CISNET Incubator Program for New Cancer Sites

New Proposed RFA Utilizing a U01 Mechanism

BSA
May 12, 2020

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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

Individual Cancer Simulation Models: (Parallel Lives with and w/o Interventions)

DEMOGRAPHICS & EARLY LIFE
Sex/Race/Year of birth
Development of risk factors

PRE-CLINICAL CANCER
Pre-cancerous lesions
Tumor initiation & growth

DIAGNOSIS AND TREATMENT
Cancer or Other Cause
Death

Summing Together Individual Histories:
Harms & Benefits of Interventions

Examples of outputs:
- Mortality
- Quality-adjusted life years
- Overdiagnosis
- Direct medical costs

Common Inputs

- Risk factor trends
- Screening behavior
- Diffusion of new treatments

Calendar Time (Model Multiple Birth Cohorts)

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
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.)

- No comprehensive national liver cancer control strategy

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
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?
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
$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
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