

Does Early Detection Save Lives?

Presented by:

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Our Mission

Breast Cancer Action carries the voices of people affected by breast cancer in order to inspire and compel the changes necessary to end the breast cancer epidemic.

BCAction's Strategic Priorities

(1) Putting Patients First



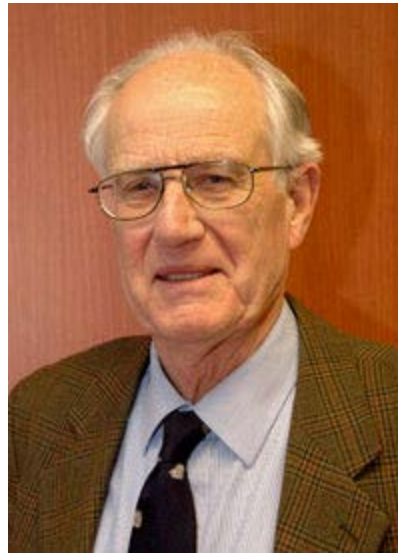
(2) Creating Healthy Environments



(3) Eliminating Social Inequities



Anthony B. Miller, MD



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The Canadian National Breast Screening Study

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Definitions

- Mammography: May be used both as a screening and diagnostic test.
 - Screening: The use of a test to detect early disease in groups of people who do not know if they have a disease.
 - Diagnosis: The use of tests in people who have symptoms or who have a positive screening test to determine if disease is present.
- Lead time: The time by which screen detection brings forward the diagnosis of breast cancer.
- Screen detected: A cancer found as a result of screening.
- Interval cancer: A cancer found after a normal screening test before the next test is due.

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Background on the Canadian National Breast Screening Study (CNBSS)


Background to the CNBSS

- In 1974 a committee established by the Canadian Association of radiologists recommended:
 - Conducting a Canadian study of the evaluation of breast screening
- In 1978 the Working Group that reviewed the US Breast Cancer Detection Demonstration Project recommended that:
 - "A trial to evaluate the magnitude of benefit and net benefit-risk in the use of mammography screening should be conducted."

CNBSS in women age 50-59 is the only trial designed to provide this necessary data.

Background to the CNBSS

- In 1973, the New York HIP trial showed that screening by mammography and breast examinations was effective in women age 50-64, but not in women age 40-49
- Before 1980, two mammography trials were ongoing in Sweden but no results had been reported
- Modern adjuvant therapy and hormone therapy for breast cancer was freely available in Canada, but not in Sweden.

