Screening

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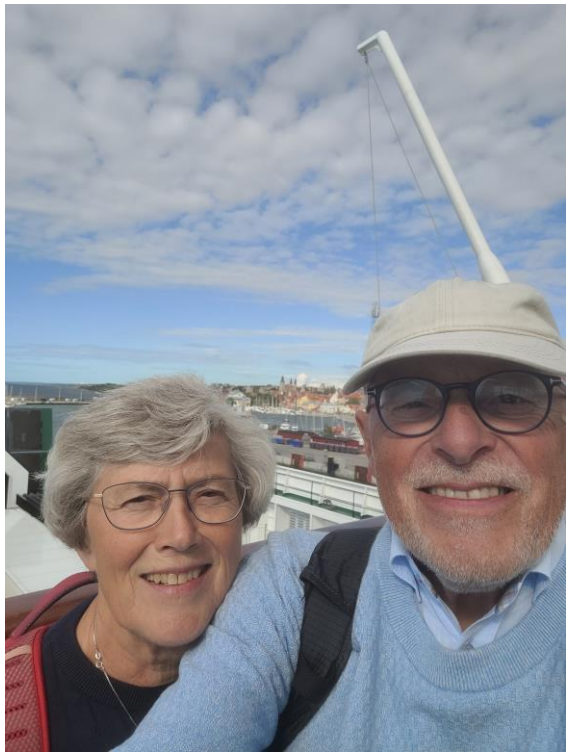
Member, Lisa Schwartz Foundation for Truth in Medicine

No financial conflicts of interest

Kitty, age 57, has just been diagnosed with early breast cancer through screening.

First reaction is shock.



Anxiety, depressed mood, looses interest in what usualy brings her joy.

She has a strong network of family and friends who are compassionate, supportive. They are emotionally affected as well.

Treatment goes well, but because of diffuse changes she undergoes mastectomy. She also receives radiation therapy and systemic therapy.

This negatively affects her self-image and quality of life, including her sex life.

As time pass, she feels better. Anxiety lessens and she enjoys life again.

She knows the disease can return even after many years and still worry from time to time, often checking for signs of recurrence.

At age 78, Kitty dies from unrelated causes.

She is thankful that breast screening saved her life.

What if everything Kitty and her family went through was unnecessary?

What if Kitty had lived to age 88 without the overtreatment?

We cannot know if an individual was overdiagnosed

We cannot know if an individual was saved

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

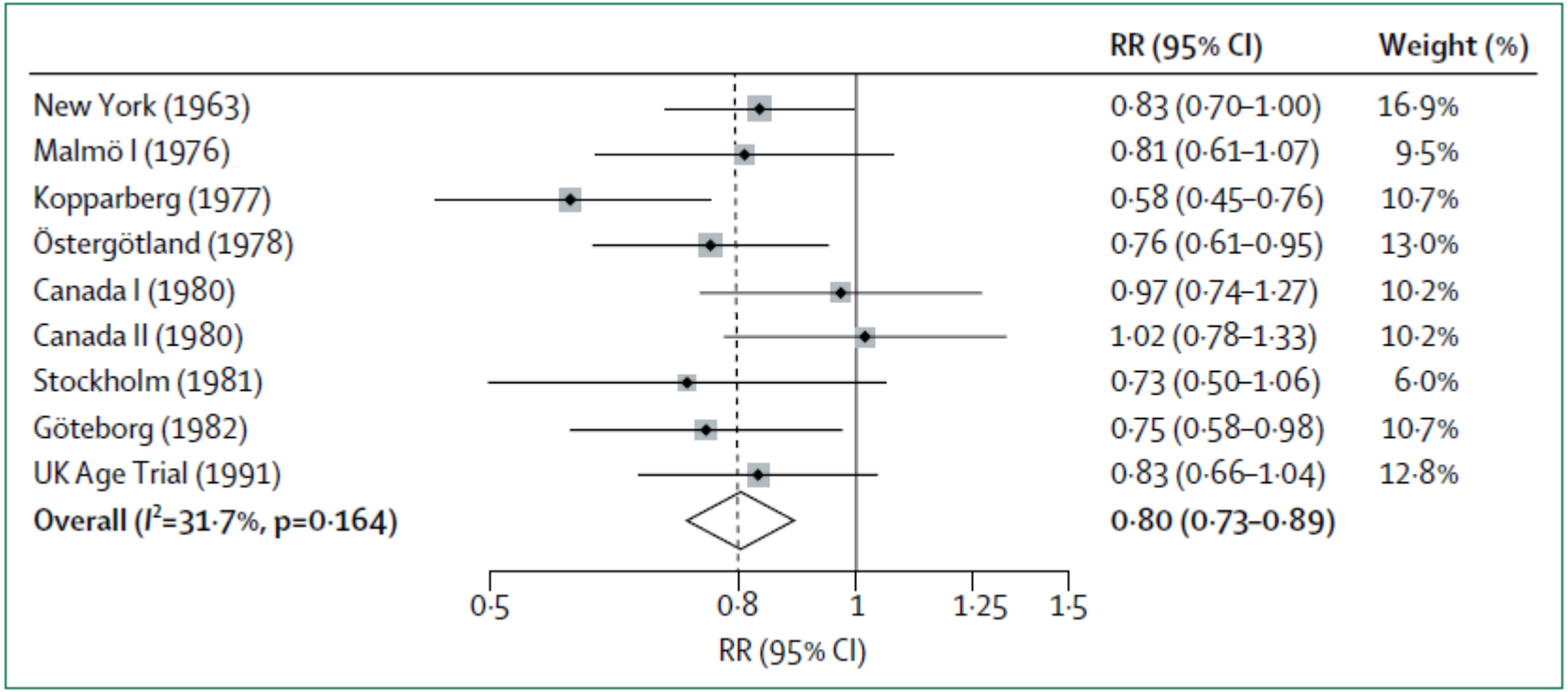
*Independent UK Panel on Breast Cancer Screening**

Lancet 2012; 380: 1778–86
Published Online
October 30, 2012
http://dx.doi.org/10.1016/

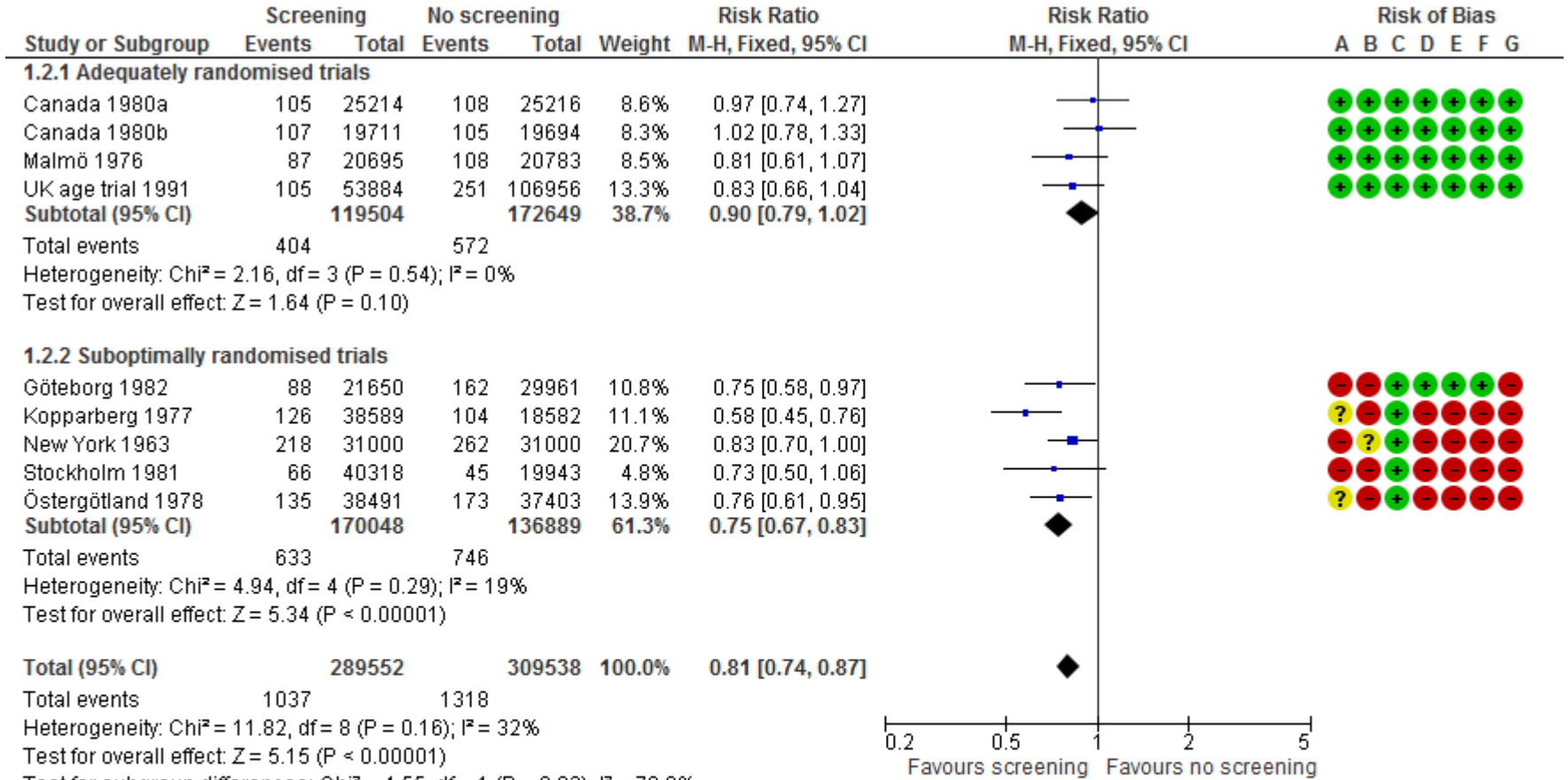
Whether breast cancer screening does more harm than good has been debated extensively. The main questions are how large the benefit of screening is in terms of reduced breast cancer mortality and how substantial the harm is in terms of overdiagnosis, which is defined as cancers detected at screening that would not have otherwise become clinically apparent in the woman's lifetime. An independent Panel was convened to reach conclusions about the

