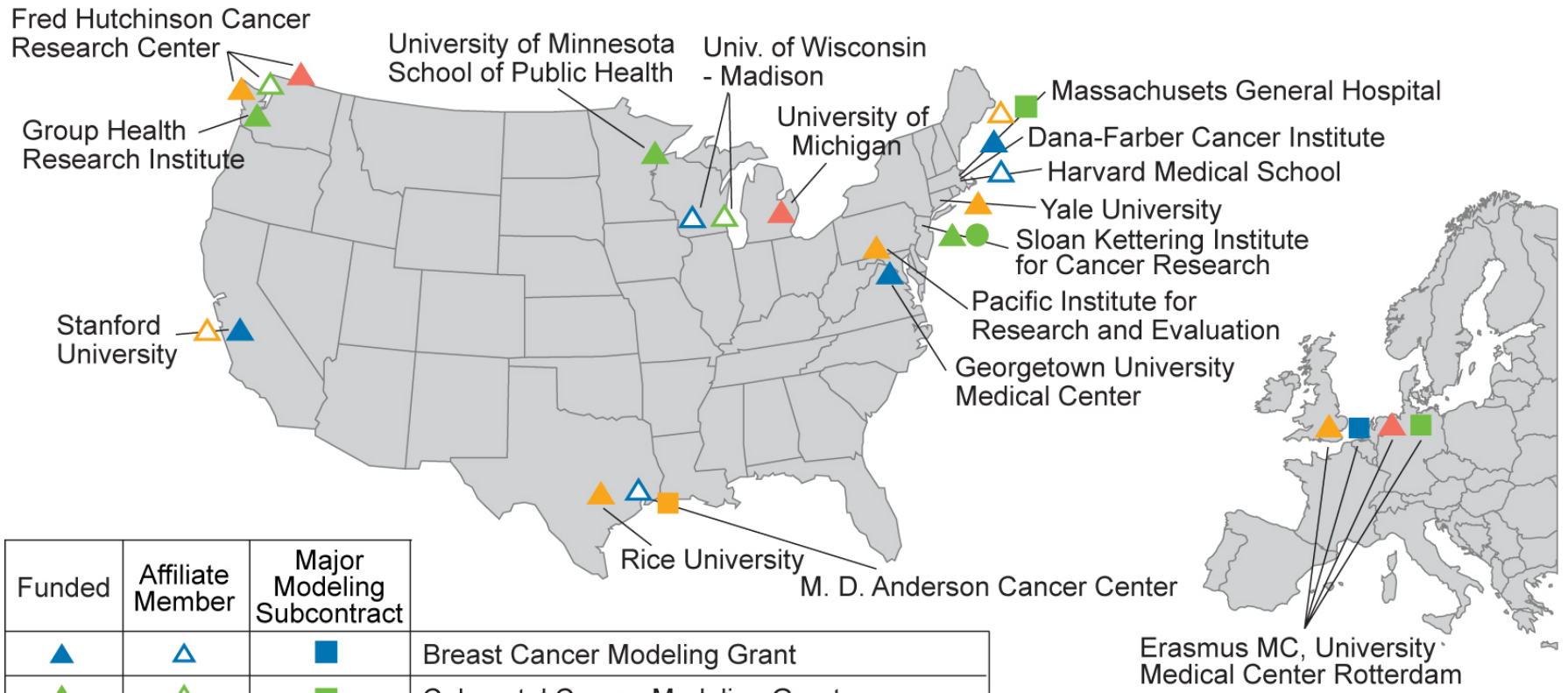
What is CISNET?

- NCI Sponsored Collaborative Consortium (U01) of simulation modelers in Breast, Prostate, Colorectal, Lung, Esophagus, and Cervical cancers formed in 2000
- Formed to learn about the drivers of population trends in cancer incidence and mortality
- Extend evidence provided by trial, epidemiologic, and surveillance data using disease modeling to guide public health research and priorities

CISNET sites



Funded	Affiliate Member	Major Modeling Subcontract	
▲	△	■	Breast Cancer Modeling Grant
▲	△	■	Colorectal Cancer Modeling Grant
●			Colorectal Cancer Coordinating Center Grant
▲	△	■	Lung Cancer Modeling Grant
▲			Prostate Cancer Modeling Grant

The New York Times

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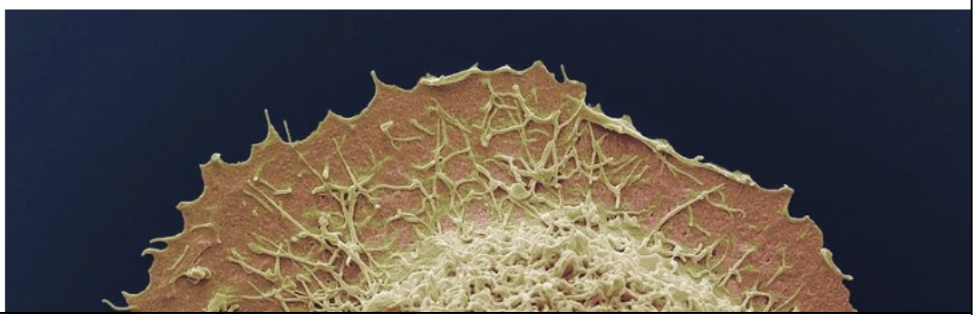
Breakthrough treatments for lung cancer and melanoma have driven down cancer mortality overall — and from 2016 to 2017 spurred the largest-ever decline.



Experts attributed the decline to the reduced smoking rates and to advances in lung cancer treatment. New therapies for melanoma of the skin have also helped extend life for many people with metastatic disease, or cancer that has spread to other parts of the body.

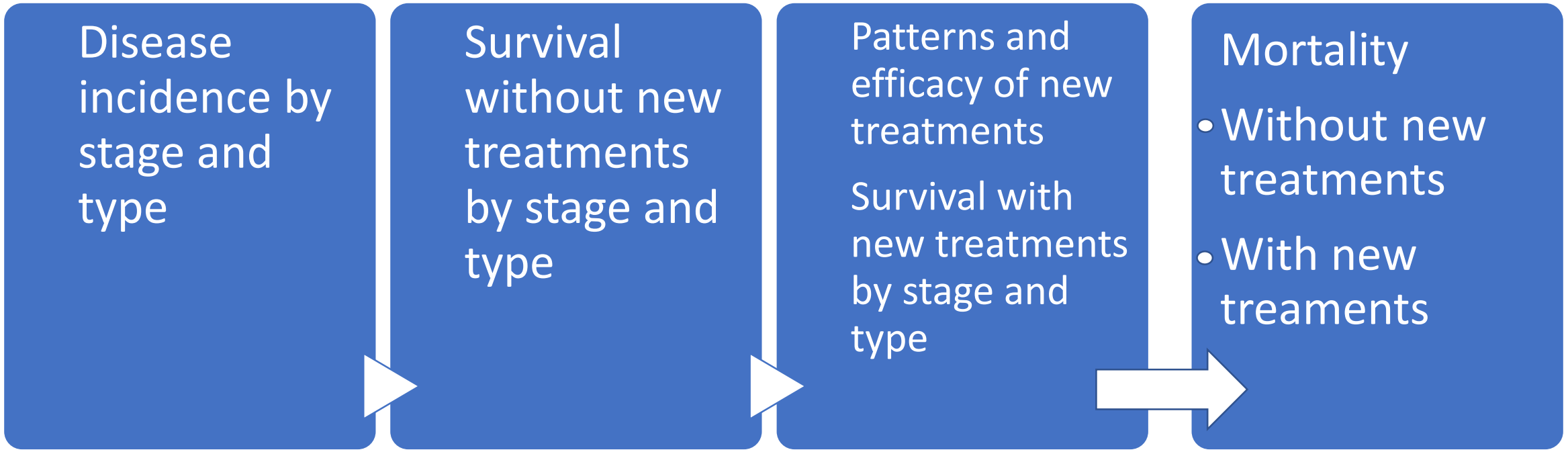
Progress has slowed for colorectal, breast and prostate cancers, however.

The rising rate of obesity among Americans, as well as significant racial and geographic disparities, likely explain why the decline in breast and colorectal cancer death rates has begun to taper off, and why the decrease in rates of prostate cancer has halted entirely.

