Cancer Intervention and Surveillance Modeling Network (CISNET)

Breast Cancer Work Group

Presented by:

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Georgetown University

CISNET Breast Cancer Collaborators

Grantees:

- Dana Farber Cancer Institute: Sandra Lee, Marvin Zelen, H. Huang, Rebecca Gelman
- Erasmus University: Harry de Koning, Nicolien van Ravesteyn, Gerrit Draisma
- Georgetown University: Jeanne Mandelblatt, Clyde Schechter, Michael Stoto
- (MD Anderson Cancer Center: Donald Berry, Mark Munsell, John Venier)
- Stanford University: Sylvia Plevritis, Bronislava Signal, Stephanie Bailey
- (University of Rochester: Andrei Yakovlev)
- (University of Wisconsin: Dennis Fryback, Marjorie Rosenberg, Natasha Stout)

Affiliates:

- University of Wisconsin : Oguzhan Alagoz, Amy Trentham-Dietz
- Harvard University: Natasha Stout
- Public Health Agency of Canada and Statistics Canada: Leslie Gaudette

National Cancer Institute: Eric Feuer, Kathleen Cronin, Angela Mariotto

Cornerstone Systems Northwest: Lauren Clarke

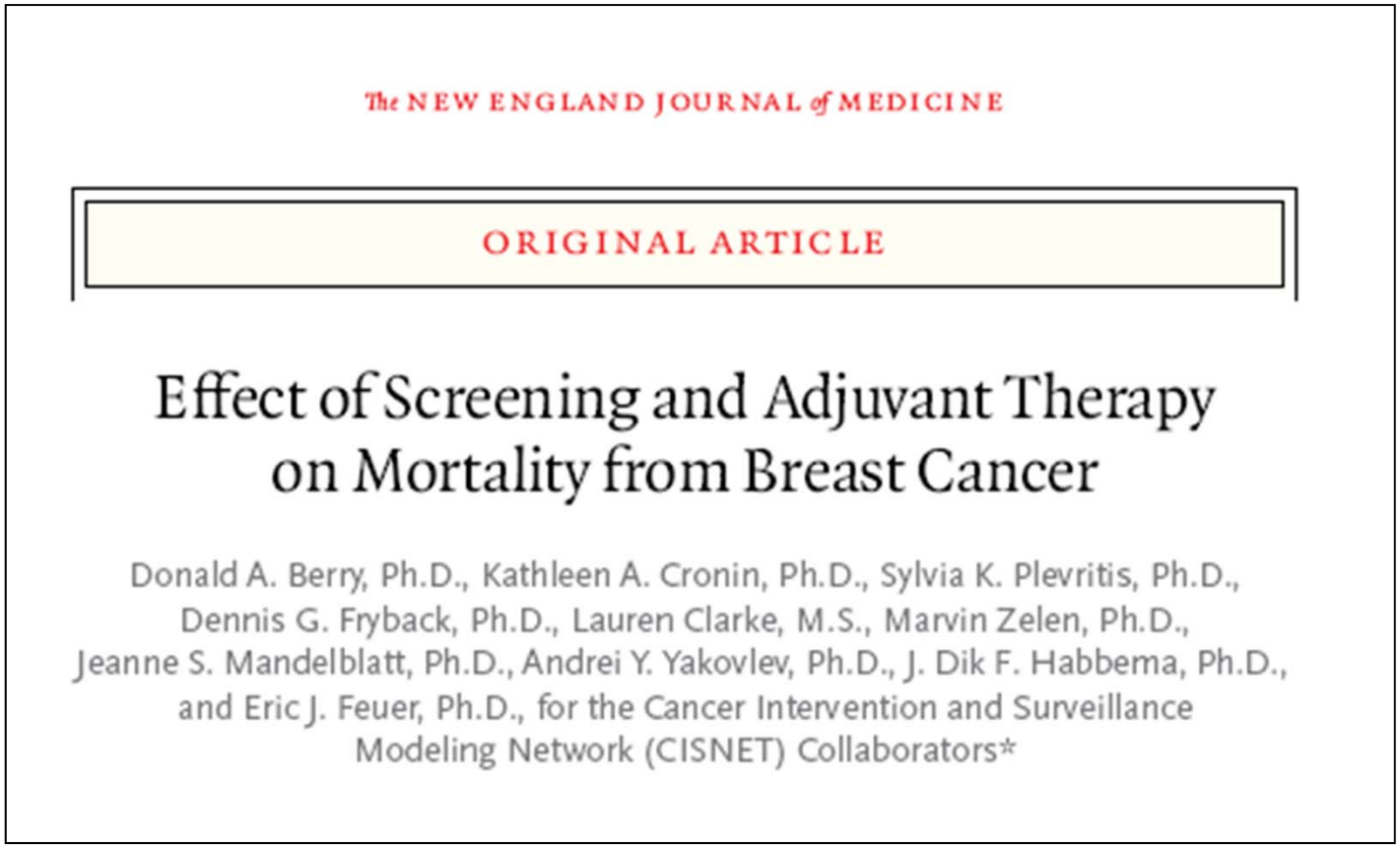
Objectives

- **Summarize scientific accomplishments**
- **Highlight collaborative research results**

Major Scientific Accomplishments

- **Publication of JNCI Monograph 2006**
- **Publication of 70 manuscripts**
- ***Evaluation of US mortality trends***
