PROSPR: Population-based Research Optimizing Screening through Personalized Regimens (with CDC)

Stephen Taplin, MD, MPH
Carrie Klabunde, PhD
Nancy Potischman, PhD
Emily Dowling, MHS
Rachel Ballard-Barbash, MD, MPH
Robert T. Croyle, PhD
Support as a Scientific Priority

- USPSTF controversy on breast cancer screening
  - Need studies of digital mammography and MRI in practice
- NIH State of the Science Conference on CRC screening use (2/10)
  - Monitor the impact of screening
- Health care reform passed and supports efforts consistent with PROSPR
  - Comparative effectiveness, prevention services, development of quality metrics
- 2010 Think Tank review with leading investigators
  - Need comprehensive data on risks and benefits of screening in practice
Clinical Guidelines

Effects of Mammography Screening Under Different Screening Schedules: Model Estimates of Potential Benefits and Harms

Jeannie S. Mandelblatt, MD, MPH; Kathleen A. Cronin, PhD; Stephanie Bailey, PhD; Donald A. Berry, PhD; Harry J. de Koning, MD, PhD; Gerrit Draisma, PhD; Hui Huang, MS; Sandra J. Lee, DSc; Mark Munsell, MS; Sylvia K. Pfeiffer, PhD; Peter Ravdin, MD, PhD; Clyde B. Schechter, MD, MA; Bronislava Sigal, PhD; Michael A. Stone, PhD; Natsuki K. Streul, PhD; Nicollin T. van Rauwendaal, MSc; John Venier, MD; Marvin Zelen, PhD; Eric J. Furer, PhD; and for the Breast Cancer Working Group of the Cancer Intervention and Surveillance Modeling Network (CISNET)

Abstract

Background: Despite trials of mammography and widespread use, optimal screening policy is controversial.

Objective: To evaluate U.S. breast cancer screening strategies.

Design: 6 models using common data elements.

Data Sources: National data on age-specific incidence, competing mortality, mammography characteristics, and treatment effects.

Target Population: A contemporary population cohort.

Time Horizon: Lifetime.

Perspective: Societal.


Memorial Sloan-Kettering Cancer Center, New York, New York 10065, USA. zuuber@mskcc.org.

Comment in:


Randomized trial of a lay health advisor and computer intervention to increase mammography screening in African American women.

Russell KM, Champion VL, Monahan PO, Millon-Underwood S, Zhao Q, Spacey N, Rush NL, Paskett ED.

Indiana University School of Nursing, 1111 Middle Drive, Indianapolis, IN 46202, USA. kartrusse@iupui.edu

Abstract

BACKGROUND: The U.S. Preventive Services Task Force requested a decision analysis to inform their update recommendations for colorectal cancer screening. OBJECTIVE: To assess life-years gained and colonoscopy colorectal cancer screening strategies and identify a set of recommendable screening strategies. DESIGN: Decision analysis using 2 colorectal cancer microsimulation models from the Cancer Intervention and Surveillance Modeling Network.
Focus on Research Translation and Implementation

- **Discoveries (e.g. genetic risk factor)**
  - T1: Epi, Cohorts, Biobanks

- **Candidate Application (e.g. test)**
  - T2: Clinical studies, RCTs

- **Evidence based Guideline/Policy**
  - T3: Implementation Research
    - Practice & Control Programs in Communities
      - T4: Outcomes Research
        - Reducing the Burden of Disease in Communities

- **Trials**
  - Phase I
  - Phase II
  - Phase III
  - Phase IV

Adapted from Khoury et al; Gen Med 2007

PROSPR
Screening is a process that breaks down in the community

Invasive cervical cancers should not occur in populations where screening is implemented well.