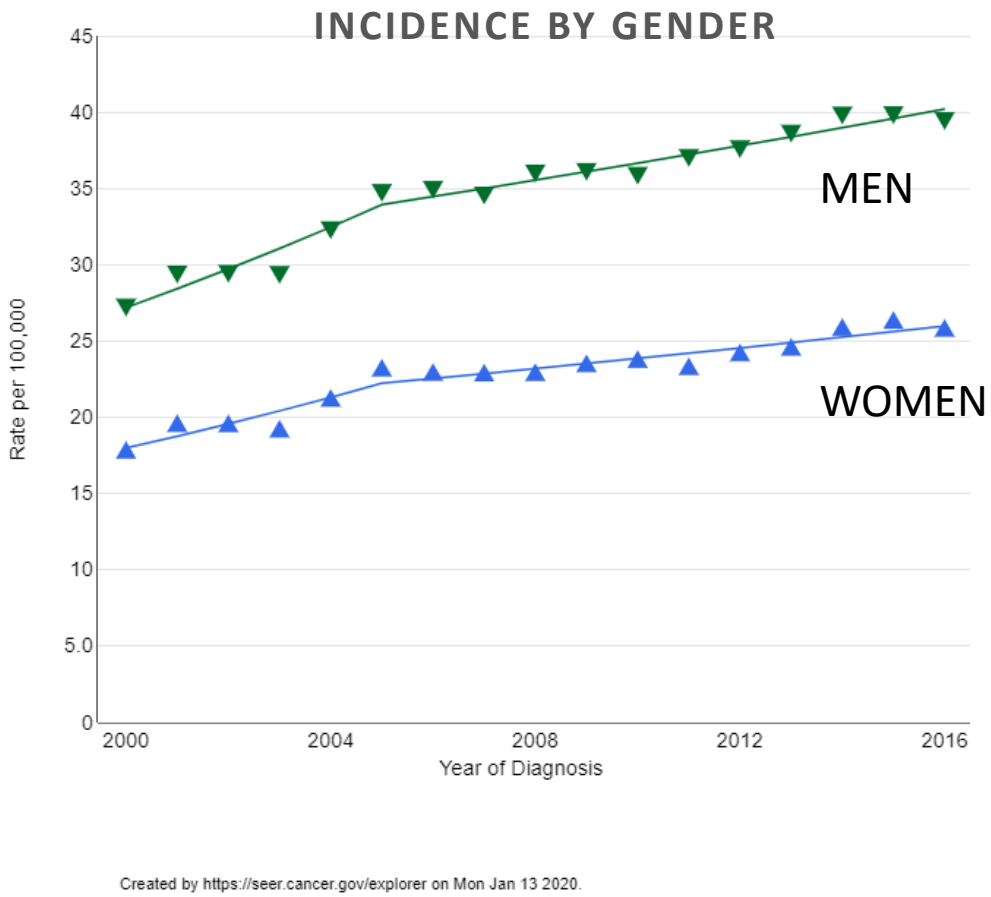
How would you check whether advances in treatment explain mortality declines?

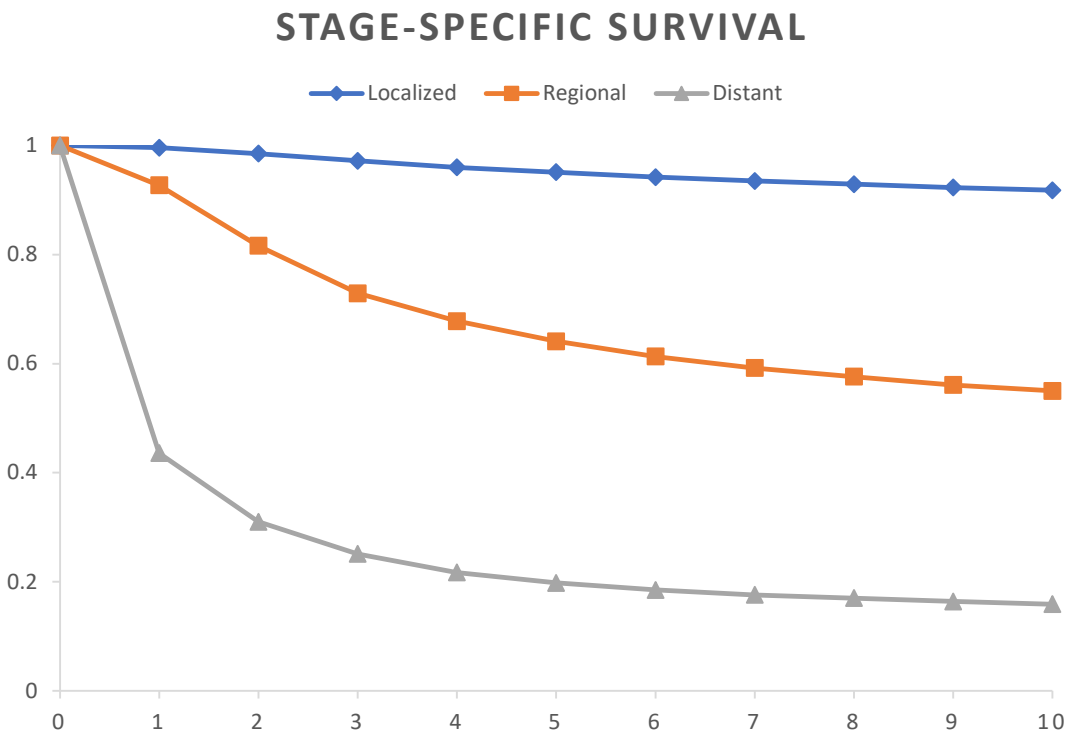
Why is this of interest ?

How would you check whether advances in treatment explain mortality declines?



