National Cancer Institute

Cancer Intervention and Simulation Modeling Network (CISNET) Funding Announcement

RFA-CA-14-012

Errata notice (NOT-CA-14-053)

Monday Oct. 6th

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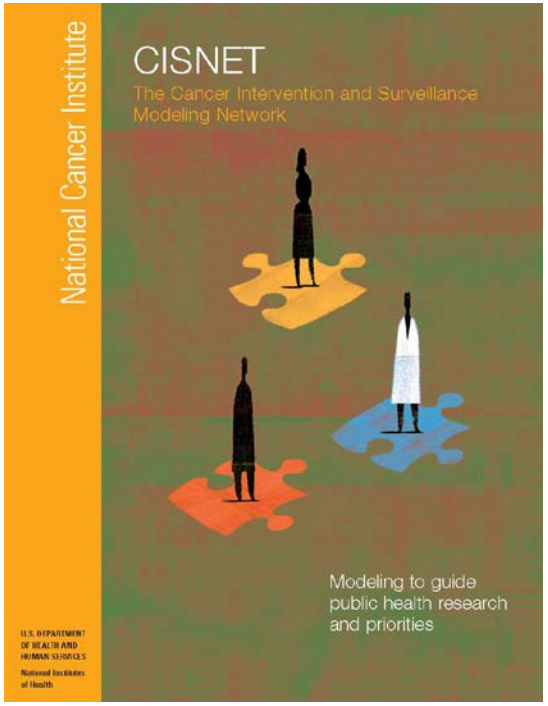
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

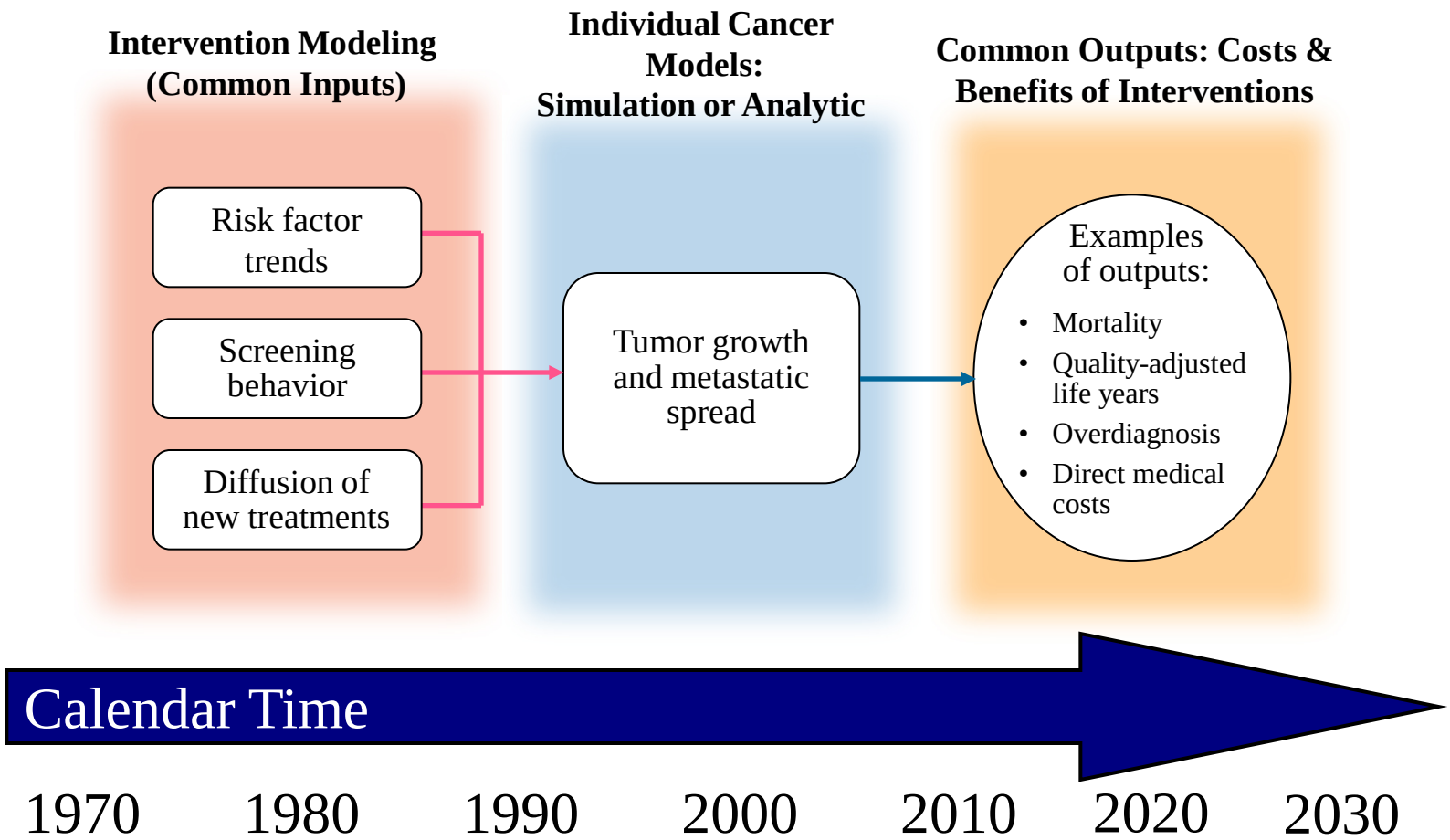
Cancer Intervention and Surveillance Modeling Network (CISNET)