Chart audits for breakdowns in the process of screening among women with invasive cervical cancer (n = 835) in 7 managed care locations with high screening rates

![Flowchart showing the process of screening with percentages:
- Risk Assessment: 56%
- No screening: 32%
- Positive test >1 year: 13%
- Diagnosis: Moderate
- Cancer or Precursor Treatment:]

Leyden JNCI 2005
Scale of Problem

- Breast, CRC, Cervical: an estimated 82 million screened each year in the U.S. ($8.8 billion)
- But screening is not optimally applied in practice
  - 1990-2000 - $6 billion paid for unnecessary screening
    - Greater mortality reduction possible by reaching more people
  - Additional reduction in CRC mortality
    - 9% greater by improving follow-up
    - 50% greater by improving the proportion of people screened

Stout JNCI 2006; Submaramanian Cancer Epidemiol Biomarkers Prev 2009
Number of Cytological Tests per 1000 Women, standardized to U.S. 2000 pop.

Source: NHIS, Paleba
Cervical Cancer Mortality Rates Standardized to U.S. 2000 Population

Source: SEER, CBS
PROSPR Objectives

- **Primary**
  - Study the comparative effectiveness and outcomes of existing and emerging cancer screening processes
    - Breast
    - Colon
    - Cervical cancer.
  - Study the balance of benefits and harms of cancer screening across *recognized* cancer risk levels

- **Secondary**
  - Share data and conduct preliminary studies relevant to future innovative research to optimize the screening process.
Examples of Potential Cancer Themes

- Strategies for estimating and communicating personalized risk, screening benefits, and harms
- Organizational and behavioral interventions to address technical and/or human factors in screening (e.g. radiologist interpretive skills, improving follow-up to abnormal tests)
- Mathematical modeling of the impact of screening improvements
Examples of Cancer-Specific Issues

- Cervical: screening impact/age, HPV type/age, impact of HPV vaccine on HPV types
- Breast: new indicators of risk, comparative effectiveness of diagnosis by MRI, ultrasound, digital mammography
- CRC: natural history of adenomas, lesion frequencies, comparative effectiveness of FOBT, fecal DNA, CT colonography, natural history of extra-colonic lesions
Examples of Trans-Cancer Issues

- Standardize CER methods for evaluating the screening process
- Foster comprehensive data collection across the process of care
- Establish US community estimates of operational characteristics of screening (i.e., true and false positive rates)
- Estimate the balance of benefits and harms across screening technologies
- Identify systematic breakdowns in the screening process and comparing them across settings and cancers
Optimize screening to:

- Improve the screening process
  - Trans-cancer measurement of the variation across communities in the frequency of steps in the screening process
  - Improvements in recruitment
  - Improvements in follow-up

- Reduce morbidity
  - Trans-cancer measurement of morbidity (harms) of screening across ages, risk groups, communities and systems of care
  - Improvements in the screening test; comparative effectiveness of screening technologies in community practice
  - Reduction in screening frequency for some people (personalization)
  - Reduction false positive testing; center studies of alternative diagnostic strategies
Population-based Research Optimizing Screening through Personalized Regimens (PROSPR)

- Imaging Center (MM, MRI, CTC)
- Endoscopy Centers (Col, Sig, CTC)
- Primary Care Practices (FOBT, Pap, HPV)

Data Capture during Screening Process:
- Facility Characteristics
- Procedure Types
- Procedure Performance/Interpretation
- Procedure Results
- Risk Factors, Demographics, Screening Hx

Funded Centers:
- Site #1
- Site #2
- Site #3
- Site #4
- Site #5

Linkage to Population-based Cancer Outcomes

Statistical Coordinating Center:
- Cervical
- Breast
- CRC

PROSPR Consulting Panel
FY11 Budget

- Up to 5 sites per cancer (3 cancers) = $13.5M/year (U54)
  - Establish network and common data elements/definitions
  - Collect the data in the course of care
  - Develop pilot projects and linkages to appropriate collaborators

- Statistical coordinating center = $1.5M/year (U01)
  - Establish data quality standards, common data elements
  - Pool data and assist with analyses with these data

- Total = $15M/year for 5 years
Why now?

- Comparative effectiveness research is a high priority for Congress
  - 2009 Senate appropriations recommendation – “NCI should research how to apply what is known in early detection”
  - Health Care Reform mandated screening reimbursement
- There are no other multi-site research initiatives addressing the entire screening process and its results
- New screening technologies are emerging in practice
  - Breast MRI, HPV DNA testing, HPV vaccine, CT colonography
  - Optimizing the screening process affects mortality