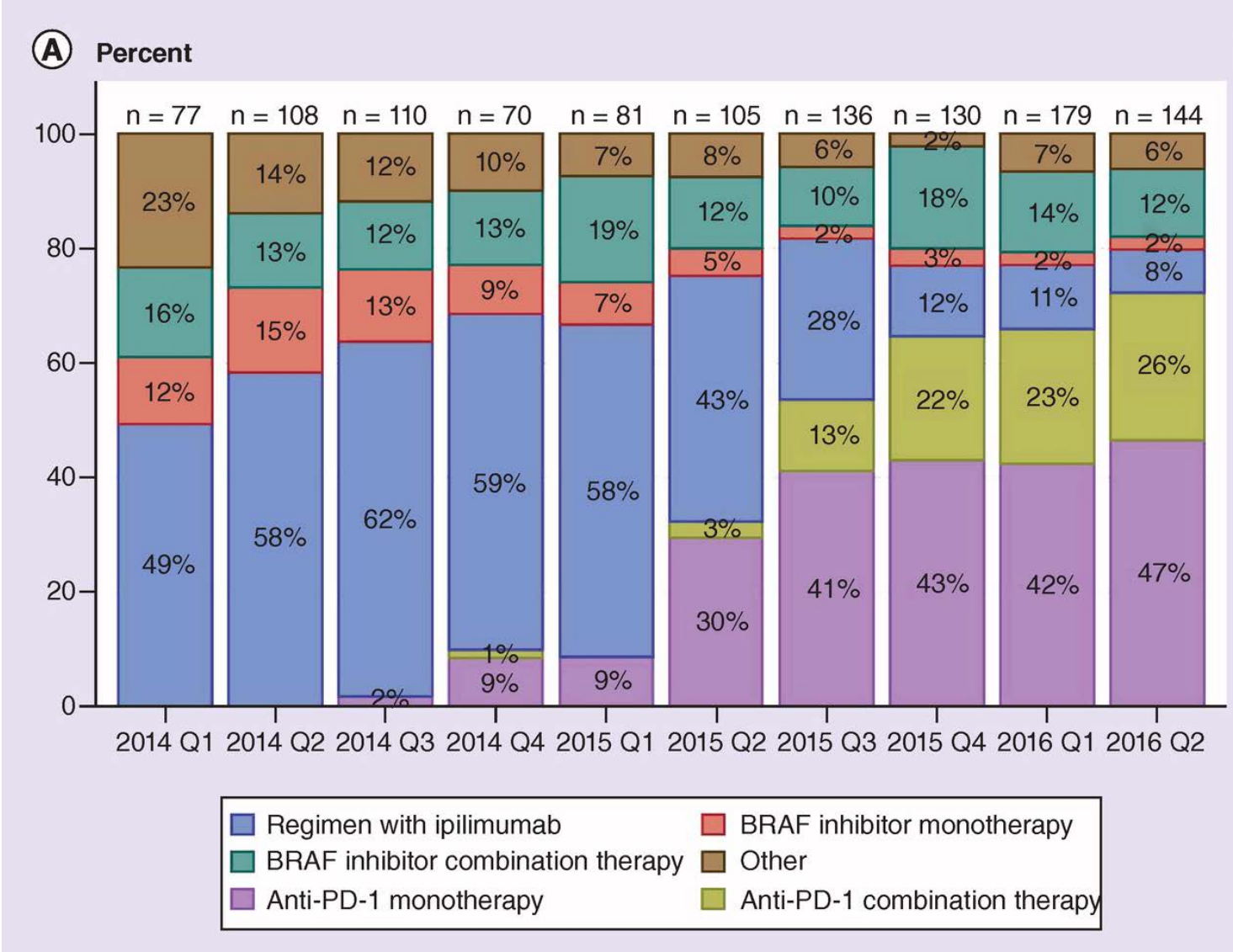
Example: Melanoma





Source: SEER

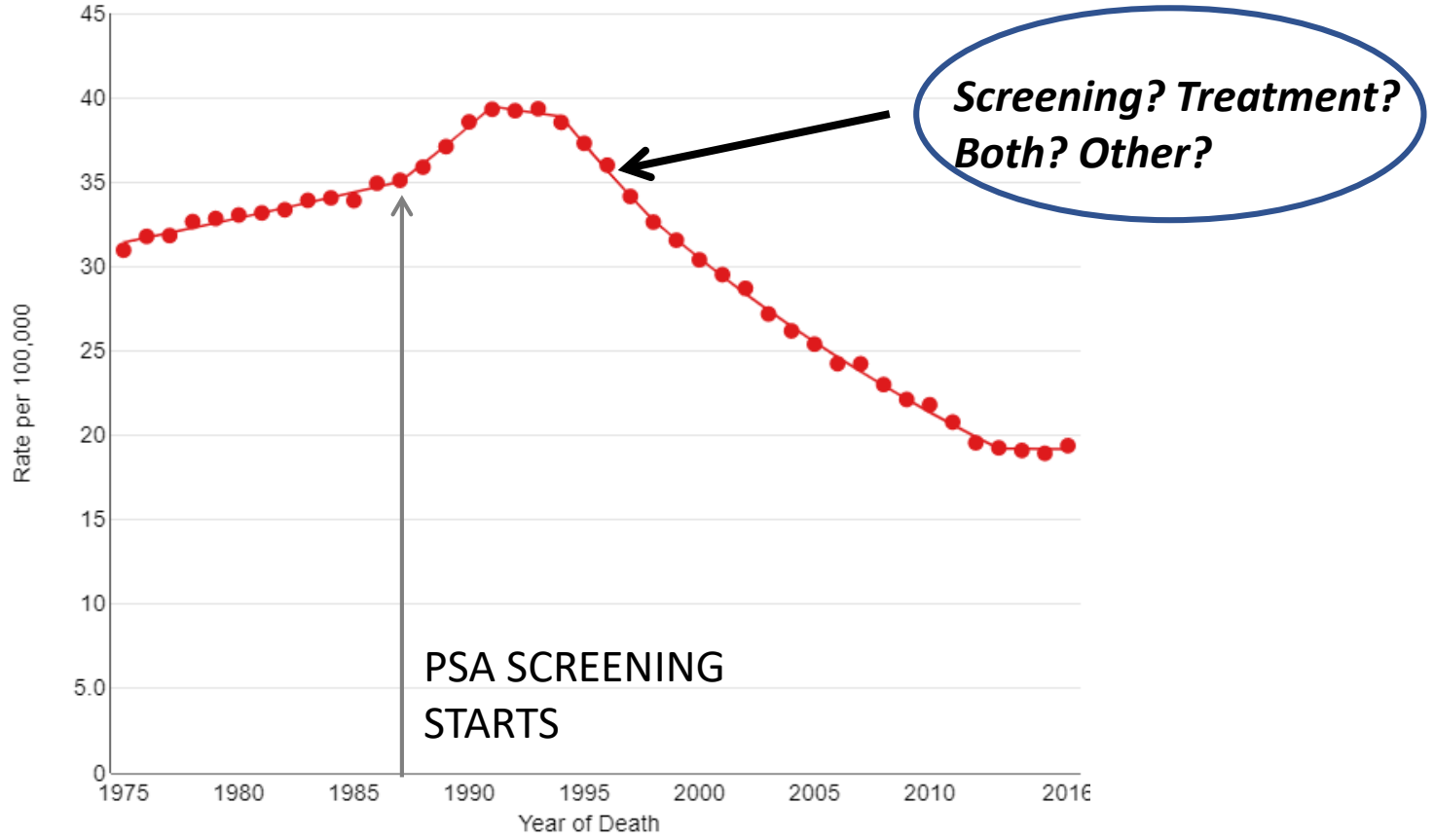
Melanoma Treatments 2014-2016



Flatiron data: Whitman et al, Future Oncol, Feb 2019

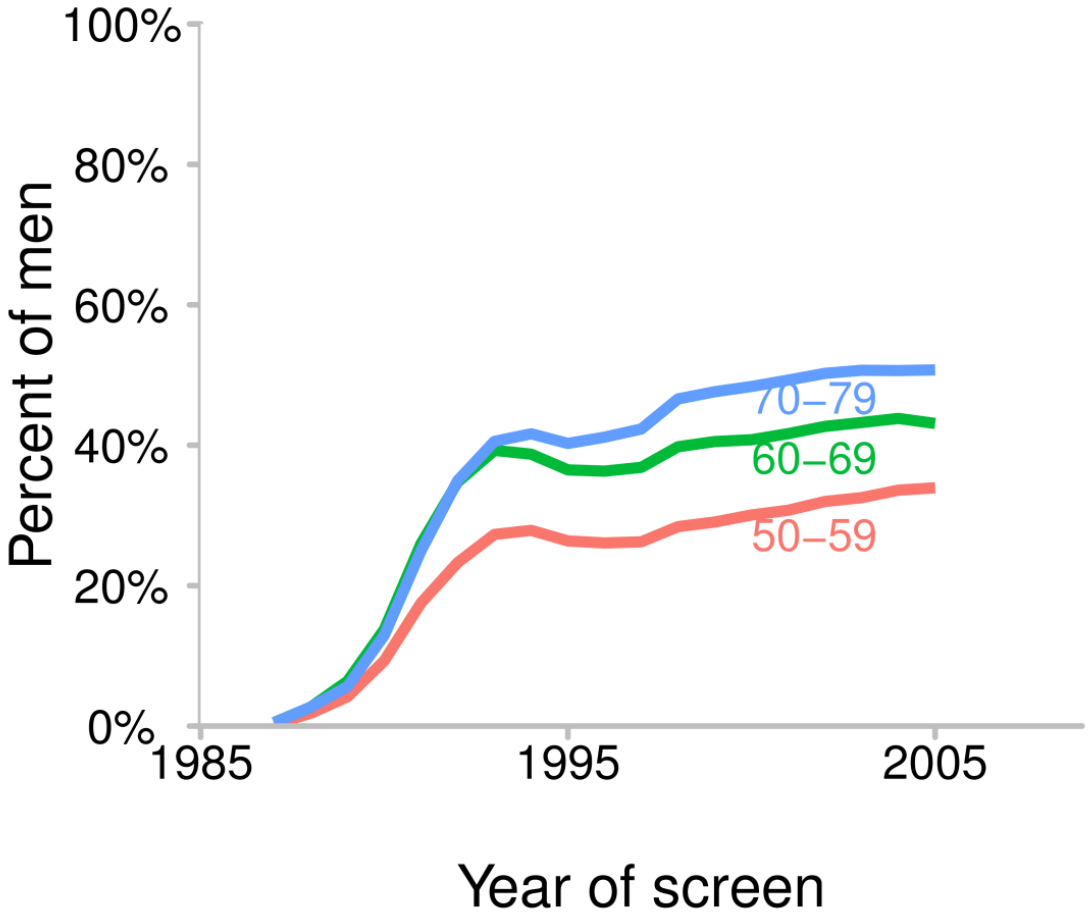
What explains prostate cancer mortality declines?

