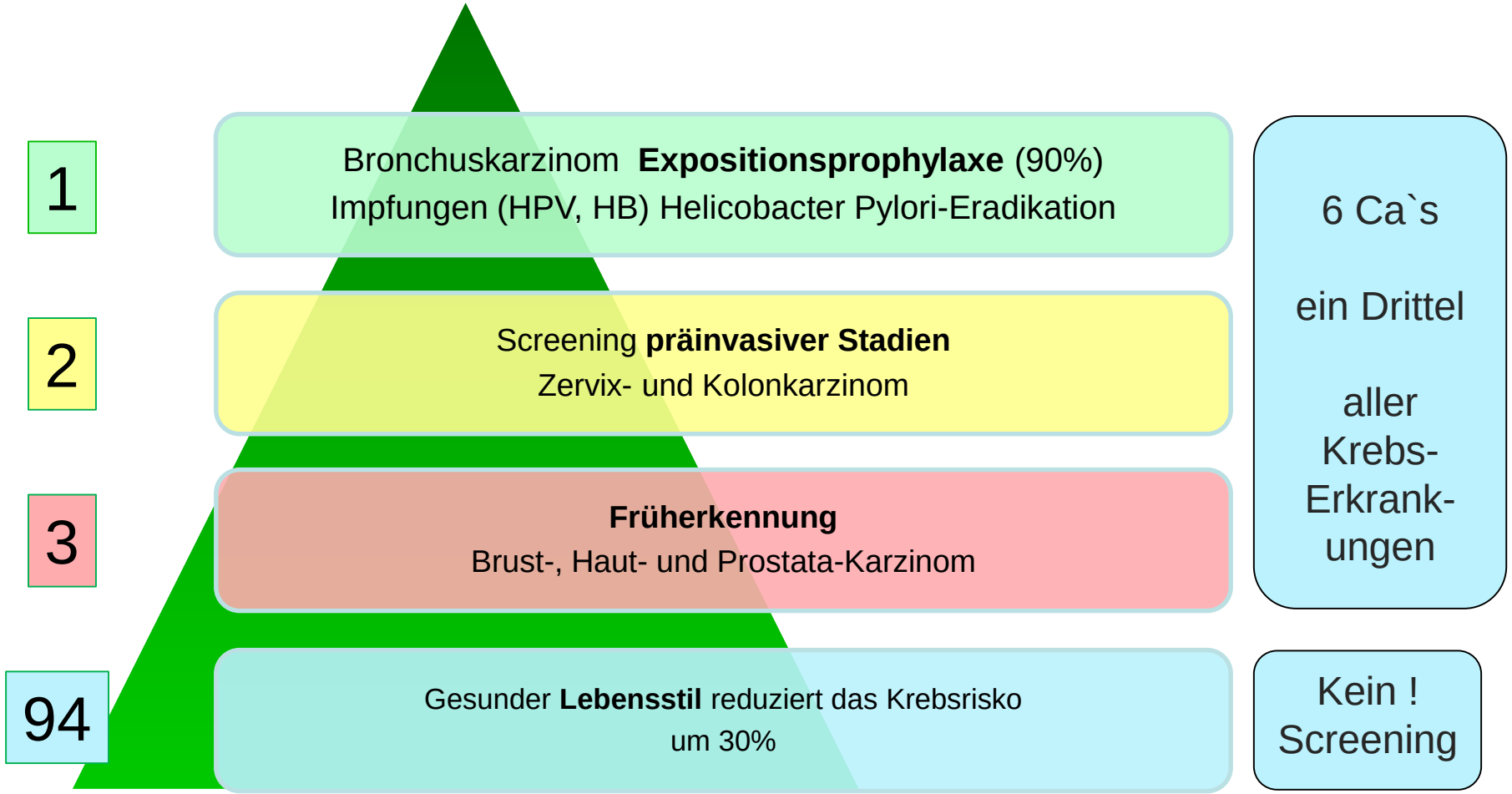
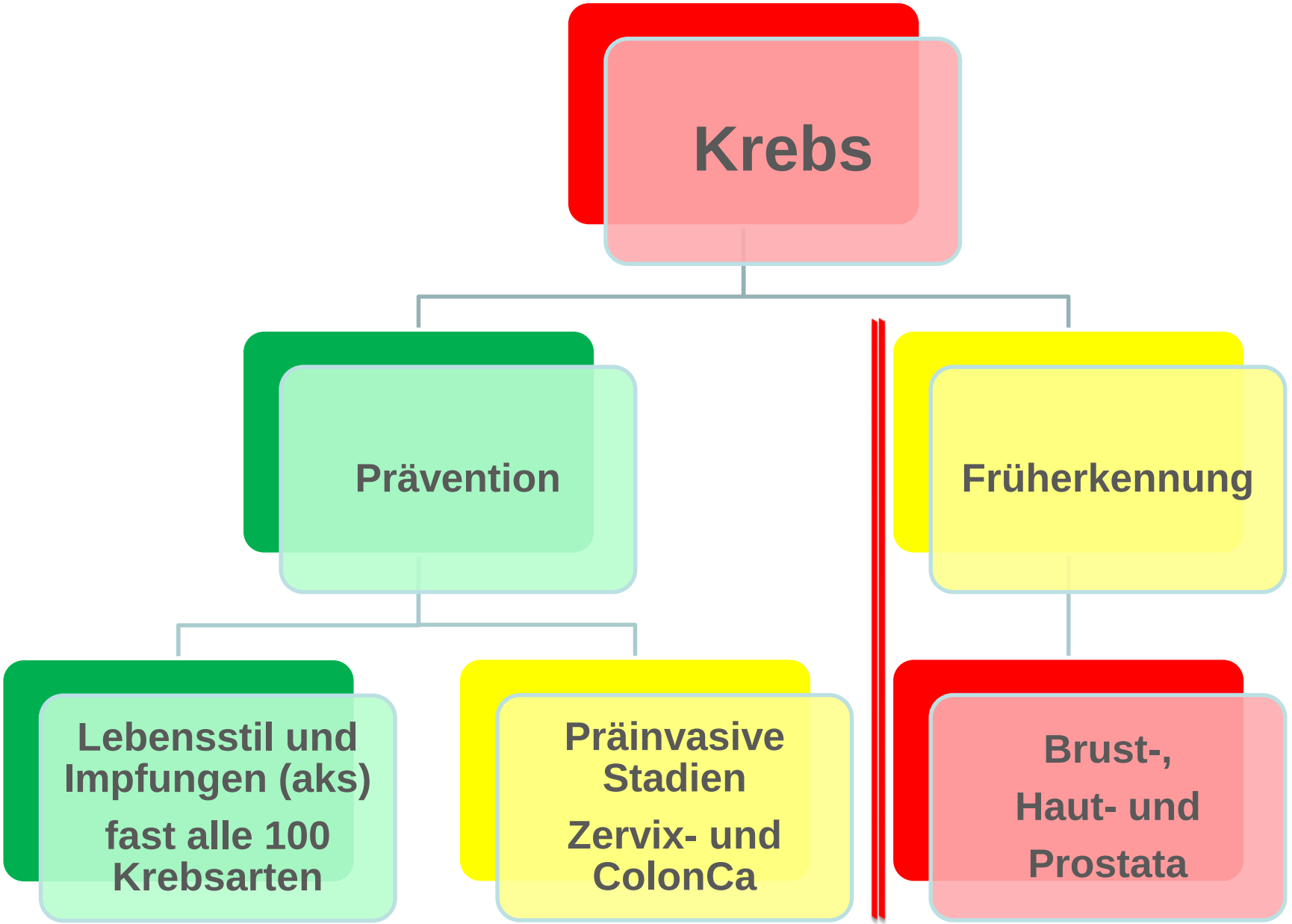
Die Krise des Krebs-Screenings - die Erfolge des Vorstadien-Screenings