one breast cancer death prevented for about every three overdiagnosed cases identified and treated.

Is this a reasonable balance?



”The Panel’s primary conclusions about breast cancer mortality are based on data reported in the Cochrane review…”



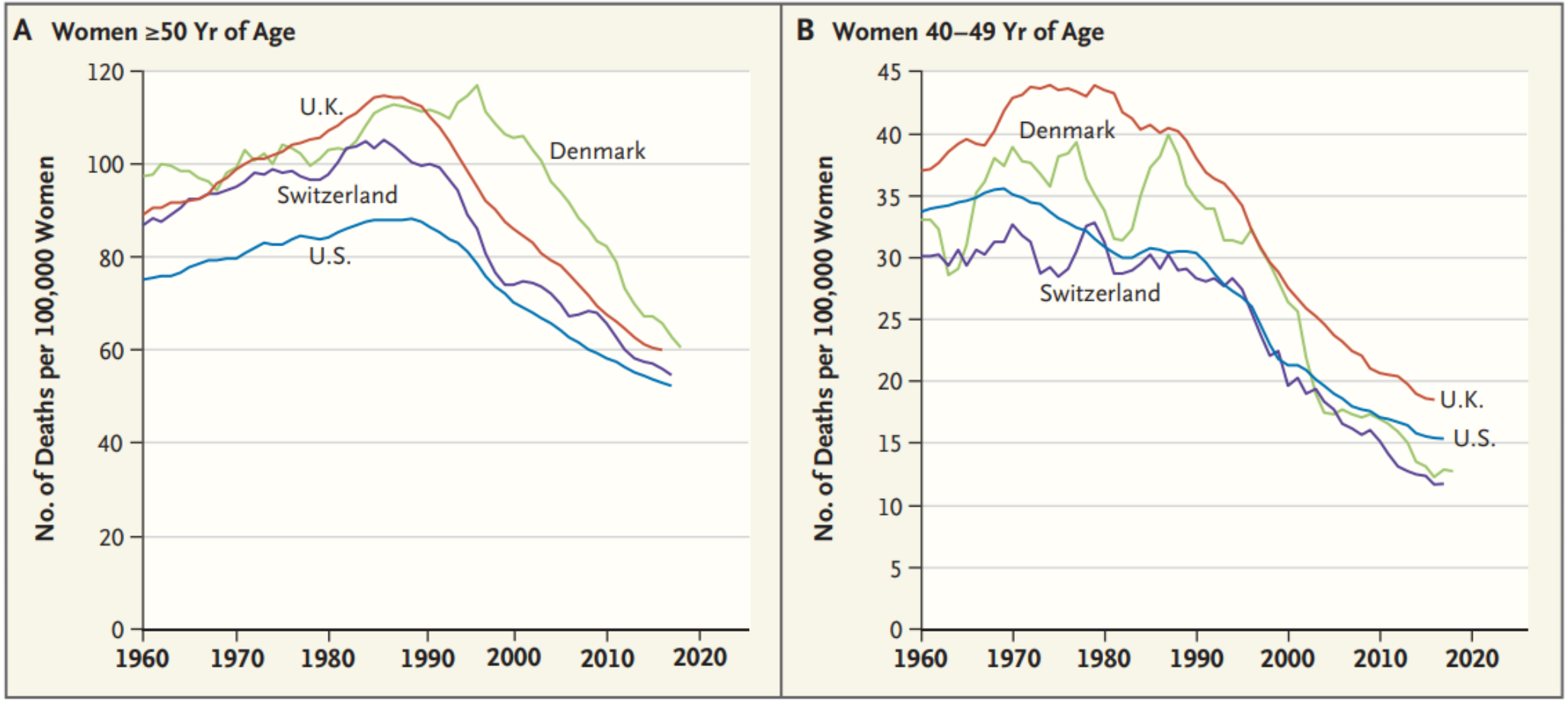
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

GRADE

”When (…) a sensitivity analysis suggests differences in estimates between studies with higher and lower risk of bias, we suggest, in accordance with the standard GRADE approach, using the estimates from the lower risk of bias studies, with no need to rate down confidence for risk of bias”

Iorio A et al. BMJ 2015;350:h870



Breast-Cancer Mortality Trends in Four Countries with Varied Screening Practices.

Trends in mortality from breast cancer are shown for women 50 years of age or older (Panel A) and women 40 to 49 years of age (Panel B) in Denmark, the United Kingdom (U.K.), the United States (U.S.), and Switzerland. More than 70% of women 50 to 70 years of age are regularly screened in Denmark, the United Kingdom, and the United States. In Denmark and the United Kingdom, there is no organized and little opportunistic screening of women in their 40s, whereas in the United States, 60% of women in this age group have been regularly screened since 1993. In Switzerland, most cantons have no organized screening program, and screening attendance is low in all age groups; the Swiss Medical Board recommended against screening mammography in all women in 2014 (see the Supplementary Appendix, available at NEJM.org). Mortality data are 3-year running averages, age-adjusted to the World Standard, and are from the Global Cancer Observatory, International Agency for Research on Cancer (IARC) Cancer Surveillance Branch.

”Monitoring the effectiveness of screening.

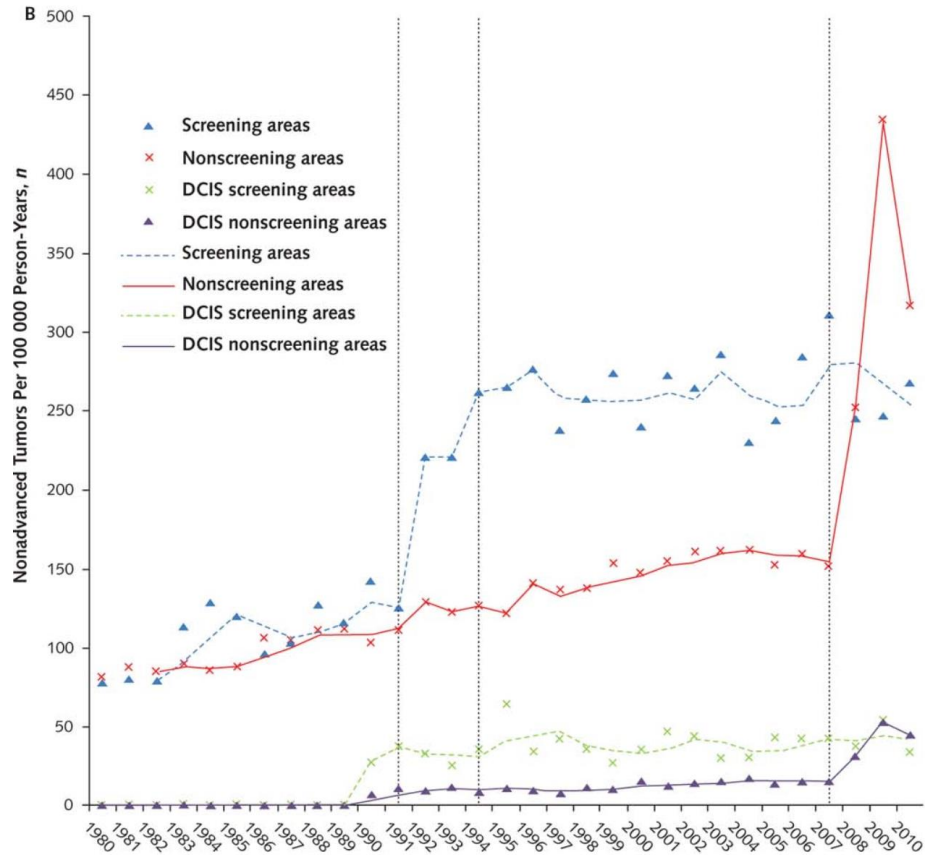
This can be done approximately by examining trends in age-specific breast cancer mortality available from routine statistics.”

