The Cancer Intervention and Surveillance Modeling Network (CISNET)

https://cisnet.cancer.gov

CISNET is a consortium of NCI-sponsored investigators who use statistical/simulation modeling to examine the impact of prevention, screening, and treatment on cancer incidence and mortality. These models can then project future trends and help determine optimal cancer control strategies. Established in 2000, CISNET comprises six cancer site groups: breast, prostate, colorectal, lung, esophageal, and cervical.

Approaches to Modeling

- **Flexible broad-based disease models** — These models incorporate the natural history of disease processes and overlay the full range of cancer control interventions.

- **Multicohort modeling**—This type of modeling captures a range of birth cohorts and the changing risk factor profiles, screening behaviors, and treatments used by each cohort as it ages.

- **Making the results of modeling efforts more transparent**—This is achieved through:

  Comparative modeling—Independent modeling efforts often yield disparate results that are difficult to reconcile. A comparative approach explores differences between models in a systematic way. In "base case" collaborations, a set of common population inputs is used across all models (e.g., dissemination patterns of screening and treatment, mortality from causes other than cancer), and common sets of intermediate and final outputs are developed. Results then are compared across models.

  Model profiles—Model profiles are standardized descriptions that facilitate the comparison of models and their results. Users can read documentation about a single model or side-by-side descriptions that contrast how models address components of the process. Journal articles seldom contain extensive model descriptions; model profiles provide more complete descriptions. Learn more: https://cisnet.cancer.gov/resources/profiles

  Model registry—The Model Registry provides overviews of each model, which are less detailed and technical than the model profiles. Learn more: https://resources.cisnet.cancer.gov/registry

Working with Researchers and Policymakers

The CISNET infrastructure informs evidence-based policy decisions, cancer control planning, and research priority setting. Examples include:

Collaborating with the U.S. Preventive Services Task Force (USPSTF) (Zauber et al., 2008; Knudsen et al., 2016; Mandelblatt et al., 2009; de Koning et al., 2013; de Koning et al., 2014; Mandelblatt et al., 2016) — CISNET models have served as a resource for USPSTF panels as they developed or revised screening guidelines for breast, colorectal, and lung cancers.

Centers for Medicare and Medicaid Services (CMS) Reports on the Cost-Effectiveness of Fecal Immunochemical Testing (FIT), CT Colonography, and DNA Stool Testing — These reports represent a joint effort with CISNET to analyze the cost-effectiveness of new screening tests for colorectal cancer and help inform CMS coverage and reimbursement decisions.

Impact of Mammography and Adjuvant Therapy on the Decline in U.S. Breast Cancer Mortality: 1975–2000 (Berry et al., 2005; CISNET Breast Cancer Collaborators, 2006; Plevritis et al., 2018) —The CISNET Breast group used a comparative modeling approach to determine the contributions of mammography and adjuvant therapy to the decline in breast cancer mortality in the U.S. The group used population data to describe the dissemination and usage patterns of mammography and adjuvant therapy in the U.S. over time. The usage patterns were coupled with seven independent modelers' syntheses of available information on the benefits of these advances (Berry et al., 2005).

Although the benefits of adjuvant therapy were more settled, controversy regarding the benefits of mammography screening persisted due to uneven results and criticism of the controlled trials on which the mortality benefits had been based. The authors (Berry et al., 2005) made the case that each factor accounted for one-half of the historic 24% decrease in mortality that was observed between 1990 and 2000. Although results based on observational data are typically validated using controlled trials, in this case, observational data (combined in a novel way using seven different models) helped to confirm mammography benefits when controlled trial results alone could not settle the debate.

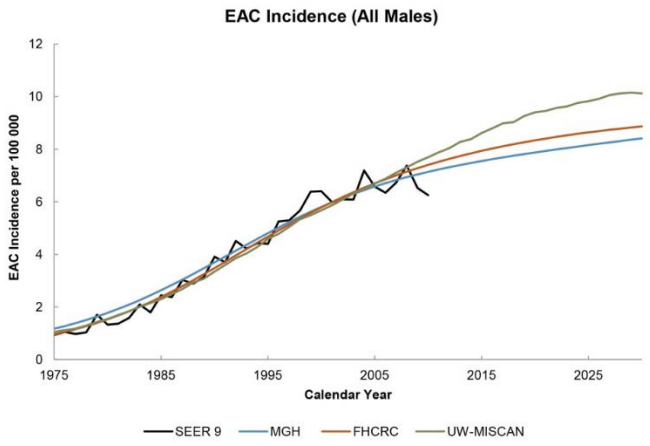
The breast cancer team has added key evidence to address the controversial questions about mammography and shows the potential role of statistical modeling of observational data in public health policy/decision making.

Although the Berry et al., 2005 landmark study quantified the relative effects of screening mammography and adjuvant treatment at a population level, those effects had not been quantified by estrogen receptor (ER) status. Breast cancer is a heterogeneous disease defined by molecular subtypes that predict treatment response and clinical outcomes, and ER is the longest-established molecular marker in use for breast cancer treatment planning.

To quantify the effects of screening and adjuvant treatment on U.S. breast cancer mortality trends by ER status from 1975–2000, the CISNET Breast group updated the landmark analysis using ER-specific model inputs (Plevritis et al., 2018; Munoz et al., 2014). All six modeling groups projected greater absolute mortality declines for ER-positive cancers than for ER-negative cancers, consistent with observed trends. For ER-positive cases, adjuvant treatment made a higher relative contribution to breast cancer mortality reduction than screening, whereas for ER-negative cases the relative contributions were similar. ER-negative cancers were less likely than ER-positive to be screen-detected (35.1% vs. 51.2%), but when screen-detected yielded a greater survival gain (5-year breast cancer survival, 35.6% vs. 30.7%).