Age-adjusted Prostate Cancer Mortality
1975-2016



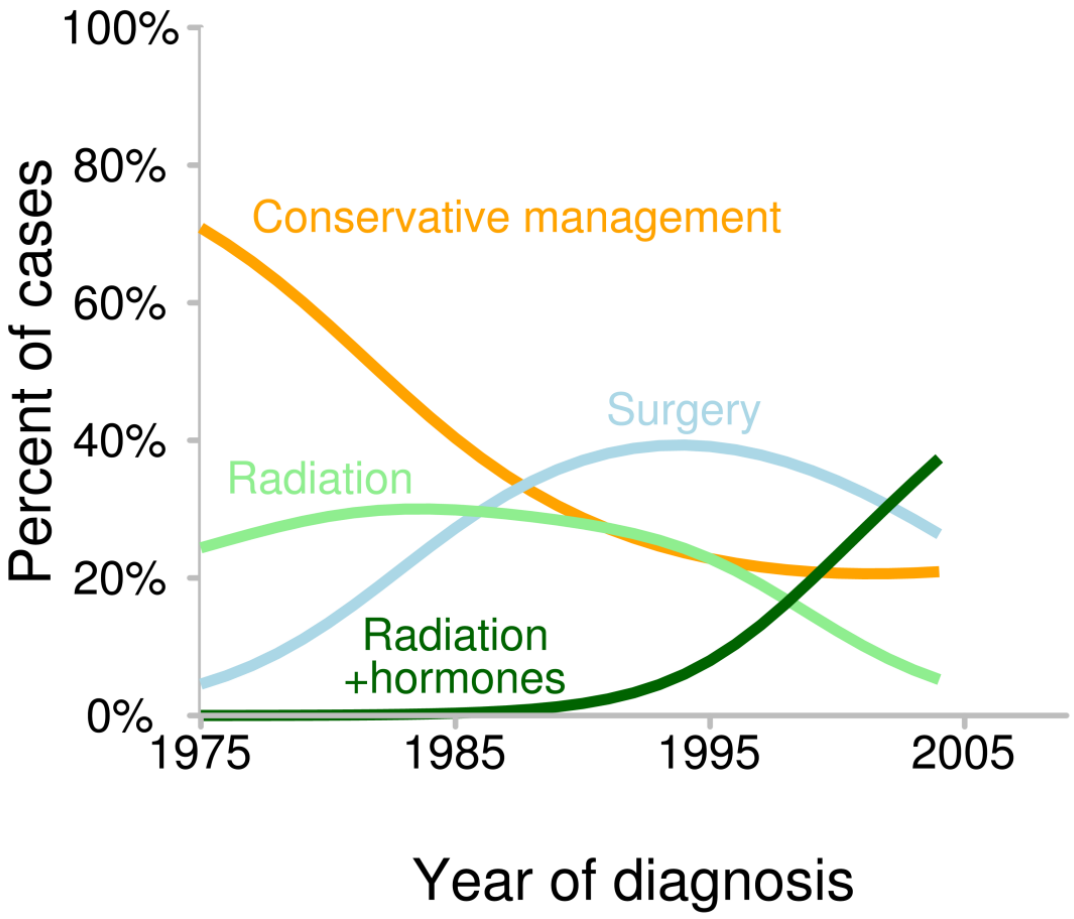
Screening and treatment dissemination

PSA screening



Mariotto et al., Cancer, 2007: NHIS and SEER-Medicare data

Initial treatments

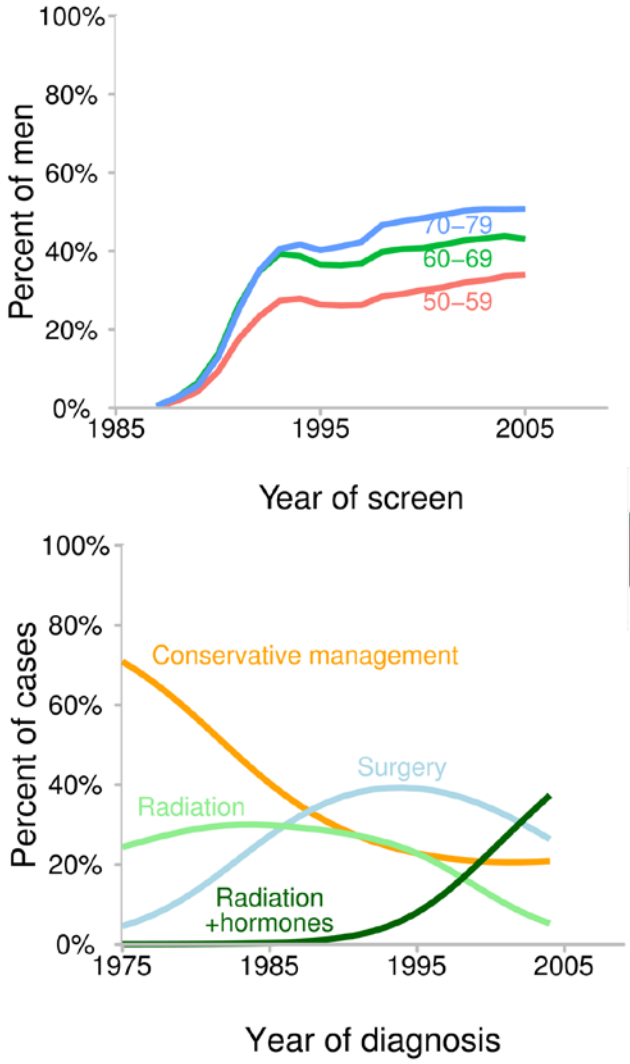


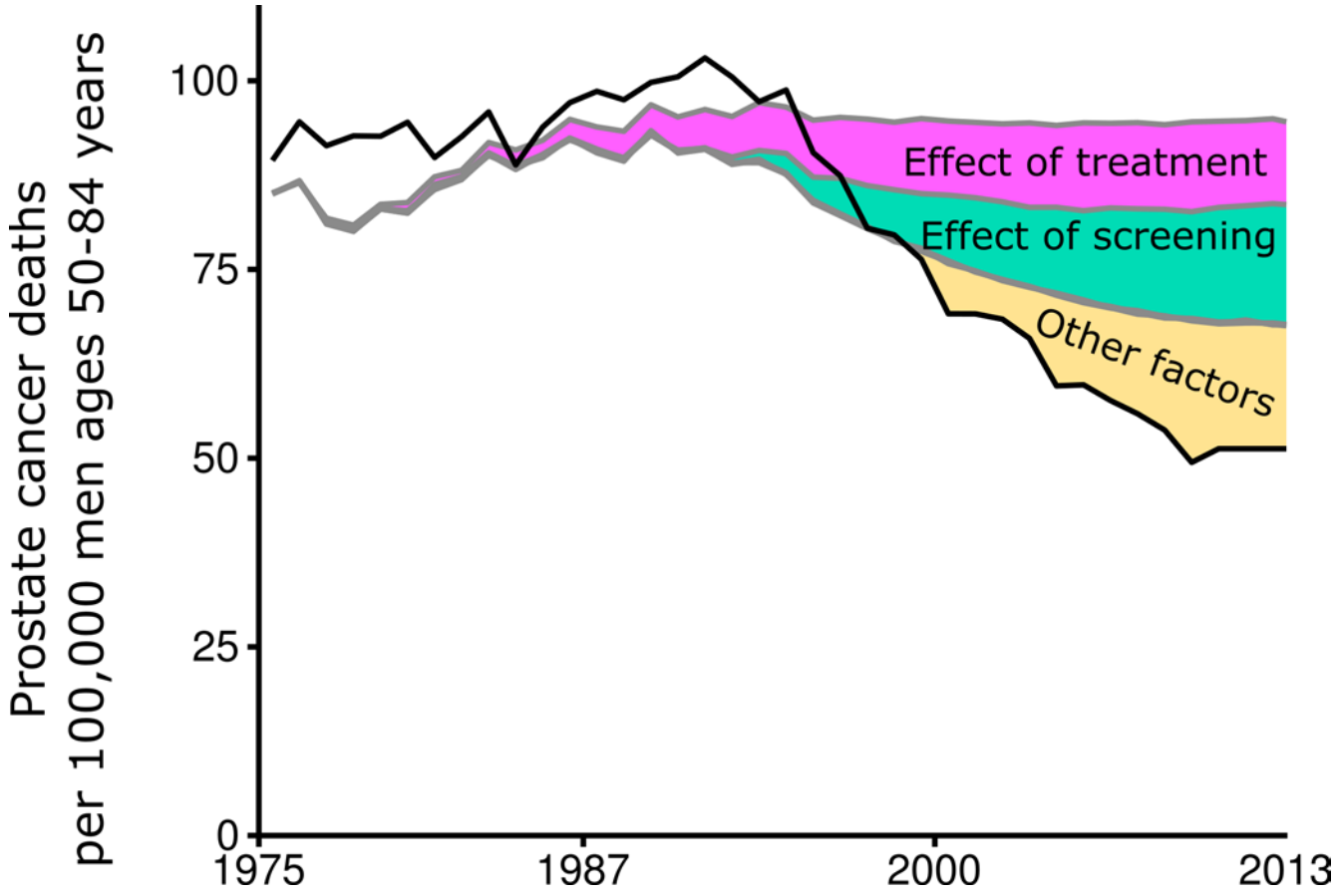
SEER and CaPSURE data

Steps to answer this question

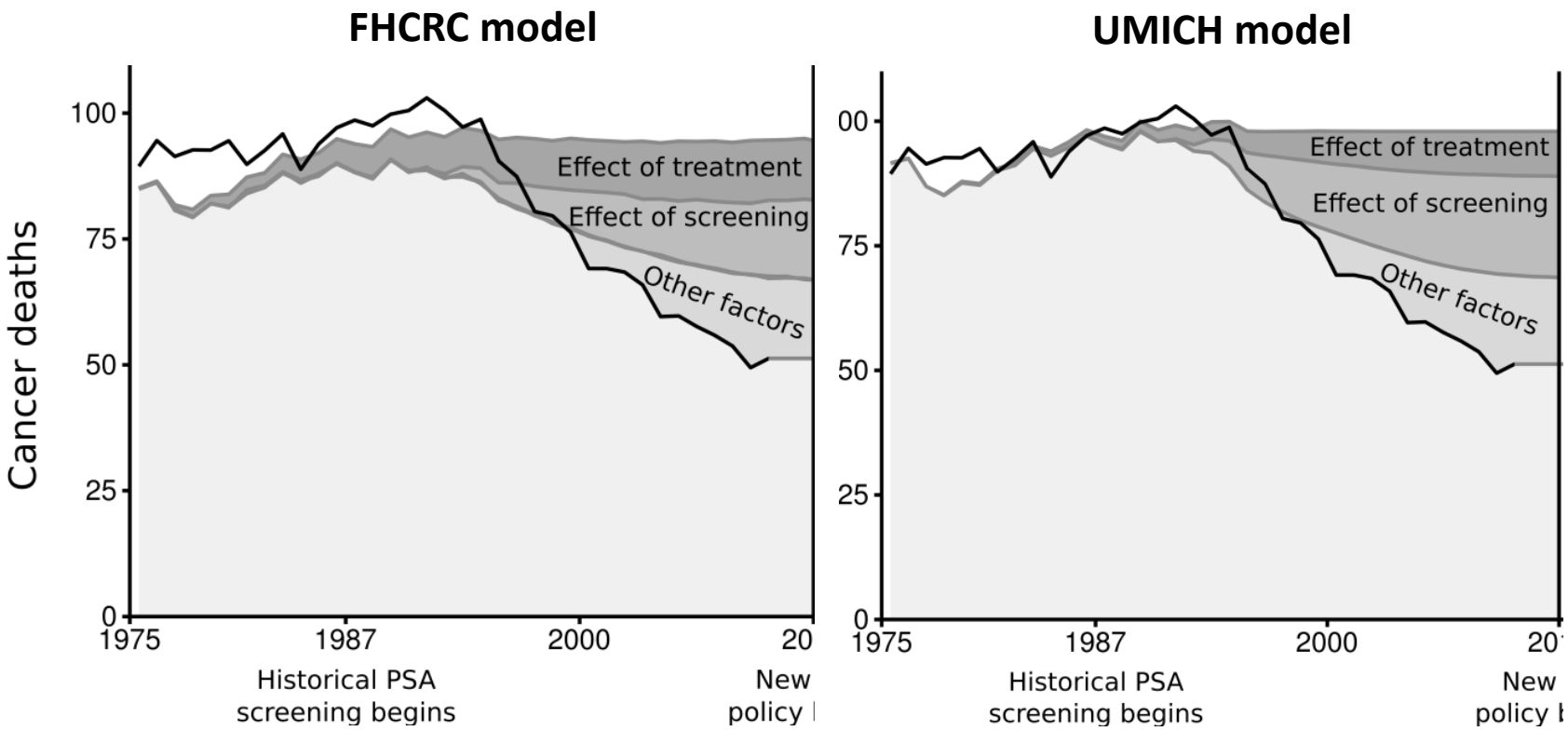
1. Understand latent incidence and progression (disease natural history)
    - Onset
    - Stage transitions
    - Survival without screening or new treatments
2. Quantify screening and treatment practices
