Mammography Screening for Breast Cancer: Lessons for Population Sciences

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The Screening Paradigm

- Identify a health problem before it causes trouble, and remove or treat it.
- Do this for everyone at risk for the disease
- This maintains health and prevents disease, both for individuals and the population.

Screening for Breast Cancer

- The earlier we find the cancer, the better.
- Screen all women at risk for breast cancer.

Canadian Task Force: Information Needed for Screening

- **Risk and severity of condition**

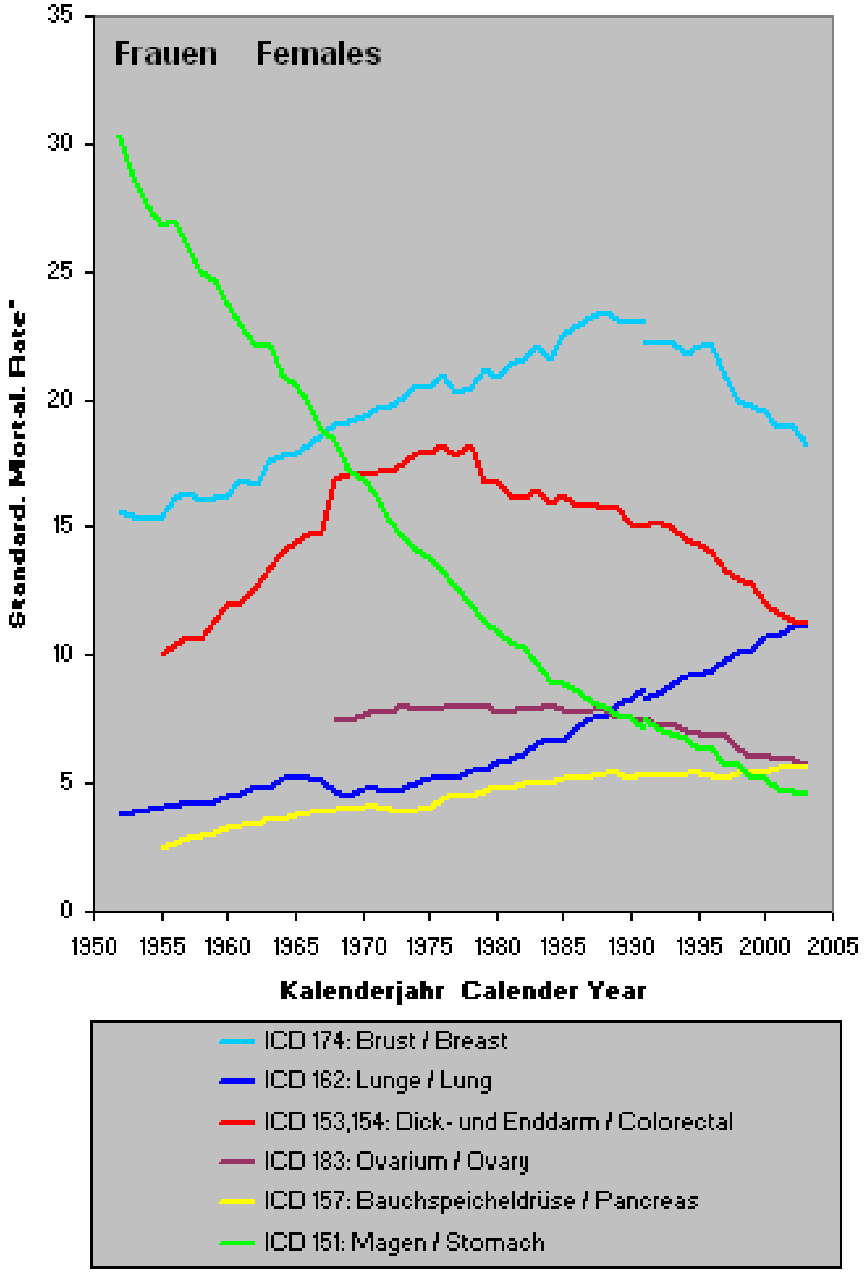
  Breast cancer incidence & mortality

- **Effectiveness of screening procedure and follow-up treatment**

  Effectiveness of screening & early treatment in preventing breast cancer mortality

- **Characteristics of the screening test**

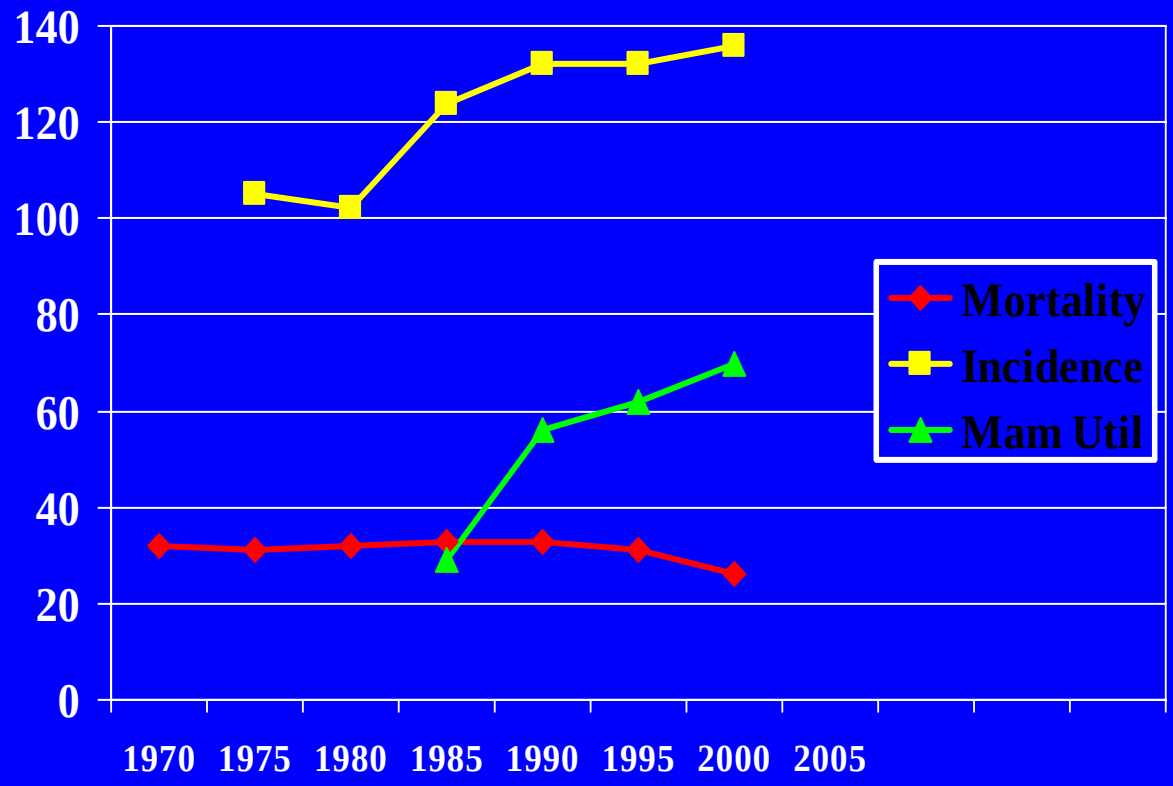
  Sensitivity, specificity, cost, simplicity, safety, acceptability, labelling effects



* vor / bevor 1990: West-Deutschland / West Germany
nach / after 1990: Deutschland / Germany

Nikolaus Becker
Evelin Deeg
Abteilung Klinische Epidemiologie
Deutsches Krebsforschungszentrum Heidelberg

History of Breast Cancer Screening in the U.S.