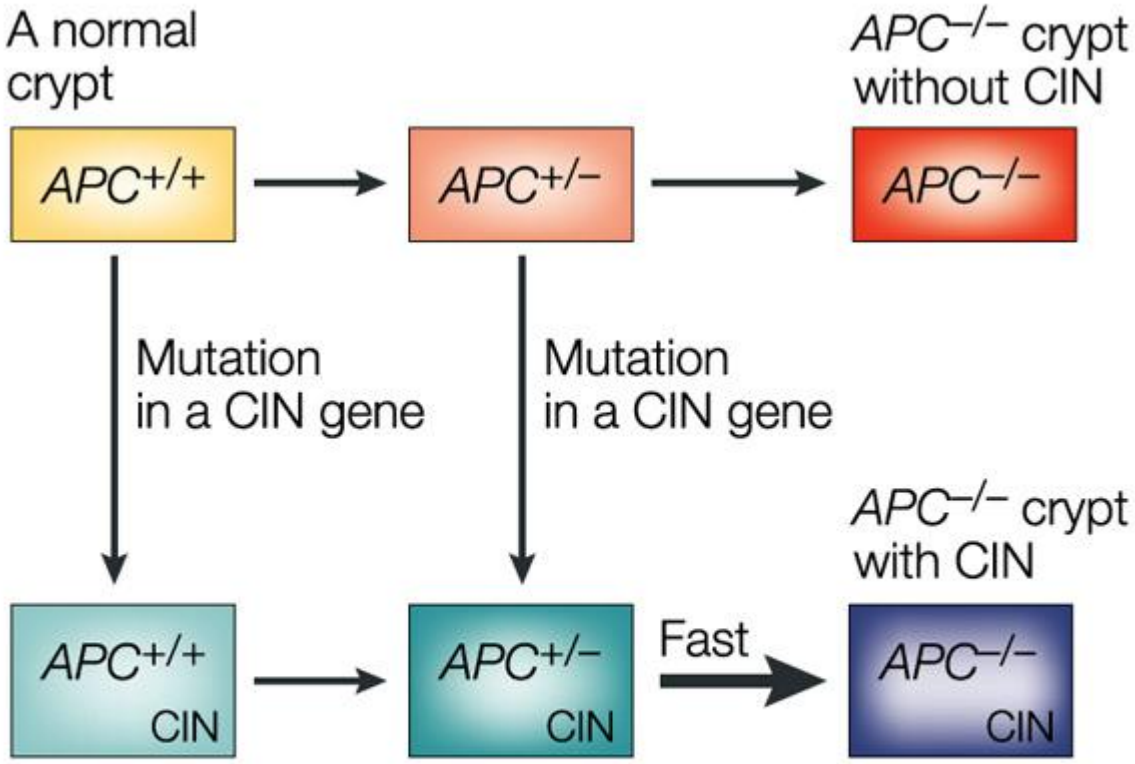
Hans Concin

aks science
aks Database
Vorarlberg Cancer Registry

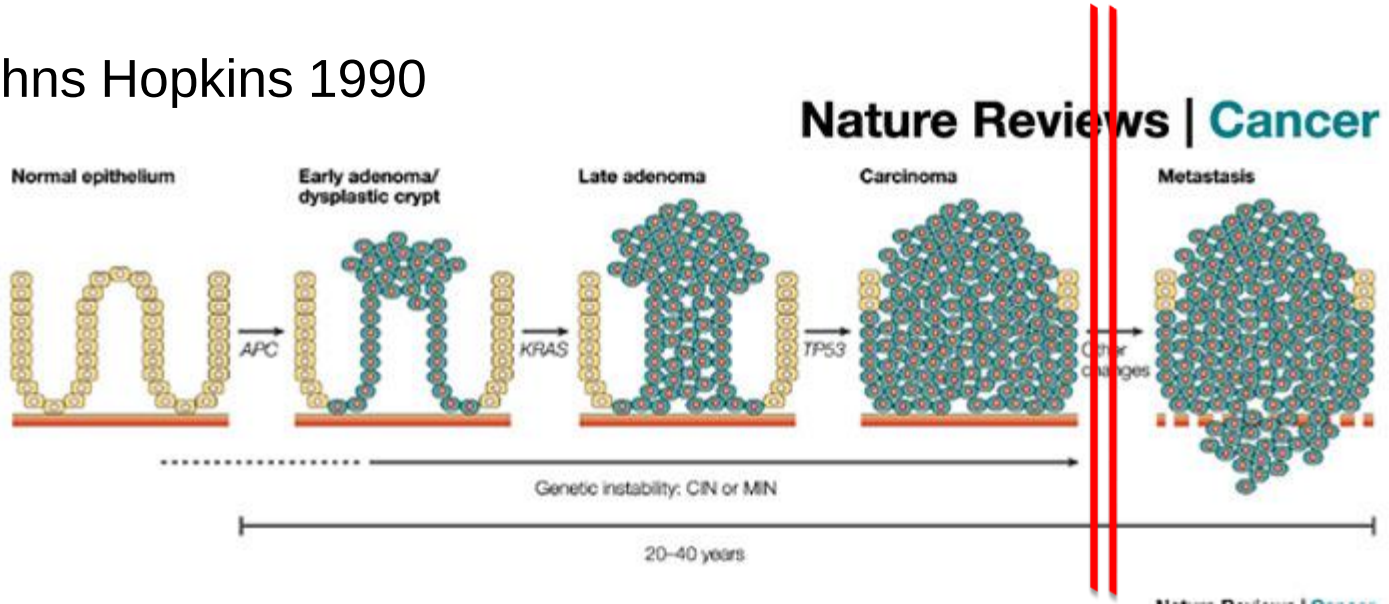
1 + 2 + 3 + 94


1
Bronchuskarzinom **Expositionsprophylaxe** (90%)
Impfungen (HPV, HB) Helicobacter Pylori-Eradikation
2
Screening **präinvasiver Stadien**
Zervix- und Kolonkarzinom
3
Früherkennung
Brust-, Haut- und Prostata-Karzinom
94
Gesunder **Lebensstil** reduziert das Krebsrisiko
um 30%
6 Ca`s
ein Drittel
aller
Krebs-
Erkrank-
ungen
Kein !
Screening

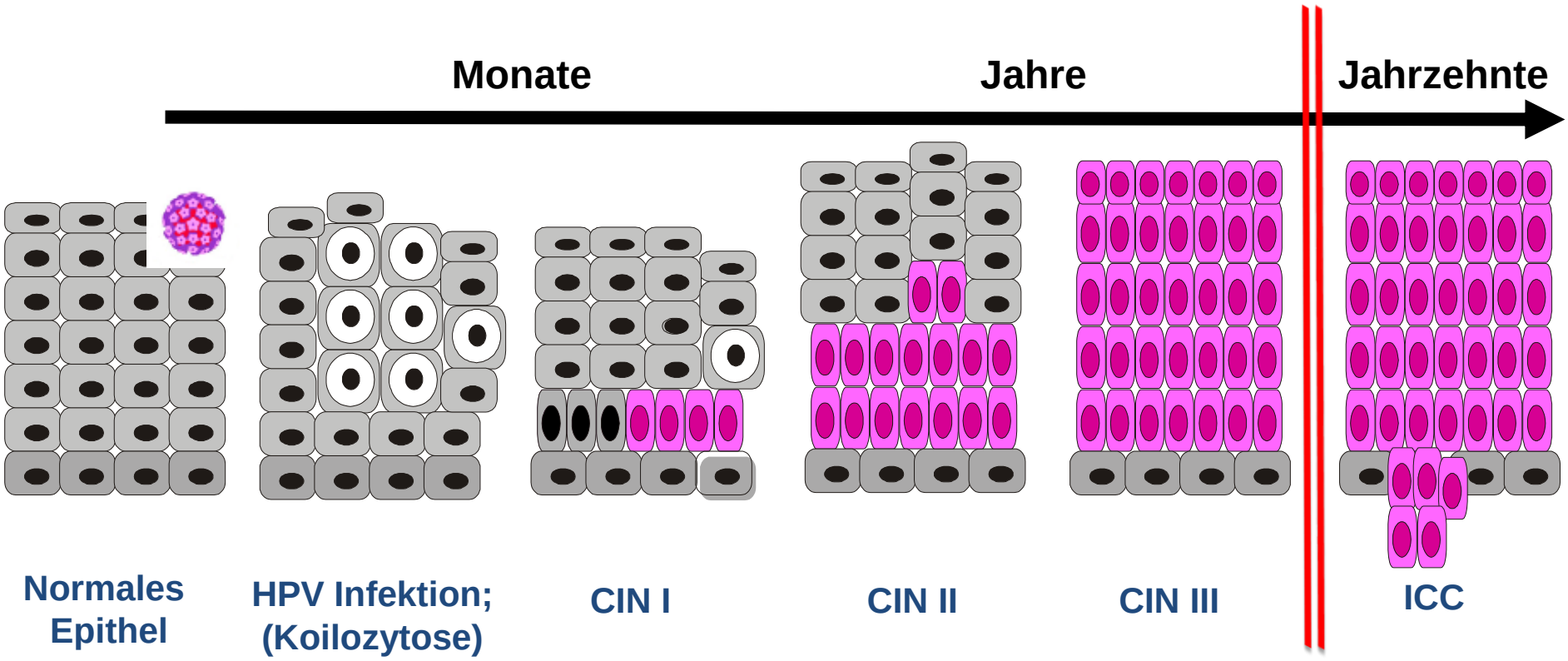

Krebs
Prävention
Früherkennung
Lebensstil und Impfungen (aks)
fast alle 100 Krebsarten
Präinvasive Stadien
Zervix- und ColonCa
Brust-,
Haut- und
Prostata



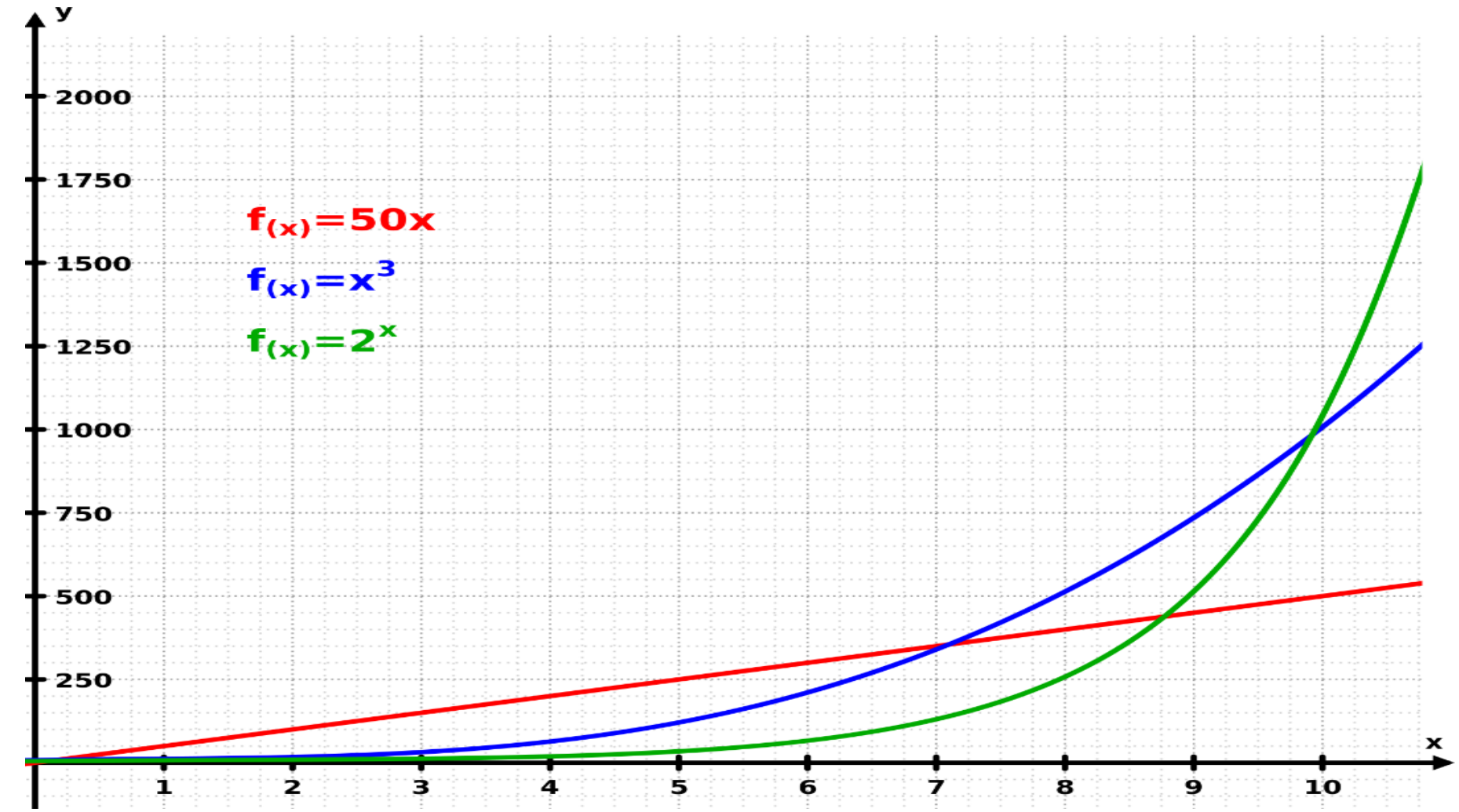
Bert Vogelstein, Johns Hopkins 1990



HPV-Infektion und Tumorentwicklung



persistierende HPV-Infektion


y
2000
1750
1500
1250
1000
750
500
250
$f_{(x)}=50x$
$f_{(x)}=x^3$
$f_{(x)}=2^x$
x
1
2
3
4
5
6
7
8
9
10

