

Cancer Intervention and Surveillance Modeling Network (CISNET)

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NCI Project Scientists:

Colorectal and Cervical: Paul Doria-Rose, DCCPS

Prostate: Angela Mariotto, DCCPS

Breast: Brandy Heckman-Stoddard, DCP

Esophageal: Ellen Richmond, DCP

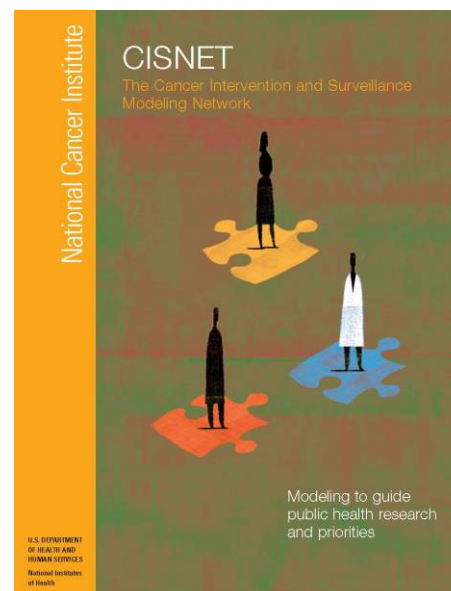
Program Director: Susan Scott, DCCPS

Cancer Intervention and Surveillance Modeling Network (CISNET)

- NCI Sponsored Collaborative Consortium (U01) of simulation modelers in Breast, Prostate, Colorectal, Lung, Esophagus, and Cervical cancers formed in 2000
- Extend evidence provided by trial, epidemiologic, and surveillance data using simulation modeling to guide public health research and priorities
 - ◆ Help address the formidable and growing gap between the rapid pace of innovation in cancer research and our ability to efficiently harness it to improve population health



<https://cisnet.cancer.gov/>

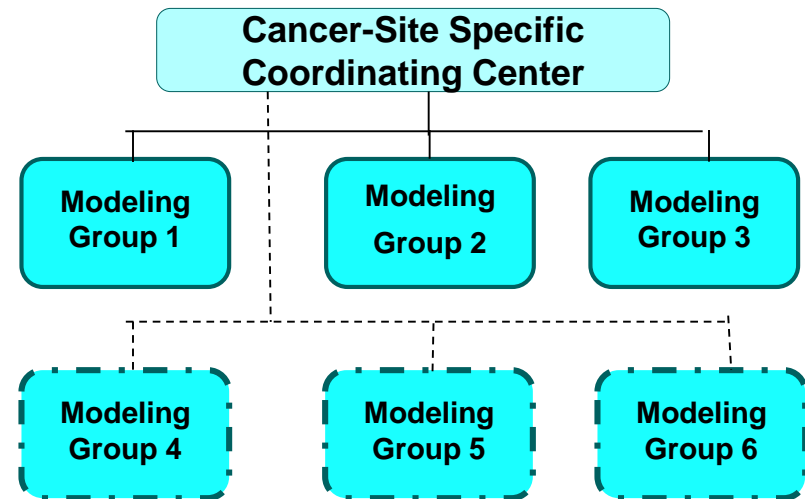


In many instances individual modeling efforts yield different results that are difficult to reconcile

