National Cancer Institute

Cancer Intervention and Surveillance Modeling Network: Reissuance Concept

NCI Board of Scientific Advisors

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

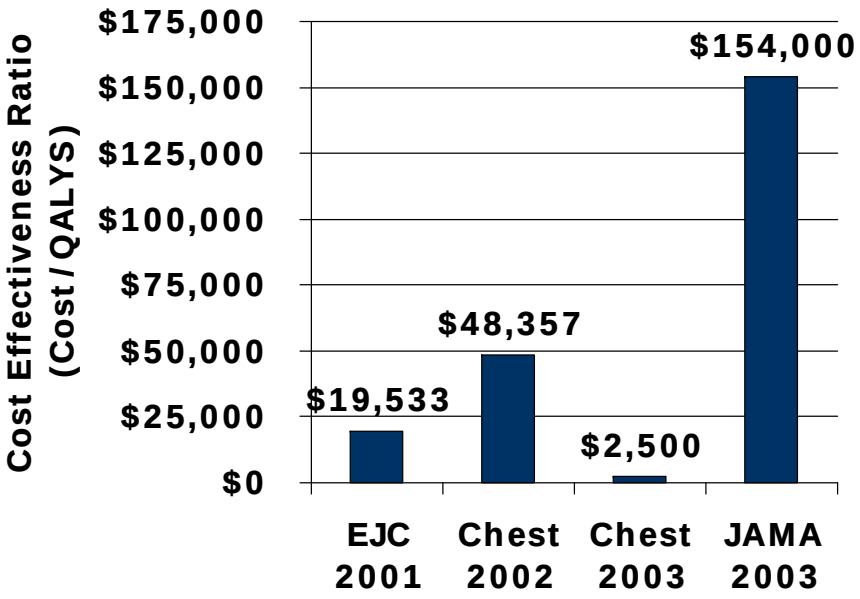
National Institutes of Health

Purpose of CISNET

- NCI Sponsored Collaborative Consortium (U01) of Modelers in Breast, Prostate, Colorectal and Lung Cancer
- Focused on bringing the most sophisticated evidence-based decision tools to:
  - Understand the impact of cancer control Interventions (screening, treatment, prevention) on current and future trends in incidence and mortality
  - Extrapolate evidence from RCT's, epidemiologic, and observational studies to determine the most efficient and cost-effective strategies for implementing technologies in the population
  - Be responsive to challenges due to the increased pace of technology, by helping to determine which new technologies are the most promising when scaled up to the population level

Comparative Modeling Approach

Older Approach: 4 Independent Studies of the Cost-Effectiveness Of CT Screening for Lung Cancer



Differences in target population, screening frequency, stage shift, assumptions about lead time and overdiagnosis, sensitivity

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 points out areas for further study in a systematic way
- Encourages cooperation instead of competition between modelers

Examples of Questions Addressed by CISNET

The NEW ENGLAND JOURNAL of MEDICINE

Landmark paper: What are the contributions of screening and adjuvant therapy on declines in breast cancer mortality?

AHRQ – ***US Preventive Services Task Force***

What are the optimal starting and stopping ages, periodicity, and combination of screening modalities to be recommended for colorectal and breast cancer screening?

CMS CENTERS for MEDICARE & MEDICAID SERVICES

National Coverage Determinations for colorectal cancer screening tests – What should CMS reimburse for new more effective screening technologies?