3. Superimpose screening and treatment practices on natural history
    - **Screening** $\rightarrow$ project implied disease stage shift and survival benefit
    - **Treatment** $\rightarrow$ project implied survival improvement

Screening, primary treatment and prostate cancer mortality





The power of comparative modeling



Gulati et al, Cancer 2014

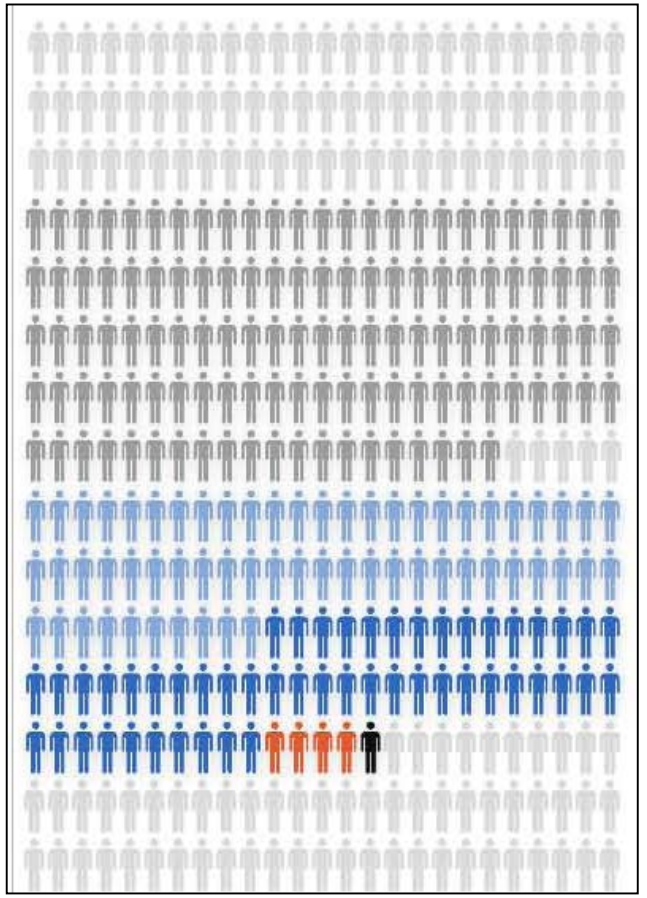
The power of a calibrated model

Level 1 evidence for policy recommendations is frequently lacking

- Age to start and stop screening
- Screening intervals and thresholds
- Tailoring recommendations for high-risk populations

Modeling is a way of conducting “virtual trials”