Screening for Breast Cancer

Seriousness of Condition

- Most common non-skin cancer in of cancers in German women (146/100,000 in Saarland, 2002)
- Most common cause of cancer death in German women (18.2/100,000)

Effectiveness of Mammography

- 8 RCTs with ~ 500,000 women
- Reduction in BC mortality

  Age 50-69 ~ 16 to 35%

  Age 40-49 ~ 15 to 25%

Mammography

- Most sensitive and specific screening test for BC

Lesson #1

Population scientists disagree on BCS

Expert Groups
BCS Recommendations

• **Cochrane** (O&G, 2001)	**No**
• **USPSTF** (2002)	**Yes for 40+ (Grade B)**
• **NCI PDQ** (2005)	**Maybe**
• **Canadian TFPHE**	**Yes for 50-65** **No for 40-49**
• **IARC**	**Yes for 50-69** **Maybe for 40-49**

SIGNE WILKINSON, PHILADELPHIA DAILY NEWS

BCS in European Countries

	Ages	Interval (Years)	No. Views
• Germany	50+	1	2/2
• Sweden	40-74	1.5-2	2/1
• UK	50-64	3	2/1
• Netherlands	50-74	2	2/1
• Norway	50-69	2	2/2
• Spain	45-64	2	1/1

Lesson # 2

Increase your awareness of, and search for, “unintended consequences” of screening.

Unintended Consequences of Breast Cancer Screening (Harms)

False-positive mammograms

Overdiagnosis (DCIS)

False-Positive Mammogram

An abnormal mammogram resulting in a recommendation for further assessment for a woman who is found ultimately not to have cancer

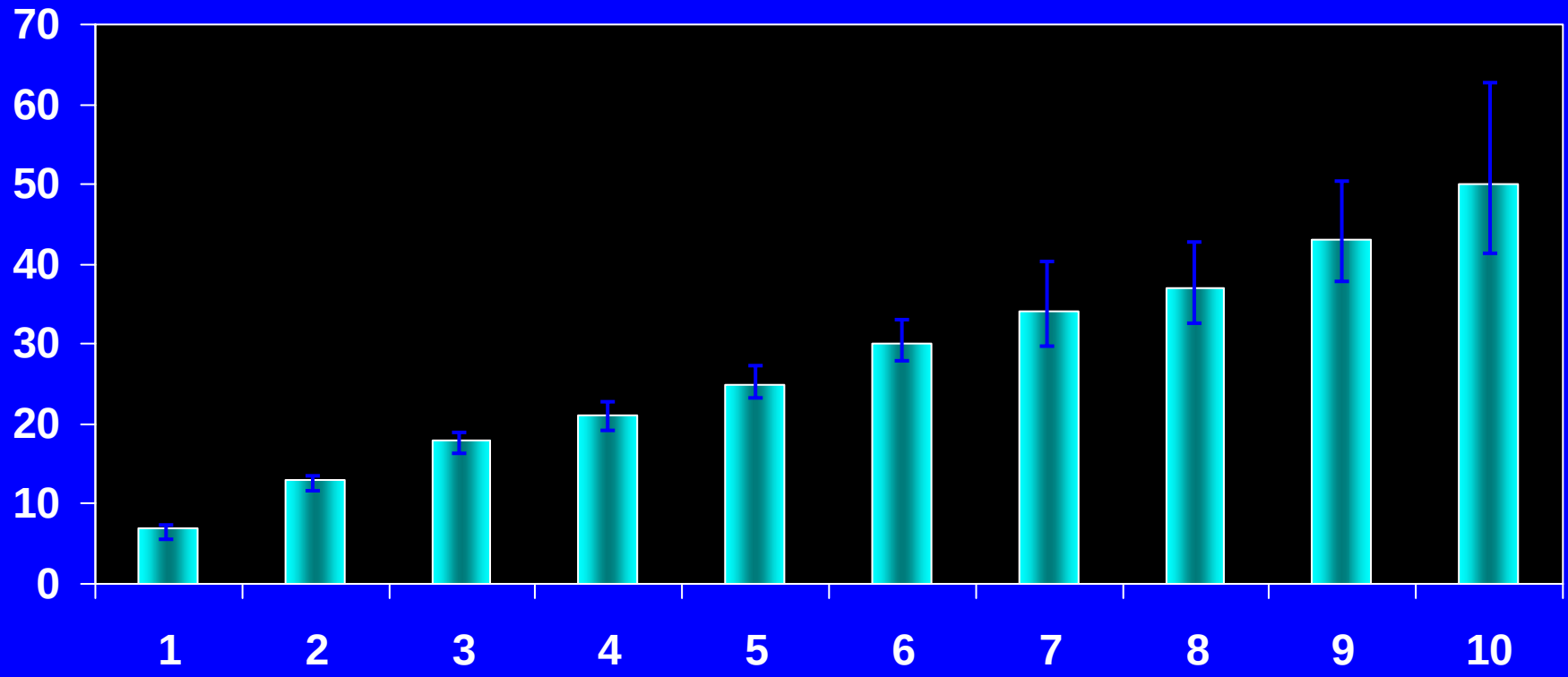
% of Abnormal Mammograms that are False-Positive

The percentage of abnormal mammograms requiring further assessment that are in women who are found ultimately not to have breast cancer

Frequency of False-Postitve Mammograms

	Abnormal mammograms (%)	% Abnl mam that are FP (%)
• Netherlands	0.9-1.4	50-56
• Norway	2.9-4.5	69-77
• UK	3-8	~88
• USA	11	96

Estimated Risk of at Least One False Positive Screening Mammogram



Consequences of F-P Mammograms

- **Financial – adds 33% to cost of screening program**
- **Personal – Causes anxiety among women**
- **Health-care utilization – Increases patient visits for non breast-related reasons**

Bottom line: Patients do not react well to hearing, "Your screening test was not quite normal."

The last well person

“If the behavior of doctors and the public continues unabated, eventually every well person will be labeled sick.”