Sir Muir Gray

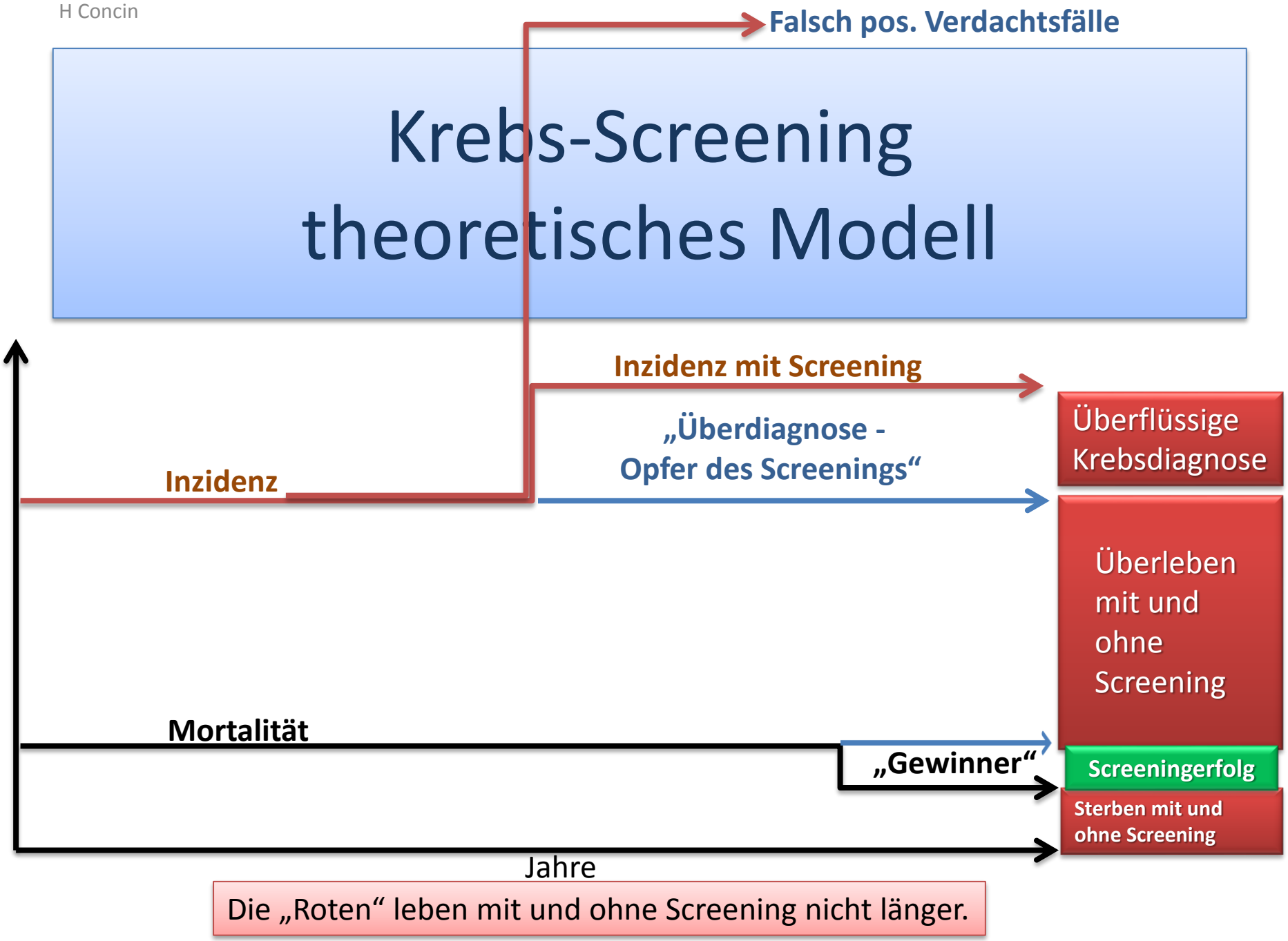
Chief knowledge officer of the

National Health Service

All screening programs
do harm;
some can do good as well

H Concin

Krebs-Screening theoretisches Modell

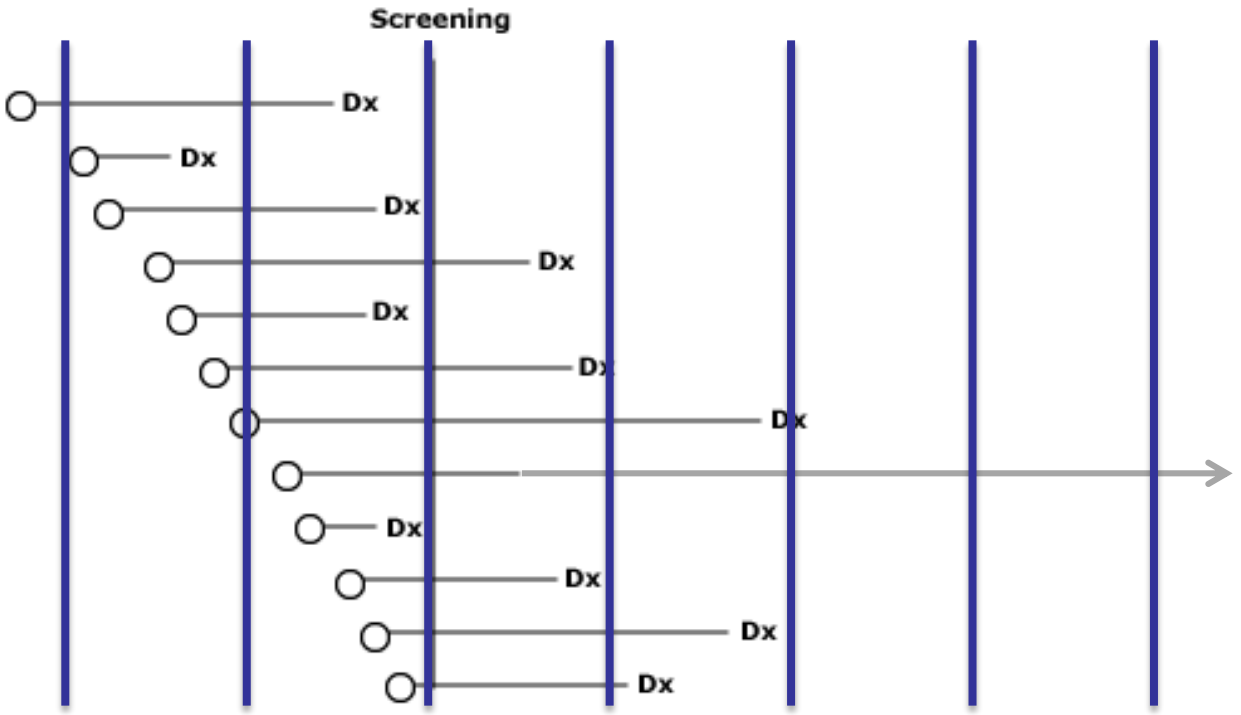


Die „Roten“ leben mit und ohne Screening nicht länger.

Screening Biases (Verzerrungen)

- ❖Volunteer/selection Bias
- ✓Length Bias
- ✓Lead-time Bias
- ✓Over-diagnosis Bias
- ✓Therapy Bias
- ✓Reporting Bias