- ***Evaluation of screening policies***
- **Describe trends in incidence by use of HRT**
- **Examine costs and benefits of different screening starting and stopping ages (by health and race group)**
- **Screening BRCA mutation carriers with MRI**
- **Methods for estimating over-diagnosis**
- **Research and policy collaborations:**
  - **Health Canada**
  - **HP 2010 mid course review**
  - **NCI Integrative Biology Program**
  - **NCI Patient Navigation Research Program**
  - **DC Dept of Health**
  - **CDC Early Breast and Cervical Cancer Detection Program**
  - **US Preventive Services Task Force**

Collaborative Results #1



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Screening and Adjuvant Therapy on Mortality from Breast Cancer

Donald A. Berry, Ph.D., Kathleen A. Cronin, Ph.D., Sylvia K. Plevritis, Ph.D., Dennis G. Fryback, Ph.D., Lauren Clarke, M.S., Marvin Zelen, Ph.D., Jeanne S. Mandelblatt, Ph.D., Andrei Y. Yakovlev, Ph.D., J. Dik F. Habbema, Ph.D., and Eric J. Feuer, Ph.D., for the Cancer Intervention and Surveillance Modeling Network (CISNET) Collaborators*

NEJM 2005; 353;1784-92

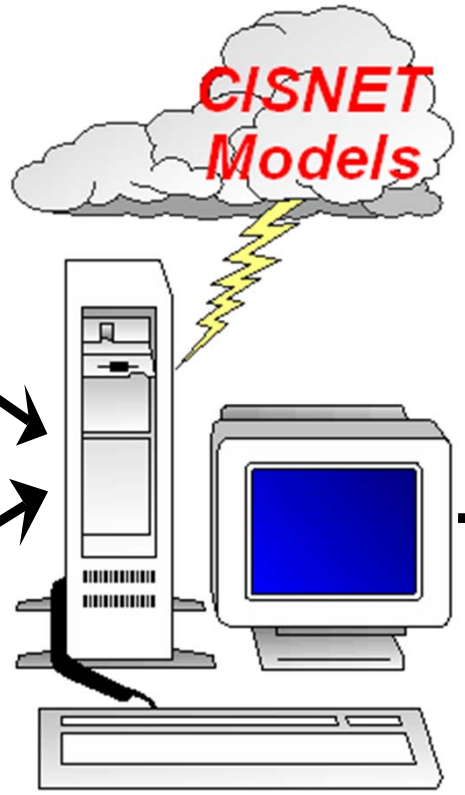
Methods for Collaborative Modeling

Population Inputs (Common to all models)

- Dissemination of Adjuvant Therapy
- Dissemination of Mammography
- Change in Background Risk
- Mortality from Other Causes