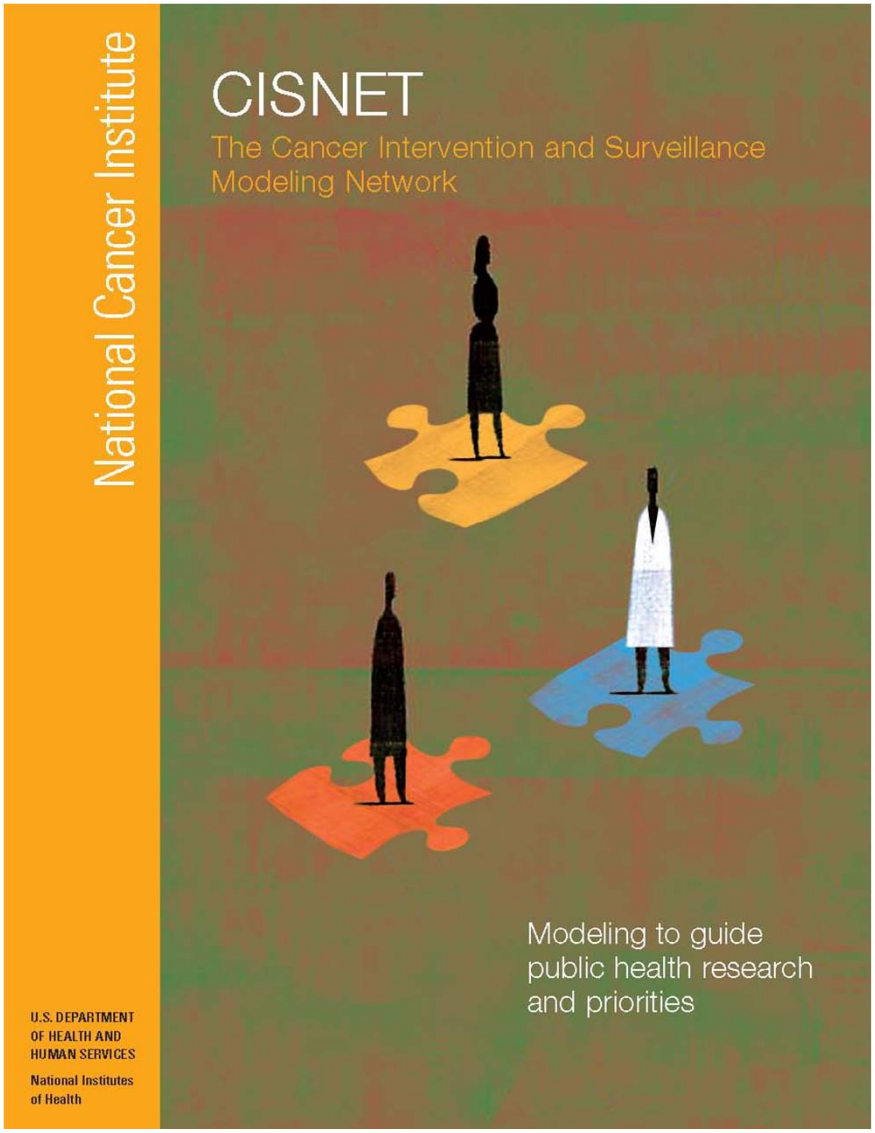
NIDA NATIONAL INSTITUTE ON DRUG ABUSE

What are the number of lung cancer deaths averted due to tobacco control efforts in the last half century?

ERSPC European Randomized Study of Screening for Prostate Cancer

Do prostate cancers dedifferentiate (change Gleason's score) during their screen-detectable preclinical phase?

For More Details on Accomplishments

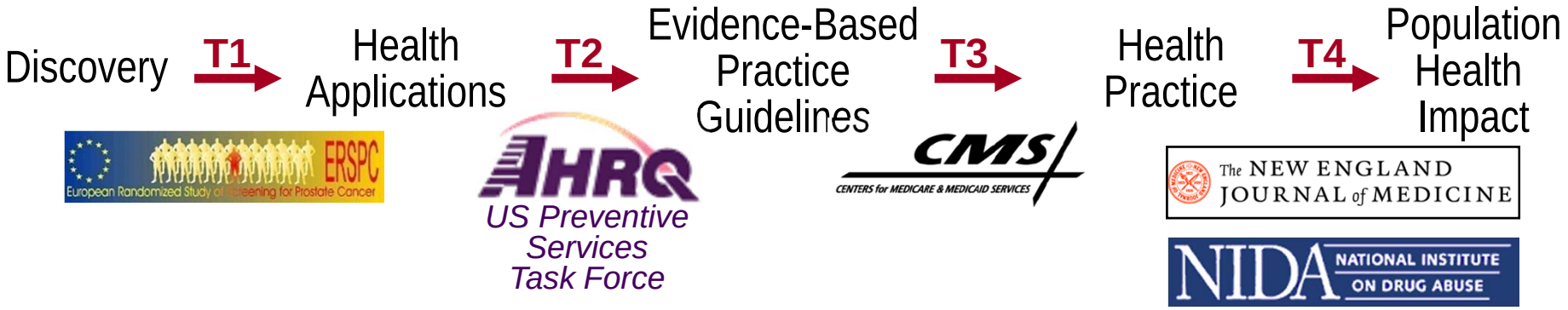


Continued Scientific Need

- Formidable and growing gap between the rapid pace of innovation in biomedicine and our ability to harness it to improve public health
  - "There is no capacity or infrastructure to meet the tsunami of basic research discoveries and move these discoveries rationally into clinical application."
    - Kathy Hudson, director of Genetics and Public Policy Center, Johns Hopkins (Health Affairs, 2008)

- Maturation of modeling in cancer sites beyond the "top 4"
  - Cervical
  - Ovarian
  - Esophagus

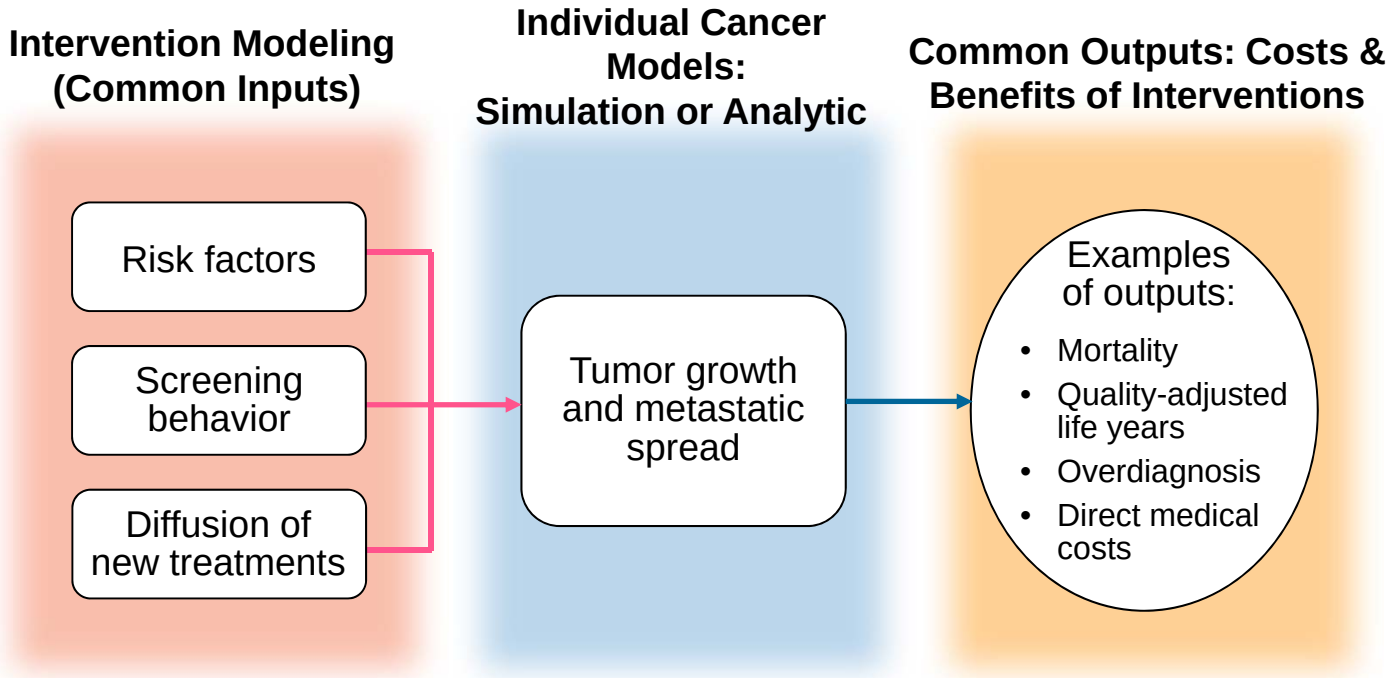
Schema for the Translation of Medical Research