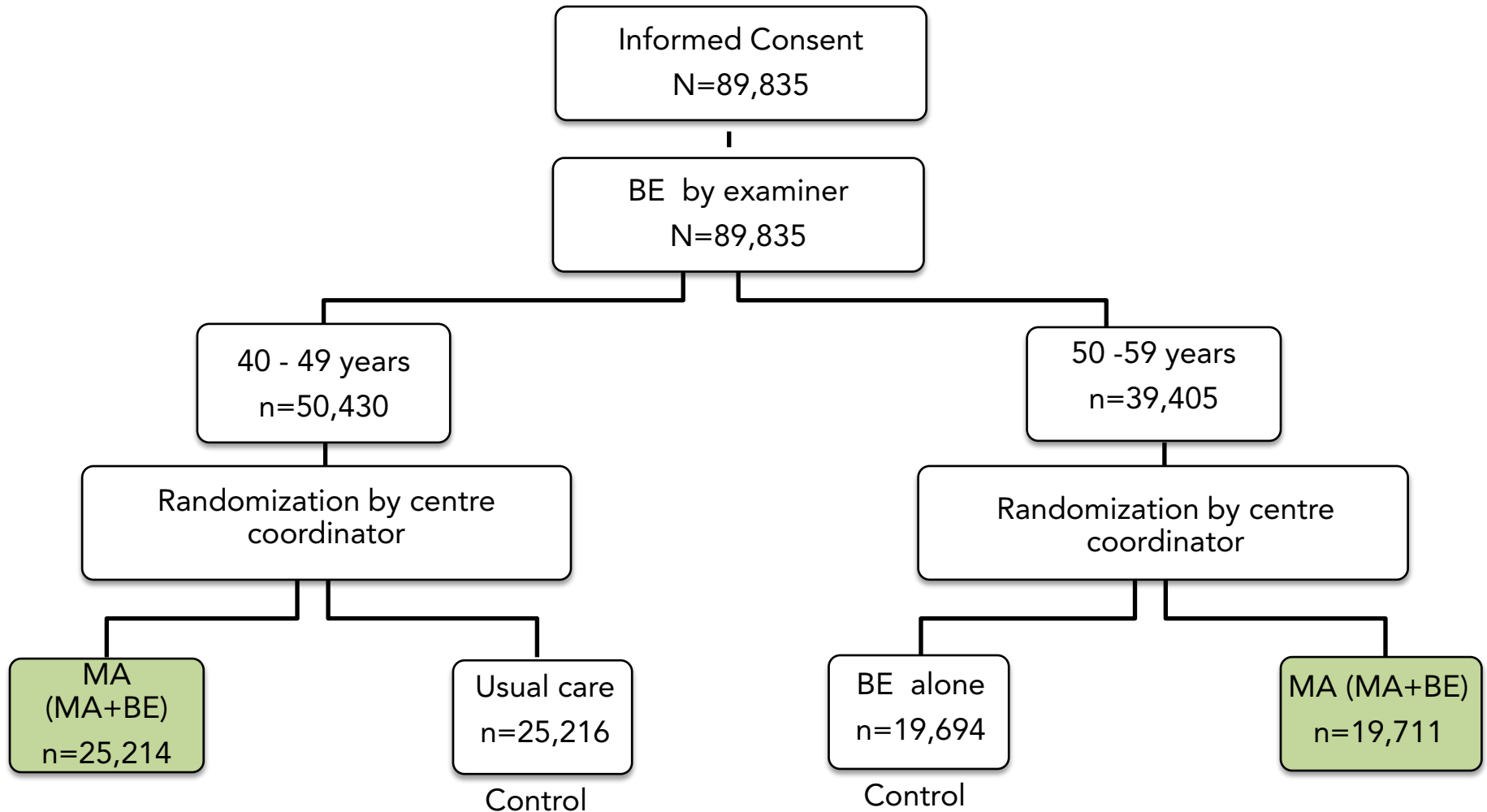


**What is
unique/important
about this study?**

Objectives of the CNBSS were different from other trials

- The efficacy of screening by mammography and breast examinations in women age 40-49 was evaluated – *the first trial specifically designed for this age group*
- We evaluated how much mammography adds to the efficacy of screening by mammography and breast examinations in women age 50-59 – *the only trial designed with this objective*