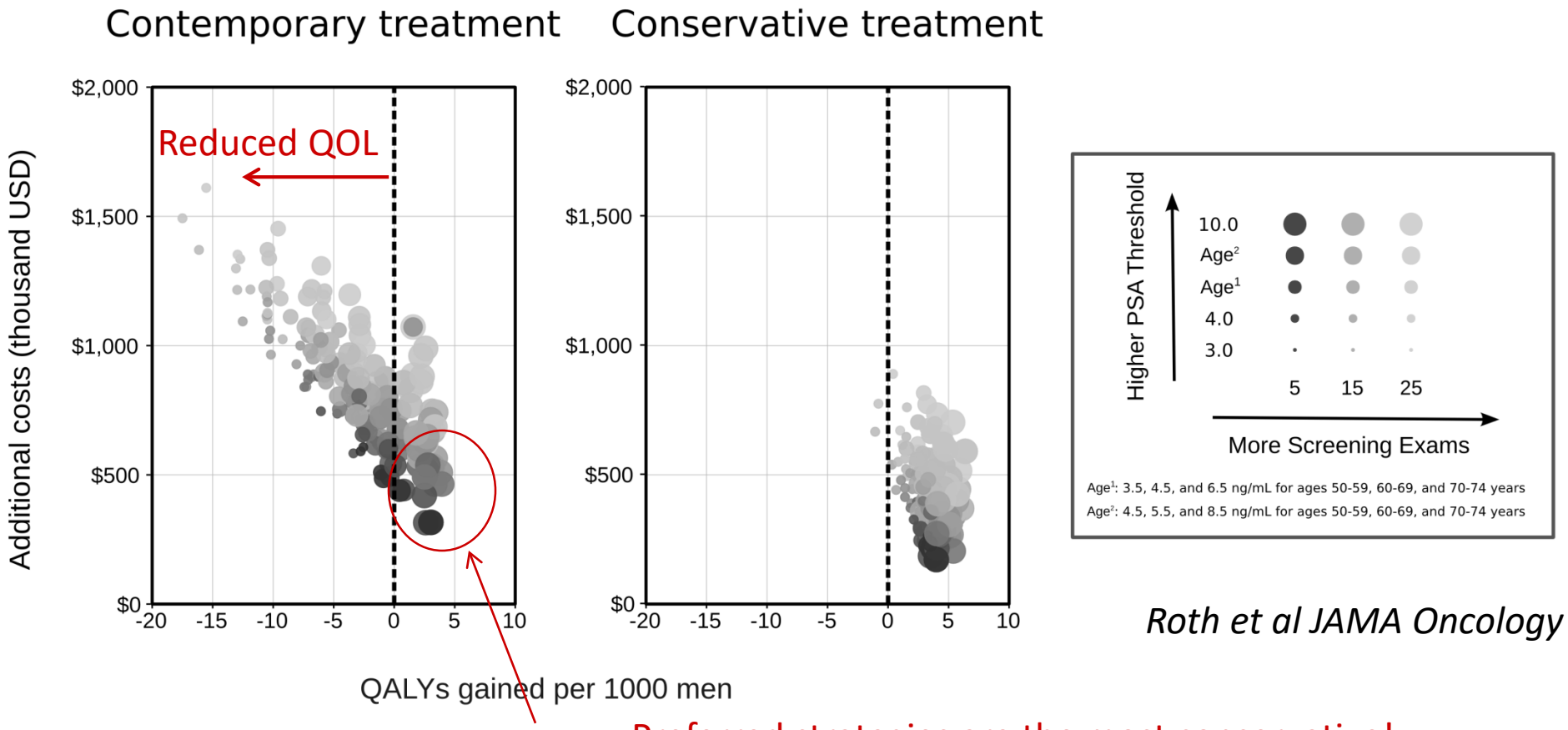
- Simulate population based on calibrated model
- Superimpose candidate policies
- Project harm-benefit tradeoffs



Original Investigation

Economic Analysis of Prostate-Specific Antigen Screening and Selective Treatment Strategies

Joshua A. Roth, PhD, MHA; Roman Gulati, MS; John L. Gore, MD; Matthew R. Cooperberg, MD; Ruth Etzioni, PhD



Roth et al JAMA Oncology 2016

Preferred strategies are the most conservative!

JAMA | Original Investigation

Association of Screening and Treatment With Breast Cancer Mortality by Molecular Subtype in US Women, 2000-2012

Sylvia K. Plevritis, PhD; Diego Munoz, MS, PhD; Allison W. Kurian, MD, MS; Natasha K. Stout, PhD; Oguzhan Alagoz, PhD; Aimee M. Near, MPH; Sandra J. Lee, ScD; Jeroen J. van den Broek, MS; Xuelin Huang, PhD; Clyde B. Schechter, MA, MD; Brian L. Sprague, PhD; Juhee Song, PhD; Harry J. de Koning, MD, PhD; Amy Trentham-Dietz, MS, PhD; Nicolien T. van Ravesteyn, PhD; Ronald Gangnon, PhD; Young Chandler, MS, MPH, DrPH; Yisheng Li, PhD; Cong Xu, PhD; Mehmet Ali Ergun, PhD; Hui Huang, MS; Donald A. Berry, PhD; Jeanne S. Mandelblatt, PhD

Original Investigation

Tobacco Control and the Reduction in Smoking-Related Premature Deaths in the United States, 1964-2012

Theodore R. Holford, PhD; Rafael Meza, PhD; Kenneth E. Warner, PhD; Clare Meernik, MPH; Jihyoun Jeon, PhD; Suresh H. Moolgavkar, MD, PhD; David T. Levy, PhD

US Preventive Services Task Force | MODELING STUDY

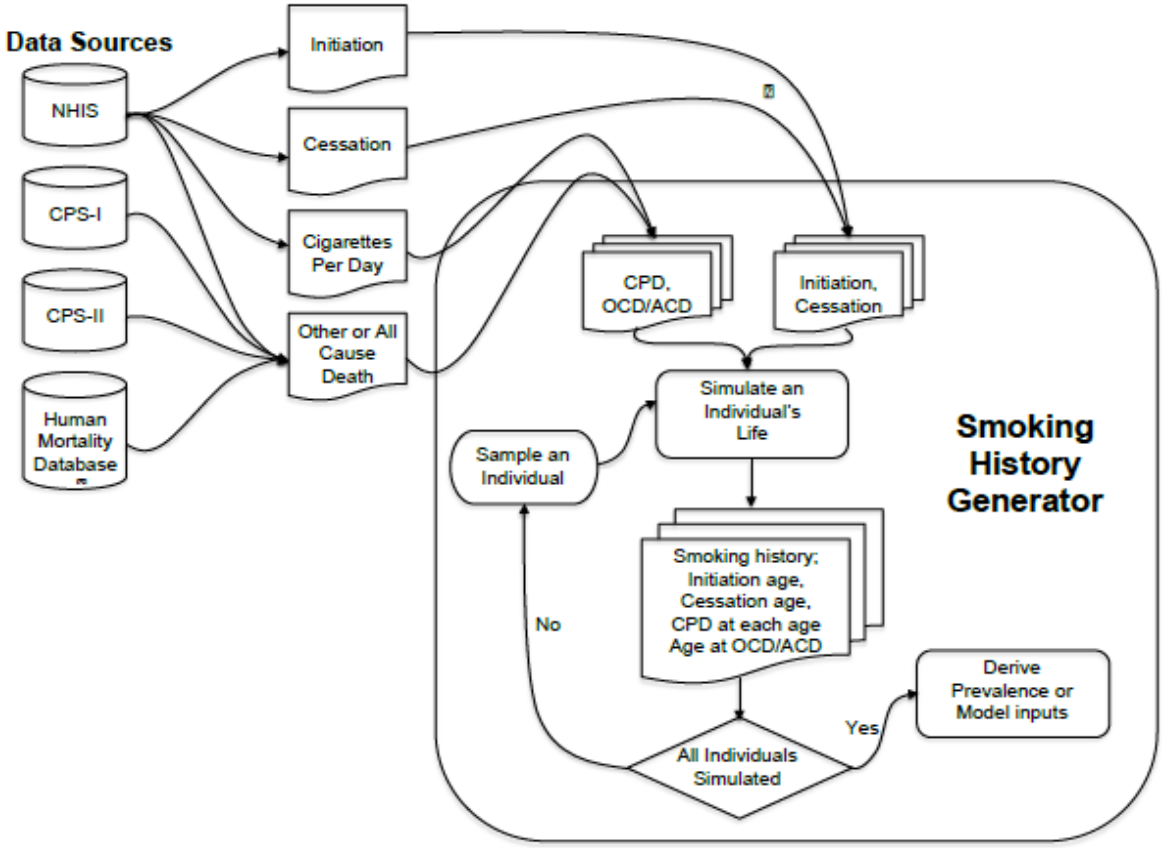
Estimation of Benefits, Burden, and Harms of Colorectal Cancer Screening Strategies