The Forrest Report, 1986

Benefits and Harms of Biennial Screening Mammography for U.S. Women in Their 40s in Terms of the Absolute Risk of Various Outcomes in the Next 10 Years.*

Outcome	Biennial Mammogram	No Mammogram	Difference
Benefits			
Death from any cause	3.0 to 3.1% (30–31 deaths per 1000 women)	3.1% (31 deaths per 1000 women)	–0.1 to 0 percentage points (≤1 *fewer* death per 1000 women)
Death from breast cancer	0.23% (2 deaths per 1000 women)	0.31% (3 deaths per 1000 women)	–0.08 percentage points (1 *fewer* death per 1000 women)
Harms			
Any false alarm	35.7% (357 events per 1000 women)	—	35.7 percentage points (357 *more* events per 1000 women)
False alarm requiring a biopsy	6.6% (66 events per 1000 women)	—	6.6 percentage points (66 *more* events per 1000 women)
Overdiagnosis	0.2% (2 events per 1000 women)	—	0.2 percentage points (2 *more* events per 1000 women)

* The 10-year risks of death from any cause and death from breast cancer are for all U.S. women 40 to 49 years of age (median age, 45 years); data are from the National Cancer Institute (https://knowyourchances.cancer.gov/custom_charts.php). No trials have shown a benefit with respect to all-cause mortality; the range provided reflects the best possible outcome (all women who avoid a breast-cancer death do not die from another cause) to the worst possible outcome (all women who avoid a breast-cancer death die from another cause). The U.S. Preventive Services Task Force modeling report (https://www.uspreventiveservicestaskforce.org/uspstf/document/draft-modeling-report/breast-cancer-screening-adults) estimated a 25% relative risk reduction in breast-cancer mortality with screening mammography.


B
Nonadvanced Tumors Per 100 000 Person-Years, n
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DCIS screening areas
DCIS nonscreening areas
Screening areas
Nonscreening areas
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EDITORIAL

Annals of Internal Medicine

Accepting the Existence of Breast Cancer Overdiagnosis

Jørgensen and colleagues (1) compare breast cancer incidence and death rates in several areas of Denmark where screening was introduced at various times in the 1990s. Although the incidence of localized disease increased with the introduction of screening, the incidence of advanced disease has not decreased. They estimate that screen-detected breast tumors have an overdiagnosis rate of 14.7% to 38.6% (excluding ductal carcinoma in situ). This is the latest of several studies using various methods and data sets to show that the phenomenon of overdiagnosis exists in breast cancer. Estimates of this overdiagnosis rate vary but range up to 54% of screen-detected localized tumors, with most estimates between 15% and 25% (2).

”If the..

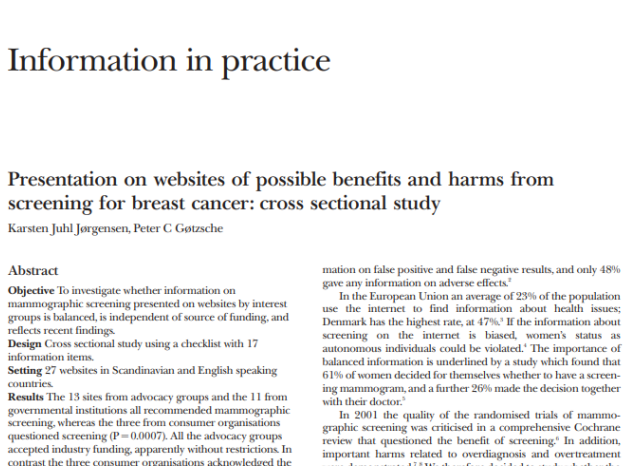
lesion fits the profile of something that killed people in the past, the natural inclination today is to assume that the lesion will grow, spread, and eventually kill. However, some of these lesions may be genomically predetermined to grow no further and may even regress. In many respects, considering all small breast lesions to be deadly and aggressive types of cancer is the pathologic equivalent of racial profiling.

Experienced clinicians have long observed that tumors, including those within the same pathologic grade, have various biological behaviors. Some tumors grow faster than others. Indeed, science has evolved to provide genomic tests that can predict more versus less aggressive tumors with a good degree of accuracy. The

Dr. Otis Brawley, then Chief Medical Officer, ACS.

What are women told?

- Headline: ”The importance of prevention.”
- ”…it is necessary to compress the breasts during the exam, which may cause mild discomfort in some women.”
- “…over a 20-year period, for every 1,000 women between the ages of 50 and 69 who undergo regular mammograms, 7-9 lives can be saved.”



Information in practice

Presentation on websites of possible benefits and harms from screening for breast cancer: cross sectional study

Karsten Juhl Jørgensen, Peter C Gøtzsche

Abstract

Objective To investigate whether information on mammographic screening presented on websites by interest groups is balanced, is independent of source of funding, and reflects recent findings.
Design Cross sectional study using a checklist with 17 information items.
Setting 27 websites in Scandinavian and English speaking countries.
Results The 13 sites from advocacy groups and the 11 from governmental institutions all recommended mammographic screening, whereas the three from consumer organisations questioned screening (P = 0.0007). All the advocacy groups accepted industry funding, apparently without restrictions. In contrast the three consumer organisations acknowledged the

mation on false positive and false negative results, and only 48% gave any information on adverse effects.[5]

In the European Union an average of 23% of the population use the internet to find information about health issues; Denmark has the highest rate, at 47%.[3] If the information about screening on the internet is biased, women's status as autonomous individuals could be violated.[4] The importance of balanced information is underlined by a study which found that 61% of women decided for themselves whether to have a screening mammogram, and a further 26% made the decision together with their doctor.[5]

In 2001 the quality of the randomised trials of mammographic screening was criticised in a comprehensive Cochrane review that questioned the benefit of screening.[6] In addition, important harms related to overdiagnosis and overtreatment

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Analysis And Comment » Public health

Content of invitations for publicly funded screening mammography

BMJ 2006 ; 332 doi: https://doi.org/10.1136/bmj.332.7540.538 (Published 02 March 2006)
Cite this as: *BMJ* 2006;332:538

Article Related content Metrics Responses Peer review

Karsten Juhl Jørgensen, research fellow (kjj@cochrane.dk)1, Peter C Gøtzsche, director1

Author affiliations

Correspondence to: K J Jørgensen

Accepted 1 December 2005

The benefits and harms of screening for breast cancer are delicately balanced and women should decide for themselves, on an informed basis. Do the invitations give enough information to enable this?

- "The Tuscany Region recently decided to extend invitations to women between the ages of 45 and 74. (…) women under the age of 50 will receive invitations annually, while those over the age of 50 will be invited every 2 years."
- "Sometimes, mammograms may detect small, slow-growing malignant tumors (about 10 out of 100 tumors found) that, if not diagnosed, would not have caused health problems for the woman. This phenomenon, called "overdiagnosis," is unfortunately inevitable because there are currently no techniques to distinguish these tumors from more aggressive ones."
- "If the mammogram shows anomalies, you will be contacted for further assessments. Only a few women (about 1 in 20) are called for additional tests like breast ultrasound or a visit to a breast specialist. There is no need to be alarmed, as most of the time, everything turns out to be normal."

Mail Online

How breast screening can HALVE the risk of death: Mammograms dramatically reduce chance of developing a fatal cancer, major new study suggests

- Women who attend at least one mammogram 37 per cent less likely to die
- For over-65s screened at least twice over three years, risk of death was halved
- Researchers looked at more than 8,000 women who died of breast cancer

BJC British Journal of Cancer

www.nature.com/bjc

ARTICLE

Clinical Study

A case-control study to evaluate the impact of the breast screening programme on mortality in England

Roberta Maroni[1], Nathalie J. Massat[1], Dharmishta Parmar[1], Amanda Dibden[1], Jack Cuzick[1], Peter D. Sasieni[2] and Stephen W. Duffy[1]

BACKGROUND: Over the past 30 years since the implementation of the National Health Service Breast Screening Programme, improvements in diagnostic techniques and treatments have led to the need for an up-to-date evaluation of its benefit on risk of death from breast cancer. An initial pilot case-control study in London indicated that attending mammography screening led to a mortality reduction of 39%.