Process of Randomization and Screening



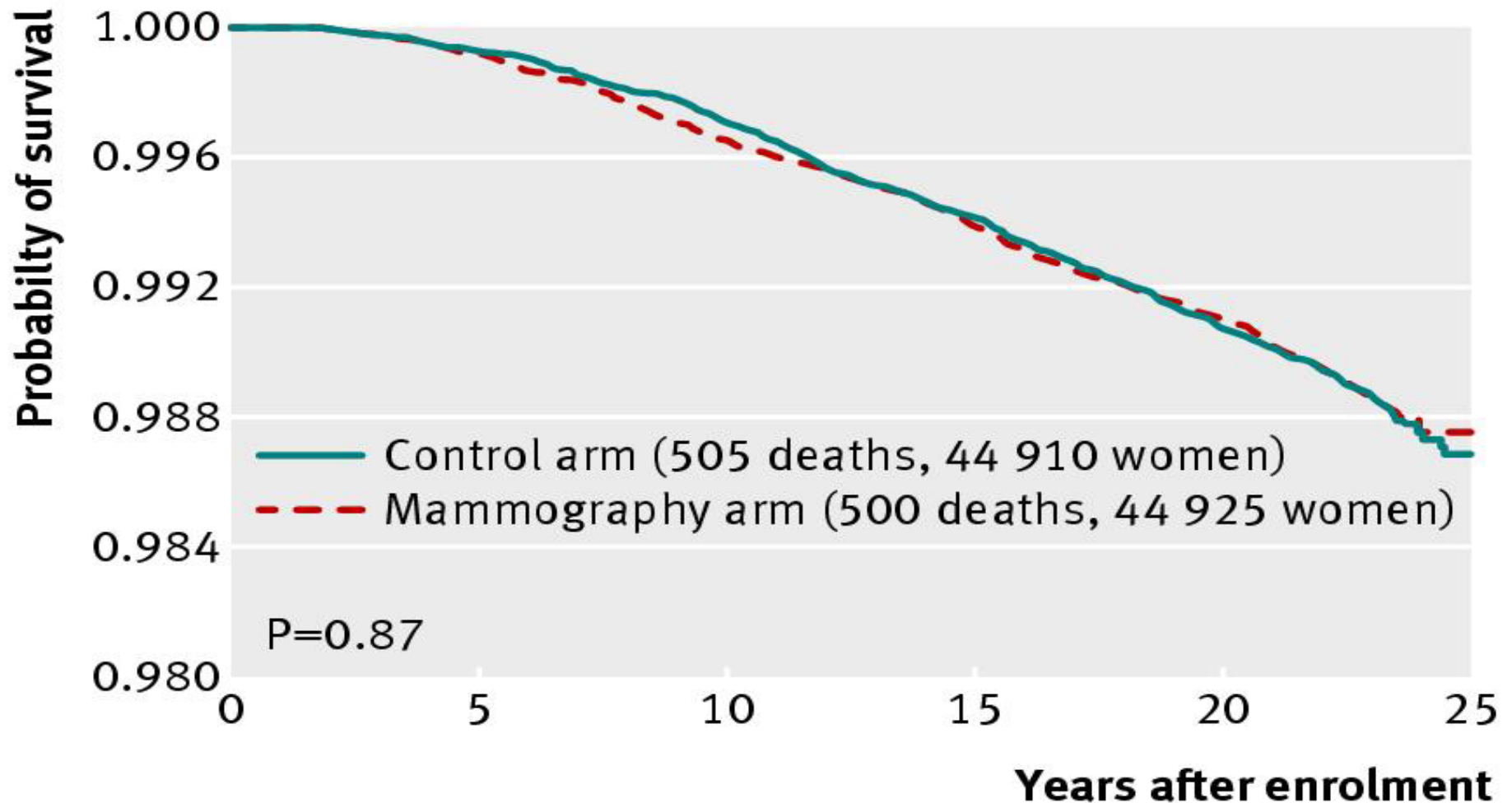
MA = Mammography

BE = Breast examination

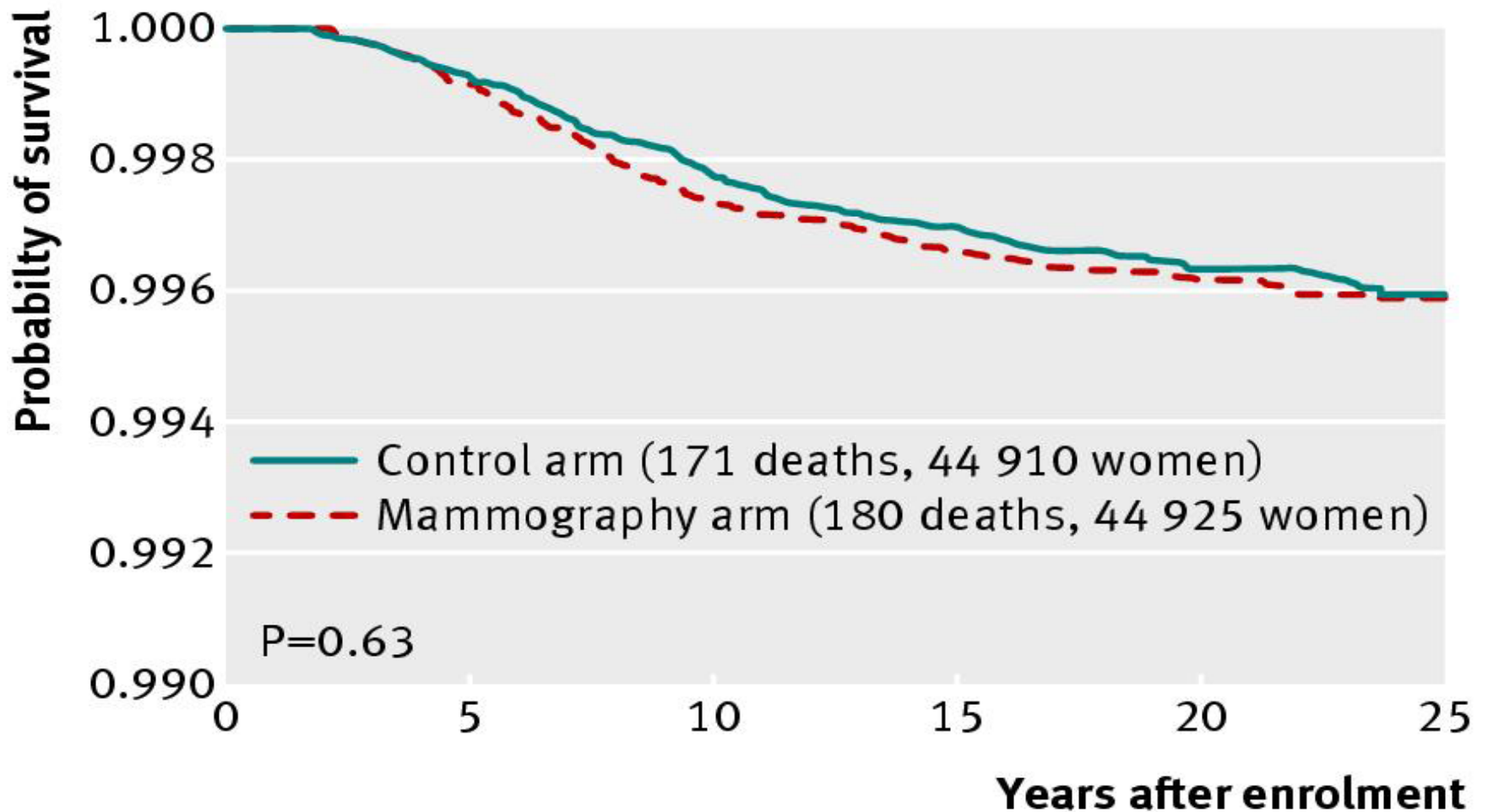
Breast cancers detected in the screening period in the CNBSS

- There were more invasive breast cancers detected in the screening period in the mammography arm than in the control arm: 666 vs. 524
- In the mammography arm, 484 were screen-detected of which 142 could not be palpated (felt)
- The palpable cancers in both arms were larger on average than the impalpable cancers in the mammography arm (2.1 cm vs. 1.2 cm)

Breast cancer specific mortality, by assignment to mammography or control arms (all participants)





Breast cancer specific mortality from cancers diagnosed in screening period



Conclusions on deaths from breast cancer in the CNBSS

- There was no difference in numbers of breast cancer deaths between the two arms, whether considering only the breast cancers diagnosed in the 5-year screening period, or in the whole period of follow-up.
- This was true both for women age 40-49 and those age 50-59.
- Thus the addition of mammography to breast examinations did not reduce deaths from breast cancer.



**How does this study
add to our knowledge
about screening
mammography?**

Potential Harms from Screening Data from the CNBSS

- False reassurance from false negative test
= Interval cancers detected as proportion of screening tests performed:
 - Mammography arm: 6/10,000 women screened
 - Control arm: 11/10,000 women screened

Conclusion: Use of mammography reduces false reassurance

Potential Harms from Screening Data from the CNBSS

- Complications from investigation of false positive test
- = Numbers of abnormal screening tests less number of screen-detected cancers as a proportion of screening tests performed:
 - In the Mammography arm: 9.7%
 - In the Control arm: 8.1%

