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 nine cancer site groups. Five cancer sites are funded from 2020-2025: breast, prostate, colorectal, lung, and cervical. Four cancer sites are funded from 2021-2026 under the CISNET Incubator Program for New Cancer Sites: bladder, gastric, multiple myeloma, and uterine.

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.html

  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) (Mandelblatt et al., 2016; Kim et al., 2018, Knudsen et al., 2021; Meza et al., 2021) — CISNET models have served as a resource for USPSTF panels as they developed or revised screening guidelines for breast, cervical, 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.

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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 comparative modeling to determine the contributions of mammography and adjuvant therapy to the decline in U.S. breast cancer mortality. Using population data, they described 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 adjuvant therapy's benefits were more settled, controversy about the benefits of mammography screening persisted due to uneven results and criticism of the controlled trials on which the mortality benefits had been based. Berry et al. (2005) showed that each factor accounted for one-half of the historic 24% decrease in mortality observed from 1990 to 2000. Although observational results 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 controversial questions about mammography and shows the potential role of statistical modeling of observational data in public health policy/decision making.

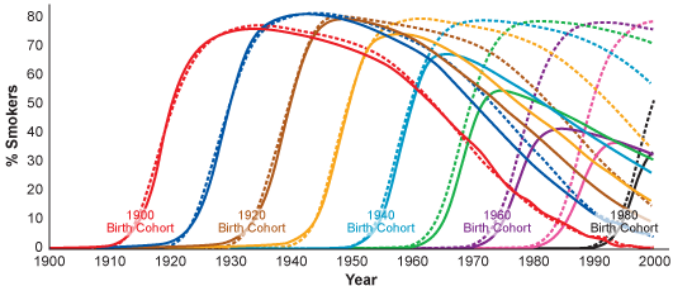
Although the 2005 landmark study quantified the relative population-level effects of screening mammography and adjuvant treatment, those effects not been quantified by estrogen receptor (ER) status. Breast cancer is a heterogeneous disease defined by molecular subtypes that predict treatment response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

Addressing State Disparities in Colorectal Cancer Screening (van der Steen et al., 2015) — Several states are implementing initiatives to provide access to colorectal cancer (CRC) screening for low-income, uninsured persons, but states differ in risk factors, budgets, and screening rates. The CISNET Colorectal group assessed which screening test would be best for a South Carolina initiative with a limited budget and found that a fecal immunochemical test (FIT)-based program would prevent more CRC deaths than a colonoscopy-based program. Using a FIT-based program resulted in nearly 8 times more persons screened and about 4 times as many CRC deaths prevented and life-years gained.

Quantifying the Impact of Tobacco Control Policies in the U.S. (Moolgavkar et al., 2012) — The CISNET Lung group's projections of tobacco control's impact 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 had the efforts been perfect. They projected smoking prevalence under different tobacco control scenarios, including no tobacco control (below).



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

Estimating the Natural History of Cervical Carcinogenesis (Burger et al., 2020) — Using four CISNET cervical models with varying underlying structures but fit to common US epidemiologic data, the CISNET Cervical group estimated the acquisition age of causal HPV infections and dwell times associated with three phases of cancer development: HPV, high-grade precancer, and cancer sojourn time. They found that the median time from HPV acquisition to cancer detection ranged from 17.5 to 26 years across the four models. Three models projected that 50% of unscreened women acquired their causal HPV infection between ages 19 and 23 years, and one projected these infections occurred at age 34 years. These validated CISNET-cervical models, which reflect some uncertainty in the development of cervical cancer, elucidate important drivers of HPV vaccination and cervical cancer screening policies and emphasize the value of comparative modeling when evaluating public health policies.

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 — provides decision makers and health professionals with estimates of the impact of four specific tobacco control policies on public health in the U.S.

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

State Colorectal Cancer Decision 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 — 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.html

Selected Publications

Alagoz O, Lowry KP, Kurian AW, et al. Impact of the COVID-19 pandemic on breast cancer mortality in the US: estimates From collaborative simulation modeling. *J Natl Cancer Inst* 2021 Jul 14. Epub 2021 Jul 14.

Berry DA, Cronin KA, Plevritis SK, et al. Cancer Intervention and Surveillance Modeling Network (CISNET) Collaborators. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005; 353:1784–92.

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Burger EA, Jansen EE, Killen J, et al. Impact of COVID-19-related care disruptions on cervical cancer screening in the United States. *J Med Screen* 2021 28:213-216.

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Etzioni R, Gulati R, Mallinger L, et al. Influence of study features and methods on overdiagnosis estimates in breast and prostate cancer screening. *Ann Intern Med* 2013; 158:831–8.

Joseph DA, Meester RG, Zauber AG, et al. Colorectal cancer screening: Estimated future colonoscopy need and current volume and capacity. *Cancer* 2016; 122:2479–86.

Kim JJ, Burger EA, Regan C, Sy S. Screening for cervical cancer in primary care: a decision analysis for the US Preventive Services Task Force. *JAMA* 2018; 320:706–714.

Knudsen AB, Rutter CM, Peterse EFP, et al. Colorectal cancer screening: an updated modeling study for the US Preventive Services Task Force. *JAMA* 2021 325:1998-2011.

Kroep S, Heberle CR, Curtius K, et al. Radiofrequency ablation of Barrett's Esophagus reduces esophageal adenocarcinoma incidence and mortality in a comparative modeling analysis. *Clin Gastroenterol Hepatol* 2017; 15:1471–1474.

Mandelblatt JS, Stout NK, Schechter CB, et al. Collaborative modeling of the benefits and harms associated with different U.S. breast cancer screening strategies. *Ann Intern Med* 2016 164:215–25.

Meza R, Jeon J, Toumazis I, et al. Evaluation of the benefits and harms of lung cancer screening with low-dose computed tomography: modeling study for the US Preventive Services Task Force. *JAMA* 2021;325:988-997.

Moolgavkar SH, Holford TR, Levy DT, et al. Impact of reduced tobacco smoking on lung cancer mortality in the United States during 1975-2000. *J Natl Cancer Inst* 2012; 104:541–8.

Munoz D, Near AM, van Ravesteyn NT, et al. Effects of screening and systemic adjuvant therapy on ER-specific US breast cancer mortality. *J Natl Cancer Inst* 2014 106:1–9.

Plevritis SK, Munoz D, Kurian AW, et al. Association of screening and treatment with breast cancer mortality by molecular subtype in US women, 2000–2012. *JAMA* 2018; 319:154–164.

Rutter CM, Knudsen AB, Marsh TL, et al. Validation of models used to inform colorectal cancer screening guidelines: accuracy and implications. *Med Decis Making* 2016; 36:604–14.

Tsodikov A, Gulati R, Heijnsdijk EAM, et al. Reconciling the effects of screening on prostate cancer mortality in the ERSPC and PLCO trials. *Ann Intern Med* 2017; 167:449–455.

Tsodikov A, Gulati R, de Carvalho TM, et al. Is prostate cancer different in black men? Answers from 3 natural history models. *Cancer* 2017; 123:2312–2319.

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.

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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