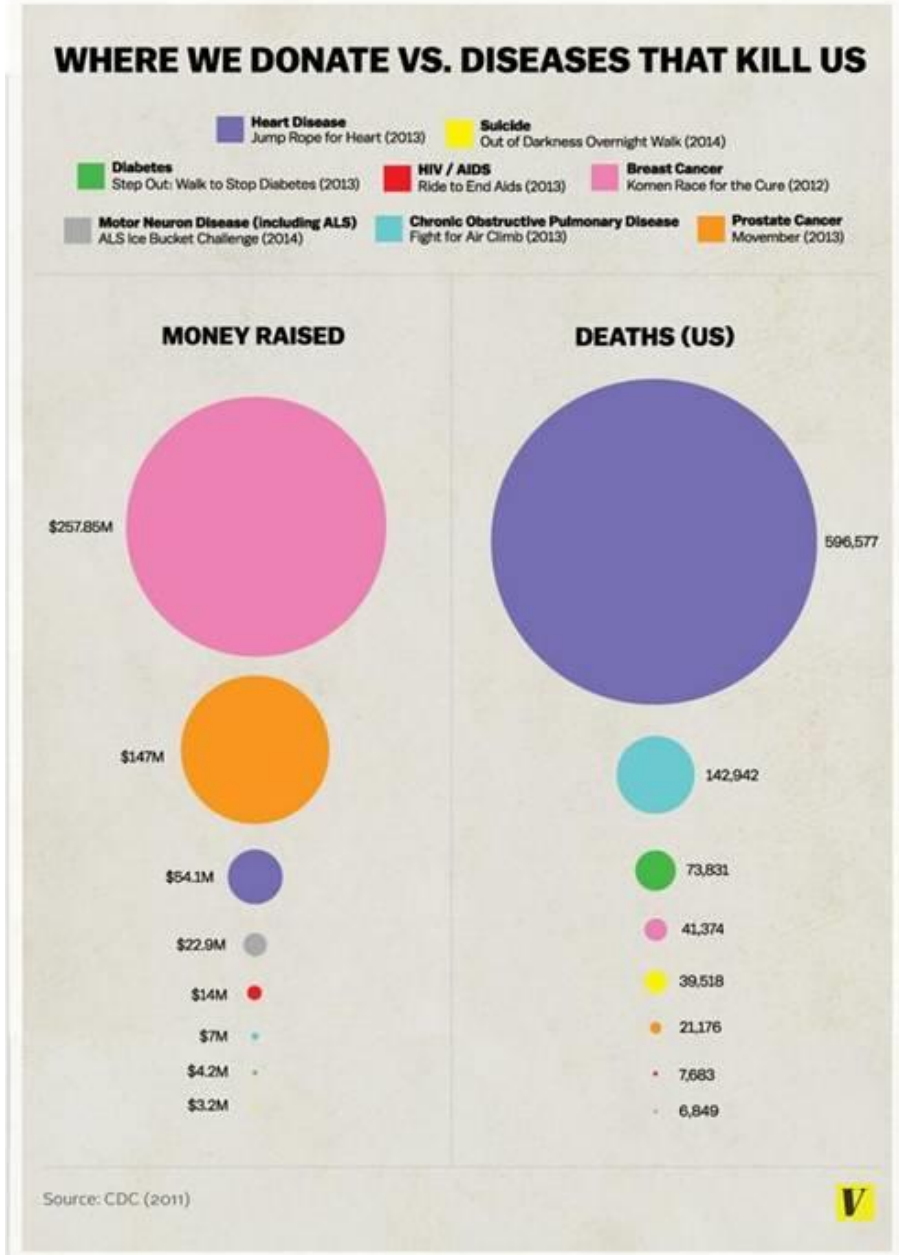
METHODS: Based on the same study protocol, an England-wide study was set up. Women aged 47–89 years who died of primary breast cancer in 2010 or 2011 were selected as cases (8288 cases). When possible, two controls were selected per case (15,202 controls) and were matched by date of birth and screening area.

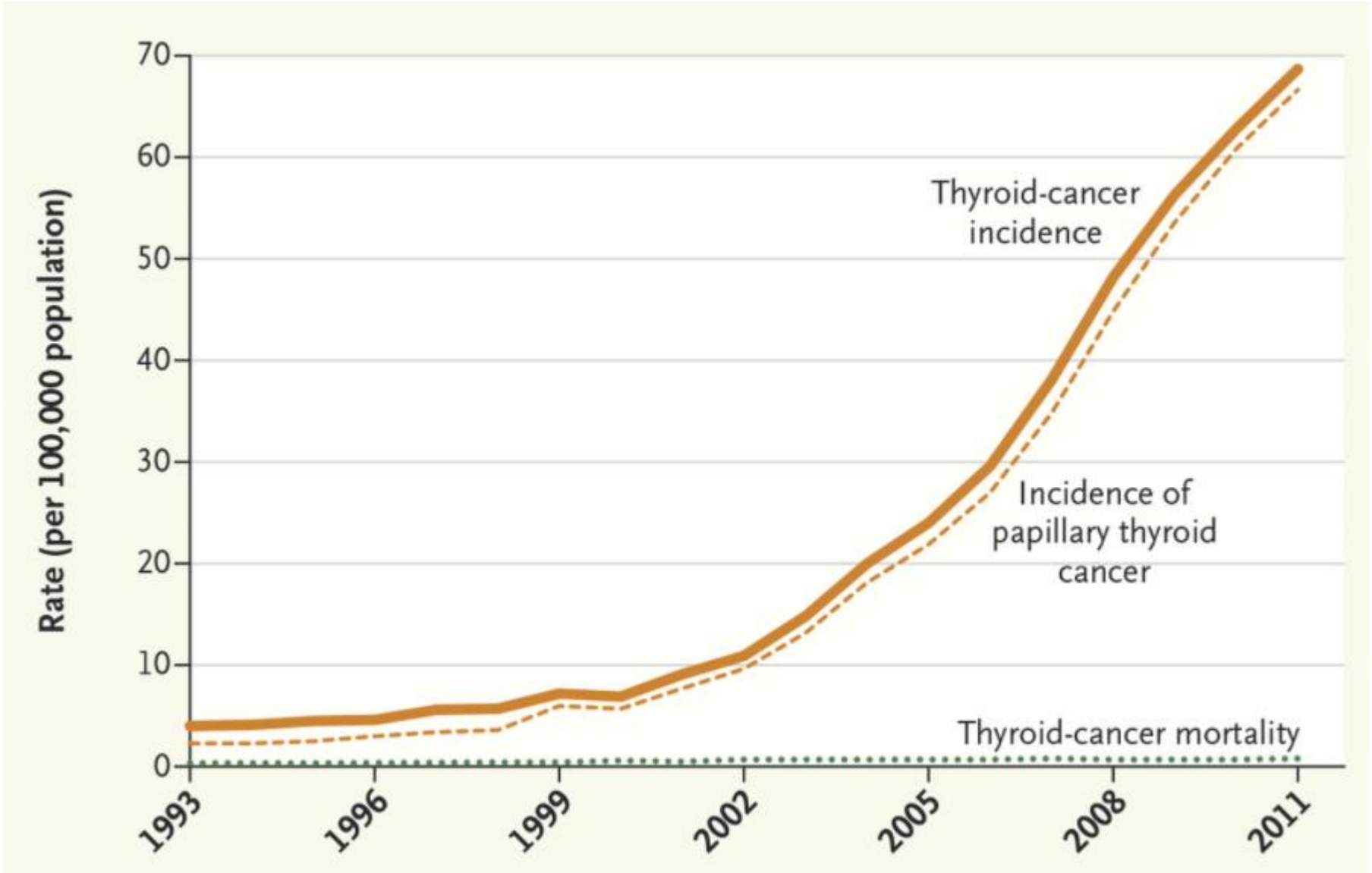
RESULTS: Conditional logistic regressions showed a 38% reduction in breast cancer mortality after correcting for self-selection bias (OR 0.62, 95% CI 0.56–0.69) for women being screened at least once. Secondary analyses by age group, and time between last screen and breast cancer diagnosis were also performed.