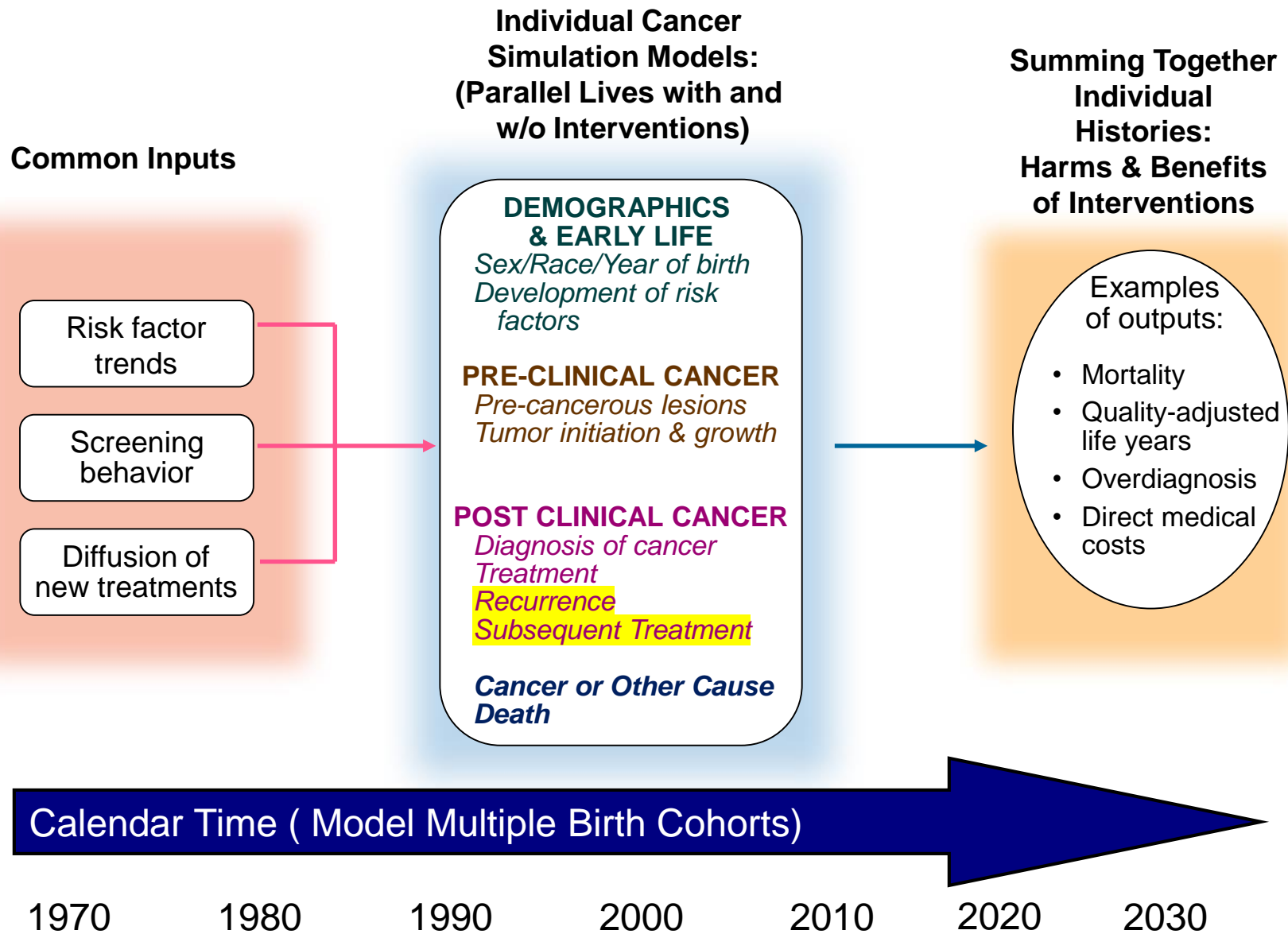
Approach Innovated by CISNET: Systematic Comparative Modeling

- Central questions to be addressed by groups collaboratively with a common set of inputs and outputs
 - ◆ Reproducibility across models adds credibility to results
 - ◆ Differences point out areas for further study in a systematic way

- Six multiple-PI grants each focused on a different cancer site with a coordinating center and between 3-6 modeling groups



- Affiliate members can join for specific collaborations



Outreach, Collaborations, and Publications



Comparison of Operative to Monitoring and Endocrine Therapy



Barrett's Esophagus Translational Research Network (BETRNet)



Population-based Research to Optimize the Screening Process (PROSPR)



Breast Oncology Local Disease (BOLD) Task Force of the NCI Breast Cancer Steering Committee

Genetics and Epidemiology of Colorectal Cancer Consortium [GECCO]



Smoking Cessation at Lung Examination: The SCALE Collaboration

Cluster Randomized Trial of PSA Testing for Prostate Cancer (CAP)



Impactful Publications

- Over 450 publications (>40 per year in most recent funding cycle)
 - 17 per year with impact factor >5
 - 7 per year with impact factor 15+

- Providing policy makers with estimates of the benefits vs. harms (including unobservable quantities such as overdiagnosis) of many different screening regimens
 - ◆ Extrapolating from the single National Lung Screening Trial regimen (3 annual screens for individuals 55-75, 30+ pack years, <15 years since quit) to facilitate the USPSTF exploring many other regimens (*Ann Intern Med*, 2014)

- Understanding the impact of advances in treatment and screening on population mortality trends
 - ◆ Quantifying the contribution of advances in mammography, chemotherapy, hormonal therapy, and targeted therapy to the decline in U.S. breast cancer mortality (*NEJM*, 2005; *JAMA*, 2018)