- NCI Sponsored Collaborative Consortium (U01) of Simulation Modelers in Breast, Prostate, Colorectal, Lung, and Esophagus Cancer formed in 2000
- Use surveillance data and simulation modeling to guide public health research and priorities



Web Site: http://cisnet.cancer.gov/

Schema for CISNET Modeling



Overview

- Each application covers a single cancer site
  - 5 current sites (breast, prostate, colorectal, lung, and esophageal cancer) and adding cervical cancer
- Open competition including current grantees and new applicants
- Put forward a comprehensive program of comparative modeling with coverage across the important cancer control areas and relevant specific priority areas for the selected organ site
- Focus on:
  - Areas of public health impact amenable to modeling
  - Take advantage of relevant new results or anticipated new results that will become available during the grant period

Relevant Dates

- Letter of Intent – October 14, 2014
- Application – November 14, 2014
- Earliest Start Date – September 1, 2015

Structure

- Each applicant team must propose the following elements:
  - Modeling Groups (approximately three to six groups per application);
  - a Coordinating Center (one per application);
  - A plan to facilitate the training and experiences of Junior Modelers

Modeling Groups

- Multiple PI applications are encouraged with the head of each modeling group being a PI
  - 3 to 6 modeling groups – the models should be complimentary
  - May propose the application, extension, refinement and/or merging of existing models. If well justified, an existing model can be reformulated using a more robust statistical/mathematical framework. However, de novo model development will NOT be supported.
  - Not all groups need to participate in every comparative modeling exercise
    - Combination of all groups (most important), some groups, and single groups
  - Could potentially have full fledged modeling groups that participate in the full range of activities, and other modeling groups that with smaller budget that participate in a limited way

Coordinating Center

- Formulating, prioritizing, and coordinating work on base case and other questions (including outside requests with new funding opportunities);
- Negotiating common requests for outside data sources; consensus building and coordinating critical evaluation of disparate results;
- Preparing inputs and collecting and processing common outputs for model comparisons;
- Coordinating synthesis papers and group responses bringing together disparate information to inform policy makers;
- Organizing conference calls and setting meeting agendas.
- Although the Coordinating Center will provide oversight, it is expected that certain coordination activities will be distributed across the modeling groups
- Generally the PI for the coordinating center is also a modeling PI, and the contact PI for the application