CONCLUSIONS: According to this England-wide case-control study, mammography screening still plays an important role in lowering the risk of dying from breast cancer. Women aged 65 or over see a stronger and longer lasting benefit of screening compared to younger women.

British Journal of Cancer (2021) 124:736–743; https://doi.org/10.1038/s41416-020-01163-2

WHERE WE DONATE VS. DISEASES THAT KILL US



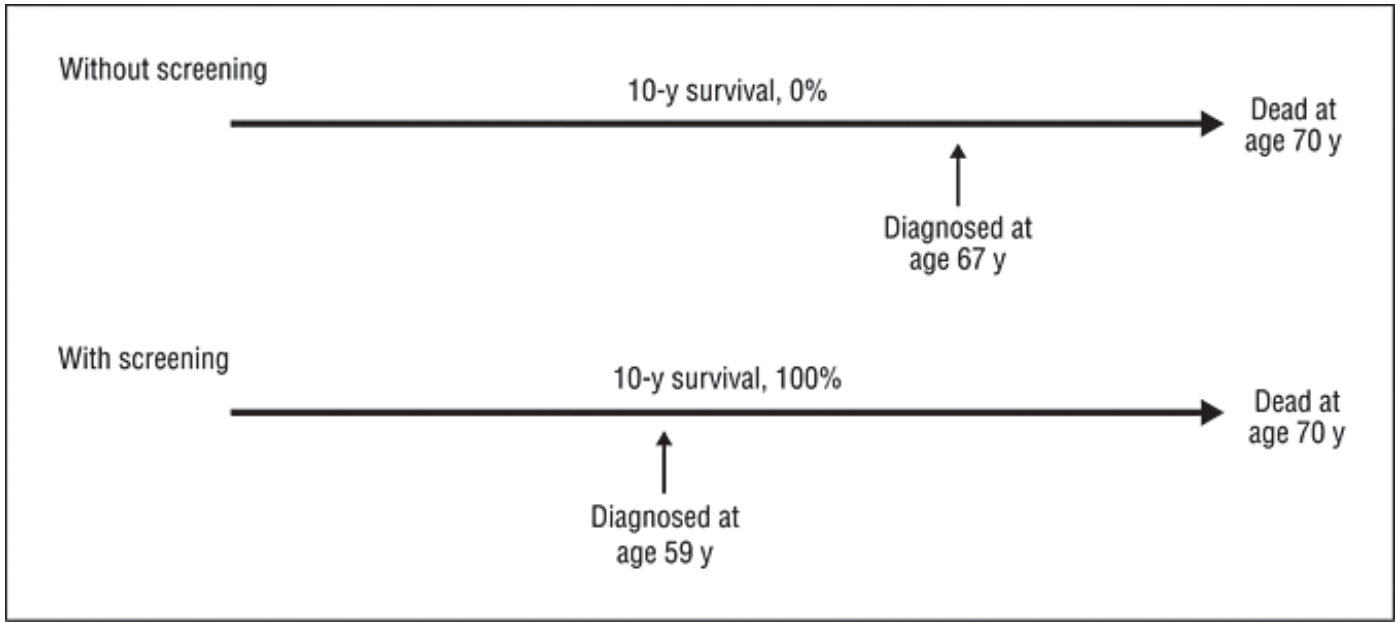


Ahn, Welch. N Engl J Med 2014;371:1765-7

What can we learn?

- South Korea has the best 5-year survival rate from thyroid cancer *in the world*
- Thyroid cancer can be cured if it is detected in time