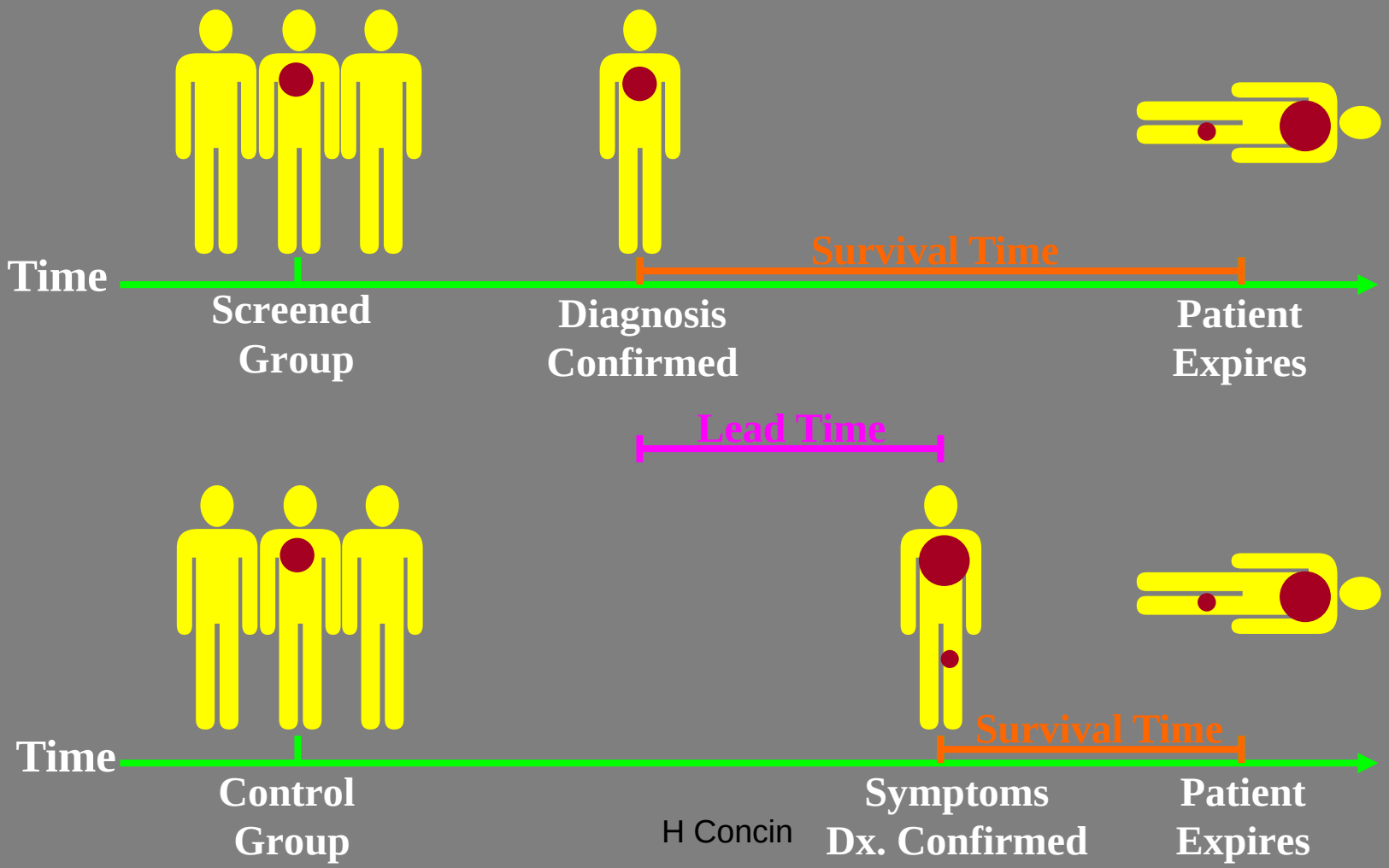
Length-time bias



Cases that progress rapidly from onset (O) to symptoms and diagnosis (Dx) are less likely to be detected during a screening examination.

Reproduced with permission from: Fletcher, RH, Fletcher, SW. Prevention. In: Clinical Epidemiology - The Essentials, 4th ed. Lippincott Williams & Wilkins, Baltimore 2005. p. 147 - 167.) Copyright © 2005 Lippincott Williams and Wilkins. http://www.lww.com

Lead Time Bias



Screening Biases

- ✓Volunteer/selection Bias
- ✓Length Bias
- ✓Lead-time Bias
- ✓Over-diagnosis Bias
- ✓Therapy Bias
- ❖Reporting Bias

Reporting Bias

Gute (Screening-) Ergebnisse werden vermehrt zur Publikation in hochrangigen Fachjournalen eingereicht.

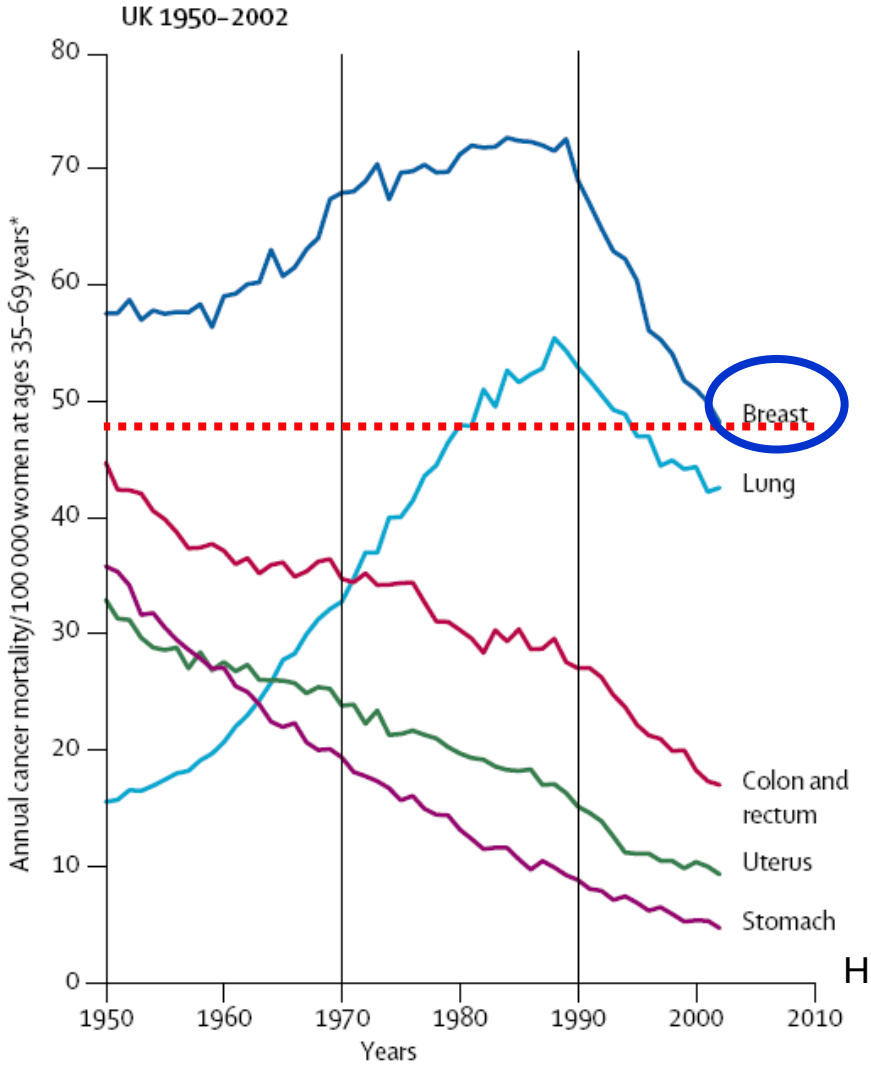
Gute (Screening-) Ergebnisse werden von den Herausgebern von Top-Journalen eher zur Publikation angenommen.

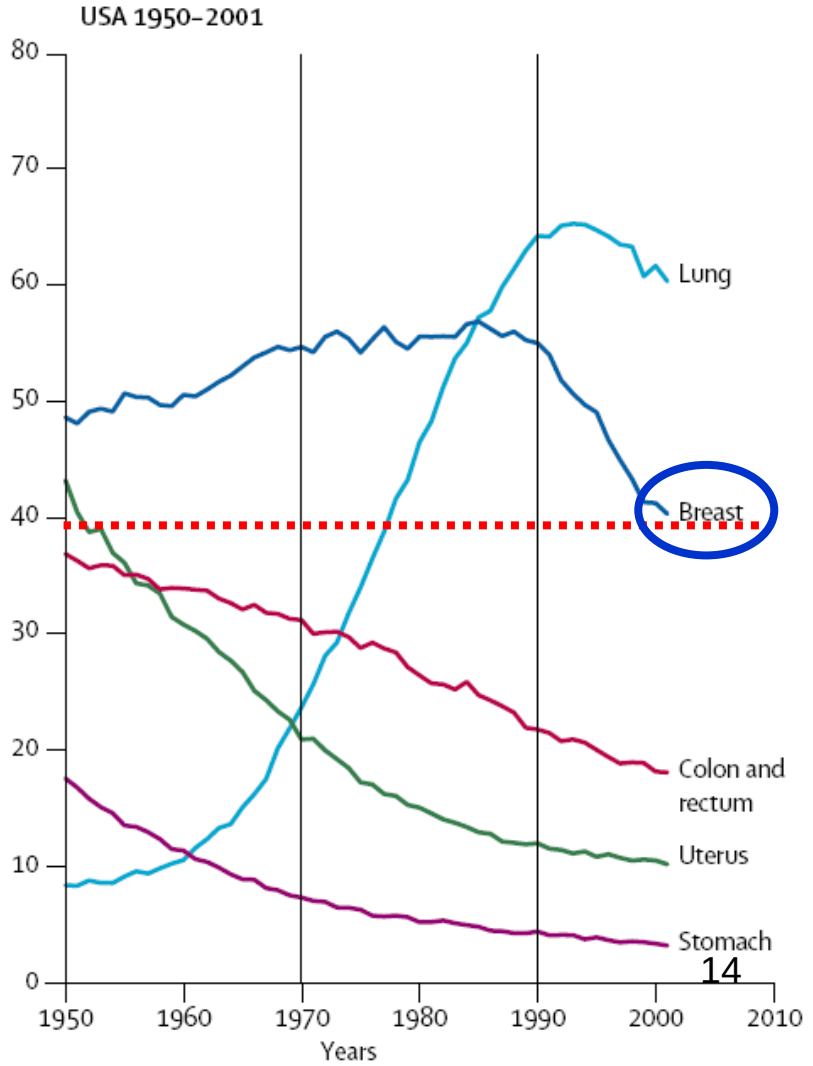
Säkulare Trends und nationale Unterschiede Mortalität häufiger Krebserkrankungen seit 1950