Plan to facilitate the training and experiences of junior modelers

- Obligation to train the next generation
- Doctoral, post-doc, junior faculty
- Could work within a single modeling group, could rotate among the groups, or even across cancer sites if can arrange
- To foster independence could give have them build a unique model component to attach to one or multiple models – could take an novel or experimental approach

Rapid Response Funds

- Respond to important cancer control issues not originally anticipated
- Examples of use of funds:
  - Gaining access to specialized expertise for particular tasks,
  - Gaining access to data sources,
  - Providing funds to modeling groups to mount important efforts not originally anticipated

Priority Areas

- NCI's way of saying that there are some important cross-cancer site issues that we would like you to focus on
- Gathered from discussions with staff at NCI, modlers, and other organizations
- Not a good idea to try to cover all of them – pick and choose those most relevant for your cancer site
- Part of the application is the justification for why you have chosen to focus on specific areas

9 Priority Areas

- ***Area 1)*** Exploring the Evolving Potential of Stratification based on Polygenic Risk for Cancer Screening and Genomic Tumor Profiles for Treatment;
- ***Area 2)*** State, Local, and International Cancer Control Planning;
- ***Area 3)*** Understanding How Screening and Treatment Work in Real-World Settings and Determining the Best Routes to Optimize the Processes;
- ***Area 4)*** Assisting in the Development of Decision Support Tools;
- ***Area 5)*** Evaluating Natural Experiments Generated as a Result of the Affordable Care Act (ACA);
- ***Area 6)*** Value of Information Analyses;
- ***Area 7***) Pan-Cancer and Pan-Disease Modeling;
- ***Area 8)*** Suggesting Optimal Routes to Reduce Health Disparities;
- ***Area 9)*** Cancer-Specific Opportunities.

Budget

- Budgets will vary, depending on the scale of work and, in particular, the number of modeling groups proposed.
- Absolute Cap - $2M total costs per year
- Suggested Caps
  - $1.2M, $1.5M, $1.8M, and $2M for 3, 4, 5, and 6 or more modeling groups, respectively (total costs).
  - Modeling Groups ($160K direct costs per year per group)
  - Coordinating Center ($90K direct costs per year)
  - Rapid Response Funds ($100K direct costs per year
- Training – included in above (modeling groups and coordinating center)
- Travel – 2 consortium meetings a year
  - Annual in DC area
  - Mid-Year – at one of the sites

Application

- Research Strategy (30 pages maximum)
  - *Sub-section A. Overall Objectives and Significance*
    - State concisely the importance and health relevance of the research described in this application by relating the specific aims to the broad, long-term objectives
  - *Sub-Section B. Team Leadership and Coordination, Advisory Groups, and Training*
    - *B.1 Team Leadership and Coordination*
    - *B.2 Training*
  - *Sub-Section C. Proposed Models and Previous Model Applications*
  - *Sub-Section D. Proposed Model Extensions, Applications and Comparative Modeling*

Review Criteria

- Significance
- Innovation
- Investigators
- Approach
- Environment
- Coordinating Center and Program Integration