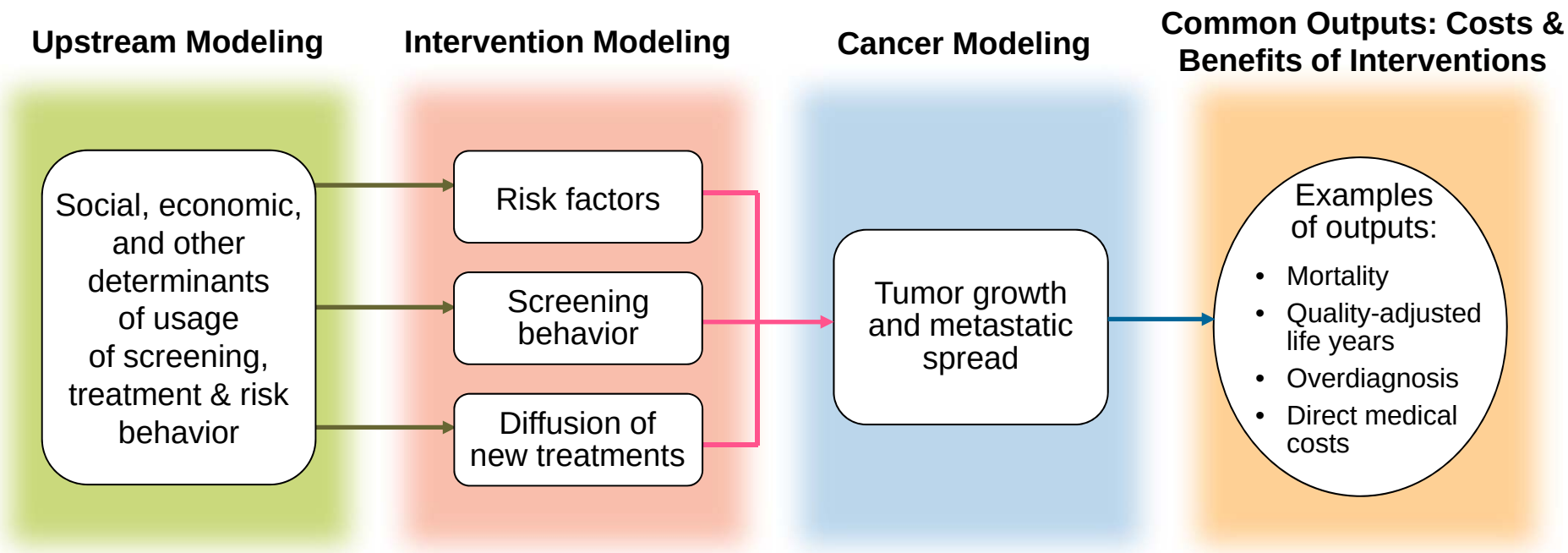
- CISNET models provide a platform for evaluating the downstream consequences of decisions and strategies that are made in earlier phases.

- New Areas for Exploration (with special emphasis on connecting from earlier phases)