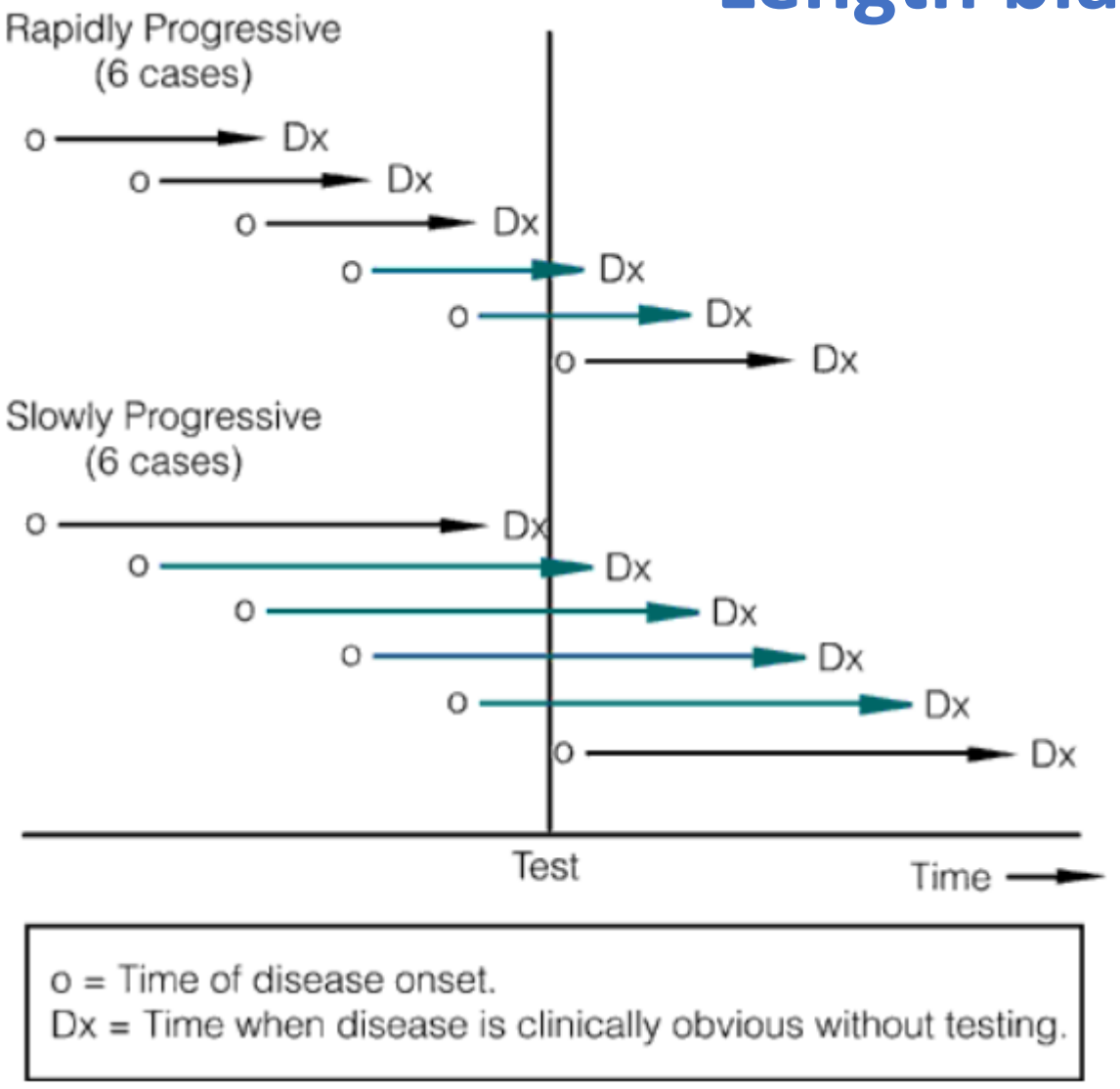
Lead-time bias

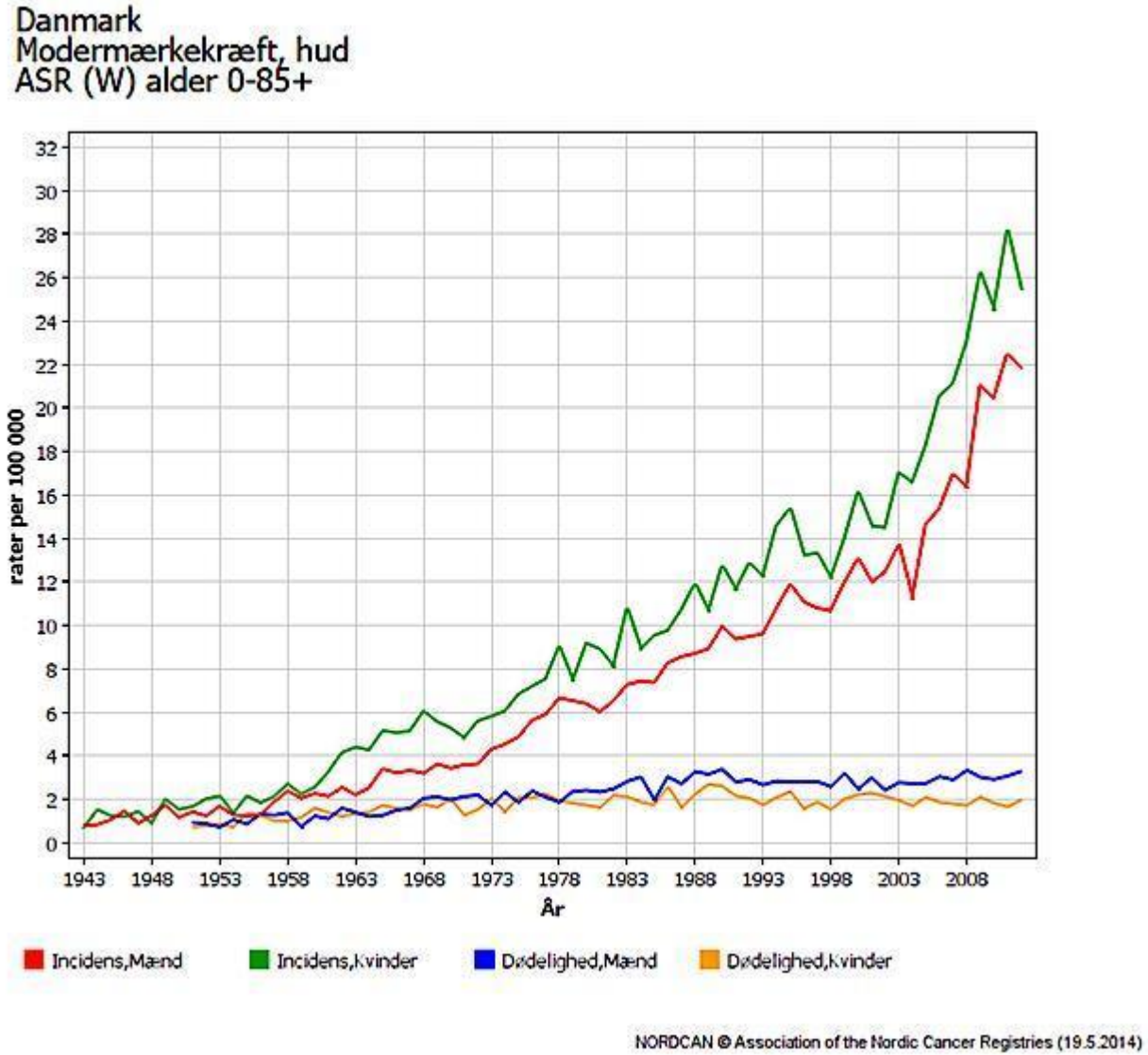


ARCHIVES OF INTERNAL MEDICINE

Welch HG et al. Arch Intern Med 2007;167:2289-2295.

Length bias


Rapidly Progressive
(6 cases)
o
Dx
Slowly Progressive
(6 cases)
Test
Time
o = Time of disease onset.
Dx = Time when disease is clinically obvious without testing.



Jørgensen KJ, Brodersen J, Gøtzsche PC. *Ugeskr Laeger* 2014;176:1250-1.

EUROMELANOMA

”Everyone should check each others skin every three months, including children. You should be completely undressed and check everywhere, also between the toes, underneath breasts, the soles of your feet – melanoma can appear everywhere.”

Cochrane Library

Cochrane Database of Systematic Reviews

Screening for reducing morbidity and mortality in malignant melanoma (Protocol)

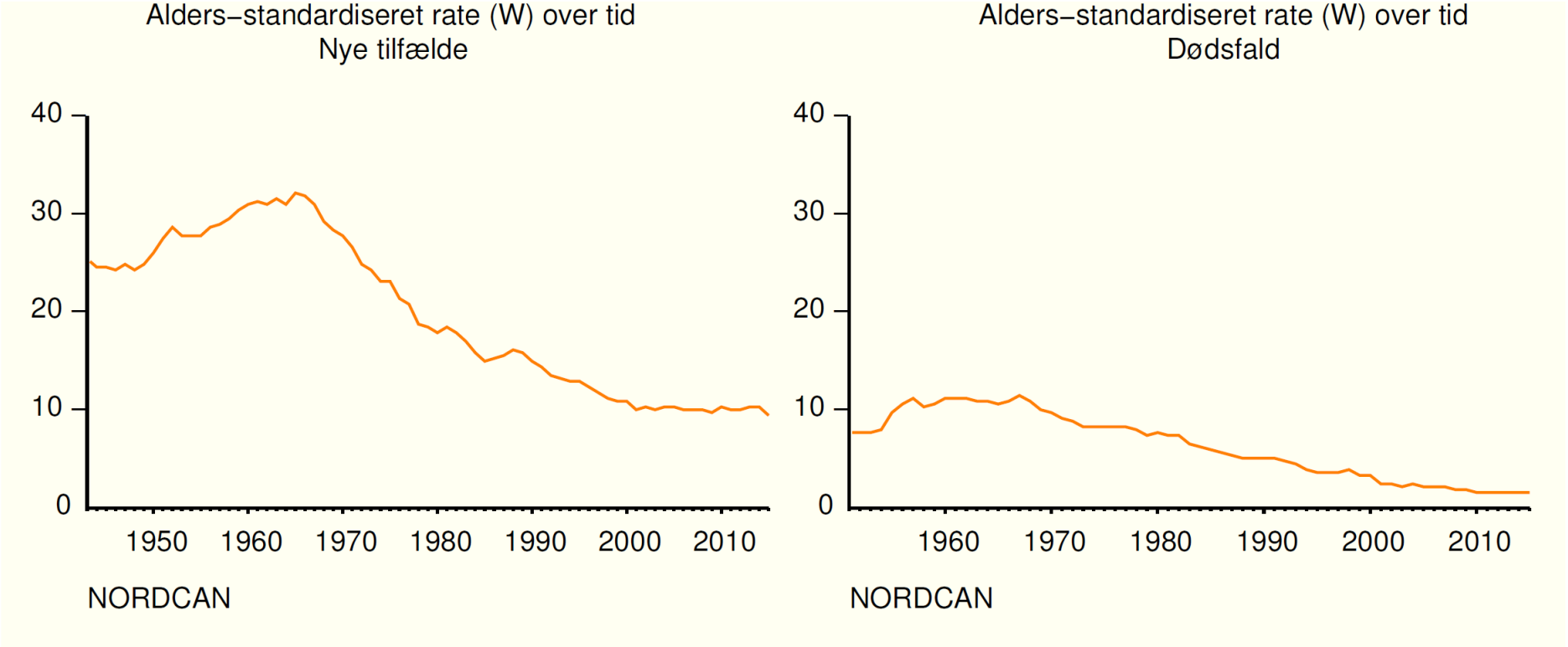
Johansson M, Brodersen J, Gøtzsche PC, Jørgensen KJ

UK National Screening Committee[1]

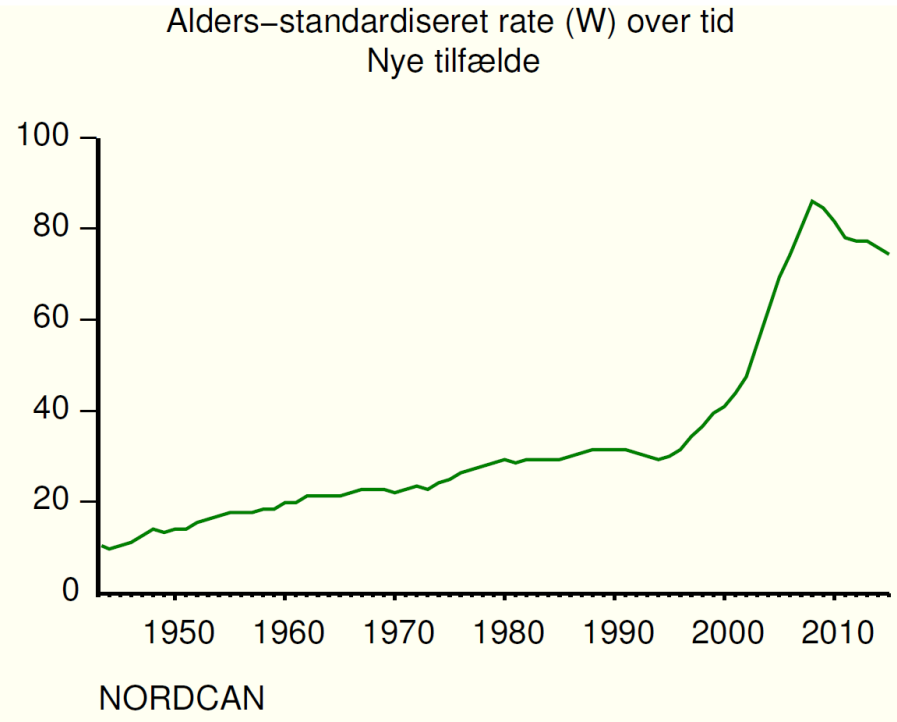
“There should be evidence from high quality Randomised Controlled Trials that the screening programme is effective in reducing mortality or morbidity.“