Conclusion: Mammography increases the numbers of false positive tests

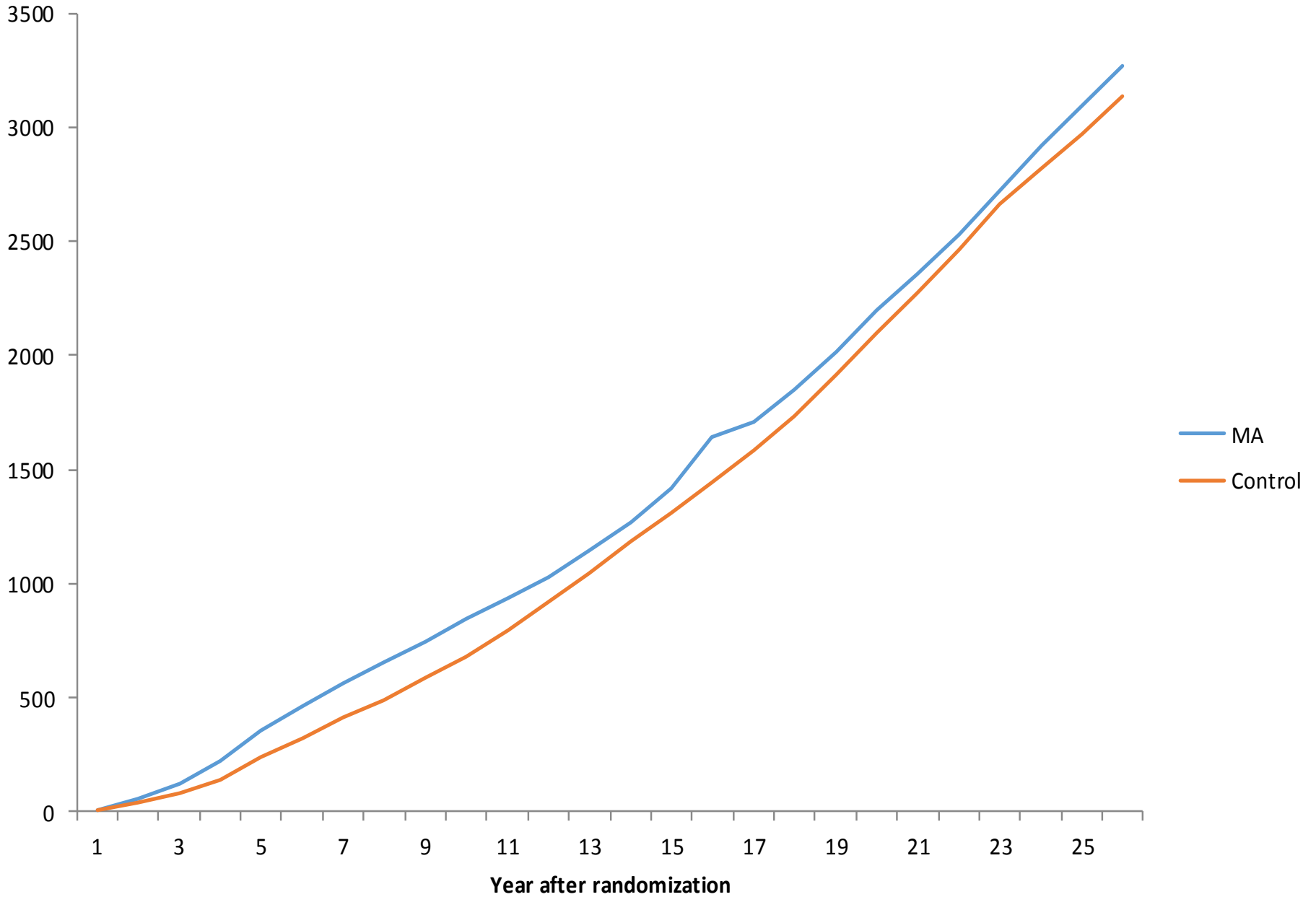
Remember: Case Detection is Not Equivalent to Benefit

- The detected cancer may not be curable, nor have its natural history modified by available treatment
- The detected cancer may never have become life-threatening in the patients lifetime (it is cured, or overdiagnosed)