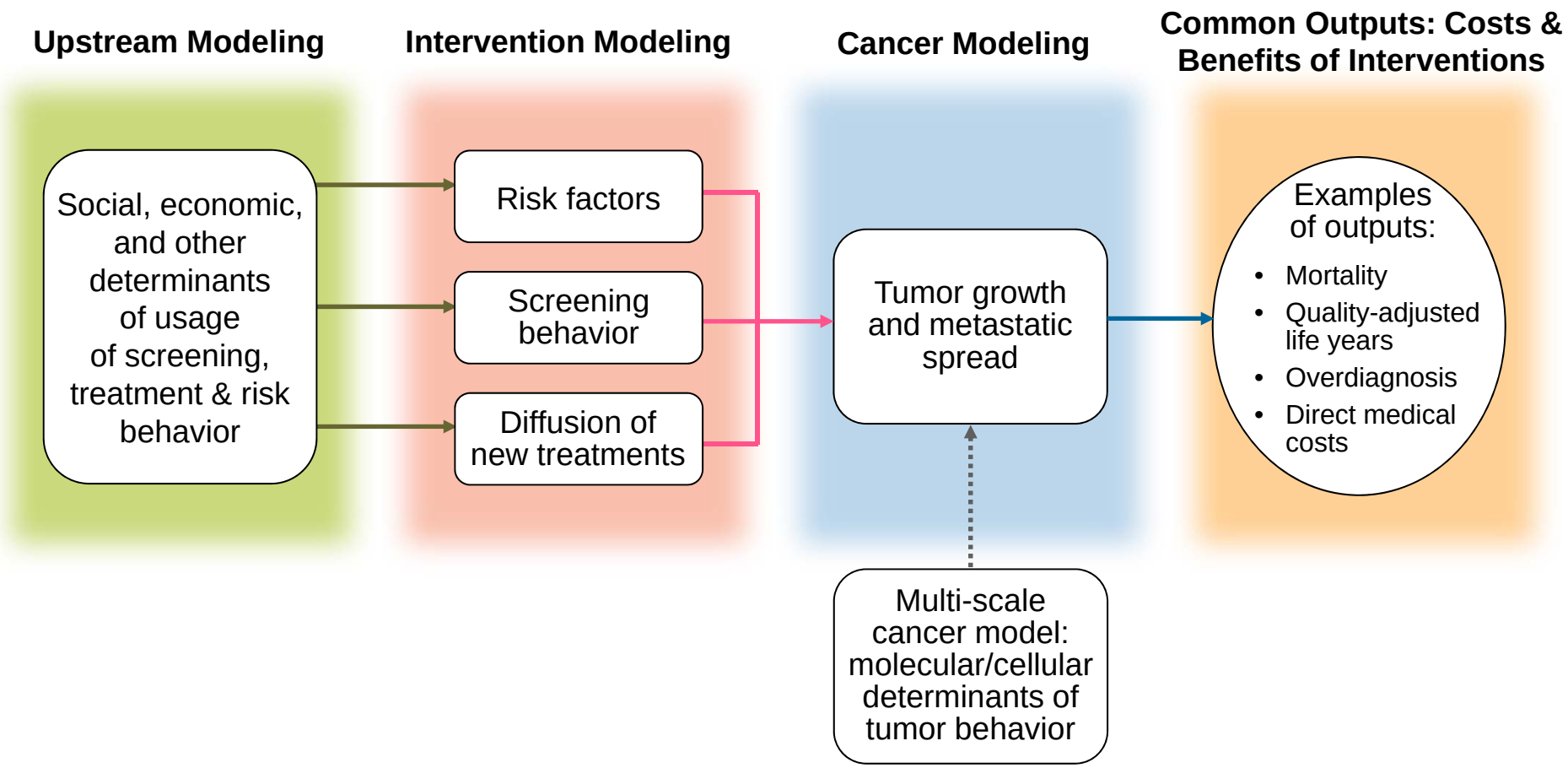
Current Schema for CISNET Modeling



Upstream Modeling

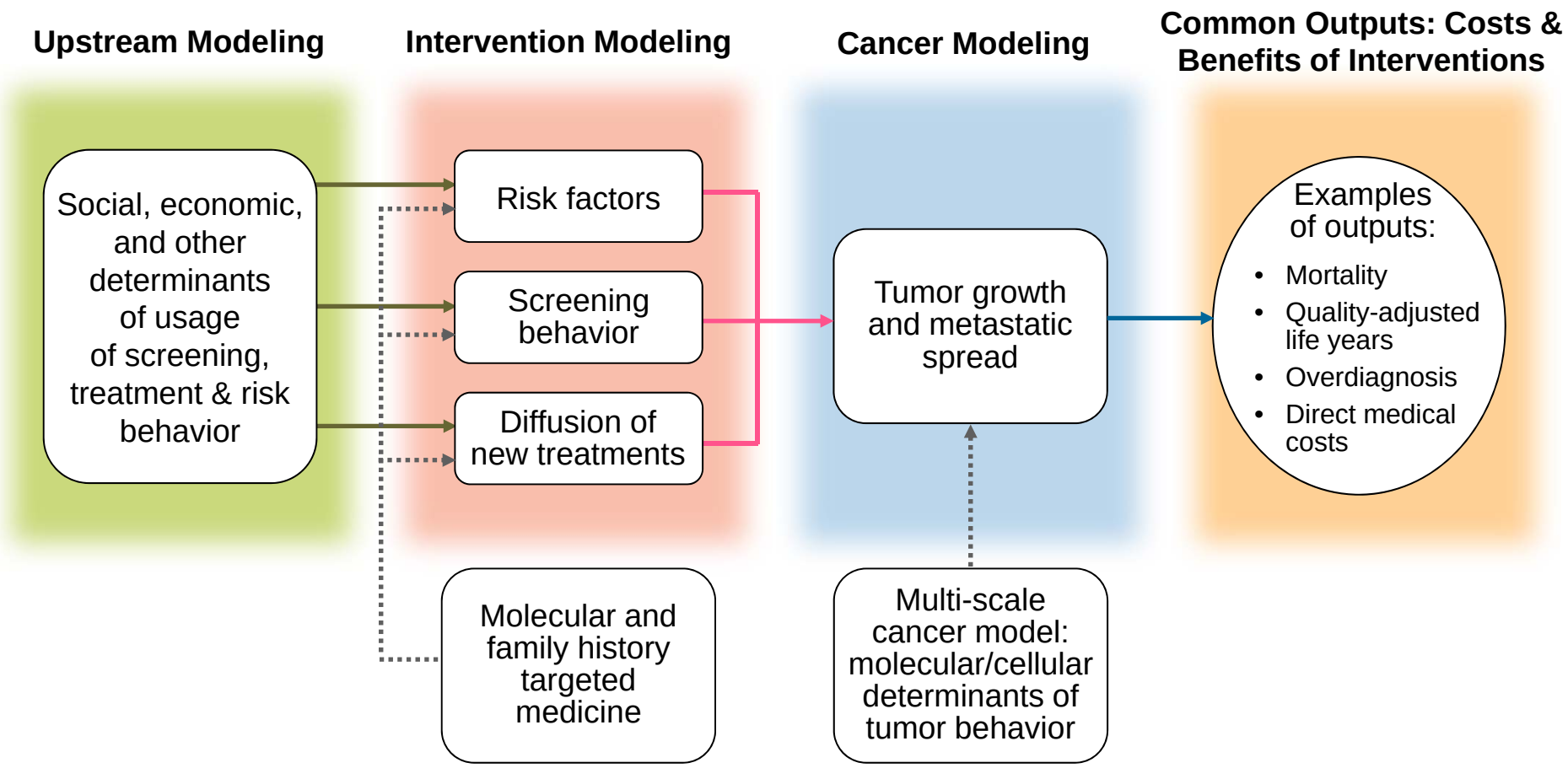


Multi-Scale Modeling



Integrative Cancer Biology Program
Division of Cancer Biology

Incorporating Genomic and Family History Risk Profiles



Integrative Cancer Biology Program
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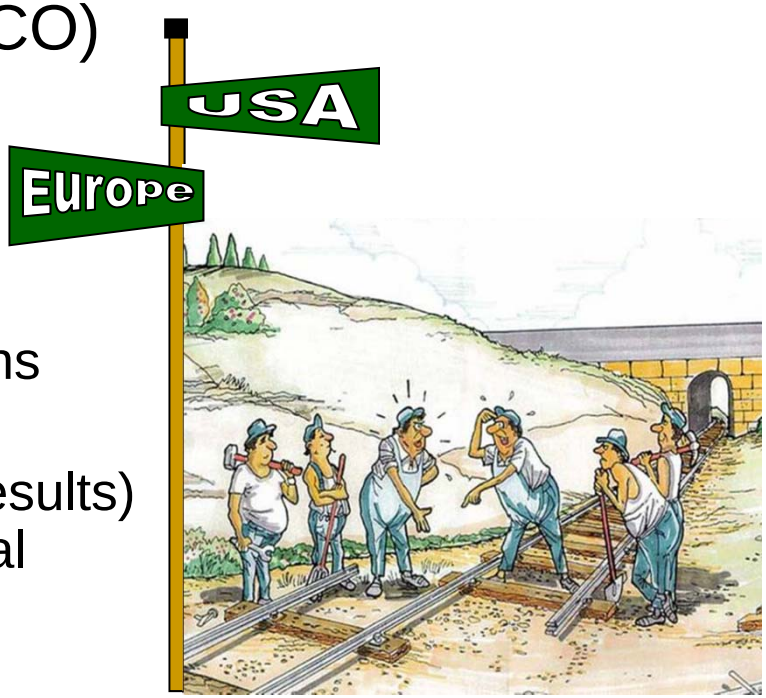
Optimizing Biomarker Development Strategies

CISNET models can provide a set of tools for EDRN investigators to:

- Project the likely impact of screening tests of given sensitivity on disease-specific deaths
- Investigate how early in the preclinical period the test needs to become sensitive in order to produce a target benefit in terms of lives saved
