National Cancer Institute

CISNET Incubator Program for New Cancer Sites

New Proposed RFA Utilizing a U01 Mechanism

BSA
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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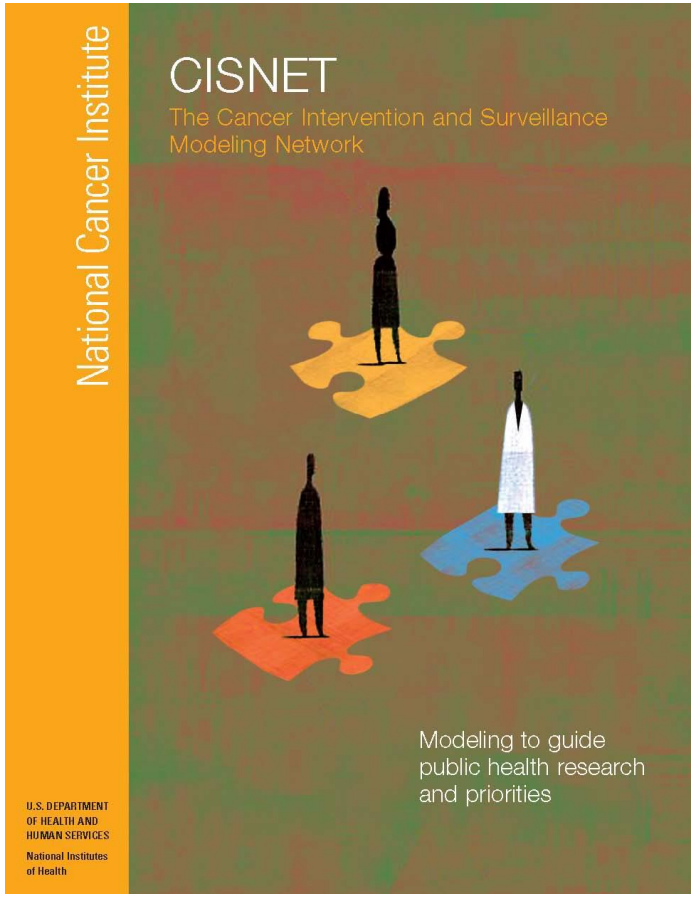
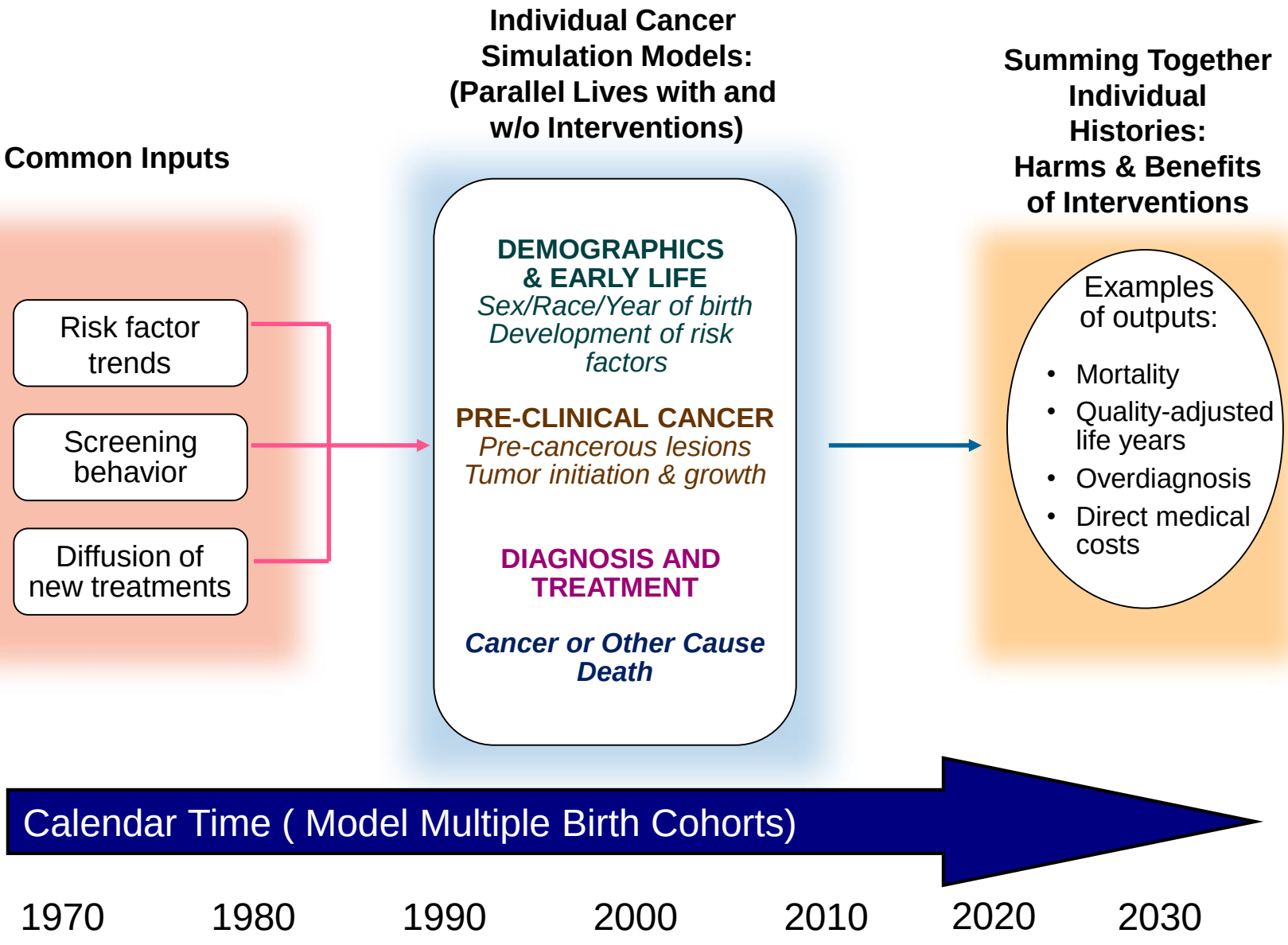
What is the Cancer Intervention and Surveillance Modeling Network (CISNET)?