Types of Overdiagnosis

- Cancer that would regress spontaneously if left alone.
- The cancer progresses too slowly to be life threatening in even the longest of lifetimes.
- The cancer progresses quickly enough to be life-threatening during a normal lifetime, but death due to a competing cause occurs prior to the date of symptomatic diagnosis had screening not occurred

Cumulative numbers of invasive breast cancers



Estimates of Overdiagnosis from CNBSS

- #of overdiagnosed invasive cases: **106**
- #of screen-detected invasive cancers: **484**
- #of non-palpable invasive cancers detected by mammography: **212**
 - ✓ **22%** (106/484) screen-detected cases overdiagnosed
 - ✓ **50%** (106/212) impalpable cases detected by mammography overdiagnosed

i.e. one overdiagnosed invasive breast cancer for every 424 women who received mammography screening in the trial.

Estimates including in situ cancer (LCIS & DCIS)

- Numbers of overdiagnosed invasive and in situ cases: **206**
- Number of screen-detected invasive and in situ cancers: **589**
- **35%** screen-detected cases overdiagnosed
- **72%** impalpable cases detected by mammography overdiagnosed

Implications of Overdiagnosis

- Overtreatment
- Our previous estimates of lead time were wrong, e.g. lead time gained by mammography is ~ 1 year, not ~ 4 years
- We need research on biomarkers (molecular markers) to identify over-diagnosed cases

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Limitations of the CNBSS study

Women older than 59 not included

- There is no reason to believe the null effect of mammography does not apply to women older than 60
- There are some reasons to fear that over-diagnosis may be greater in women older than 60

We used 1980's mammography

- But the other trials on which people depend to show mammography reduces breast cancer deaths used similar or older mammography
- Our cancer detection rates were at least as high as these other trials

Some have criticized our Randomization Method

However:


- Independent review for Canadian National Cancer Institute confirmed appropriateness
- We have data on all participants that confirms the groups were balanced on breast cancer risk factors (e.g. family history)
- Equal numbers referred for review at first screen
- Death rate same in both groups for 25 years



**How does this study of
Canadian women apply
to the diversity of
communities here in
the US?**

Very well, but remember:


- Information disseminated has to be compatible with the community's culture
- Although there are women at risk of breast cancer in every community, the degree of risk varies
- Canada's universal healthcare system means that there are no financial barriers to accessing appropriate care

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**What are the
important takeaways
from the study?**

Conclusions on the CNBSS

- Annual mammography does not result in a reduction in breast cancer specific mortality for women aged 40-59 beyond that of physical examination alone or usual care in the community.
- The value of mammography screening should be reassessed.
- Overdiagnosis is a serious consequence of mammography screening, and research into its amelioration and reduction in overtreatment is urgently needed.

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Other screening mammography studies