- Given specified test characteristics, project benefits and costs associated with different regimens of screening

Translation of Trial Results into Clinical Guidelines and Public Health Policy

- European (ERSPC) and US (PLCO) prostate cancer screening trials differ with respect to:
  - Screening protocols, test positive criteria, compliance with biopsy recommendations, treatment patterns
  - ERSPC (efficacy trial – established protocol for follow-up of abnormal results) PLCO (effectiveness trial – individual physicians determine follow-up)

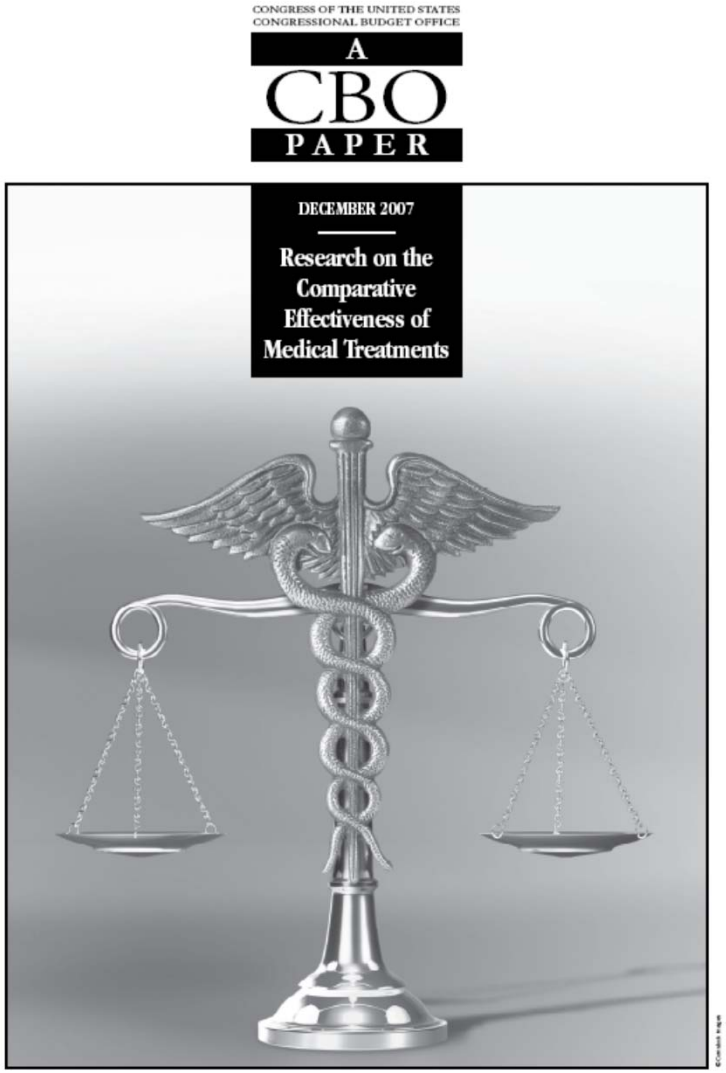


- Probable co-existence of overdiagnosis for some and mortality benefits for others will further complicate guidelines.