Frauen im Alter von 35 – 69 Jahre

*Early Breast Cancer Trialists' Collaborative Group (EBCTCG)**

Lancet 2005; 365: 1687–1717



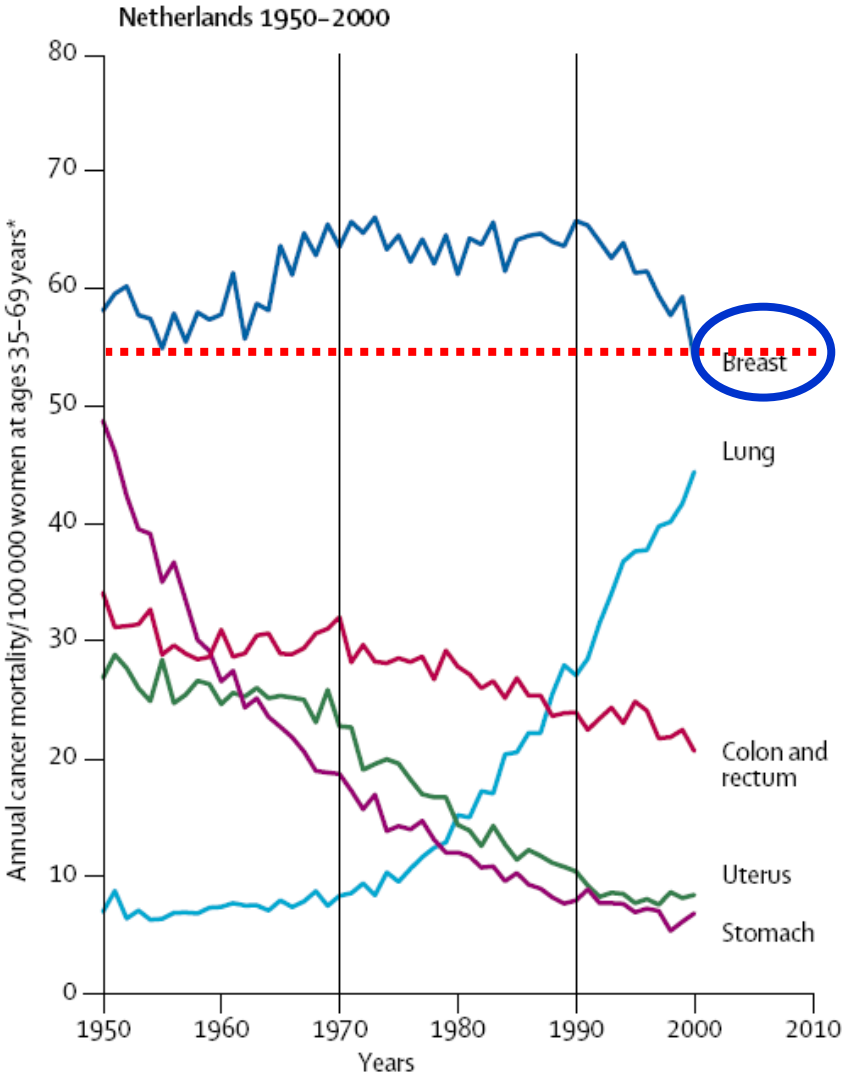


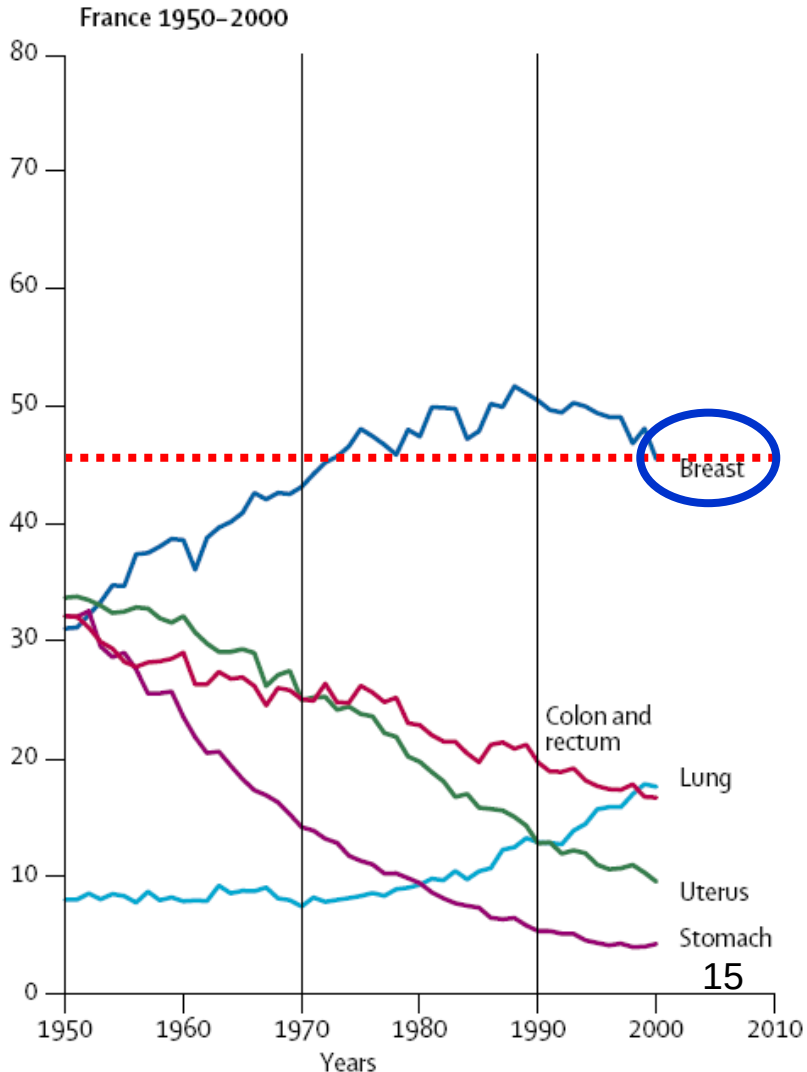
Säkulare Trends und nationale Unterschiede Mortalität häufiger Krebserkrankungen seit 1950

Frauen im Alter von 35 – 69 Jahre

*Early Breast Cancer Trialists' Collaborative Group (EBCTCG)**

Lancet 2005; 365: 1687–1717



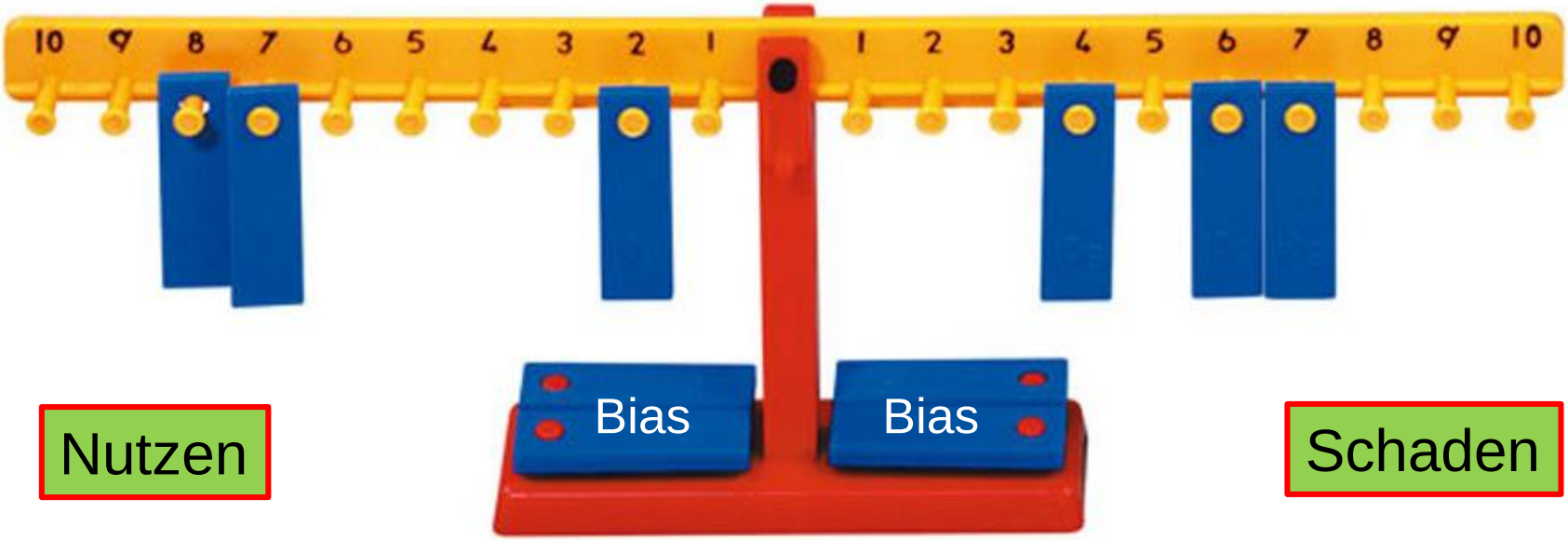


Qualität im Screening

Sensitivität

Qualität nach EU-LL

Spezifität



Nutzen

Schaden

Brustkrebsfrüherkennung

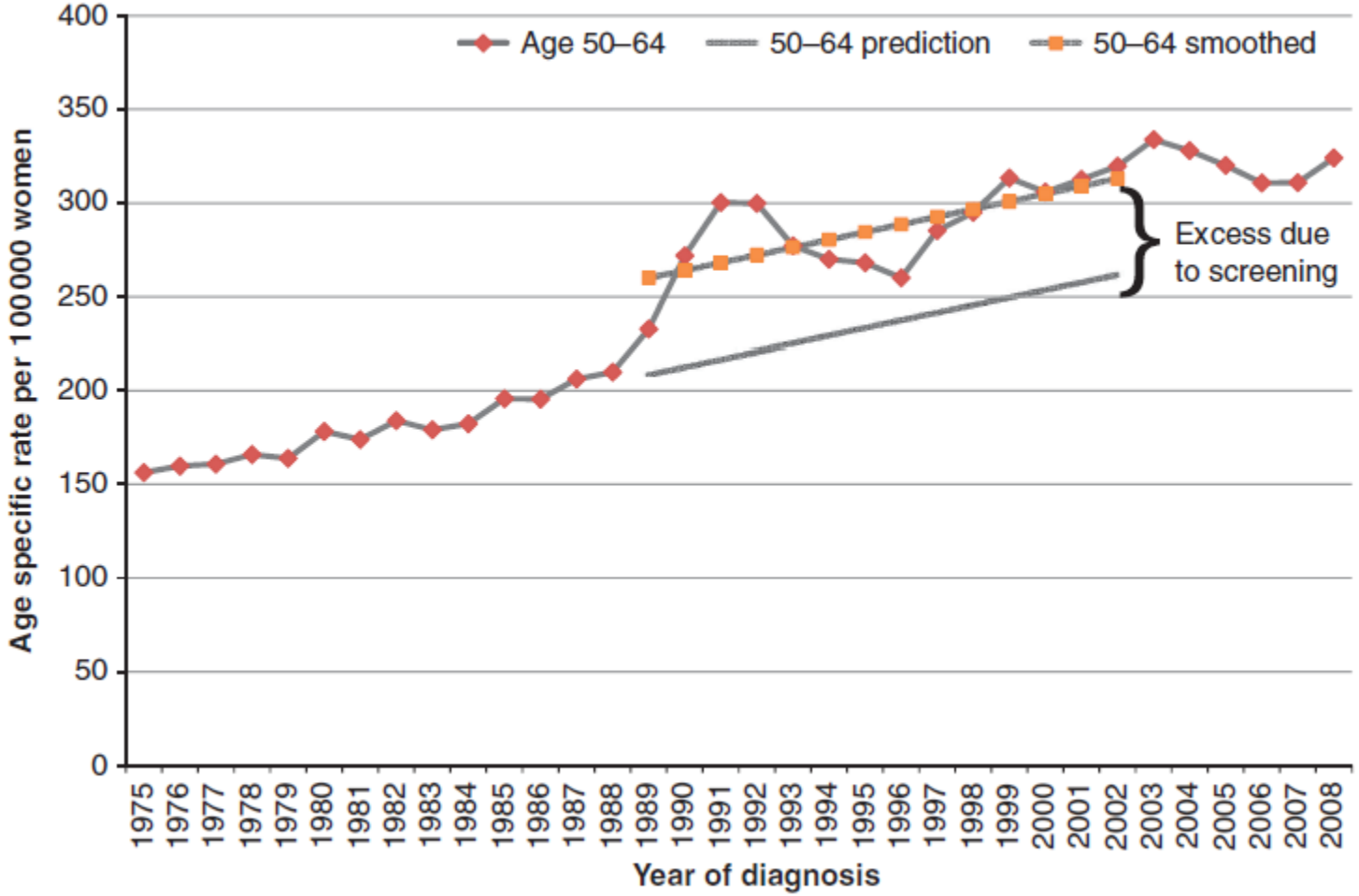
Mammographie-Screening

die wichtigsten Publikationen
2010 -2014

Woloshin S, Schwartz L M **The benefits and harms of mammography screening: understanding the trade-offs.**