- NCI Sponsored Collaborative Consortium (U01) of simulation modelers in Breast, Prostate, Colorectal, Lung, Esophagus, and Cervical cancers
  - Approved to continue through FY24
- Comparative modeling approach with 3-6 independent modeling groups per cancer site: adds credibility to results
  - One multiple PI grant per cancer site with a coordinating center
- Purpose: provide link between complex evidence & actionable public health strategies
  - Assist the USPSTF in developing screening guidelines

Framework for CISNET Population Modeling



Motivation and Purpose of CISNET Incubator Program

- Questions that CISNET-type models can address extend well beyond the 6 current sites

- Translate CISNET's model of success to cancer sites for which there has been nascent/ limited population modeling efforts to date and little to no comparative modeling

What is the State of Population Modeling in Cancers Beyond the Six Included in CISNET?

- Fewer existing models, and not as well developed
- Because of a lack of consistent funding, most are "one-off" efforts that focus on a single limited portion of cancer control spectrum
  - Importance of including synergies across the spectrum
- No (or very limited) comparative modeling
  - Some post publication comparisons of models and results – difficult to do because of so many things varying simultaneously
- Availability of new data resources to inform models
  - Large observational databases and specialized linkages, e.g. linkage between SEER hepatocellular carcinoma cases and state hepatitis registries

Incubator Program

- Smaller Scale: Multiple PI grants with 2-3 independent modeling groups that will share common data sources and compare their models as they are developed
- One modeling group will serve as the coordinating center for that site
  - Formulating, prioritizing, and coordinating work;
  - Negotiating common requests for outside data sources;
  - Preparing inputs and collecting and processing common outputs for model comparisons / critical evaluation of disparate results
- Require that no more than one PI on an incubator application can also be a PI on a concurrently funded CISNET grant