Comparative Effectiveness Research

- "… a rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients." CBO, 2007

- Modeling can integrate evidence, extend available evidence from intermediate to long term outcomes, and balance trade-offs
  - E.g. Radical prostatectomy vs. conservative management for prostate cancer (survival benefit vs. urinary and sexual dysfunction)



Other Areas

- Modeling to suggest optimal routes to reduce health disparities
- Development of interactive decision tools
- Evaluation of diagnostic tests

Budget

- Up to 6 linked cancer-site specific groups of awards
  - 2-5 collaborating modelers within each group
  - Average of $900K total cost per year for each linked group of awards
  - 5 year awards
- Collaborative Study Funds
  - $600K per year in Years 2-5
  - Set up to provide a systematic mechanism to facilitate collaborations (either with gov't or non-gov't) who bring timely cancer control issues amenable to modeling
  - Funds would pay for time of collaborators, time of CISNET investigators, data acquisition, etc.

Budget Summary

	FY10	FY11	FY12	FY13	FY14
Grant funds	$5.40M	$5.40M	$5.40M	$5.40M	$5.40M
Collaborative Study Funds	_____	$0.60 M	$0.60M	$0.60M	$0.60M
Total	$5.40M	$6.00M	$6.00M	$6.00M	$6.00M

Responses to Subcommittee Questions

What is the rationale for the increase in the budget?

- Budget
  - Current budget: about $3.75M per year
  - Proposed: Year 1: $5.4M, Years 2-5: $6M per year

- Three reasons for increase:
  - (1) increase from original 4 to up to 6 cancer sites
  - (2) slightly larger awards to individual PI's to accommodate:
    - (a) adding various model components – possibly through subcontracts with specialized modelers (e.g. multi-scale modelers, up-stream modelers)
    - (b) adding more multi-disciplinary expertise
  - (3) $0.6M collaborative study funds in years 2-5

Accomplishments in terms of the full initiative: # of models, # of model applications, cross-over of models among cancer sites

- 18 models (5 lung, 7 breast, 3 colorectal, 3 prostate)
  - Affiliate members (2 lung, 1 colorectal)
- Model applications: 90 papers
- No cross over models per se, since model development for each cancer is unique with respect to the biology of the cancer, the data sources, and the state of RCT evidence
  - Methodologic advances do have broad applicability across cancer sites:
    - 48 methodology papers

Status of Implementing External Review Recommendations (Especially Pilot Studies in New Areas)

- Pilot Studies in New Areas
  - Multi-Scale Modeling
    - 2 pilot studies in breast and lung cancer with ICBP
  - Incorporating Genomic and Family History Risk Profiles
    - Formulating plans for possible use of stimulus money to fund pilot projects in this area
  - Health Disparities
    - Pilot project with ACS to model the factors underlying divergent patterns of colorectal cancer mortality rates for blacks and whites

- Use of Modeling to Evaluate Diagnostic Tests
  - New area suggested by external review and added to concept
  - Initiated discussions with Diagnostic Imaging Branch, DCTD
  - Have applied for stimulus package funds on comparative effectiveness research in this and other areas

Future Expectations in Terms of New Model Development vs. Model Application

- No new models developed from scratch (even in newly added cancer sites)

- Emphasis on:
  - Updating models based on new evidence
  - Model applications
  - Adding modules to existing CISNET models to allow expansion into new areas

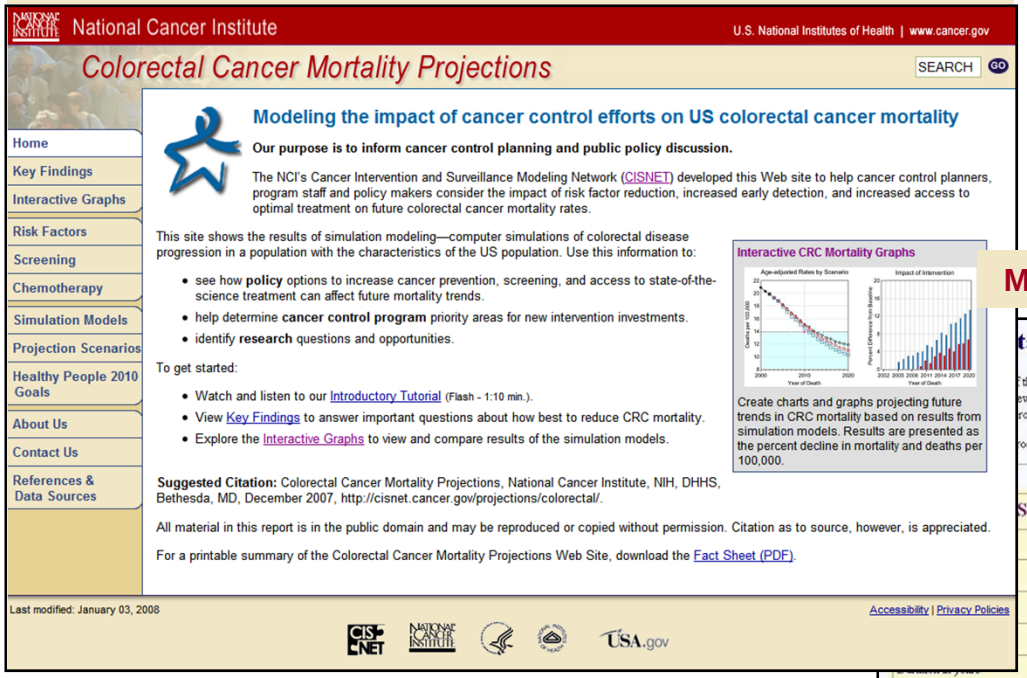
Suggesting Optimal Routes to Reduce Health Disparities