Clifton Meador, MD
NEJM 1994;330:440

Predicting Cumulative Risk of False-Positive Mammograms

Highest risk woman – 98 % after 1 mammogram

Young age (40), estrogen user, 3 previous biopsies, family hx of BC, no comparison with previous mammogram, 3 yrs between screens, radiologist tends to call positive mammograms

Lowest risk woman – 5% after 9 mammograms

Old age (70), no estrogen, no breast biopsies, no fm hx of BC, mammogram compared to previous one, 1 yr between screens, radiologist does not tend to call positive mammograms

Christiansen et al, JNCI, 2000

Cumulative Risk of a FP Mammogram after 10 Screens

	Norway	USA
	%	%
Abnormal mammograms	2.9 – 4.5	7.1
FP mammograms	69 – 78	92
Risk of FP after 10 screens	20.8	49.1

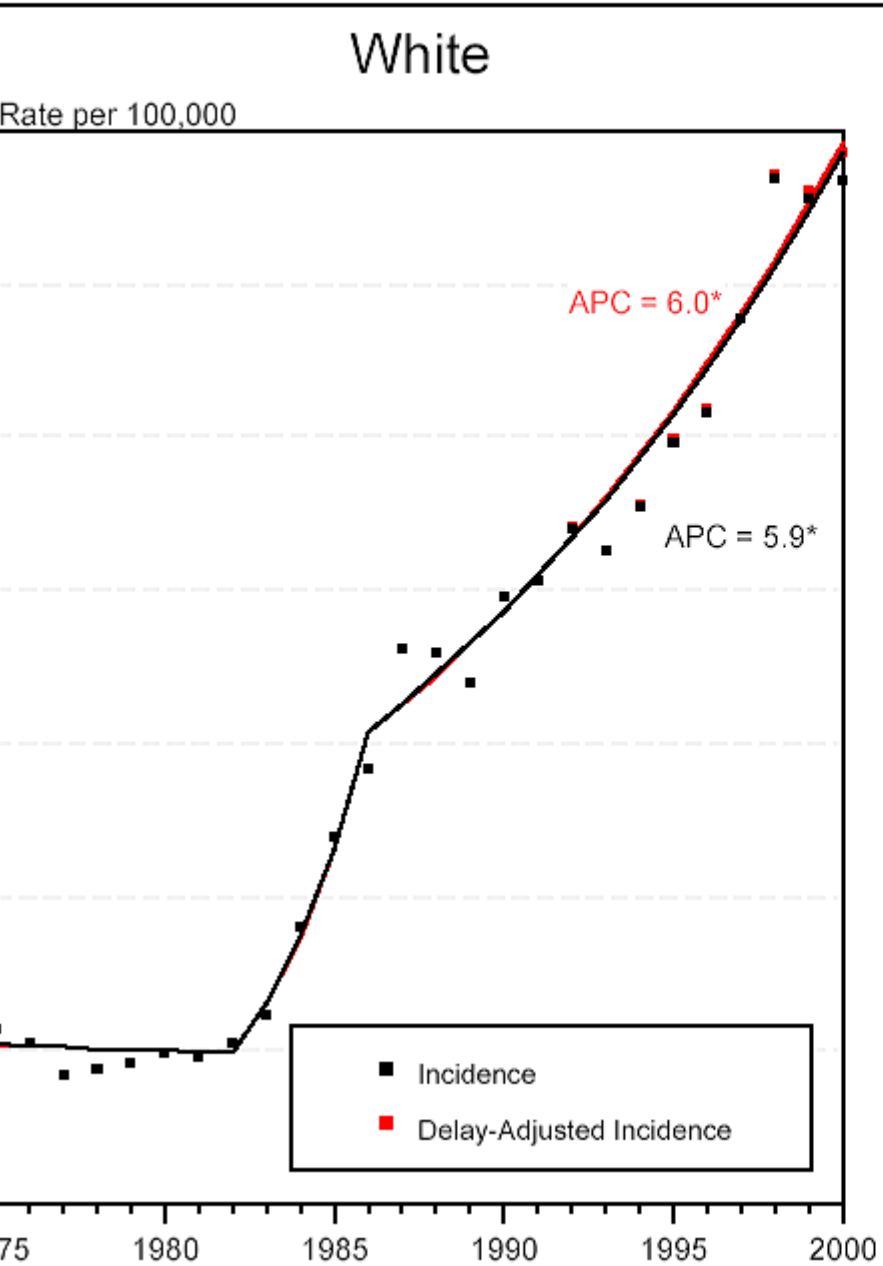
Hofvind et al, Cancer 2004

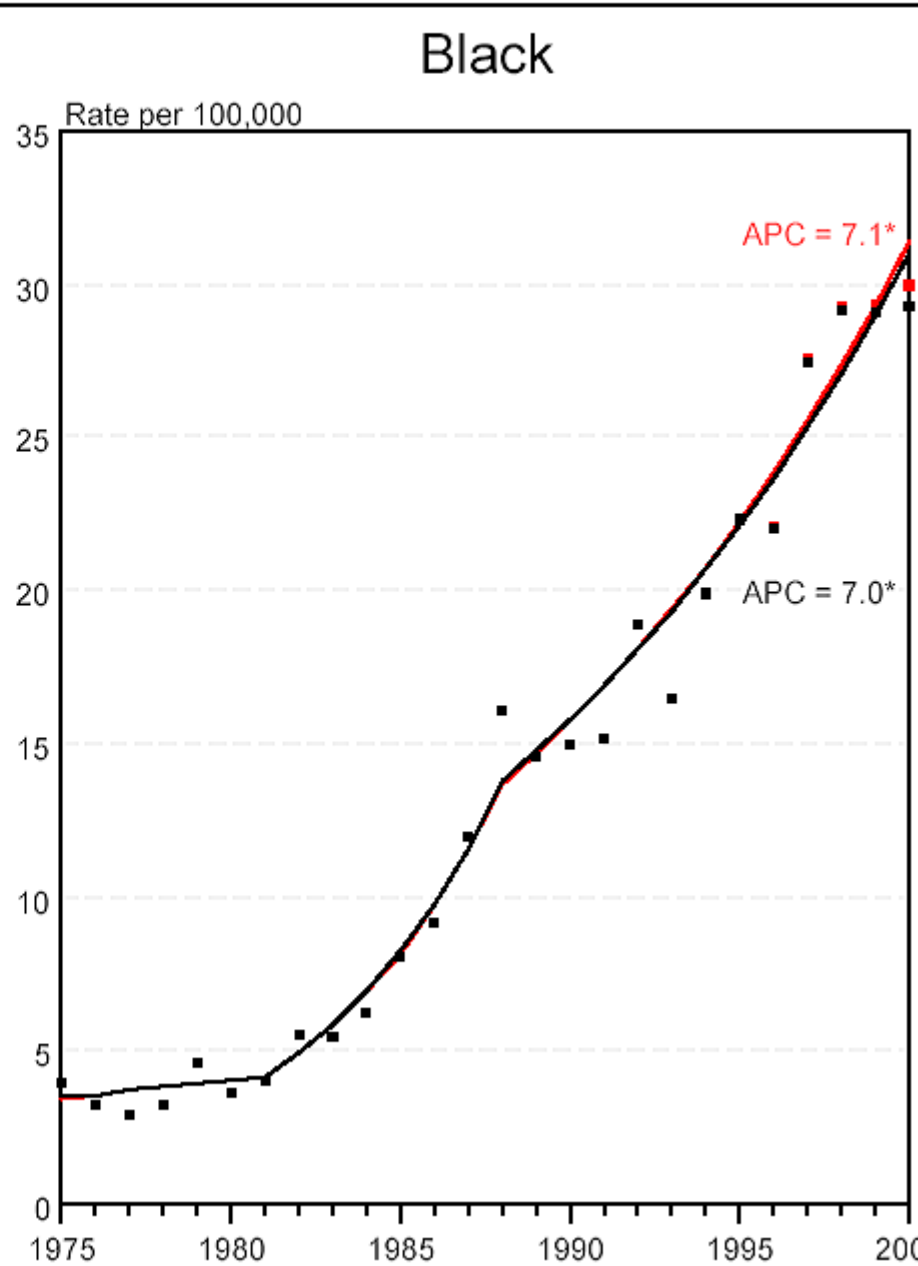
Elmore et al, NEJM 1998

Overdiagnosis

Ductal Carcinoma in Situ (DCIS)

SEER Incidence and Delay Adjusted Incidence Rates+
Female Breast Cancer *(In Situ)*, by Race





DCIS - Prognosis

- Almost all women survive in first 9 years (Ernster et al, 1996)
- Recurrent cancers over 12 years (Fisher et al, 2001)

	All Recurrences	Invasive Recurrences
	%	%
Lumpectomy	31.7	14.1
Lumpectomy & Radiation	15.7	7.8

Lesson # 3 – The Modern Screening Quandry

- Technology can find lesions that look but don’t act like cancer in large numbers of people
- We do not know which of these lesions will progress to act like cancer
- The quandry - what to do?