JAMA 2010 January 13; 303(2): 164-5

Mortalität	**40 – 49 Jahre**	**50 – 59 Jahre**
kein Screening	**3.5 / 1000**	**5.3 / 1000**
Screening regelmäßig	**3.0 / 1000**	**4.6 / 1000**
Todesfälle verhindert	**0.5 / 1000**	**0.7 / 1000**



Breast cancer age-specific incidence rates, England 1975–2008, age 50–64 with expected, observed and smoothed data.

BRITISH JOURNAL OF CANCER Report 2232 bjc 2013

Table. Change in Incidence and Mortality of Cancers Over Time From 1975 to 2010 as Reported in Surveillance, Epidemiology and End Results[1]

Change[a]	Incidence			Mortality		
	Per 100 000		% Change	Per 100 000		% Change
	1975	2010[b]		1975	2010[b]	
Example 1						
Breast[c]	105.07	126.02	20	31.45	21.92	−30
Prostate	94	145.12	54	30.97	21.81	−30
Lung and bronchus[d]	52.26	56.68	8	42.56	47.42	11
Example 2						
Colon	41.35	28.72	−31	28.09	15.51	−45
Cervical	14.79	6.71	−55	5.55	2.26	−59
Example 3						
Thyroid	4.85	13.83	185	0.55	0.51	−7
Melanoma	7.89	23.57	199	2.07	2.74	32

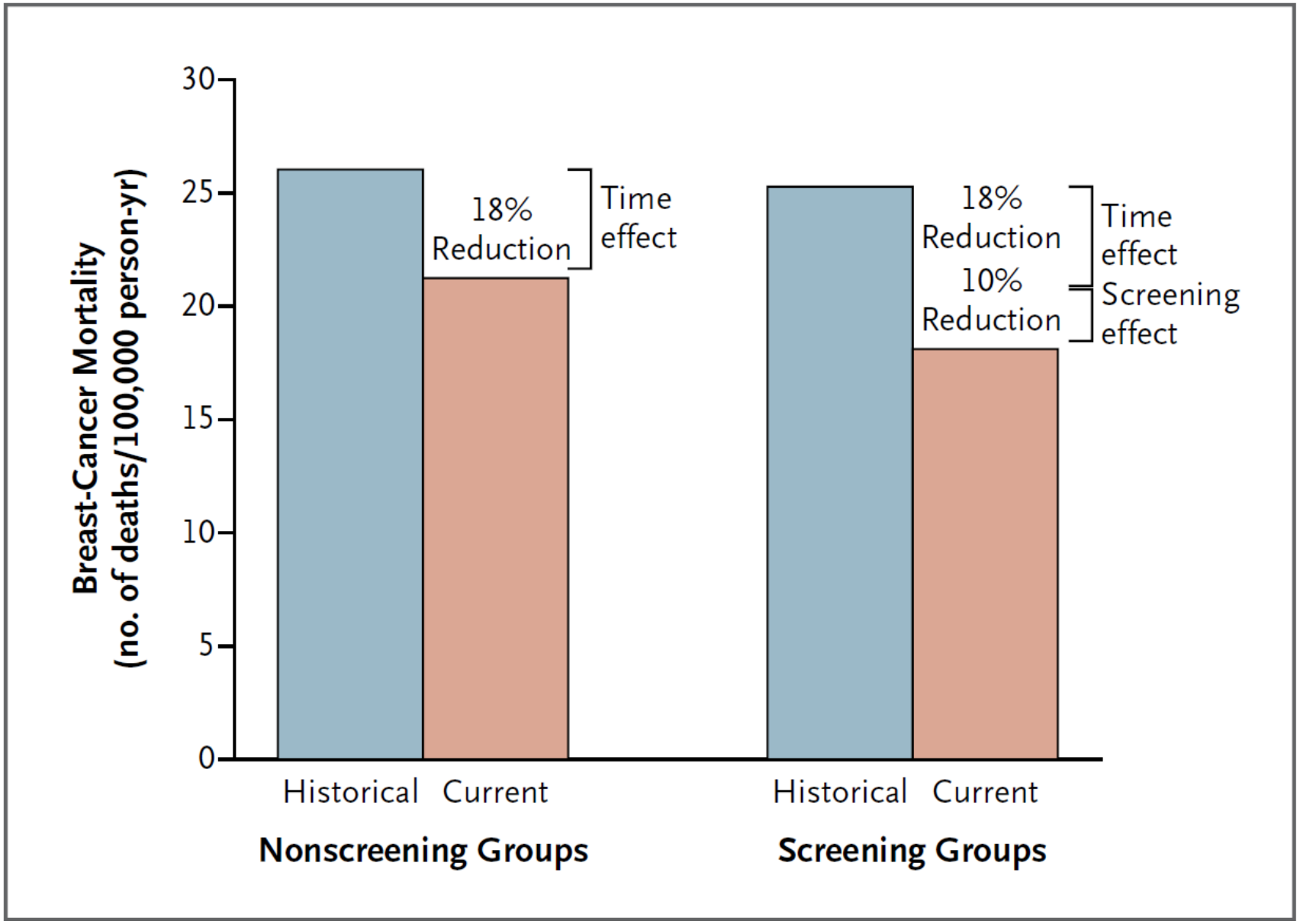
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 23, 2010 VOL. 363 NO. 13

Effect of Screening Mammography on Breast-Cancer Mortality in Norway

CONCLUSIONS

The availability of screening mammography was associated with a reduction in the rate of death from breast cancer, but the screening itself accounted for only about a third of the total reduction. (Funded by the Cancer Registry of Norway and the Research Council of Norway.)



H Concin: vereinfachte Rechnung: Alter 50 bis 70 Jahre – 5% haben eine BrCa Diag. 2% sterben daran, Reduktion um 10% = 2/1000, NN-Screen über 20 Jahre: 500

BMJ

RESEARCH

Breast cancer mortality in organised mammography screening in Denmark: comparative study

Karsten Juhl Jørgensen, researcher,[1] Per-Henrik Zahl, senior researcher,[2] Peter C Gøtzsche, professor[1]

[1]The Nordic Cochrane Centre, Rigshospitalet, University of Copenhagen, Denmark

[2]Norwegian Institute of Public Health, Oslo, Norway

Correspondence to: K J Jørgensen kj@cochrane.dk

Cite this as: *BMJ* 2010;340:c1241

ABSTRACT

Objective To determine whether the previously observed 25% reduction in breast cancer mortality in Copenhagen following the introduction of mammography screening was indeed due to screening, by using an additional screening region and five years additional follow-up.

Design We used Poisson regression analyses adjusted for

non-screened areas and in age groups too young to benefit from screening, and are more likely explained by changes in risk factors and improved treatment than by screening mammography.

INTRODUCTION

Comprehensive systematic reviews of randomised trials

Conclusions

We were unable to find an effect of the Danish screening programme on breast cancer mortality.

The reductions in breast cancer mortality we observed in screening regions were similar or less than those in non-screened areas and in age groups too young to benefit from screening, and are more likely explained by changes in risk factors and improved treatment than by screening mammography.

ORIGINAL ARTICLE

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.

From the Quality Department, St. Charles Health System, Central Oregon, and the Department of Radiation Medicine, Oregon Health and Science University, Portland (A.B.); the University of Texas Medical School at Houston, Houston (A.B.); and the Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine at Dartmouth, Hanover, NH (H.G.W.). Address reprint requests to Dr. Bleyer at 2500 NE Neff Rd., Bend, OR 97701, or at ableyer@gmail.com.

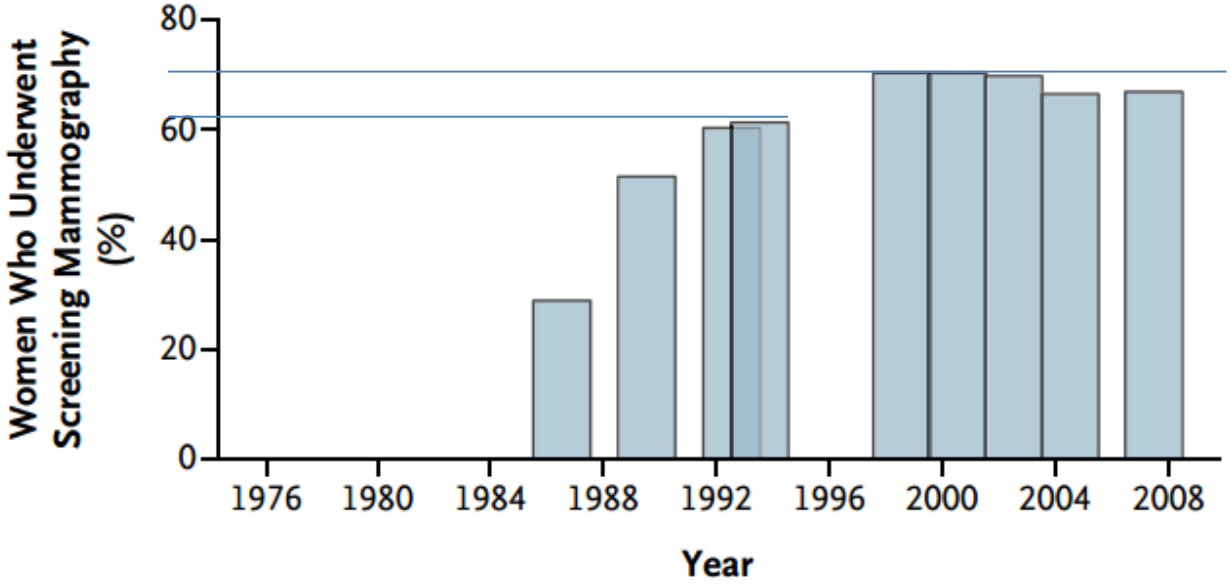
N Engl J Med 2012;367:1998-2005.
DOI: 10.1056/NEJMoa1206809