- Moving beyond standard racial/ethnic characterizations
  - Education/Income
  - Insurance Status
  - Geographic Disparities

- Search for the largest leverage points to reduce disparities in mortality rates as a function of:
  - Risk Factors: smoking rates, obesity, other risk factors
  - Screening rates, follow-up to abnormal screening
  - Treatment, quality of care

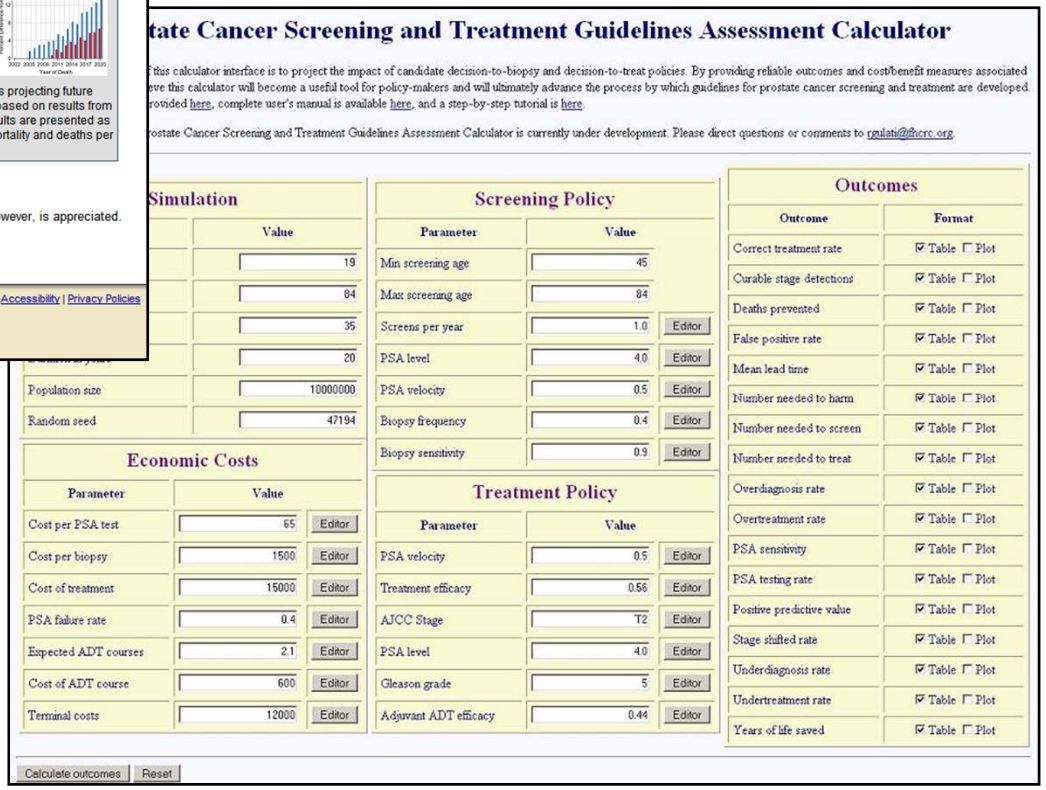
Interactive Policy-Level Decision Tools

Colorectal Cancer Mortality Projections Website



- Allow cancer control planners and policy makers to explore the impact of varying key parameters involved in their decision making.

Mock-Up of Prostate Cancer Policy Assessment Calculator



- Ensure that the tools are understandable and relevant for target audiences.

Evaluation of Diagnostic Tests

- A large number of diagnostic tests (conducted for symptoms or for known disease) are not supported by empirical studies showing that they affect patient outcomes

- Example: Assistance to CMS in making coverage decisions about indications for using PET imaging
  - Which cancers
  - Diagnosis, staging, restaging and monitoring response to treatment

Use of the Collaborative Linked Mechanism

- Group proposals will incorporate plans for joint collaborative analyses, rather than having to change plans after the award
- The group as a whole would coordinate to provide coverage of the new areas (with some groups specializing in specific areas)
  - Groups could bring in and share specialized modeling expertise (e.g. upstream modelers, multi-scale modelers)
- Since groups could decide who they want to work with, it would reward PI's who are perceived as collaborative
- Coordination of group activities would be built into the application, rather than funding it separately

Cooperative Agreement Mechanism (U01)

- Facilitate comparative modeling
- Allow access to a broader array of data resources and multi-disciplinary expertise
- Provide a forum for discussion of validation and other methodologic issues
- Collaboration with NCI staff will assist in:
  - Ensuring responsiveness of the consortium to evolving surveillance and cancer control issues
  - Attaining research goals and catalyzing collaborations with outside groups who often approach NCI seeking assistance
  - Knowledge of and access to potential data resources

