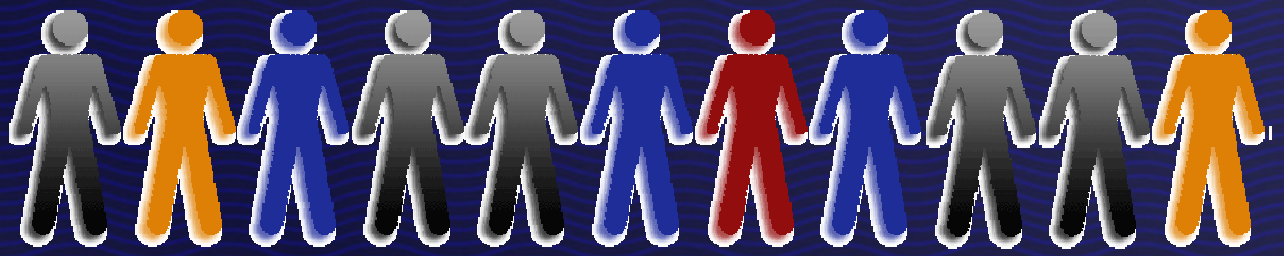
Cancer Risk Prediction Models:
A Workshop on Development, Evaluation, and Application



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Sponsored by
Division of Cancer Control and Population Sciences
Division of Cancer Epidemiology and Genetics
Office of Women's Health

National Cancer Institute, National Institutes of Health,
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Workshop Overview and Objectives

Andrew N. Freedman, Ph.D

Applied Research Program, DCCPS, NCI

Risk Prediction Models for Cancer

Absolute Risk Assessment Models

- Estimates the probability of developing cancer over a defined period of time

Genetic Susceptibility Risk Models

- Estimates the likelihood of detecting a mutation in a cancer susceptibility gene in a given family or individual

Applications

- Planning intervention trials
- Estimating the population burden of disease
- Clinical decision making and creating benefit/risk indices
- Identifying individuals at high risk and designing prevention strategies

Development

Risk Factors

- Environmental
  - Demographic, reproductive, smoking, medications, etc.
- Genetic
  - Family history
  - High penentrance alleles
  - Low penentrance polymorphisms
- Clinical and Biological markers
  - Blood pressure, cholesterol, enzyme levels, protein expression, etc.
- Interactions

Development

Data

- Cohort, case-control, nested case-control, family and clinical studies, SEER and population surveys
- Expert opinion

Risk Calculation

- Empirical, logistic regression, proportional hazards, Bayesian analyses, log Incidence, Markov models/decision theory

Evaluation

Reliability or Calibration

- Ability of a model to predict incidence of a disease in a group of individuals

Discriminatory Accuracy

- Measures a model's ability to discriminate at the individual level among those who develop disease from those who do not

Internal Validity

- Data-splitting, cross validation, bootstrapping

External Validity

- New independent sample

Absolute Risk Models

Coronary Heart Disease

- Framingham Coronary Risk Prediction Model (Kannel et al. Am J Cardiol, 1976)

Breast Cancer

- BCDDP “Gail” Model: (Gail et al. JNCI, 1989)
- CASH “Claus: Model: (Claus et al. AJHG, 1991)
- Group Health (Taplin et al. Cancer,1991)
- DevCan (Feuer et al. JNCI, 1993)
- NHS (Rosner et al. JNCI, 1996)

Risk models for predicting carrier status for cancer susceptibility genes

BRCA1/2

- Couch et al. NEJM, 1997.
- Shattuck-Eidens et al. JAMA, 1997.
- Frank et al. JCO, 1998.
- BRCAPRO: Berry et al. JNCI 1997, Parmigiani, AJHG, 1998.
- Hartge et al. AJHG, 1999.

Why this Workshop? Why Now?