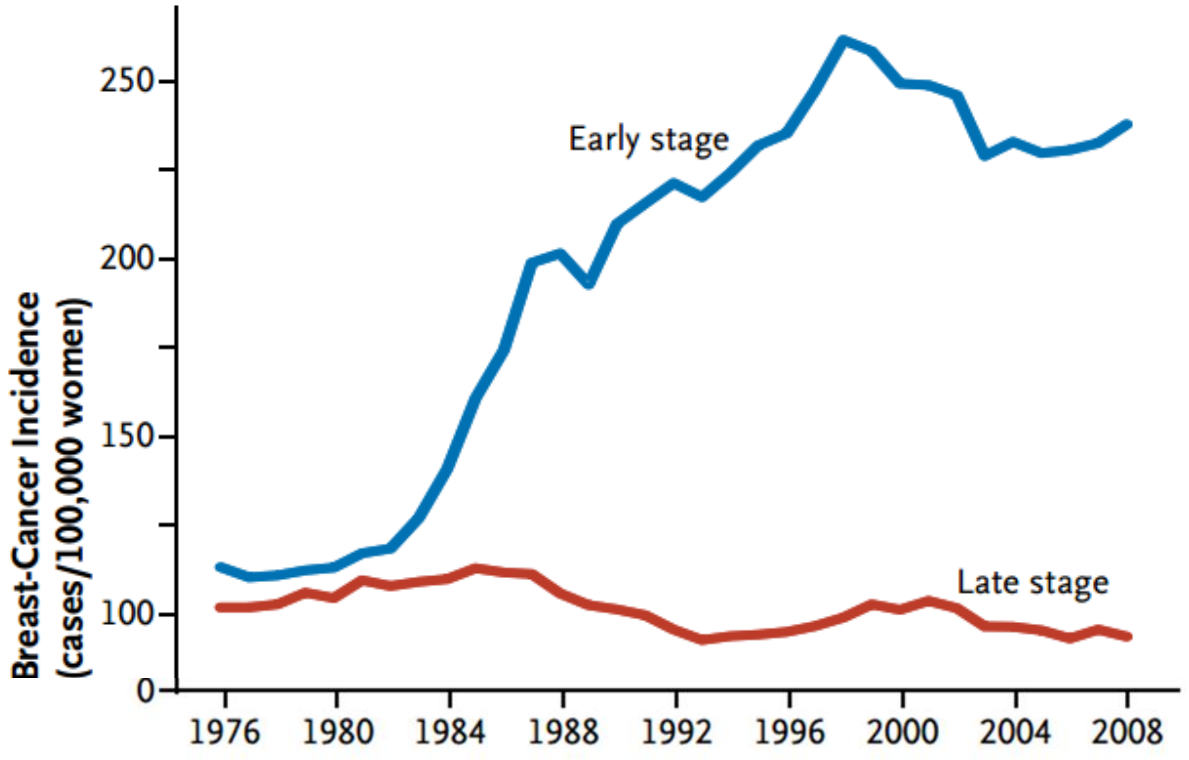
ABSTRACT

Conclusions

Despite substantial increases in the number of cases of early-stage breast cancer detected, screening mammography has only marginally reduced the rate at which women present with advanced cancer. Although it is not certain which women have been affected, the imbalance suggests that there is **substantial overdiagnosis, accounting for nearly a third of all newly diagnosed breast cancers, and that screening is having, at best, only a small effect on the rate of death from breast cancer.**

A **Women 40 Yr of Age or Older**





ORIGINAL ARTICLE

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.

N Engl J Med 2012; 367:1998-2005 | November 22, 2012 | DOI: 10.1056/NEJMoa1206809

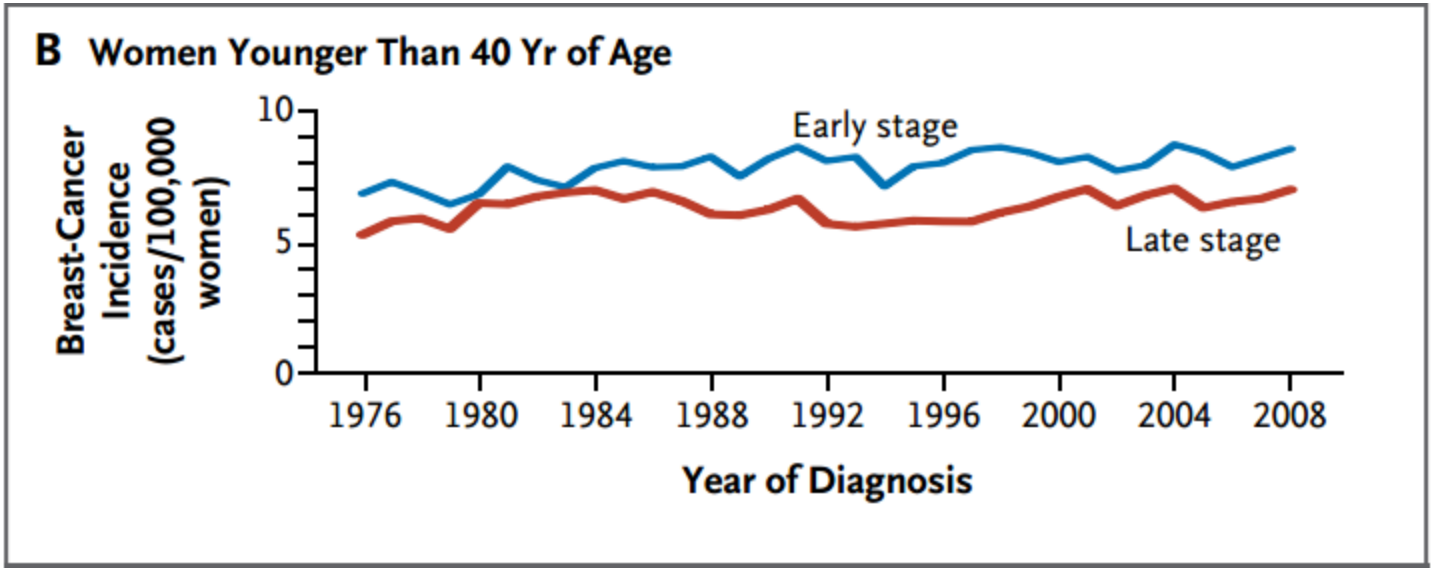


Figure 1. Use of Screening Mammography and Incidence of Stage-Specific Breast Cancer in the United States, 1976–2008.

Panel A shows the self-reported use of screening mammography and the incidence of stage-specific breast cancer among women 40 years of age or older. Panel B shows the incidence of stage-specific breast cancer among women who generally did not have exposure to screening mammography — those younger than 40 years of age.

ORIGINAL ARTICLE

Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.

N Engl J Med 2012; 367:1998-2005 | November 22, 2012 | DOI: 10.1056/NEJMoa1206809

Conclusions

Despite substantial increases in the number of cases of early-stage breast cancer detected, screening mammography has only marginally reduced the rate at which women present with advanced cancer.
Although it is not certain which women have been affected, the imbalance suggests that there is substantial overdiagnosis, accounting for nearly a third of all newly diagnosed breast cancers, and that screening is having, at best, only a small effect on the rate of death from breast cancer.

Schlussfolgerungen

Trotz erheblichem Anstieg der entdeckten Zahl von Brustkrebs-Frühstadien, hat das Mammographie-Screening nur geringfügig die Rate der Frauen mit Krebs im fortgeschrittenen Stadium reduziert. Obwohl es nicht sicher ist, welche Frauen betroffen sind, deutet das Ungleichgewicht darauf hin, dass es eine erhebliche Überdiagnose gibt, die fast ein Drittel aller neu diagnostizierten Brustkrebsfälle ausmachen und dass das Screening, im besten Fall nur einen geringen Einfluss auf die Sterberate von Brustkrebs hat.

RESEARCH

J R Soc Med 2013: 106: 234–242.

Breast cancer mortality trends in England and the assessment of the effectiveness of mammography screening: population-based study

Toqir K Mukhtar • David RG Yeates • Michael J Goldacre

Unit of Health-Care Epidemiology, Department of Public Health, University of Oxford, Oxford OX3 7LF, UK

Correspondence to: Toqir K Mukhtar. Email: toqir.mukhtar@dph.ox.ac.uk

JRSM JOURNAL OF THE ROYAL SOCIETY OF MEDICINE

ow an effect of
ncer mortality in

DECLARATIONS

Competing interests

None declared

Funding

This work was supported by the English National Institute for Health Research (ref. RNC/035/02). The funding source had no influ-

Conclusions

We permuted the data in a number of different ways, over an observation period of 39 years, but the data show that, at least as yet, there is no evidence of an effect of mammographic screening on population-level breast cancer mortality.

Participants Women who died from breast cancer in the Oxford region

REPORT

BJC

British Journal of Cancer (2013) 108, 2205–2240 | doi: 10.1038/bjc.2013.177

The benefits and harms of breast cancer screening: an independent review

A report jointly commissioned by Cancer Research UK and the Department of Health (England) October 2012.

M G Marmot*[,1], D G Altman[2], D A Cameron[3], J A Dewar[4], S G Thompson[5], M Wilcox[6] – The Independent UK Panel on Breast Cancer Screening

[1]*UCL Department of Epidemiology and Public Health, UCL Institute of Health Equity, 1-19 Torrington Place, London WC1E 7HB, UK;* [2]*Centre for Statistics in Medicine, University of Oxford, Botnar Research Centre, Windmill Road, Oxford, OX3 7LD, UK;* [3]*University of Edinburgh Cancer Research Centre and NHS Lothian, Western General Hospital, Edinburgh, EH4 2XR, UK;* [4]*Department of Surgery and Molecular Oncology, Medical School, Ninewells Hospital, Dundee DD1 9SY, UK;* [5]*Department of Public Health and Primary Care, University of Cambridge, Strangeways Research Laboratory, Worts Causeway, Cambridge CB1 8RN, UK and* [6]*Independent Cancer Patient's Voice, 17 Woodbridge Street, London EC1R 0LL, UK*

1. SUMMARY

Marmot and colleagues acknowledged the limitations of their review, …

… on the basis of their estimate of
one death from breast cancer avoided for every 235 women invited to screening, they concluded that the UK breast screening programme should continue.