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Details of Priority Areas

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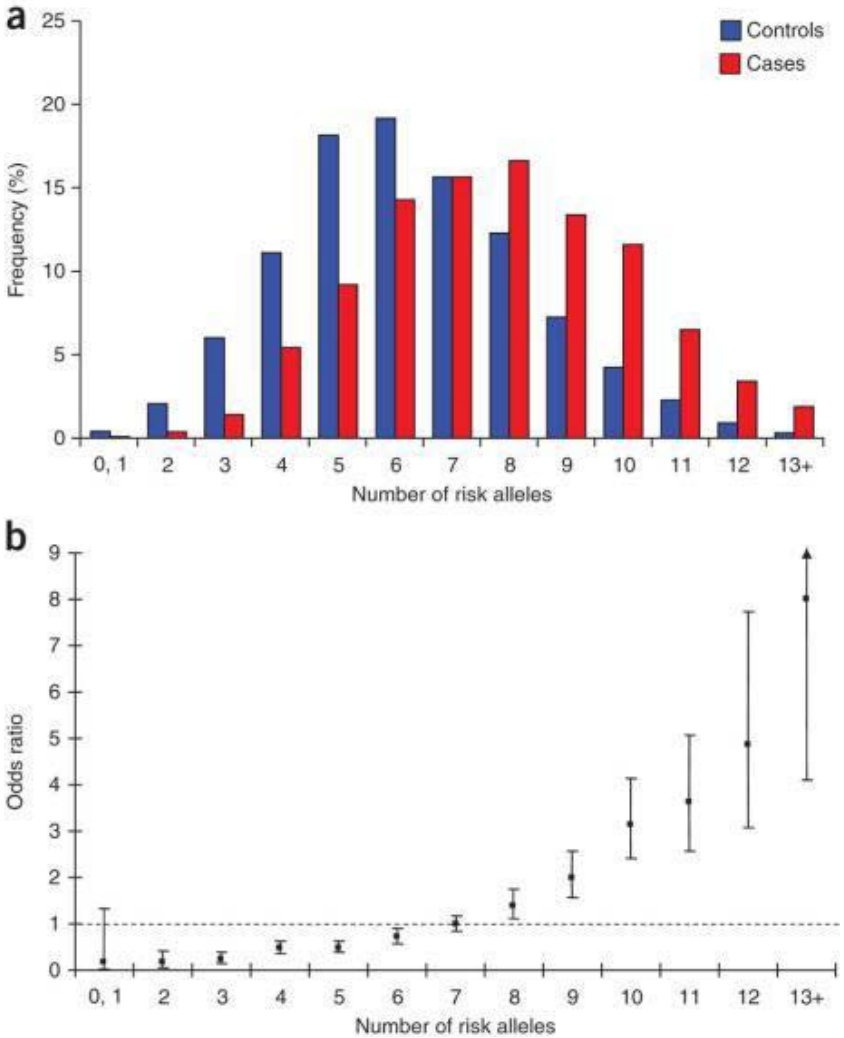
Priority Area 1: Polygenic Risk and Family History

- Polygenic risk - traits where the genetic component is determined by many genes with individually small effects
  - Stratifies across the risk spectrum – potential to identify both high and low risk strategies (unlike family history)
  - Currently level of risk discrimination is not great for common cancers, but has potential to improve in the next 5 years
- Should polygenic risk be the first or last factor considered?
  - How do we best integrate genetic and nongenetic factors?



Cumulative impact of 10 variants on chronic lymphocytic leukemia risk.
Crowther-Swanepoel et al. Common variants at 2q37.3, 8q24.21, 15q21.3 and 16q24.1 influence chronic lymphocytic leukemia risk. Nature Genetics 42, 132–136 (2010)

Genomics (continued)

- What is the impact of SNPs on the natural history of disease?
  - Can common variants identified by GWAS and other approaches go beyond characterizing just cancer vs. control to more specific characterization of cancer (aggressive/non-aggressive disease, adenomas, size/type of adenomas, etc)?
- Using Results from The Cancer Genome Atlas (TCGA) and Other Data Sources
  - Genomic characterization of disease (e.g. triple negative breast cancer and beyond)
  - Genomic risk stratification for treatment

Priority Area 2: Assisting in State, Local, and International Cancer Control Planning

- Extend models previously applied on national level to state, local, and international context.
- Pilot projects funded by CDC supplements:
  - Example: CRC screening in South Carolina – Prior program spending $1M per year on colonoscopy screening for uninsured. Modeling suggested many more lives saved if paid for biennial FIT.
- Internationally, cancer control planning in middle income countries (e.g. South America, Caribbean, Far East, Middle East, Eastern Europe) is an opportunity for CISNET to make an impact

Priority Area 3: Understanding How Screening Works in Real-World Settings and Determining the Best Routes to Optimize the Process