Open Competition:
Continuation of Current
Cancer Sites
(Up to 6 multiple-PI U01's)



Cross-CISNET Program Activities

- Cross-cancer site collaborations (continued)
- Programmers Interest Group (continued)
- **NEW** Junior Investigators Career Enhancement (JUICE) Program

- Types of questions that CISNET can help answer are becoming even more ubiquitous
 - ◆ **Cervical** – Should screening recommendations change as vaccinated populations reach screening age?
 - ◆ **Colorectal** – What mix of screening modalities for CRC might work best in underserved populations in the US and in middle and lower income countries?
 - ◆ **Breast** – Can the interface between randomized trials of active surveillance for DCIS of the breast and modeling help us better understand & manage this condition?
 - ◆ **Esophageal** – Can low cost minimally invasive mass screening serve as a cost-effective triage for upper endoscopy to detect Barrett’s esophagus?
 - ◆ **Prostate** – Are there strategies for PSA screening that more effectively “thread the needle” of maximizing mortality reduction while minimizing overdiagnosis? What are the most effective strategies for initiating and terminating active surveillance that can minimize the harms of overdiagnosis?
 - ◆ **Lung** – What strategies for the management of suspicious nodules (e.g. Lung-Rads, volumetrics) are most effective for minimizing false positives, while maximizing sensitivity? Could strategies be individualized to take into account personal preferences?

9 Priority Areas to Focus Modeling Efforts

1. *Precision Screening and New Screening Technologies*
2. *Precision Treatment*
3. *Overdiagnosis and Active Surveillance*
4. *Decision Aids (Individual and Policy)*
5. *Understanding Screening in Real-World Settings and Determining the Best Routes to Optimize the Processes*
6. *State, Local, and International Cancer Control Planning*
7. *Suggesting Optimal Routes to Reduce Health Disparities*
8. *Methods Development*
9. *Cancer Site-Specific Opportunities*

Ongoing priorities set by Organ Sites Specific Steering Committees:

- Specific aims as specified in grant application and selected from the priority areas;
- New topics of timely relevance
- Outside inquiries from other NCI staff, NCI sponsored consortia, guideline setting organizations & other outside researchers and organizations

- Evolving “big data” resources from electronic claims, labs, and health records, and their potential linkage to population-based registry data, will generate detailed information on first-line and salvage therapies and dose, recurrence, and the genomic characterization of disease
- Types of questions
 - ◆ Population impact of therapies
 - ◆ Quantifying possible overdiagnosis of recurrence – e.g. biochemical PSA-based recurrence
 - ◆ Value-based “threshold pricing” of new therapies – cost set so that the cost effectiveness ratio is equal to established regimens
 - ◆ When is genomic characterization of tumors cost effective
 - ◆ Trial design and evaluation – considering different endpoints, eligibility criteria, extrapolating long-term outcomes including QALYs (esp. important in de-escalation trials), simulating the chance of a positive trial result as a function of trial design options

Junior Investigators Career Enhancement (JUICE) Program

- Modeling oriented data scientists are in high demand and short supply
 - ◆ Learning to be a modeler is a combination of book learning and mentored opportunities
- In the last round of CISNET, a junior investigators initiative sponsored webinars, lunch sessions at meetings, networking opportunities, but was largely an unfunded mandate
 - ◆ Help junior investigators *”squeeze”* more out of their CISNET experiences
 - ◆ Target – pre-docs, post-docs, junior faculty across CISNET
- A cross-CISNET JUICE workgroup would be formed to plan and implement ideas
- Examples:
 - ◆ Small awards to junior investigators across CISNET to work on innovative and creative small projects
 - ◆ Fund visits to other CISNET sites to take advantage of the breadth of CISNET approaches
 - ◆ Develop mini-curriculum on special advanced topics of interest

- Strict budget constraints on direct costs per year for each component
 - ◆ \$180K per modeling group (3-6 groups)
 - ◆ \$110K for coordinating center
 - ◆ \$100K rapid response funds
 - ◆ \$40K for JUICE program

- Total cost per year – 6 awards (average of 4 modeling groups per cancer site)
 - ◆ Average \$1.66M per award - \$10M for 6 awards
 - ◆ \$50M over the total funding period (FY20-FY24)

Mathematical models, oversimplified, unrealistic, and even false in some respects, force analysts to confront possibilities that would not have occurred to them otherwise

A Beautiful Mind by Sylvia Naser
(the biography and movie about John Nash - the developer of game theory)

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