Cancer Risk Prediction Models published in the last 2-3 years or currently in development

- Harvard Cancer Risk Index
- Lung
- Melanoma
- Prostate
- Colorectal
  - HNPCC (MLH1 and MSH2)
- Breast
  - BRCA1/2
  - Extension of existing models

2005 NCI Bypass Budget, Genes and Environment

- "Refine cancer risk prediction methods/models to integrate genetic and environmental determinants of cancer among diverse populations"

Personalized Medicine and Genetic Profiling

"By the year 2010, it is expected that predictive genetic tests will be available for as many as a dozen common conditions, allowing individuals who wish to know this information to learn their individual susceptibilities and to take steps to reduce those risks for which interventions are or will be available."

- Collins FS, McKusick VA. Implications of the Human Genome Project for Medical Science. JAMA 2001;285:540-544.

Why This Workshop?
Why Now?

- Websites:
  - srab.cancer.gov/devcan/
  - www.mskcc.org/
  - www3.utsouthwestern.edu/cancergene/
  - Bcra.nci.nih.gov/
  - www.yourcancerriskharvard.edu/index.htm
- Books:
  - Handbook of Breast Cancer Risk Assessment
  - Handbook of Cancer Risk Assessment and Prevention
- International Society of Cancer Risk Assessment and Management (ISC-RAM)
- Companies in the US and UK offering testing of multiple genetic polymorphisms for genomic profiling for a number of chronic diseases

Current opportunities in Cancer Risk Prediction

- Large cohort and case-control datasets and consortiums
- Evidence for effective screening, intervention and prevention strategies in high risk individuals and in the general population
- Promising new biomarkers
- New risk prediction methodologies and evaluation techniques
- Progress in research for communicating risk, decision-making and decision aids
- Chemoprevention trials
- Modeling cost-effectiveness and burden of disease by stratifying the population by risk and intervention

Important Questions: Application

- What are the strengths and limitations of cancer risk prediction models?
- For which applications are these risk prediction models most useful?
- How useful are these risk prediction models at the individual level?
- What discriminatory accuracy is needed to be useful in clinical decision-making?

Important Questions: Development

- How much can we improve discriminatory power at the individual level with the addition of risk/genetic factors to the models?
- Do we need to develop specific risk models for subgroups of the population (e.g. minorities)?
- Are there genetic, biologic, hormonal or behavioral risk factors or markers that are particularly promising for risk prediction for cancer?
- How can we effectively combine genetic, clinical, and biological risk factors with epidemiologic risk factors into absolute risk models?

Important Questions: Evaluation

- What current models require validation? What quantitative criteria should be used to assess the performance of risk models for various purposes?
- Are ROC curves the best measure of discriminatory accuracy?
- How should one describe the uncertainties in predictions from model misspecification?
- How transferable are absolute risk projections from one population to another?

Other Questions:

- **What resources are needed to improve cancer risk prediction models?**

- How should cancer risk prediction models be disseminated to health care providers, patients, and the public?
- How can they be used effectively to improve cancer education and risk communication?
- Monograph

Workshop Agenda

Day 1

- Session I: Applications of Cancer Risk Prediction Models
- Session II: Poster Session
- Session III: Goals and Issues in the Development of Cancer Risk Prediction Models for Various Purposes
- Lunch: Lessons Learned from Cardiovascular Risk Models
- Session IV: Risk Assessment Models for Predicting Cancer Susceptibility Genes and Cancer Risk
- Session V: Breakout Sessions
- Poster Session: Revisited

Day 2

- Session VI: Validation and Evaluation Methodology
- Session VII: Report from Breakout Sessions

Breakout Sessions:

Session I:

Intervention studies, clinical decision-making, and population prevention strategies

- Focus on breast cancer

Session II:

Intervention studies, clinical decision-making, and population prevention strategies

- Focus on lung, CRC, melanoma and cancers other than breast

Session III:

Genetic susceptibility

Session IV:

Evaluation and validation

Thank You!

Co-Chair

- Ruth Pfeiffer, DCEG, NCI

Planning Committee

- Rachel Ballard-Barbash, DCCPS, NCI
- Graham Colditz, Harvard Medical School
- Mitchell Gail, DCEG, NCI
- Patricia Hartge, DCEG, NCI
- Daniela Seminara, DCCPS, NCI

- Mary Jane Kissel, Nova Research Corp.
- Geoff Tobias, DCEG, NCI

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Participants