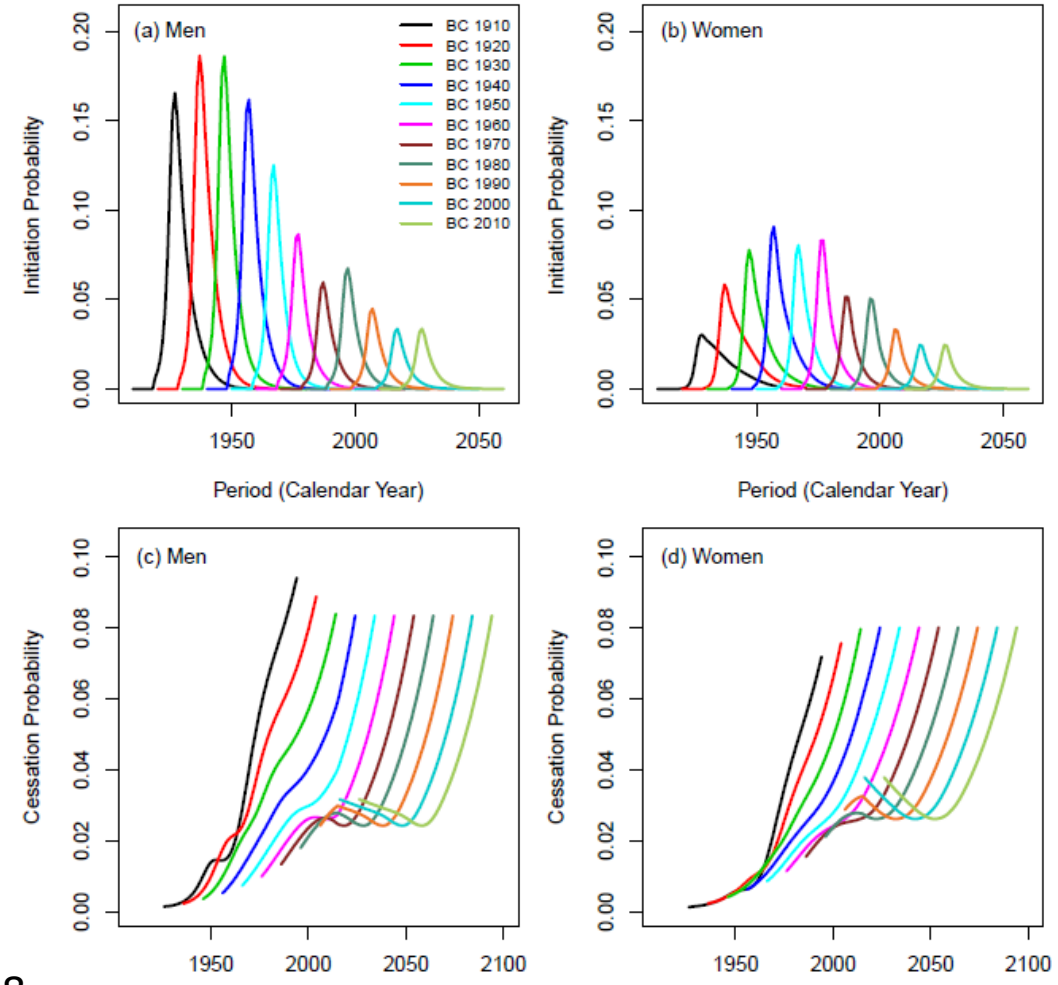
Modeling Study for the US Preventive Services Task Force

Amy B. Knudsen, PhD; Ann G. Zauber, PhD; Carolyn M. Rutter, PhD; Steffie K. Naber, MSc; V. Paul Doria-Rose, DVM, PhD; Chester Pabiniak, MS; Colden Johanson, BA; Sara E. Fischer, MPH; Iris Lansdorp-Vogelaar, PhD; Karen M. Kuntz, ScD

https://cisnet.cancer.gov/

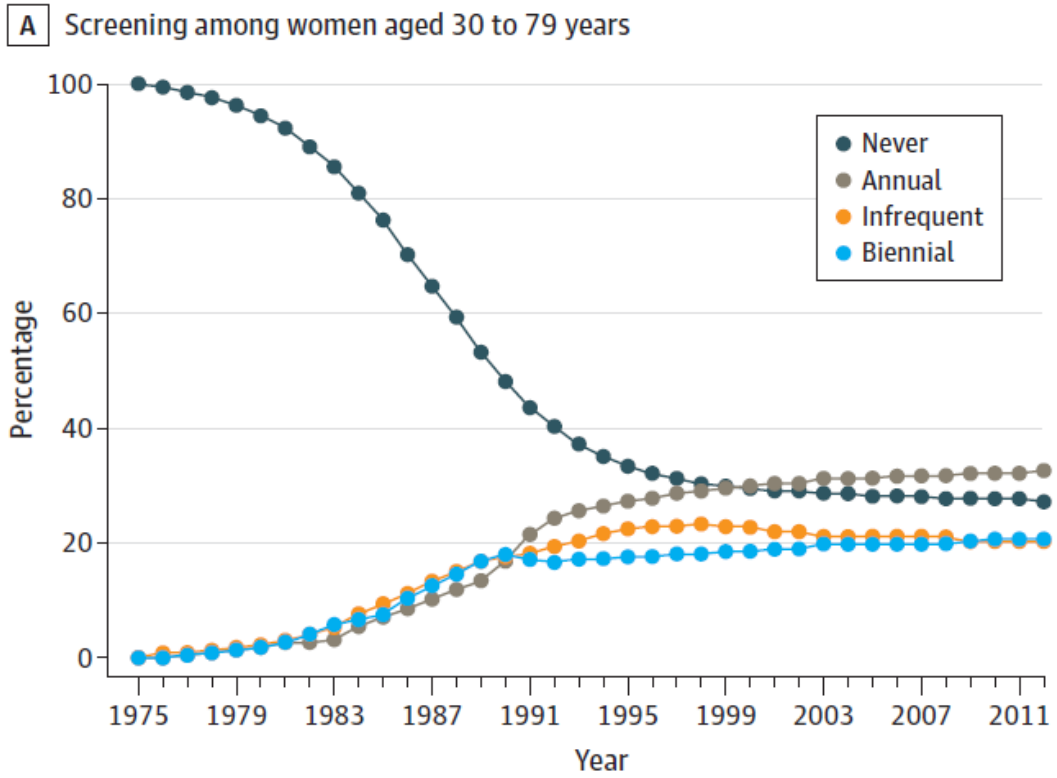
Smoking generator for CISNET lung models