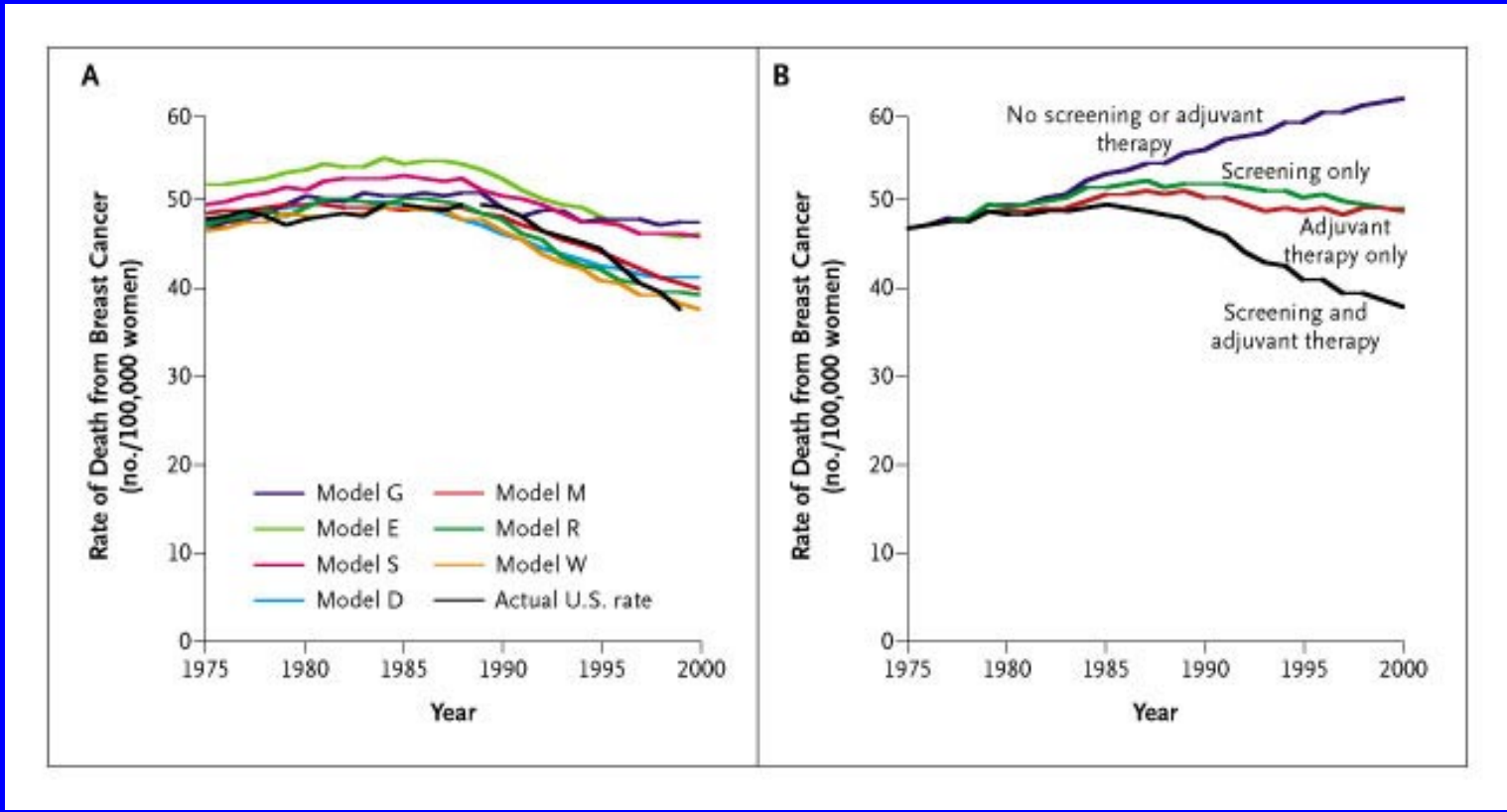
Monitoring Screening Programs

- Breast Cancer Mortality Rate
- Rate of advanced cancers
- Stage distribution
- Prevalence rate and rate of interval cancers
- Participation rate
- Recall rate

Commission of the European Communities (2001)

Lesson # 4
Interaction between Breast Cancer Screening & Treatment

Death from Breast Cancer among Women 30 to 79 Years of Age from 1975 to 2000 (Panel A) and under Hypothetical Assumptions about the Use of Screening Mammography and Adjuvant Treatment (Panel B)