Model Specific Inputs and Assumptions

- Efficacy of Treatment
- Tumor Growth Rates and Metastatic Spread
- Operating Characteristics of Screening (e.g., sensitivity, lead time)
- Consequences of Screening (e.g., stage shift, over diagnosis)
- Post Diagnosis Survival by Tumor Characteristics

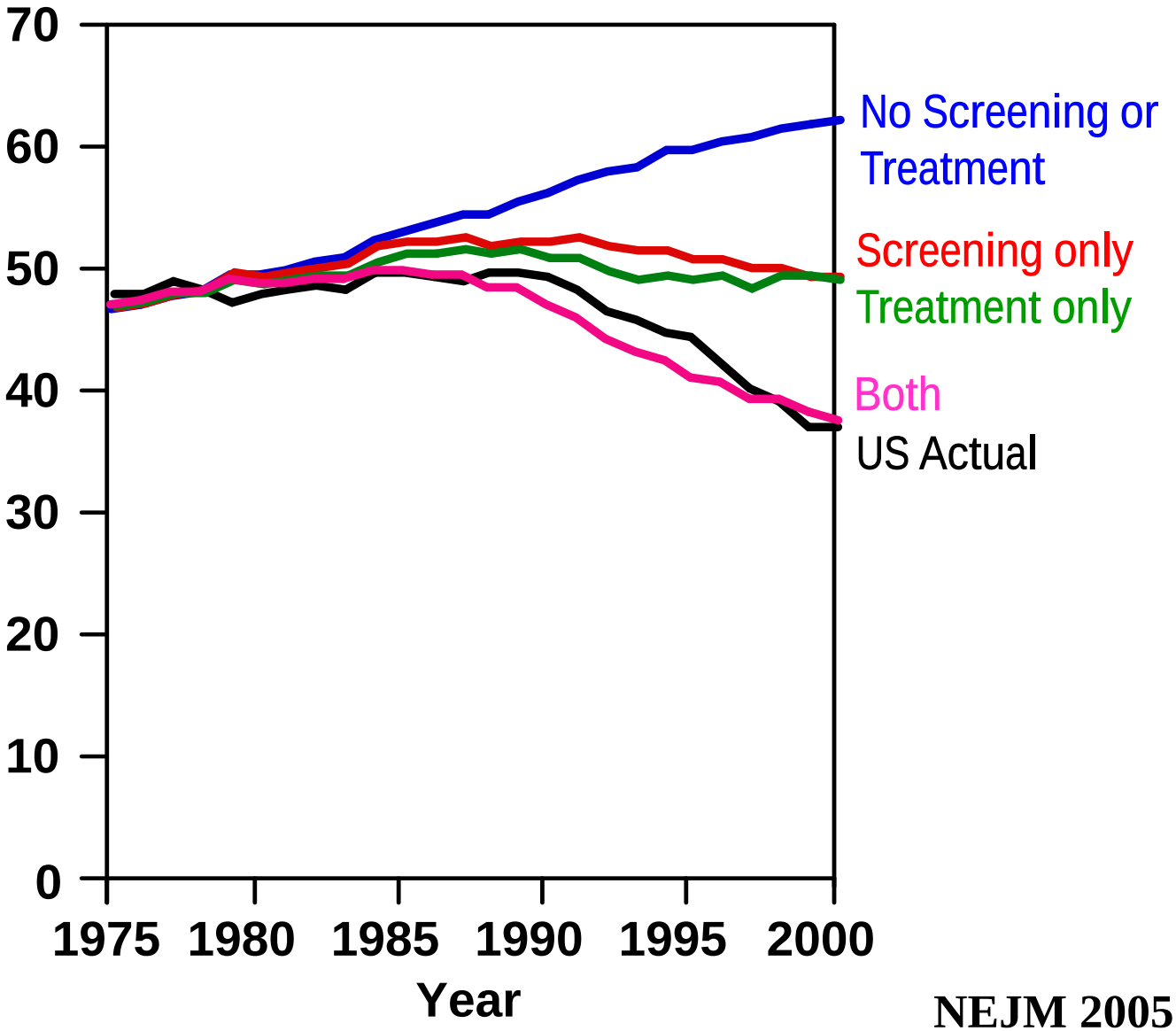


Predicted Incidence
Predicted Mortality

Based on:

- Treatment Alone
- Screening Alone
- Treatment and Screening

Exemplar Results: Mortality Rate per 100,000 Women 30-79 under Various Scenarios



NEJM 2005; 353;1784-92

Collaborative Results: Percent Reductions in BC Mortality due to Adjuvant Rx and Screening

Table 3. Estimated Reductions in the Rate of Death from Breast Cancer in 2000 Attributed to Adjuvant Treatments and Screening.*

Model	Tamoxifen	Chemotherapy	Both Therapies	Screening	Overall
	percent (percent of reduction)				
D (Dana–Farber Cancer Institute)	6.1	6.1	12.0 (35)	22.7 (65)	32.9
E (Erasmus University Medical Center)	12.0	9.6	20.9 (58)	15.3 (42)	30.9
G (Georgetown University)	7.7	7.0	14.6 (54)	12.4 (46)	24.9
M (M.D. Anderson Cancer Center)	10.7	9.5	19.5 (65)	10.6 (35)	27.5
R (University of Rochester)	NA	NA	19.0 (72)	7.5 (28)	25.6
S (Stanford University)	8.9	6.9	14.9 (47)	16.9 (53)	29.9
W (University of Wisconsin–Madison)	12.5	8.9	20.8 (51)	20.3 (49)	38.3

* Values are point estimates from each model; percentages in parentheses are the percentages of the overall reduction that are attributable to treatment or screening. NA denotes not applicable.

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N Engl J Med 2005;353:1784-1792

Conclusions and Press Coverage

- **Observational data and modeling provided additional evidence to help answer a question that RCT's had not completely settled:**

"What seems most important is that each team found at least some benefit from mammograms. The likelihood that they are beneficial seems a lot more solid today than it did four years ago, although the size of the benefit remains in dispute"

***New York Times* Editorial Oct. 22, 2005**

Continuing Collaborative Work

- **Analysis of the effect of new "generations" of systemic therapy regimens based on age, stage and ER/PR and HER2 status:**
  - **Hormonal (tamoxifen, aromatase Inhibitors)**
  - **Chemotherapy (e.g., taxanes, anthracycline and dose dense regimens)**
  - **Herceptin**

Collaborative Results #2

The Role Of Modeling in Developing Mammography Recommendations for the United States Preventive Services Task Force:

What can results of 6 models tell the us about benefits and harms of 20 screening schedules that vary by:

Initiation ages?

Cessation ages?

Rescreening interval?