- Mortality gains from idealized trial settings may be considerably attenuated when practiced on a larger population scale
  - Recent USPSTF draft lung cancer screening recommendations are based on results from major screening centers, but e.g. variation in how suspicious nodules are identified and followed up may lead to smaller realized benefits in the population
- Develop partnerships between CISNET and those who collect cancer screening process data in community settings
  - Population-based Research Optimizing Screening through Personalized Regimens (PROSPR), Cancer Research Network, Breast Cancer Surveillance Consortium

Priority Area 4: Supporting the Development of Decision Aids

- The Need (example):
  - USPSTF Breast Recommendations:
    - The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms.
  - Most physicians do not have the time or background to: (1) know the risks of harms and benefits for this patient (or even the average patient), (2) elicit values, and (3) help a patient integrate the various harms and benefits and with their values
- Modeling cannot solve all of these problems, but working in support of decision analysts, they can contribute information useful to # 1 above

What can CISNET models contribute to?

- Decision Aids
  - Tools to Allow Individuals to Elucidate Harms and Benefits and to Weigh Potential Choices Given their Personal Preferences
  - Tools to Allow Health Care Professionals to Guide Shared Decision Making
  - Evaluation of the Benefits versus Costs (esp. time) of Shared Decision Making

- Decision Support Tools
  - Tools that aid physicians in making decisions –e.g. tools to help radiologists make decision about call backs

Priority Area 5
Evaluating Natural History Experiments Caused as a Result of the Affordable Care Act (ACA)

- As the affordable care act is implemented across the country (in some cases differently in different places), there will be opportunities to explore the differential impact on health care outcomes

- Modeling is an ideal way to explore these relationships, and allows for control of confounding factors, time lags between policy changes and their impact, and statistical variation
  - An example of using modeling to explore a natural experiment
    - Shaw et al. An ecologic study of prostate-specific antigen screening and prostate cancer mortality in nine geographic areas of the United States. Am J Epidemiol. 2004 Dec 1;160(11):1059-69.

Affordable Care Act (continued)

- Phase in for ACA (2010-2015)
- Opportunities for modeling, e.g.,
  - Declines in health disparities
  - BRCA counseling about genetic testing for women at higher risk
  - Elimination of cost sharing for mammography, colonoscopy
- Surveys will be enhanced to support research on the impact of ACA
  - BRFSS, NHIS, National Ambulatory Care Survey, MEPS

Priority Area 6: Value of Information (VOI) and Value of Research (VOR) Analyses

- The amount a decision maker would be willing to pay for information prior to making a decision or potential economic losses associated choosing suboptimal policies when that decision is made with uncertain information
  - VOI - evaluate the impact of individual decisions (e.g. the decision to get an additional scans or tests prior to starting therapy)
  - VOR – evaluate the impact of additional research (e.g. the decision to conduct additional laboratory studies to better understand a mechanism of action prior to launching a large expensive cancer prevention study)
- One prior limitation of the development of VOI/VOR analyses has been the effort necessary to build appropriate models
  - CISNET models since they can take advantage of much of the existing model structure and data which has already been accumulated and incorporated into the models

Priority Area 7: Pan Cancer and Pan Disease Modeling

- Prior work is mostly on single cancer sites
- Work on risk factors common across cancers
  - Development of other cause lifetables as a function of risk factors, co-morbidities, etc.
- SNP's with pleiotropic effects that affect the risk of multiple cancers
- Comprehensive characterization of cancers is redefining how cancers are classified
  - Communalities in somatic alterations across cancer sites may lead to discoveries of treatments that are effective across cancers

Priority Area 8: Suggesting Optimal Routes to Reduce Health Disparities

- Modelers are encouraged to explore both the source of disparities and the best leverage points to reduce them.

- If possible, move beyond the standard racial/ethnic characterizations of health disparities and utilize data sources that will enable modeling as a function of disparities in terms of income/education, insurance status, geography, and access to health care.

Priority Area 9: Cancer Site Specific Opportunities

- Areas potentially outside of other priority areas that are specifically important for this cancer site
- Examples:
  - Important new study results that will become availabile during the grant period
  - Evaluate specific new cancer control strategies and/or technologies that have (or will) become available during the grant period