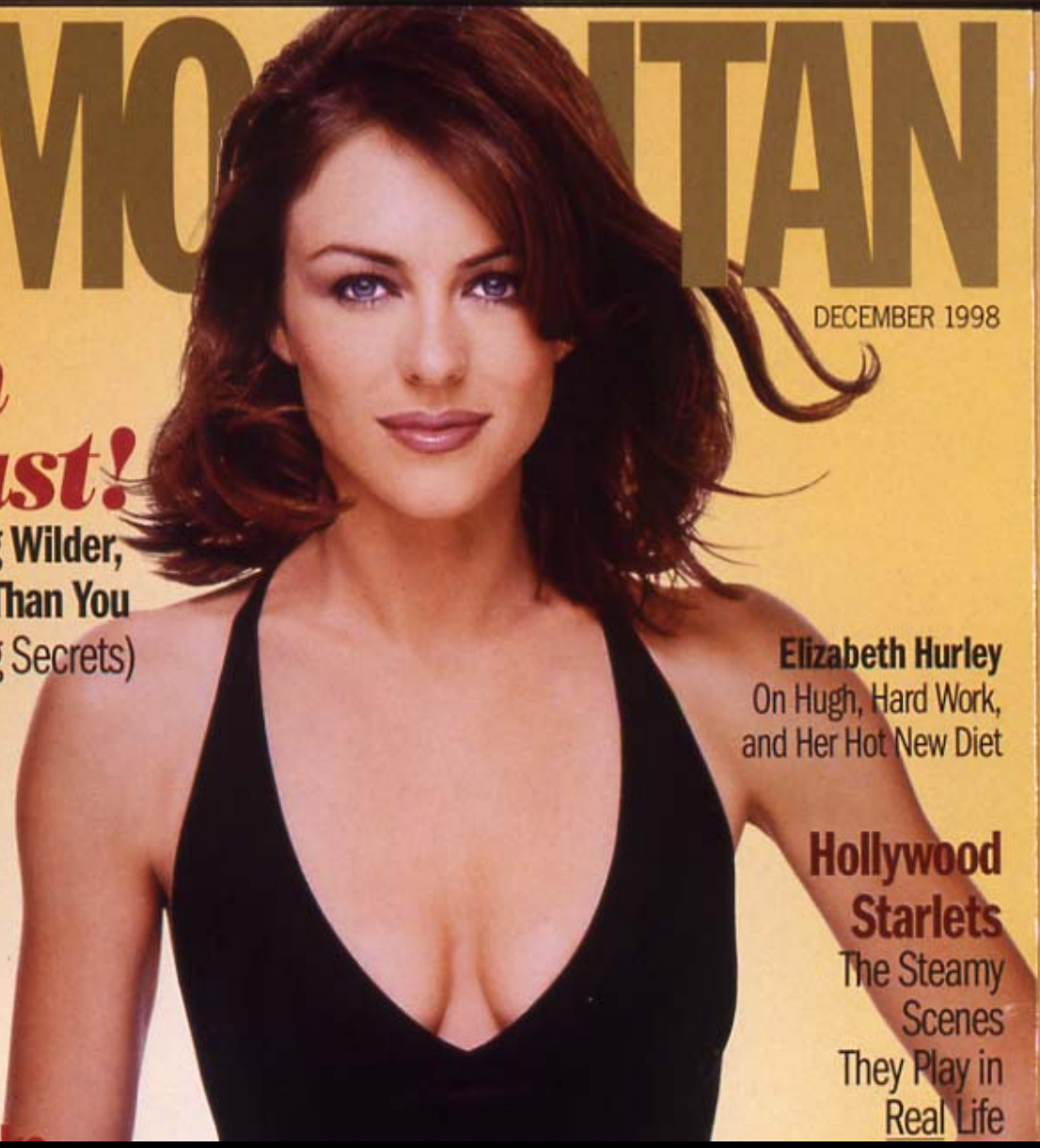


Berry, D. A. et al. N Engl J Med 2005;353:1784-1792

Lesson #5
The Social Context of Breast Cancer Screening

COSMOPOLITAN

DECEMBER 1998



Unleash Your Lust!

Find Out Who's Having Wilder, Hotter, and More Sex Than You
(and Steal Their Sizzling Secrets)

Elizabeth Hurley
On Hugh, Hard Work, and Her Hot New Diet

Should You Say "I Love You?"
5 Don't-Blow-It Moves for Scary New-Man Moments

Hollywood Starlets
The Steamy Scenes They Play in Real Life

50

Fear of Breast Cancer

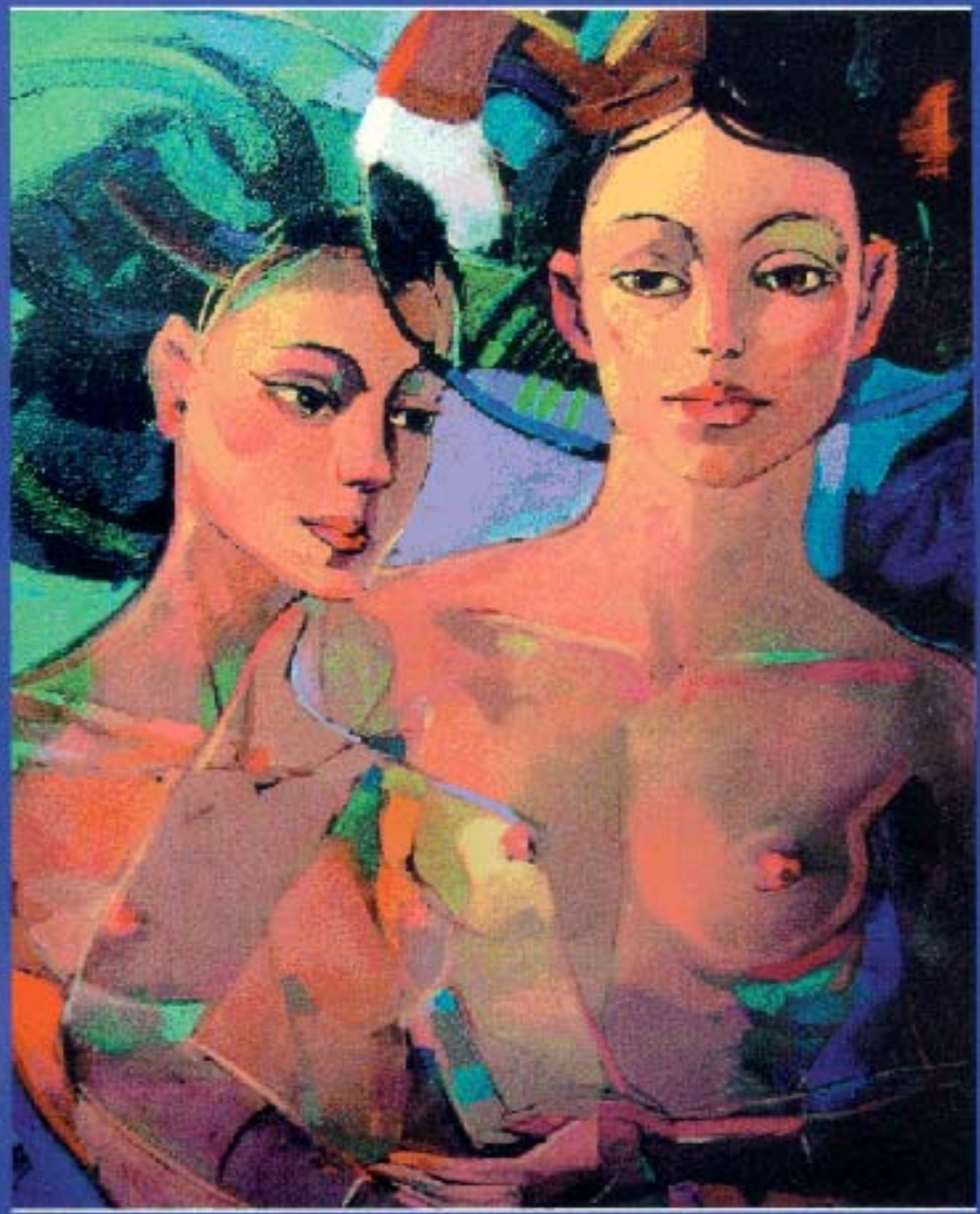
Community Survey

20-25%	Worried about breast cancer
40 – 50%	Feared finding breast cancer
70 – 85 %	Thought looking for it makes women worry