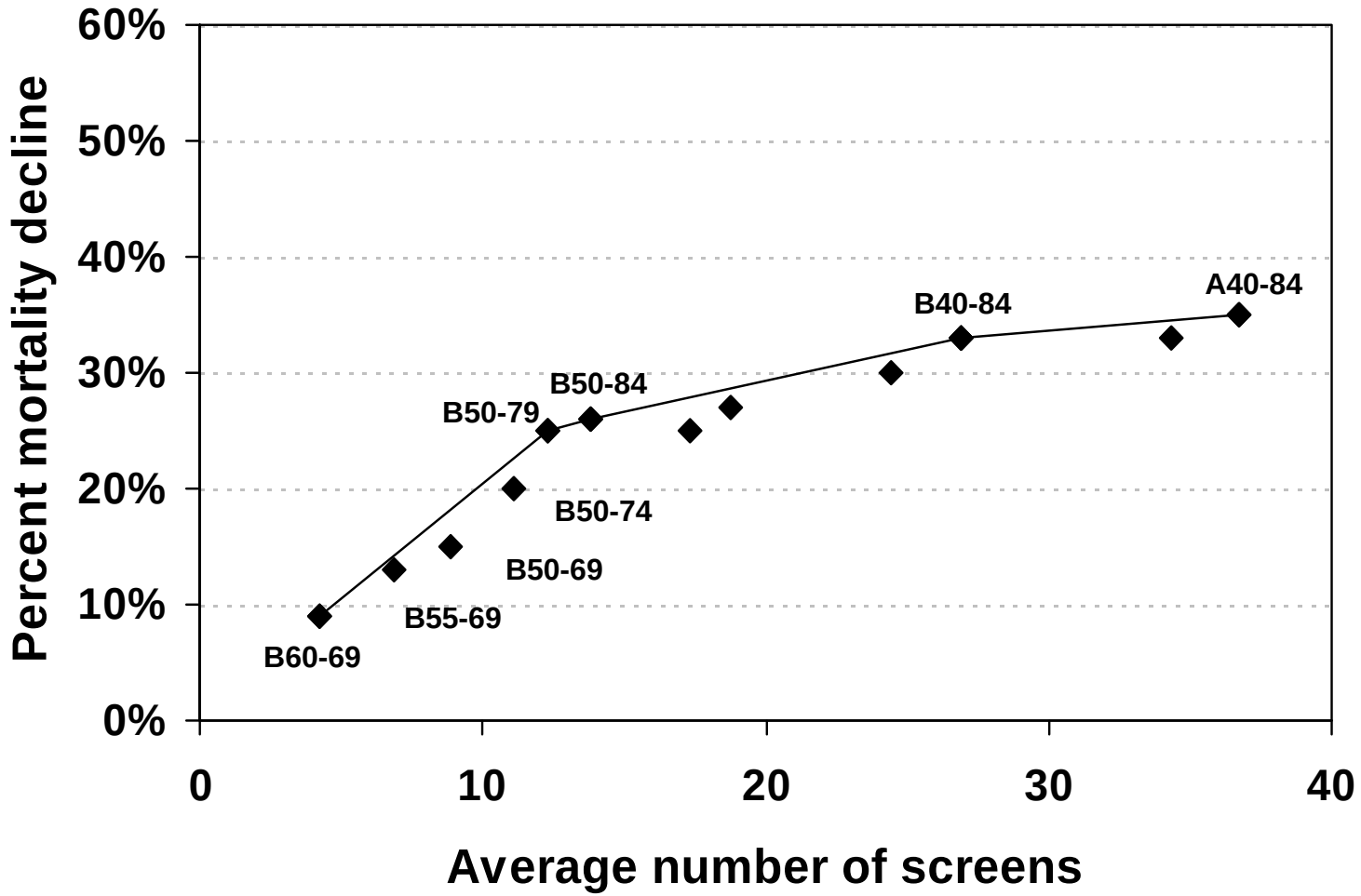
Results: Non-dominated Strategies by Model and # of Mammograms

Percent mortality reduction vs. no screening

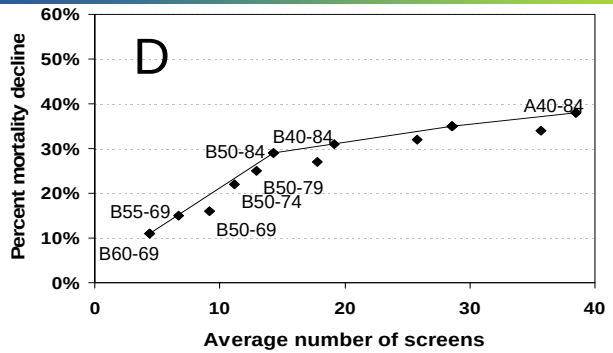
Screening Strategies	Average # of screens per woman	Models					
		W	M	G	D	S	E
B 60-69	4	12%	21%	11%	9%	9%	13%
B 55-69	7	19%	24%	15%	12%	13%	18%
B 50-69	9	23%	28%	17%	13%	15%	23%
B 50-74	11	28%	28%	21%	18%	20%	27%
B 50-79	12	30%	28%	24%	21%	25%	29%
B 50-84	14	33%	28%	25%	24%	26%	31%
B 40-84	18	39%	31%	28%	26%	27%	37%
A 40-84	37	54%	32%	32%	32%	35%	49%