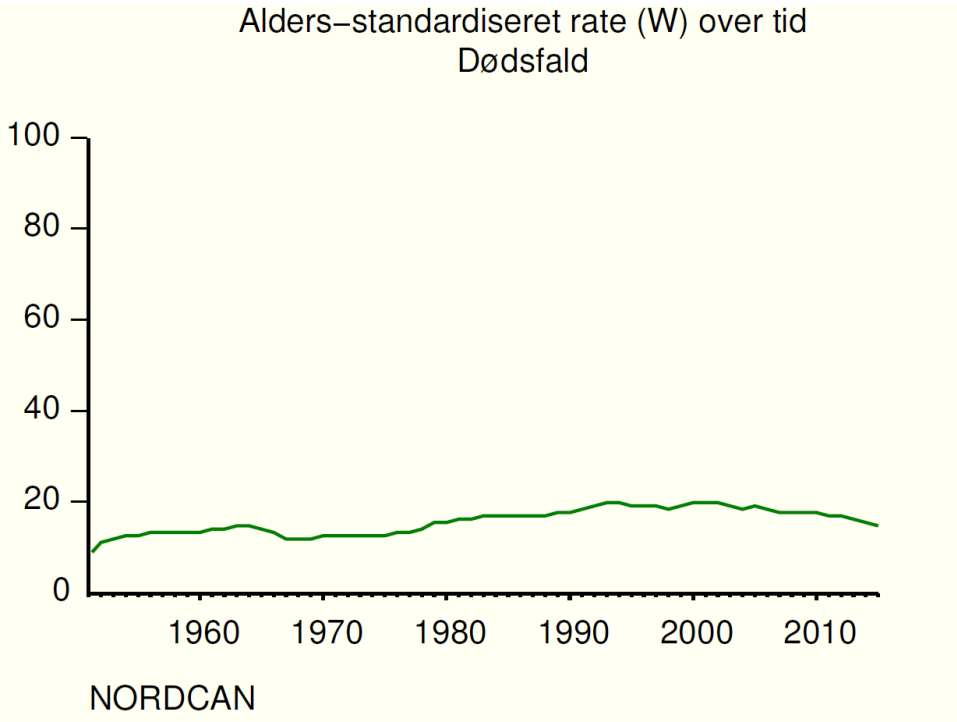
1. http://www.screening.nhs.uk/criteria

Cervical cancer in Denmark



Prostate cancer in Denmark





Ovarian cancer population screening and mortality after long-term follow-up in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial

Usha Menon, Aleksandra Gentry-Maharaj, Matthew Burnell, Naveena Singh, Andy Ryan, Chloe Karpinskyj, Giulia Carlino, Julie Taylor, Susan K Massingham, Maria Raikou, Jatinderpal K Kalsi, Robert Woolas, Ranjit Manchanda, Rupali Arora, Laura Casey, Anne Dawnay, Stephen Dobbs, Simon Leeson, Tim Mould, Mourad W Seif, Aarti Sharma, Karin Williamson, Yiling Liu, Lesley Fallowfield, Alistair J McGuire, Stuart Campbell, Steven J Skates, Ian J Jacobs, Mahesh Parmar

Interpretation The reduction in stage III or IV disease incidence in the MMS group was not sufficient to translate into lives saved, illustrating the importance of specifying cancer mortality as the primary outcome in screening trials. Given that screening did not significantly reduce ovarian and tubal cancer deaths, general population screening cannot be recommended.

Funding National Institute for Health Research, Cancer Research UK, and The Eve Appeal.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial

H.J. de Koning, C.M. van der Aalst, P.A. de Jong, E.T. Scholten, K. Nackaerts, M.A. Heuvelmans, J.-W.J. Lammers, C. Weenink, U. Yousaf-Khan, N. Horeweg, S. van 't Westeinde, M. Prokop, W.P. Mali, F.A.A. Mohamed Hoesein, P.M.A. van Ooijen, J.G.J.V. Aerts, M.A. den Bakker, E. Thunnissen, J. Verschakelen, R. Vliegenthart, J.E. Walter, K. ten Haaf, H.J.M. Groen, and M. Oudkerk

- 6583 men screened vs 6612 not screened
- 160 vs 210 deaths from LC (RR 0.76; 0.61-0.94)
- NNS for 10 years and 22,600 CT scans: 132 (my calculation)
- 40 more cases after 10 years
- 264 false positives needed ”workup” (2069 ”indeterminate”)

Table 4. Cause of Death of Deceased Male Participants at 10 Years of Follow-up or until the Data-Cutoff Date of December 31, 2015.*

Variable	Screening Group (N=868)	Control Group (N=860)	Total (N=1728)	Rate Ratio (95% CI)
		number (percent)		
Cause of death — no. (%)				
Lung cancer	160 (18.4)	210 (24.4)	370 (21.4)	0.76 (0.62–0.94)
No lung cancer after cause-of-death review, no other specification	6 (0.7)	11 (1.3)	17 (1.0)	0.55 (0.17–1.61)
Other neoplasm	318 (36.6)	289 (33.6)	607 (35.1)	1.10 (0.94–1.30)
Cardiovascular disease	189 (21.8)	181 (21.0)	370 (21.4)	1.05 (0.85–1.29)
Respiratory disease	42 (4.8)	43 (5.0)	85 (4.9)	0.98 (0.62–1.53)
Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	37 (4.3)	20 (2.3)	57 (3.3)	1.86 (1.05–3.37)
Diseases of the digestive system	30 (3.5)	21 (2.4)	51 (3.0)	1.43 (0.79–2.63)
External causes of illness and death	24 (2.8)	19 (2.2)	43 (2.5)	1.27 (0.67–2.45)
Endocrine, nutritional, and metabolic diseases	21 (2.4)	9 (1.0)	30 (1.7)	2.34 (1.03–5.80)
Diseases of the nervous system	9 (1.0)	19 (2.2)	28 (1.6)	0.48 (0.19–1.10)
Other cause of death	26 (3.0)	28 (3.3)	54 (3.1)	0.93 (0.52–1.65)
Unknown	6 (0.7)	10 (1.2)	16 (0.9)	0.60 (0.18–1.83)
Total person-yr at risk	62,298	62,484	124,782	
All-cause mortality — deaths per 1000 person-yr	13.93	13.76	13.85	1.01 (0.92–1.11)

Possible explanations

- Lack of power?
- No blinded outcome assessment?
- 11 of 50 misclassified LC death would make results NS
- Complications with ”workup” and treatment?
- **Do not dismiss risk of bias trials!**

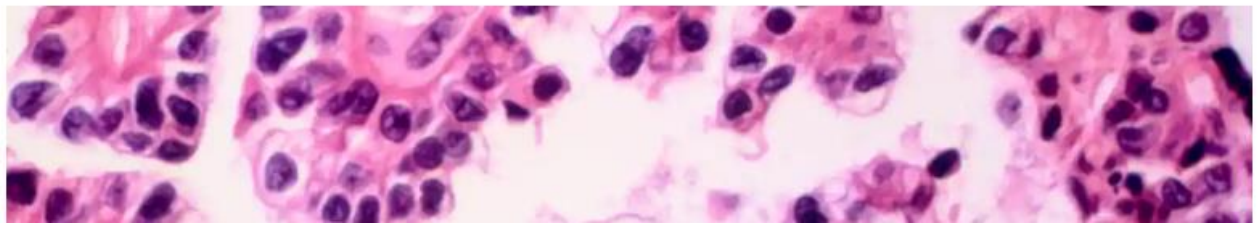
UK National Screening Committee

”All the cost-effective primary prevention interventions should have been implemented as far as practicable”

This article is more than **1 year old**

'Holy grail of cancer research': doctors positive about early detection blood test

Blood tests called liquid biopsies show signs of finding 10 different types of cancer at an early stage



Challenges

- Doubtful experience with blood tests for cancer (PSA og CA-125)
- Tested in 1,005 patients with know cancers (8 types)
- Not shown to improve prognosis
- More advanced cases shed more cells
- How often tested? Which age group? Which risk factors?
- Problems with overdiagnosis not known
- Inventors from Johns Hopkins has started business and sells test for 500 Euros

Cohen JD et al. Science 2018;359:936.