Survey of Women in Their 40s

Overestimated risk of dying >20-fold

Overestimated risk of developing breast cancer ~ 6 fold

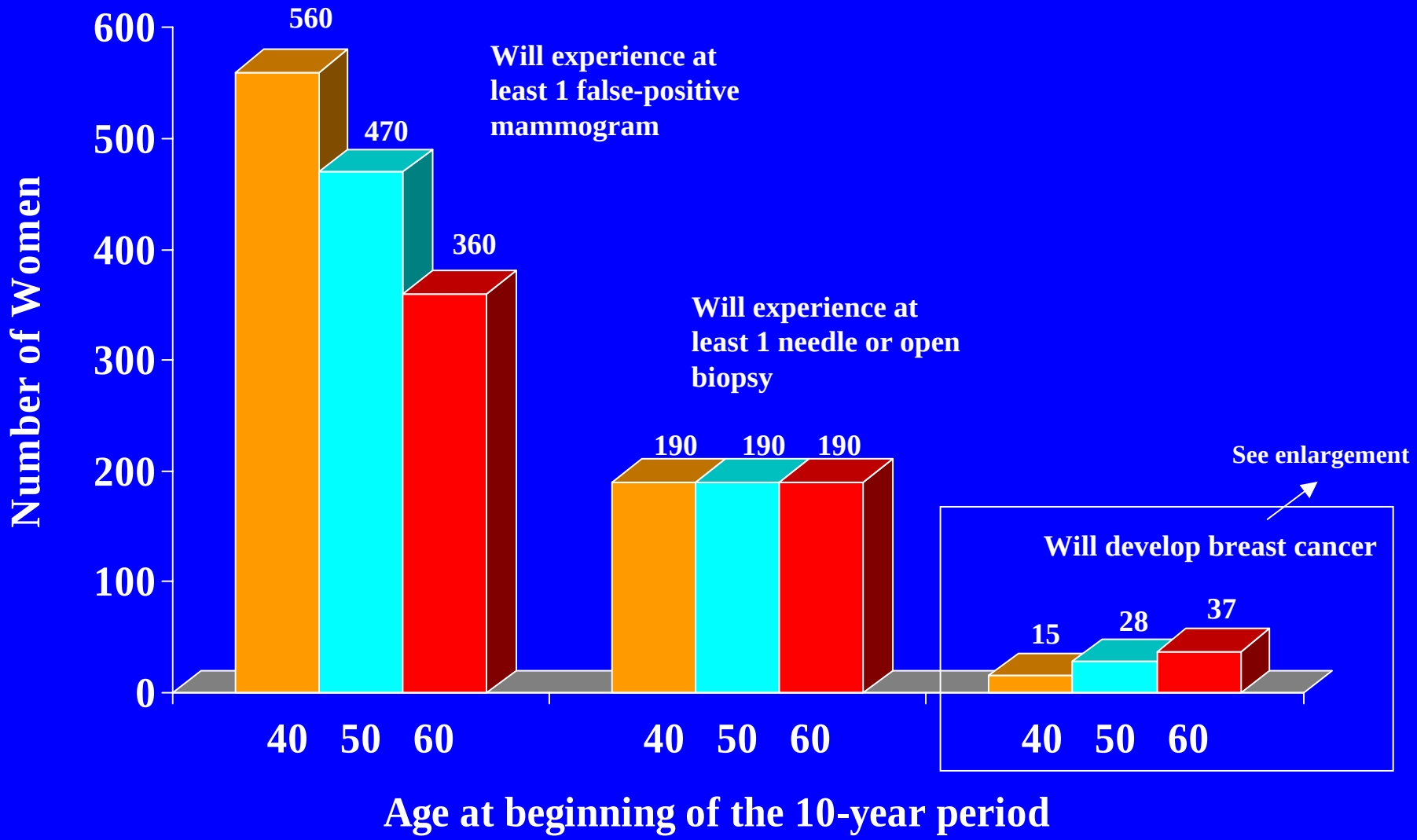


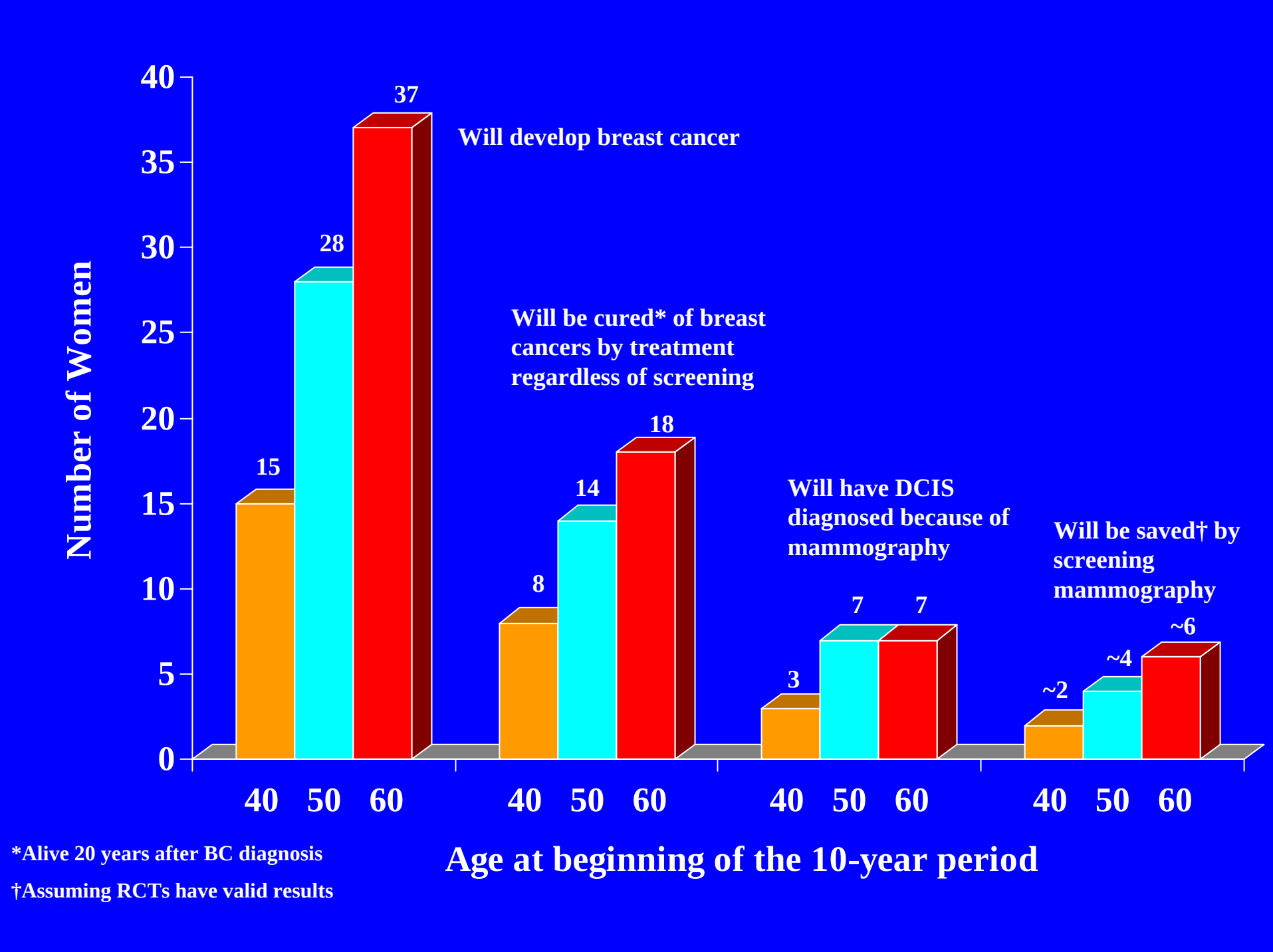
European guidelines for quality assurance in mammography screening

Third Edition

6th Lesson
Study How to Communicate with the Public

What happens when 1000 women get a screening mammogram every year for 10 years?