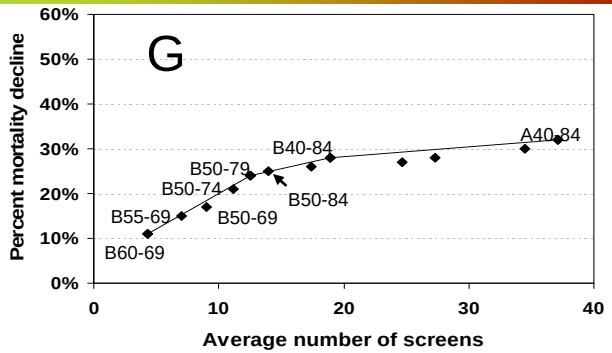
A = Annual B = Biennial

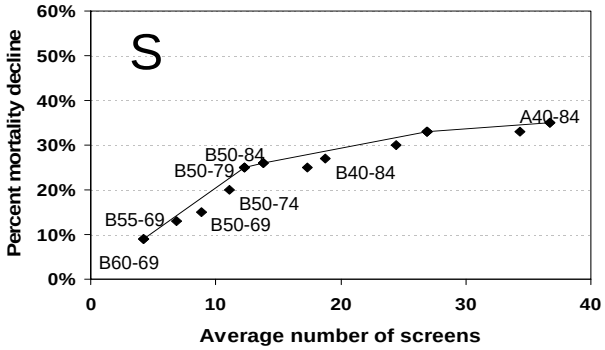
Efficiency Frontier of Non-dominated Strategies for % Mortality Decline– *Exemplar Model*

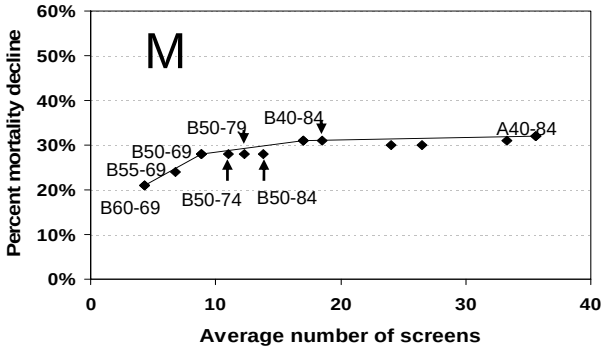


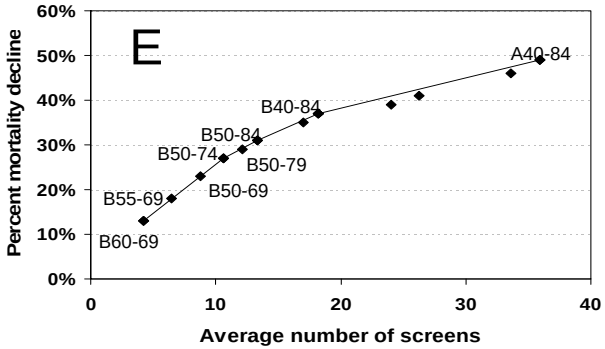
Efficiency Frontier by Model – Percent Breast Cancer Mortality Reduction

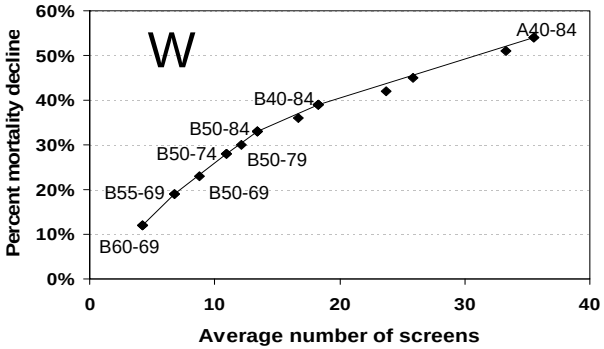












Conclusions

- Six models produce consistent results on the ranking of screening strategies
- Biennial approaches are the most “efficient”
- There are small additional benefits with strategies that begin at age 40 as compared to age 50
- There is uncertainty in results for upper ages and harms associated with DCIS due to limits in primary knowledge base
- Collaborative modeling can inform policy and clinical recommendations