Status of Implementing External Review Recommendations

- More Comparative Modeling Aimed at Understanding Model Differences
  - Joint modeling work
    - Some focused on large policy questions (e.g. role of screening and adjuvant therapy on the decline in breast cancer mortality)
    - Others focused on hypothetical exercises aimed at understanding model differences (e.g. how long after a single colonoscopy at age 50 does it take for age-specific CRC incidence rates to return to background levels)
  - Model Profiler – on-line templated model documentation to aid in model transparency
  - Publications on model differences

Funding History

- Originally funded in two phased in rounds (FY00 and FY02)
- Refunded in FY05 – total of 15 grants funded in breast, prostate, colorectal and lung cancer
- 8 Affiliate Members (Funded through other mechanisms – joined CISNET collaboration)

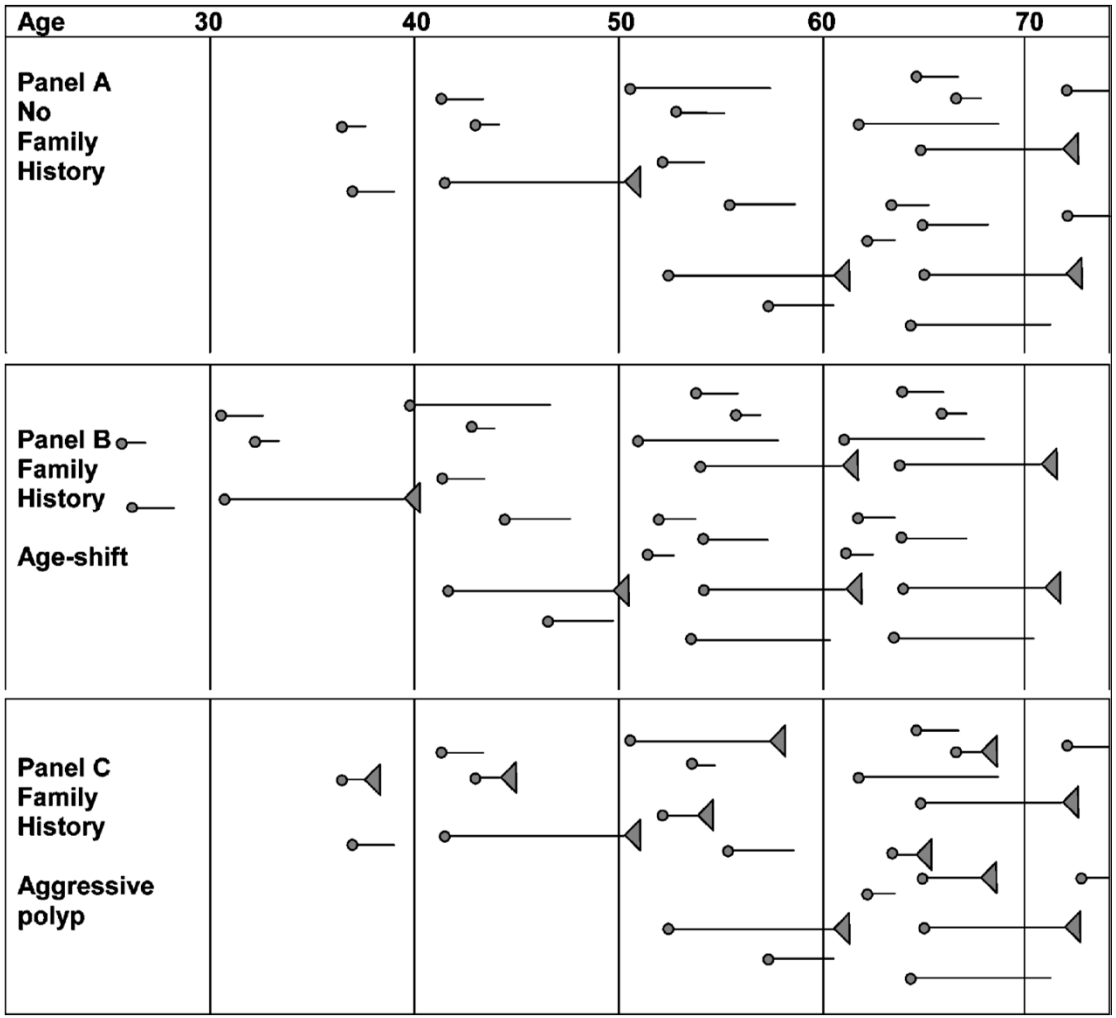
Optimizing Biomarker Development Strategies

Preclinical Exploratory	*PHASE 1*	*Promising directions identified*
Clinical Assay and Validation	*PHASE 2*	*Clinical assay detects established disease*
Retrospective Longitudinal	*PHASE 3*	*Biomarker detects preclinical disease and a "screen positive" rule defined*
Prospective Screening	*PHASE 4*	*Extent and characteristics of disease detected by the test and the false referral rate are identified*
Cancer Control	*PHASE 5*	*Impact of screening on reducing burden of disease on population is quantified*

Building Capacity and a Unique Approach to Modeling

- Flexible-Broad Based Disease Models
  - Able to incorporate the full range of cancer control interventions
- Multiple-Birth Cohort Modeling
  - Construct the actual US experience rather than a single hypothetical birth cohort
- Comparative Modeling
  - Central questions to be addressed by all groups with a common set of inputs and outputs
    - Reproducibility across model adds credibility to results
    - Differences points out areas for further study in a systematic way
- Transparency in Modeling Structure and Assumptions
  - Standardized web-based documentation across models

How Should Screening Schedules for Colorectal Cancer be Modified for Individual with A Family History?



Ramsey et al. Cancer Epidemiol Biomarkers Prev, 2005