Number of Women
40
35
30
25
20
15
10
5
0
37
28
15
18
14
8
7
7
3
~6
~4
~2
Will develop breast cancer
Will be cured* of breast cancers by treatment regardless of screening
Will have DCIS diagnosed because of mammography
Will be saved† by screening mammography
40 50 60
40 50 60
40 50 60
40 50 60
Age at beginning of the 10-year period
*Alive 20 years after BC diagnosis
†Assuming RCTs have valid results

Screening Programs: Lessons for Population Scientists

- RCTs are necessary but not sufficient
- "Unintended consequences" are far more common than cancer
- Screening picks up premalignant lesions that will not develop into cancer
- Treatment advances will effect screening
- The social context of cancer and screening is important
- Communication to the lay public is key

EBM Controversies

oes mammography work in younger women (under age 50)?

oes mammography work at all?

Lancet Cochrane Review by Olsen and Gotzsche in 2000 and 2001

- 5 of 8 studies (and part of a 6th) flawed
- Remaining 2 ½ studies showed no effect of mammography

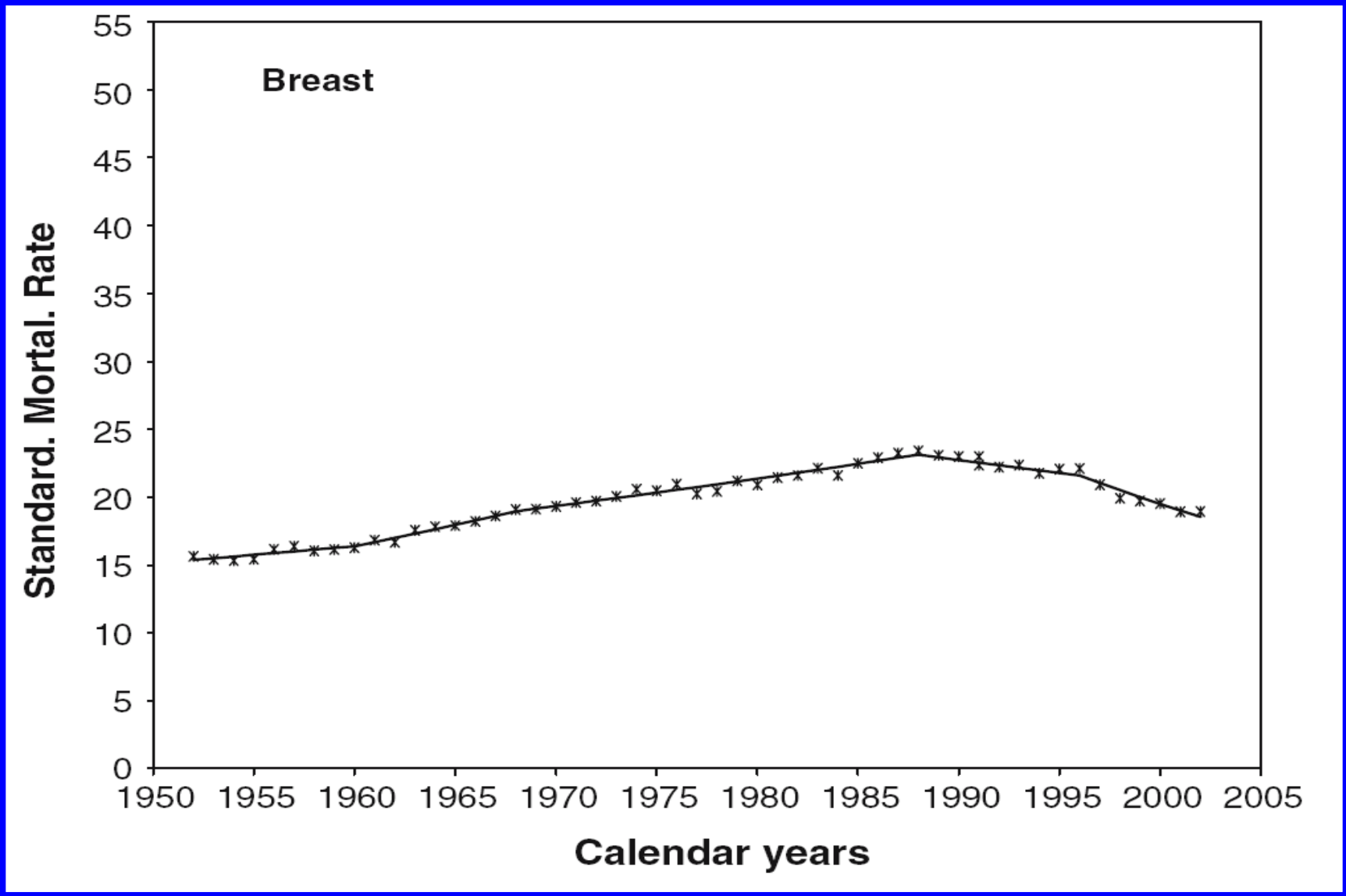
What were the "Fatal Flaws"?

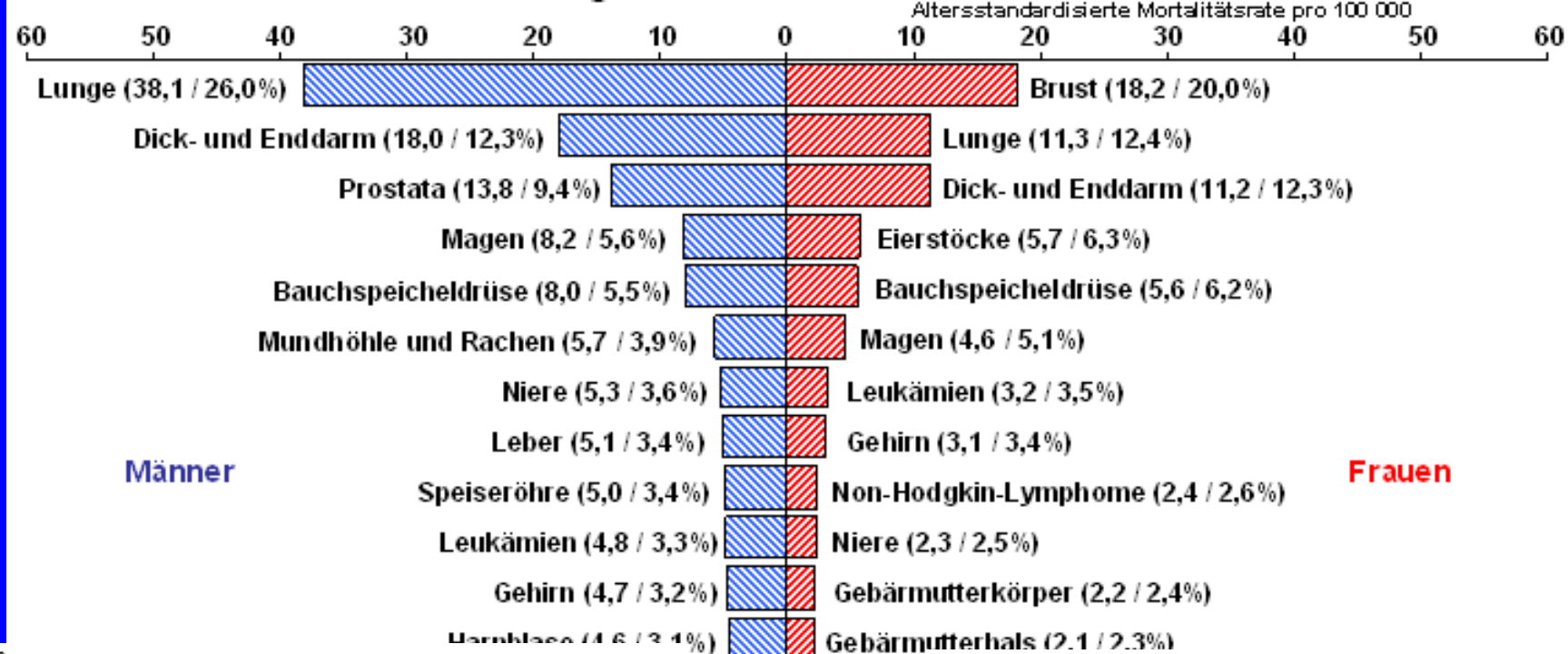
- Unequal distribution of characteristics