However, they also reported that
“for every breast cancer death prevented, approximately three overdiagnosed cases will be identified and treated.”

BMJ

BMJ 2013;346:f385 doi: 10.1136/bmj.f385 (Published 23 January 2013)

VIEWS & REVIEWS

PERSONAL VIEW

Harms from breast cancer screening outweigh benefits if death caused by treatment is included

Michael Baum *professor emeritus of surgery, Division of Surgery and Interventional Science, University College London, London WC1E 6BT, UK*

Each new intake of medical students to my surgical "firm" started off with a tutorial where I posed a rhetorical question: "Why do we screen for cancer?" To which the inevitable answer would be, "To catch it early, sir." Wrong. The question should be reframed, as "Does screening for cancer improve length or quality of life?" All other outcomes are surrogates.

The clinical trials of screening for breast cancer that informed the recent Marmot review[1] made no attempt to measure quality of life, but a surrogate for that might be mastectomy rate in

as overdiagnosis rates increase then the importance of the relatively rare lethal toxicities of treatment increase.

If we accept the Marmot estimate of reduction in cause specific mortality of 20%, then, as adjuvant systemic therapy developed over the years since the data accumulated to provide this estimate, we would now have to screen 2500 women for 10 years to avoid one breast cancer death (box 1). This estimate is much lower than in the Marmot report, which dismissed the impact of improvements in treatment.

“Does screening for cancer improve length or quality of life?”

Michael Baum *professor emeritus of surgery, Division of Surgery and Interventional Science,*
University College London

BMJ 23 January 2013

BMJ

BMJ 2014;348:g366 doi: 10.1136/bmj.g366 (Published 11 February 2014)

RESEARCH

Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial


OPEN ACCESS

Anthony B Miller *professor emeritus*[1], Claus Wall *data manager*[1], Cornelia J Baines *professor emerita*[1], Ping Sun *statistician*[2], Teresa To *senior scientist*[3], Steven A Narod *professor*[1 2]

[1]Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario M5T 3M7, Canada; [2]Women's College Research Institute, Women's College Hospital, Toronto, Ontario M5G 1N8, Canada; [3]Child Health Evaluative Services, The Hospital for Sick Children, Toronto, Ontario, Canada

Abstract

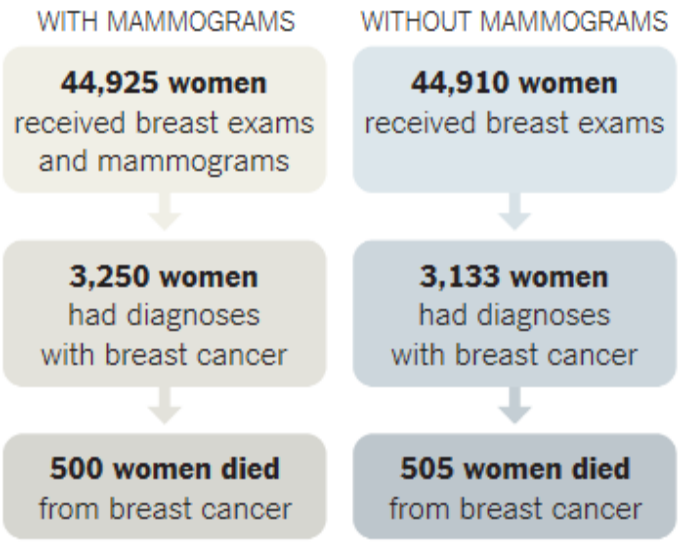
Objective To compare breast cancer incidence and mortality up to 25

Conclusion Annual mammography in women aged 40-59 does not reduce mortality from breast cancer beyond that of physical examination

The New York Times

Study Results

A large, 25-year study of Canadian women aged 40 to 59 found no benefit for women who were randomly mammograms. FEB. 11, 2014



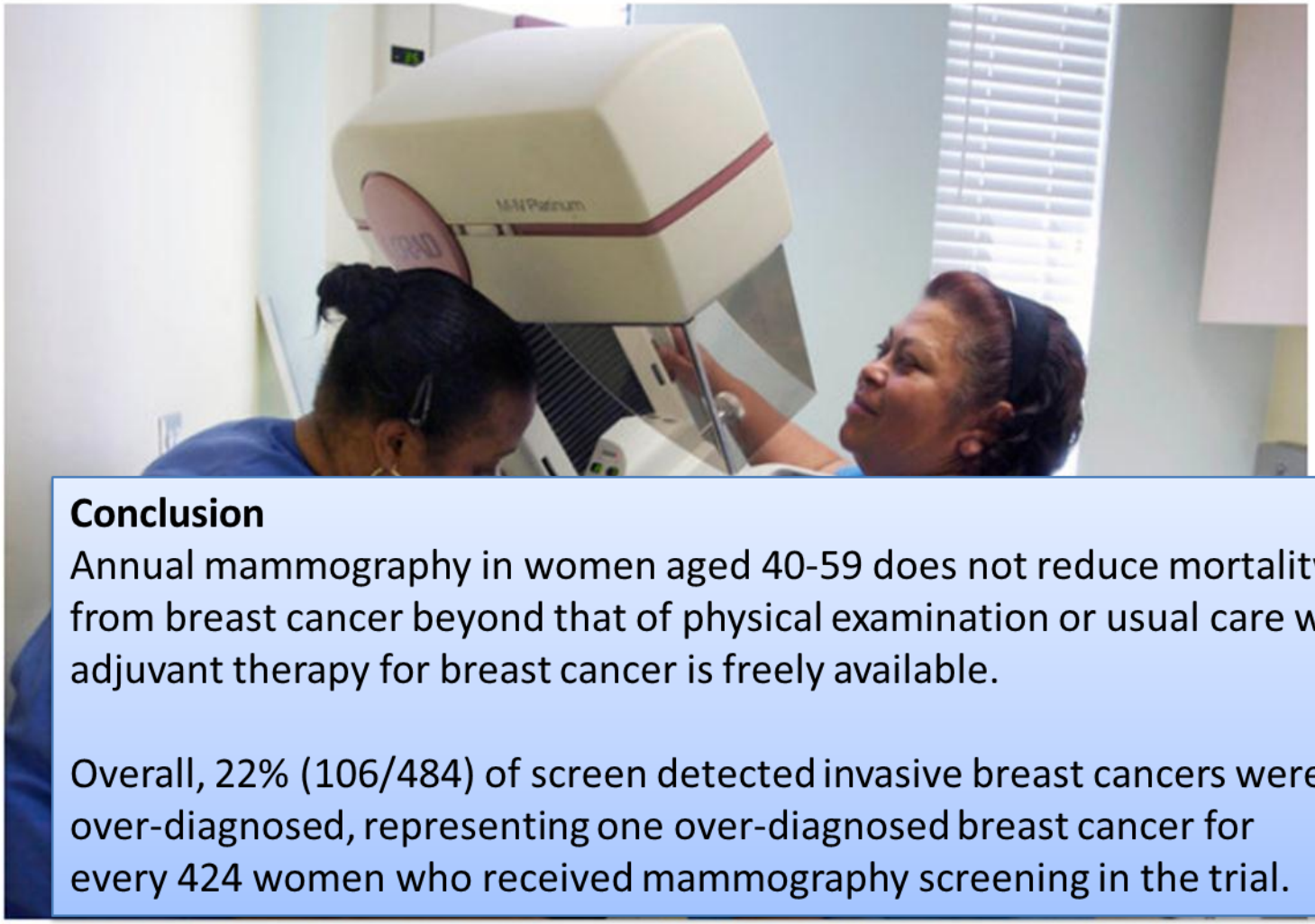
The death rate from breast cancer was the same in both groups, but **1 in 424 women** who had mammograms received unnecessary cancer treatment, including surgery, chemotheraphy and radiation.

Source: British Medical Journal

The New York Times

Vast Study Casts Doubts on Value of Mammograms

ssigned to have



Conclusion

Annual mammography in women aged 40-59 does not reduce mortality from breast cancer beyond that of physical examination or usual care when adjuvant therapy for breast cancer is freely available.

Overall, 22% (106/484) of screen detected invasive breast cancers were over-diagnosed, representing one over-diagnosed breast cancer for every 424 women who received mammography screening in the trial.

Nearly 75 percent of American women 40 and over say they had a mammogram in the past year.

DAMIAN DOVARGANES / ASSOCIATED PRESS

Falsche Befunde von Brustkrebs und unnötige Behandlungen:

Das Swiss Medical Board rät vom systematischen Mammografie-Screening in der Schweiz ab.

UNIVERSITY OF TORONTO
DALLA LANA SCHOOL OF PUBLIC HEALTH

Health Sciences Building, 155 College Street

Toronto, ON, M5T 3M7, Canada

February 17, 2012

To whom it may concern

I am writing in support of the application by Prof. Dr. med. Gabriele Nagel, MPH for funds to evaluate the organized mammography screening program in Vorarlberg. Given the increasing uncertainty of the validity of many of the randomized screening trials conducted in Sweden which have largely been the basis for the initiation of breast screening in many countries, it is critical that programs such as those in Vorarlberg where data are available that enable linkage of the records of screened women with breast cancer incidence and mortality data be carefully conducted. Prof. Nagel and her colleagues have proposed an innovative cohort study that will permit such an evaluation. An important contribution of their proposal will be to determine the extent to which regular clinical breast examinations impact on the outcome of mammography screening, and the relevance of risk factors such as obesity and diabetes.

I have known Dr Nagel since I spent 1999-2003 as Head of the Division of Clinical Epidemiology of Deutsches Krebsforschungszentrum, Heidelberg, and I have a high opinion of her expertise and experience. I have agreed to provide advice and assistance to Dr Nagel and her colleagues during the course of this project

Sincerely

Anthony B. Miller, MD, FRCP,

Professor Emeritus

Director, Canadian National Breast Screening Study