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

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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.
Mortality by site

Cancer Statistics, 2020

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

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?

- Disease incidence by stage and type
- Survival without new treatments by stage and type
- Patterns and efficacy of new treatments
  - Survival with new treatments by stage and type
- Mortality
  - Without new treatments
  - With new treatments
Example: Melanoma

INCIDENCE BY GENDER

MEN

WOMEN

STAGE-SPECIFIC SURVIVAL

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? Treatment? Both? Other?

PSA SCREENING STARTS

Year of Death

Rate per 100,000
Screening and treatment dissemination

PSA screening

- Percent of men
- Year of screen

Initial treatments

- Percent of cases
- Year of diagnosis

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

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** → project implied disease stage shift and survival benefit
   - **Treatment** → project implied survival improvement
Screening, primary treatment and prostate cancer mortality

Graphs showing the percentage of men screened and the percent of cases treated with conservative management, radiation, surgery, or radiation + hormones over time. A line graph illustrates the effect of treatment, screening, and other factors on prostate cancer deaths per 100,000 men ages 50-84 years.
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
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

Reduced QOL

Preferred strategies are the most conservative!

Roth et al JAMA Oncology 2016
Original Investigation


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; Golden Johanson, BA; Sara E. Fischer, MPH; Iris Lansdorp-Vogelaar, PhD; Karen M. Kuntz, ScD

https://cisnet.cancer.gov/
Smoking generator for CISNET lung models

Data Sources
- NHIS
- CPS-I
- CPS-II
- Human Mortality Database

Smoking History Generator
- Initiation
- Cessation
- Cigarettes Per Day
- Other or All Cause Death
- CPD, OCC/ACD
- Initiation, Cessation
- Simulate an individual’s Life

Sample an Individual
- No
- Smoking history: Initiation age, Cessation age, CPD at each age, Age at OCC/ACD
- Derive Prevalence or Model inputs
- All individuals simulated

Graphs:
(a) Men
(b) Women
(c) Men
(d) Women

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
CISNET models driven by practice patterns

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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, Ruilin Chen, Nicole Pratt, Christian G. Reich, Jon Duke, David Madigan, George Hripcsak, Patrick B Ryan

Original Investigation | Diabetes and Endocrinology
Association of Hemoglobin A1c 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

Rehlt Vehik, PhD, Kenneth Jung, PhD, Alejandro Schuler, MS, Juan M. Banda, PhD, Eze Week Park, MD, PhD, Sanghyeong Jn, MS, Li Li, MS, MD, Jed T. Oksilt, PhD, Ripa W. Johnson, MD, PhD, Mark M. Sheehy, PhD, Hue Xu, PhD, Yongail Wai, PhD, Kartik Narasimhan, PhD, George Hripcsak, MD, MS, Peng Jin, MS, Mui Van Zandt, ES, Anthony Biedard, ES, Christian G. Reich, MD, James Weaver, MPH, MS, Martijn J. Schuemie, PhD, Patrick B. Ryan, PhD, Allison Calahan, PhD, Nigam H. Shah, MBBS, MD

Characterizing treatment pathways at scale using the OHDSI network

George Hripcsak, Patrick B. Ryan, Jon D. Duke, Nigam H. Shah, Rae Woong Park, Vojtech Huser, Marc A. Suchard, Martijn J. Schuemie, Frank J. DeFalco, Adler Perotta, Juan M. Banda, Christian G. Reich, Lisa M. Schilling, Michael E. Matheny, Daniella Meeker, Nicole Pratt, and David Madigan
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!

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

Many thanks to Roman Gulati