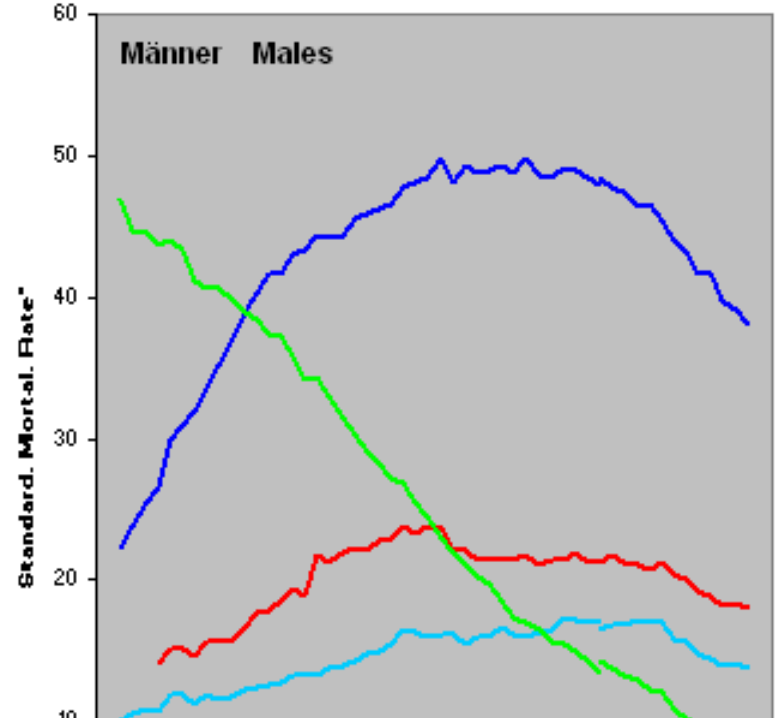
  E.g., breast lumps in HIP, age in Swedish studies, SES in Edinburgh
- Varying numbers of women reported
- Combined Swedish studies showed no overall mortality reduction
- Cause of death not always masked (HIP)

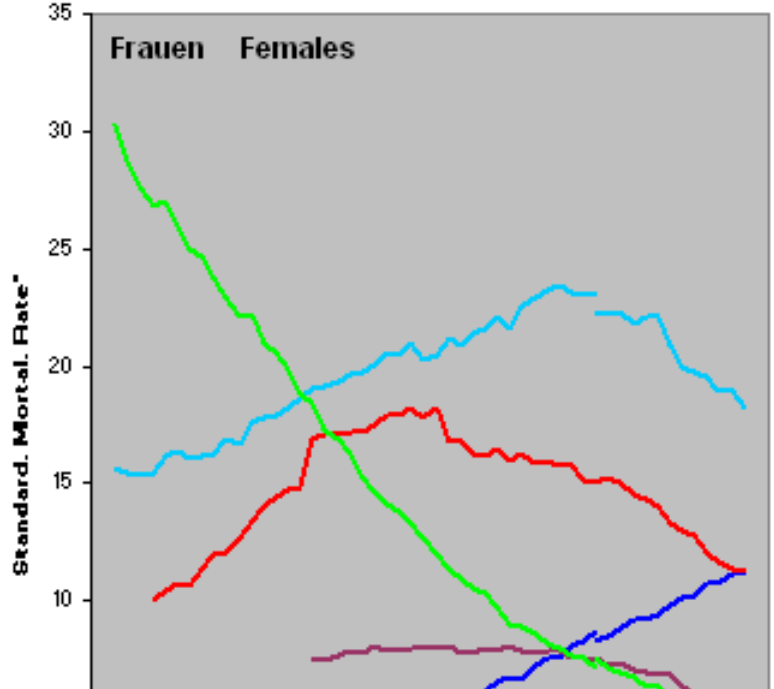
Answers by Investigators

- Varying numbers
  - Age versus dates of birth
  - Late exclusion of some ineligible women
- Unequal distribution of characteristics
  - Cluster randomization in some studies
  - Small absolute differences
  - Some differences biased against screening
- Latest update of Swedish studies found decrease in overall mortality


Breast
Standard. Mortal. Rate
55
50
45
40
35
30
25
20
15
10
5
0
1950
1955
1960
1965
1970
1975
1980
1985
1990
1995
2000
2005
Calendar years


Altersstandardisierte Mortalitätsrate pro 100 000
60 50 40 30 20 10 0 10 20 30 40 50 60
Lunge (38,1 / 26,0%)
Dick- und Enddarm (18,0 / 12,3%)
Prostata (13,8 / 9,4%)
Magen (8,2 / 5,6%)
Bauchspeicheldrüse (8,0 / 5,5%)
Mundhöhle und Rachen (5,7 / 3,9%)
Niere (5,3 / 3,6%)
Leber (5,1 / 3,4%)
Speiseröhre (5,0 / 3,4%)
Leukämien (4,8 / 3,3%)
Gehirn (4,7 / 3,2%)
Männer
Brust (18,2 / 20,0%)
Lunge (11,3 / 12,4%)
Dick- und Enddarm (11,2 / 12,3%)
Eierstöcke (5,7 / 6,3%)
Bauchspeicheldrüse (5,6 / 6,2%)
Magen (4,6 / 5,1%)
Leukämien (3,2 / 3,5%)
Gehirn (3,1 / 3,4%)
Non-Hodgkin-Lymphome (2,4 / 2,6%)
Niere (2,3 / 2,5%)
Gebärmutterkörper (2,2 / 2,4%)
Gebärmutterhals (2,1 / 2,3%)
Frauen


Männer Males
Standard. Mortal. Rate*
60
50
40
30
20


Frauen Females
Standard. Mortal. Rate*
35
30
25
20
15
10

For all we do in medicine, we must determine

“the benefits of medical interventions in relation to their hazards and costs.”

Kerr L. White, MD