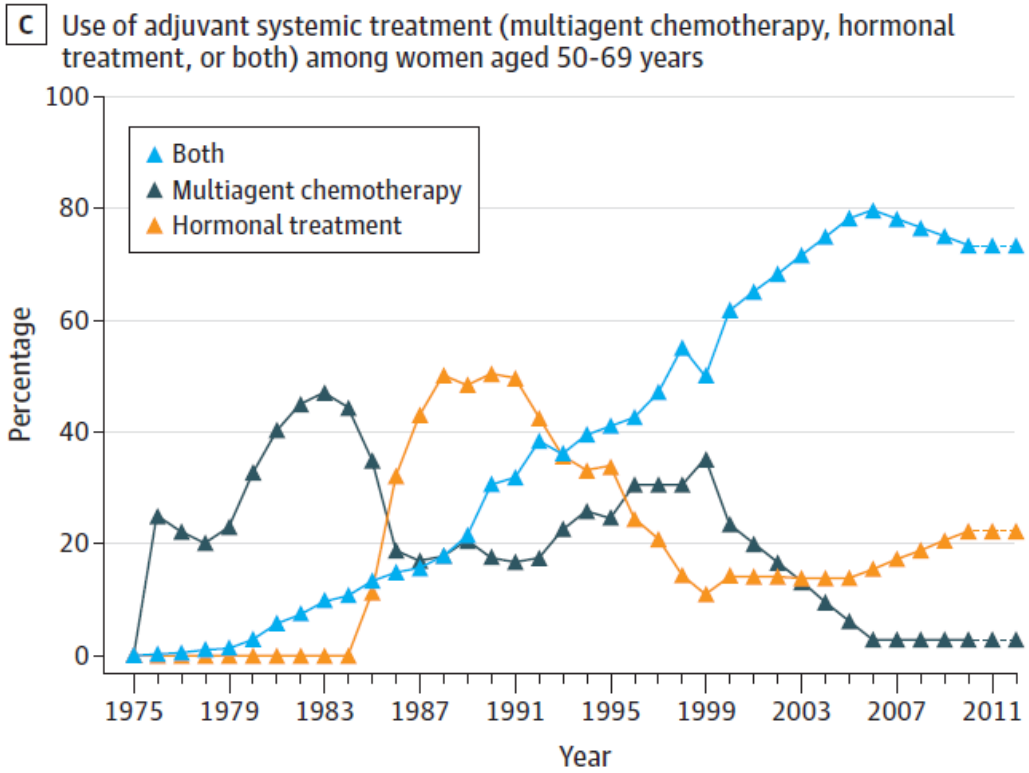




Appendix to Jeon et al, Annals of Internal Medicine November 2018

Screening and treatment for CISNET breast models

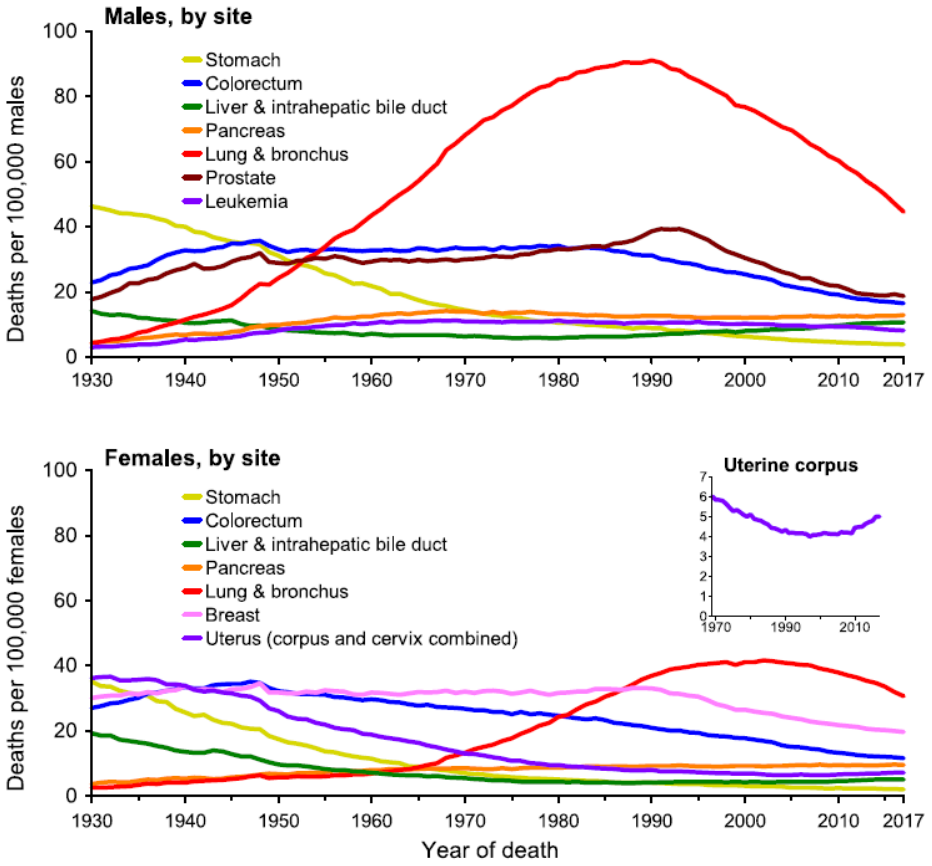




Plevritis et al JAMA 2018

In conclusion

- Cancer trends are a potential treasure trove of information
  - → Effectiveness of new interventions and treatments on outcomes
  - → Benefits and harms of novel diagnostic technologies
  - → Disparities in disease
- Cancer trends are also easily misinterpreted
- Validly learning from cancer trends requires close study of the patterns of exposure and care driving outcomes



CISNET models driven by practice patterns

Etiology, exposures, behaviors driving disease onset

- Smoking
- Obesity

Early detection and diagnosis

- Screening frequencies
- Biopsy referral criteria and compliance
- Imaging technologies for diagnosis and staging

Treatment

- Primary treatment following diagnosis
- Secondary and salvage treatment following recurrence
- Surveillance following diagnosis

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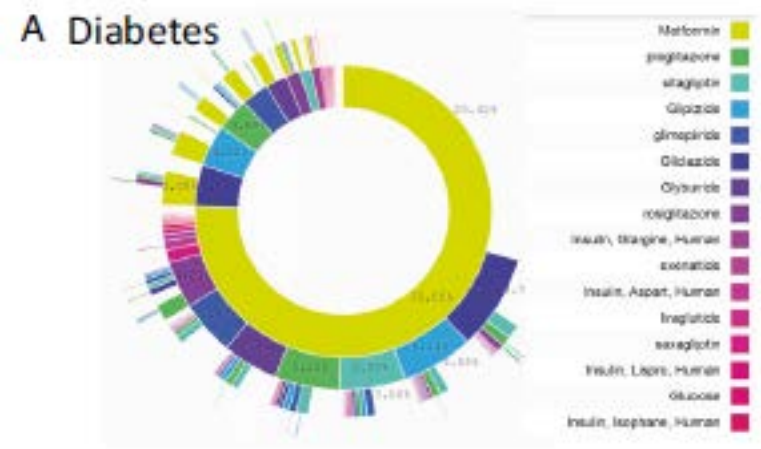
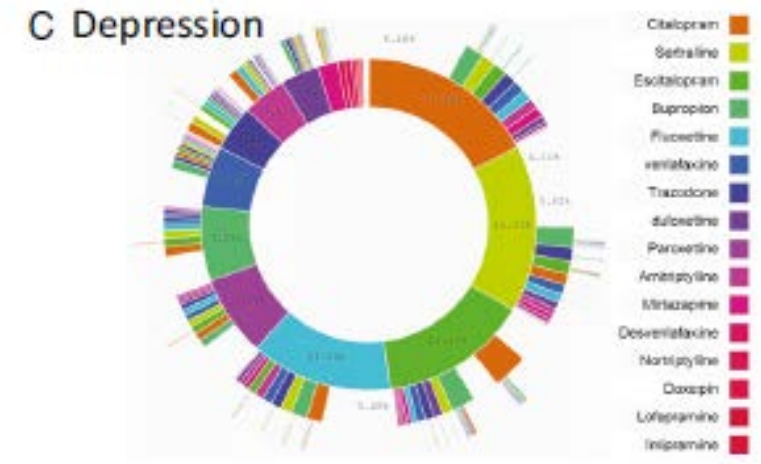
Salivating over OHDSI





Comprehensive comparative effectiveness and safety of first-line antihypertensive drug classes: a systematic, multinational, large-scale analysis

Marc A Suchard, Martijn J Schuemie, Harlan M Krumholz, Seng Chan You, RuiJun Chen, Nicole Pratt, Christian G Reich, Jon Duke, David Madigan, George Hripcsak, Patrick B Ryan

JAMA Network Open

Original Investigation | Diabetes and Endocrinology

Association of Hemoglobin A_{1c} Levels With Use of Sulfonylureas, Dipeptidyl Peptidase 4 Inhibitors, and Thiazolidinediones in Patients With Type 2 Diabetes Treated With Metformin

Analysis From the Observational Health Data Sciences and Informatics Initiative

Rohit Vashisht, PhD; Kenneth Jung, PhD; Alejandro Schuler, MS; Juan M. Banda, PhD; Rae Woong Park, MD, PhD; Sanghyung Jin, MS; Li Li, MS, MD; Joel T. Dudley, PhD; Kipp W. Johnson, MD, PhD; Mark M. Shervey, PhD; Hua Xu, PhD; Yonghui Wu, PhD; Karthik Natrajan, PhD; George Hripcsak, MD, MS; Peng Jin, MS; Mui Van Zandt, BS; Anthony Reckard, BS; Christian G. Reich, MD; James Weaver, MPH, MS; Martijn J. Schuemie, PhD; Patrick B. Ryan, PhD; Alison Callahan, PhD; Nigam H. Shah, MBBS, PhD

Characterizing treatment pathways at scale using the OHDSI network

George Hripcsak[a,b,c,1], Patrick B. Ryan[c,d], Jon D. Duke[c,e], Nigam H. Shah[c,f], Rae Woong Park[c,g], Vojtech Huser[c,h], Marc A. Suchard[c,i,j,k], Martijn J. Schuemie[c,d], Frank J. DeFalco[c,d], Adler Perotte[a,c], Juan M. Banda[c,f], Christian G. Reich[c,l], Lisa M. Schilling[c,m], Michael E. Matheny[c,n,o], Daniella Meeker[c,p,q], Nicole Pratt[c,r], and David Madigan[c,s]

Questions of intense interest

- Recent trends in novel androgen-targeting treatments for prostate cancer? Immunotherapies for melanoma?
- Changes in dose of radiation therapies and cancer-specific survival?
- Changes in imaging technologies used in cancer staging? Has this changed the definition of early versus late stage?
- How do hormonal treatments for prostate and breast cancer impact risk of cardiovascular disease and other-cause death?
- Distributions of various sequences of therapies for ovarian cancer?
- For all of these questions
  - Racial/ethnic disparities
  - Geographic variation

Discussion

Thank you!

If interested in discussion potential collaborations with the prostate or other CISNET groups please email me!

retzioni@fredhutch.org

CISNET website is at https://cisnet.cancer.gov/

Many thanks to Roman Gulati