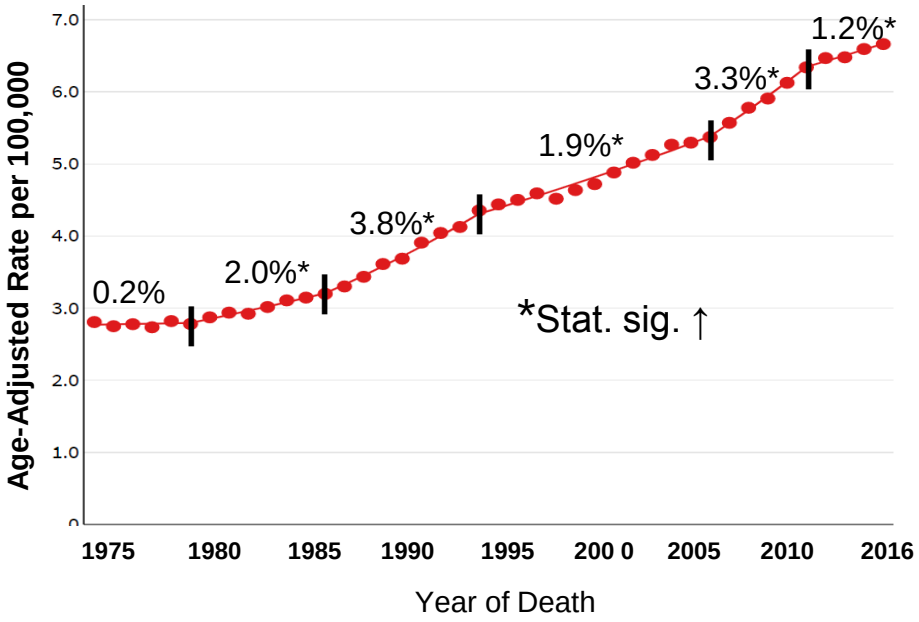
What Are We Looking For?

- Up to the research community to make the case that a cancer site is amenable to this type of modeling and would have impactful public health benefits
- We are looking for cancer site specific proposals where:
  - Applicants bring together separate nascent modeling efforts focusing on important cancer control applications
  - Data sources exist to inform the models (especially the preclinical natural history)
  - Potential interventions or strategies are sufficiently well developed to provide estimates of their operating characteristics
  - Priority will be given to applications that propose modeling feasible cancer control opportunities at different points across the cancer control spectrum

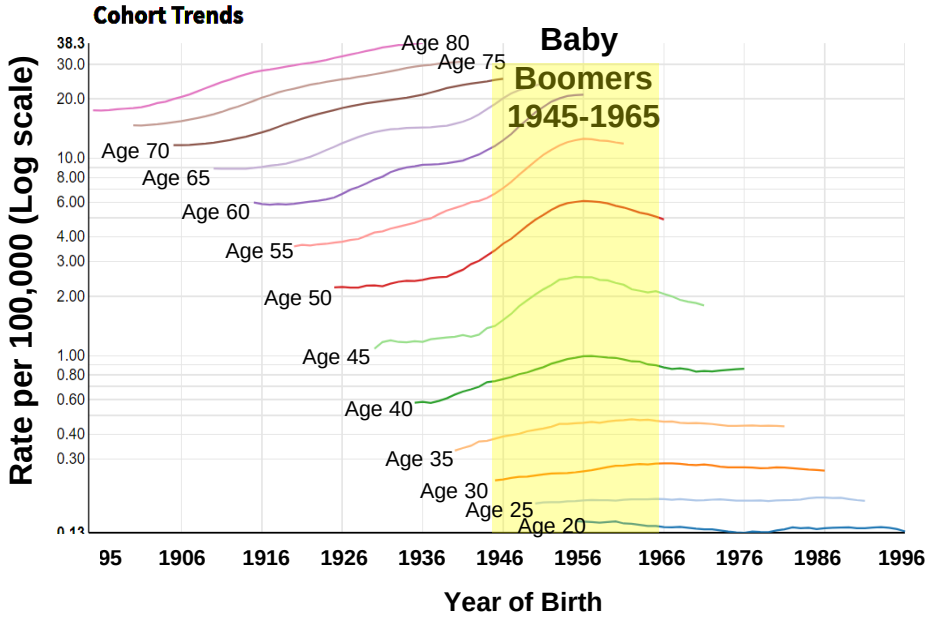
Liver Cancer as an Example

- 42,000 cases, 32,000 deaths per year (2019 est.)