Interpreting Estimates of Overdiagnosis (Etzioni et al., 2013) — The CISNET Prostate and Breast Groups reviewed widely varying definitions and estimates of overdiagnosis and provided guidance for policymakers on evaluating estimates based on the specific definition used, the study context in which it is measured, and the estimation method.

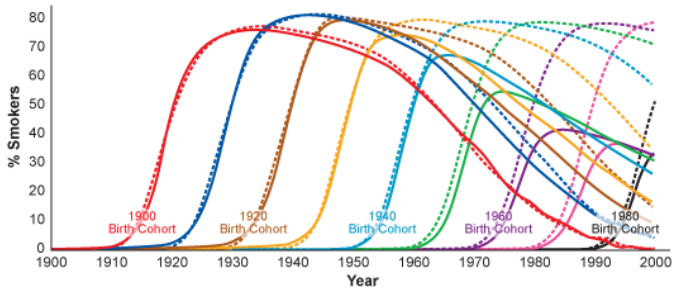
Predicting Trends in Esophageal Adenocarcinoma (EAC) Incidence and Mortality — Although esophageal squamous cell carcinoma incidence has been declining in the U.S. and other parts of the western world, EAC incidence has experienced an alarming five-fold increase over the past four decades. There is no consensus regarding the causes of this increase, although increasing prevalence of gastroesophageal reflux disease related to increases in abdominal obesity, and wider eradication of *H. pylori* infection have been suggested, among others. A joint analysis by the CISNET Esophageal Group (Kong et al., 2014) used three independent mathematical models to analyze EAC incidence and mortality rates among men and women aged 20-84 years in the U.S. during 1975–2010. They then projected the rates to 2030. Despite the differences in mathematical formalisms among the three models, their projections (below, males) suggest that the EAC incidence rate will continue to increase. Thus, improving screening and surveillance protocols for EAC continues to be a critical public health need.



(Reprinted with permission from AACR)

Addressing State Disparities in Colorectal Cancer Screening (van der Steen et al., 2015) — Several states across the U.S. are implementing initiatives to provide access to colorectal cancer screening for low-income, uninsured persons. However, states differ in risk factors, budgets, and screening rates. The Colorectal Working Group assessed which screening test would be best for a state-based (South Carolina) initiative with a limited budget and found that a fecal immunochemical test (FIT)-based program would prevent more colorectal cancer deaths than a colonoscopy-based program. Using a FIT-based program resulted in nearly eight times more individuals being screened and approximately four times as many colorectal cancer deaths prevented and life-years gained, compared to the colonoscopy program.

Quantifying the Impact of Tobacco Control Policies in the U.S. (Moolgavkar et al., 2012) — The Lung Working Group's initial projections of the impact of tobacco control on lung cancer mortality from 1975–2000 highlighted the number of lung cancer deaths avoided due to tobacco control efforts that were implemented, and an upper bound on how many more deaths could have been avoided if the efforts had been perfect. The authors also projected smoking prevalence under different tobacco control scenarios, including no tobacco control (below).



Estimated percentages of white male smokers in the US population (solid lines) based on survey data and hypothesized percentages that would have been observed if tobacco control efforts had never been initiated (dashed lines). (Adapted with permission from JNCI)

Policy and Individual Decision Tools

CISNET has developed several web-based tools to aid policymakers, health professionals, and individuals in making decisions about risk reduction approaches, screening, and health care policies.

Tobacco Control Policy Tool — This tool provides decision makers and health professionals with estimates of the impact of four specific tobacco control policies on public health in the U.S.

Mammograph Outcomes Policy (Mammo OUTPut) Tool — This tool provides health care policy makers with quantitative data on the tradeoffs of benefits and harms related to the age of mammography screening initiation in different groups of women.

State Colorectal Cancer Decision Tool — This tool provides state decision makers and health professionals with planning tools for their area's colorectal cancer screening programs.

Decision Tool for Women with BRCA Mutations — This tool is designed for joint use by women with BRCA mutations and their health care providers, to guide management of cancer risks.

Learn more about these tools at https://cisnet.cancer.gov/resources/policy.

Selected Publications

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van der Steen A, Knudsen AB, van Hees, et al. Optimal colorectal cancer screening in states' low-income, uninsured populations—the case of South Carolina. *Health Serv Res* 2015; 50:768–89.

Weinstein MC, O'Brien B, Hornberger J, et al. ISPOR Task Force on Good Research Practices—Modeling Studies. *Value Health* 2003; 6: 9–17.

Zauber AG, Lansdorp-Vogelaar I, Knudsen AB, Wilschut J, van Ballegooijen M, Kuntz KM. Evaluating test strategies for colorectal cancer screening: a decision analysis for the U.S. Preventive Services Task Force. *Ann Intern Med* 2008; 149:659–69.

For a complete list of publications, visit https://cisnet.cancer.gov/publications/.

Collaboration Opportunities

CISNET invites inquiries from outside groups regarding collaborations on cancer control issues that are amenable to modeling. Visit https://cisnet.cancer.gov/working/ or contact Dr. Eric Feuer for more information.

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