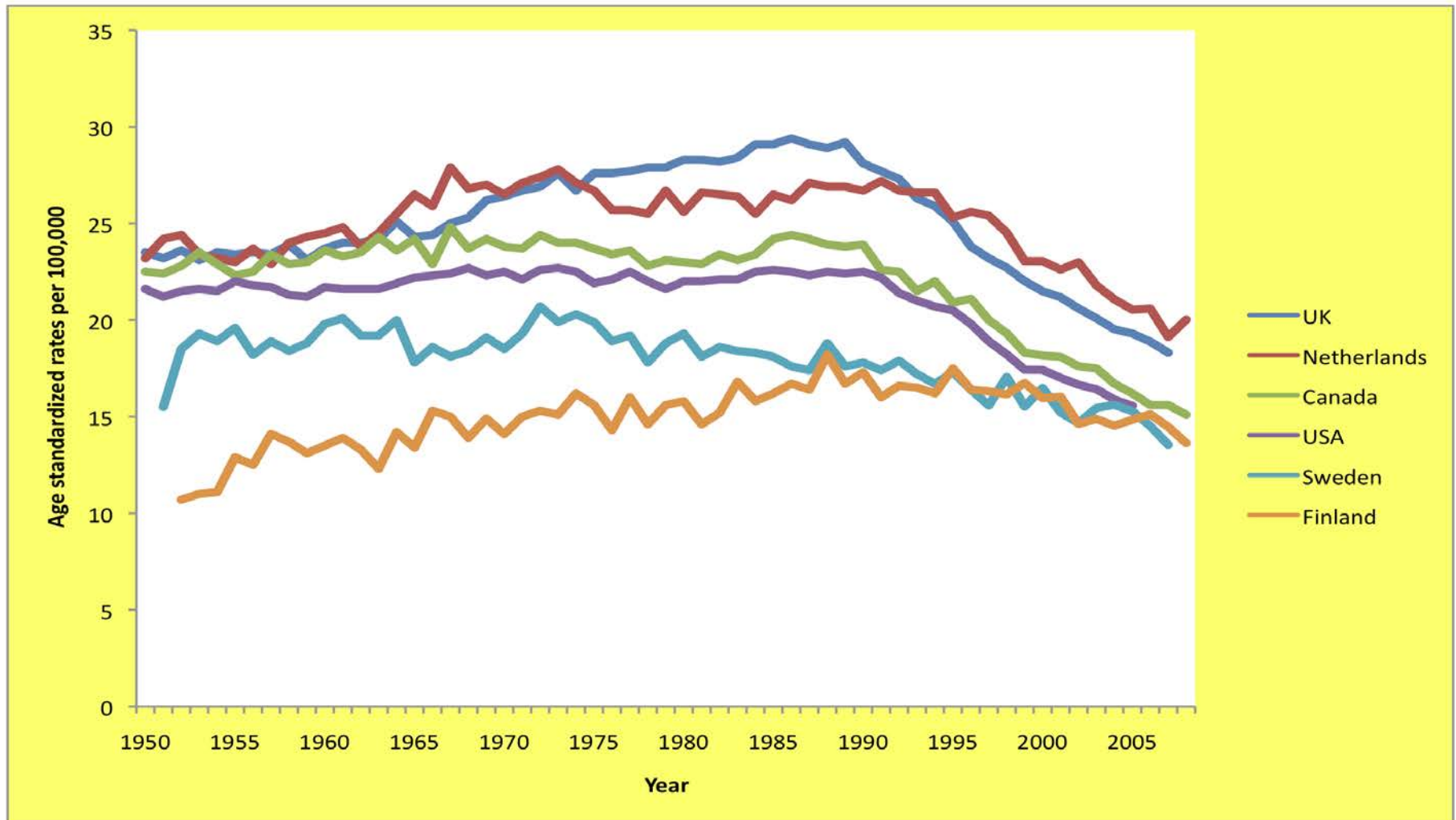
Summary of the trials of mammography alone


- In Sweden 4 trials: Malmö, Two-county, Stockholm, Gothenburg
- Commenced 1976, 1977, 1981, 1982
- Only in Two-county trial was a significant effect of mammography screening found
- In UK: "Age" trial 39-41, commenced 1991(-1997) non-significant effect found

Comments on Swedish Trials, used to justify mammography screening

- In an overview analysis, benefit only confirmed for women age 60-69
- Several used cluster randomisation
- Balance between compared arms has not been confirmed
- Modern adjuvant therapy was not available

Trends in breast cancer mortality



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**Last thoughts about
the impact, value &
importance of this
study?**

Conclusions

- 1) In the CNBSS, death rates from breast cancer were the same in women who got mammograms and those who did not.
- 2) One in five breast cancers found by mammography screening and treated did not pose a threat to women's health.
- 3) There is no benefit to finding breast cancers before they can be felt.
- 4) Studies showing a benefit for mammograms were performed before improved treatments for breast cancer were available.

Review resources from presentation

- **Research:** Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial, *Feb 2014*
- **Webinar:** *The Oversimplification of Early Detection*, Mar 2013
- **Book:** *The Big Squeeze: A Social and Political History of the Controversial Mammogram* by Handel Reynolds, MD
- **Book:** *Overdiagnosed: Making People Sick in the Pursuit of Health* by H. Gilbert Welch

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