Age-Adjusted U.S. Liver Cancer Mortality by Year of Death



Age-Specific U.S. Liver Cancer Mortality by Birth Cohort



- No comprehensive national liver cancer control strategy

Exemplar Liver Cancer Questions Amenable To Modeling

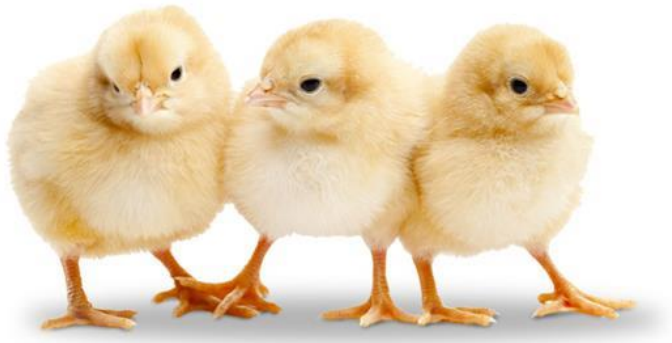
- What is the estimate of the attributable fraction of liver cancer cases that come though each of the 4 major pathways:
  (1) Hepatitis B (vaccine at birth starting in 1991)
  (2) Hepatitis C (large undiagnosed pool, expensive but effective Tx)
  (3) Obesity → Nonalcoholic Fatty Liver Disease (NALFD)
  (4) Heavy Alcohol Use

- How can we determine the most impactful interventions along these pathways and optimize their timing and frequency to reduce liver cancer incidence/mortality and health disparities?
  - Interventions include: vaccinations and reducing risk factors; screening (e.g. for hepatitis); and therapeutic interventions

- Who should be screened for liver cancer and how often?
  - Impact of compliance issues for current 6 month screening interval
  - Relevance of new biomarkers for precision screening and treatment

Some Other Examples of Potential Cancer Sites

- **Thyroid Cancer:** When should thyroid nodules be biopsied, who should consider active surveillance for low-risk thyroid cancer, and when should active treatment be initiated?
- **Anal Cancer:** What is the efficacy of highly targeted screening (e.g. men who have sex with men, HIV+, HPV+) using the anal pap test for early detection of anal cancer -- what regimen should be used? What might be the impact of home collection of samples for screening?
- **Bladder Cancer:** In what situations and under what regimen can those Dx with low-risk bladder cancers undergo active surveillance and what type of surveillance after Tx is cost effective?



Priority Areas

- Same priority areas as main RFA, but new incubator sites will spend considerable time on model development/refinement and consideration and study of data sources to inform the models.

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*
   - Optimizing Strategic Opportunities in Prevention

Budget

- $180K direct cost per modeling group (2 or 3 per cancer site)
- $90K direct costs coordinating center
- $40K direct costs contribution to junior investigators program
- 4 awards (e.g. 2@2 modeling groups and 2@3 modeling groups)
  - $4M total costs per year
  - $20M total costs over 5 years

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Thanks to CISNET Project Team

Cancer Site-Specific Project Scientists
Angela Mariotto (DCCPS) – Prostate
Paul Doria-Rose (DCCPS) – Cervical and Colorectal
Brandy Heckman-Stoddard (DCP) – Breast
Ellen Richmond (DCP) – Esophageal
Rocky Feuer (DCCPS) – Lung

Program Director: Susan Scott (DCCPS)

Questions?

Examples of the Types of Questions That CISNET-Type Models Can Answer

- Understanding of national trends;
- Evaluating the potential lifetime harms and benefits of new strategies and technologies (including costs and cost effectiveness);
- Population screening guidelines and individualized screening strategies;
- Gauging the impact of competing cancer control strategies
- Characterizing community screening practices and processes
- State and local cancer control planning
- Serving as the basis for policy and individual decision aids
- Interpretation of trial results and the design of new trials;
- Characterizing and targeting opportunities to alleviate health disparities;
- Screening in special populations

How will the Incubator Program be Integrated Into the Main CISNET Program?

- One year lag in starting
- Incubator program will share meetings with the main CISNET investigators:
  - Take advantage of experience and approaches used by current network of existing cancer sites (e.g. smoking history generator or HPV transmission models)
  - Contribute to and join in CISNET Junior Investigators Program and Model Accessibility Group
- NCI program staff will help grantees gain knowledge and access to data sources, and connect with relevant NCI consortia, opportunities, and priorities

Evaluating Success

- Demonstrating that the available evidence is sufficient to build a credible model, especially of the natural history of disease
  - Model's results can be validated against independent evidence not used in model development
- Reasonable consistency can be found between independently developed models
  - When disagree – find the source of the inconsistency and determine whether one model needs to be corrected or whether the state of knowledge is insufficient to resolve the issue
- Model applications demonstrating opportunities across the cancer control spectrum where modeling can assist in optimizing choices that will have significant public health benefit
- Cancer sites that are successful in the incubator phase will be considered for inclusion to join the competition as a regular cancer site in potential future rounds