Analysis

Health screening needs independent regular re-evaluation

BMJ 2021 ; 374 doi: https://doi.org/10.1136/bmj.n2049 (Published 27 September 2021)
Cite this as: *BMJ* 2021;374:n2049

Fabienne G Ropers, consultant1, Alexandra Barratt, professor2, Timothy J Wilt, professor3, Stuart G Nicholls, researcher4, Sian Taylor-Phillips, professor5, Barnett S Kramer, consultant6, Laura J Esserman, professor7, Susan L Norris, doctor8, Lorna M Gibson, consultant9, Russell P Harris, emeritus professor10, Stacy M Carter, director11, Gemma Jacklyn, consultant2, Karsten Juhl Jørgensen, chief physician12

Author affiliations

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Conclusions

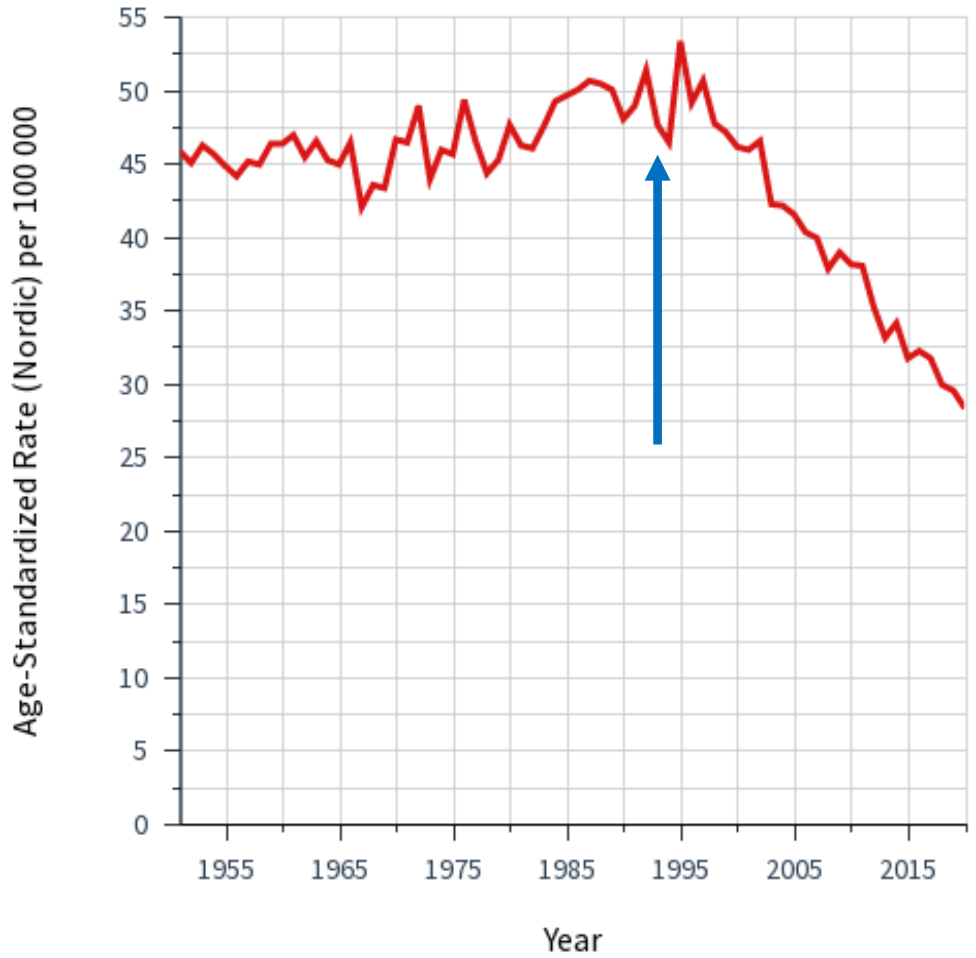
- Earlier detections with screening can be highly valuable. It can also do more harm than good.
- Weighing benefits against harms is subjective and value judgements cannot be determined through science.
- It is harder to make healthy people better than those who are sick.
- The continued justification of screening programmes should be re-evaluated periodically based on EBM priciples by impartial panels with broad skillsets.
- Changes to existing screening practices can be randomised.

Thank you!

Age-Standardized Rate (Nordic) per 100 000 , Mortality, Females

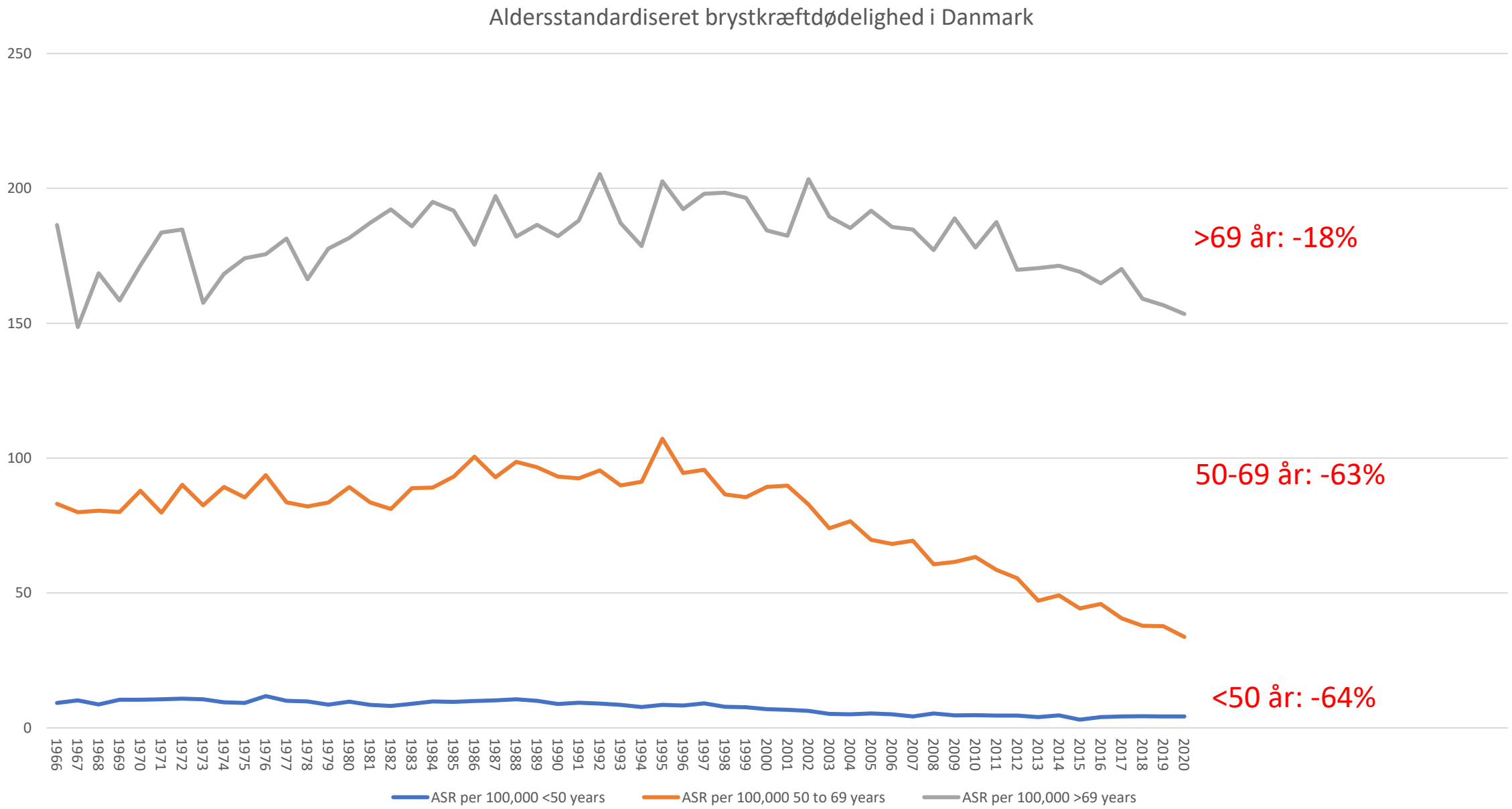
Denmark

Breast



NORDCAN
Association of the Nordic Cancer Registries

International Agency for Research on Cancer
World Health Organization


Aldersstandardiseret brystkræftdødelighed i Danmark
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100
50
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>69 år: -18%
50-69 år: -63%
<50 år: -64%
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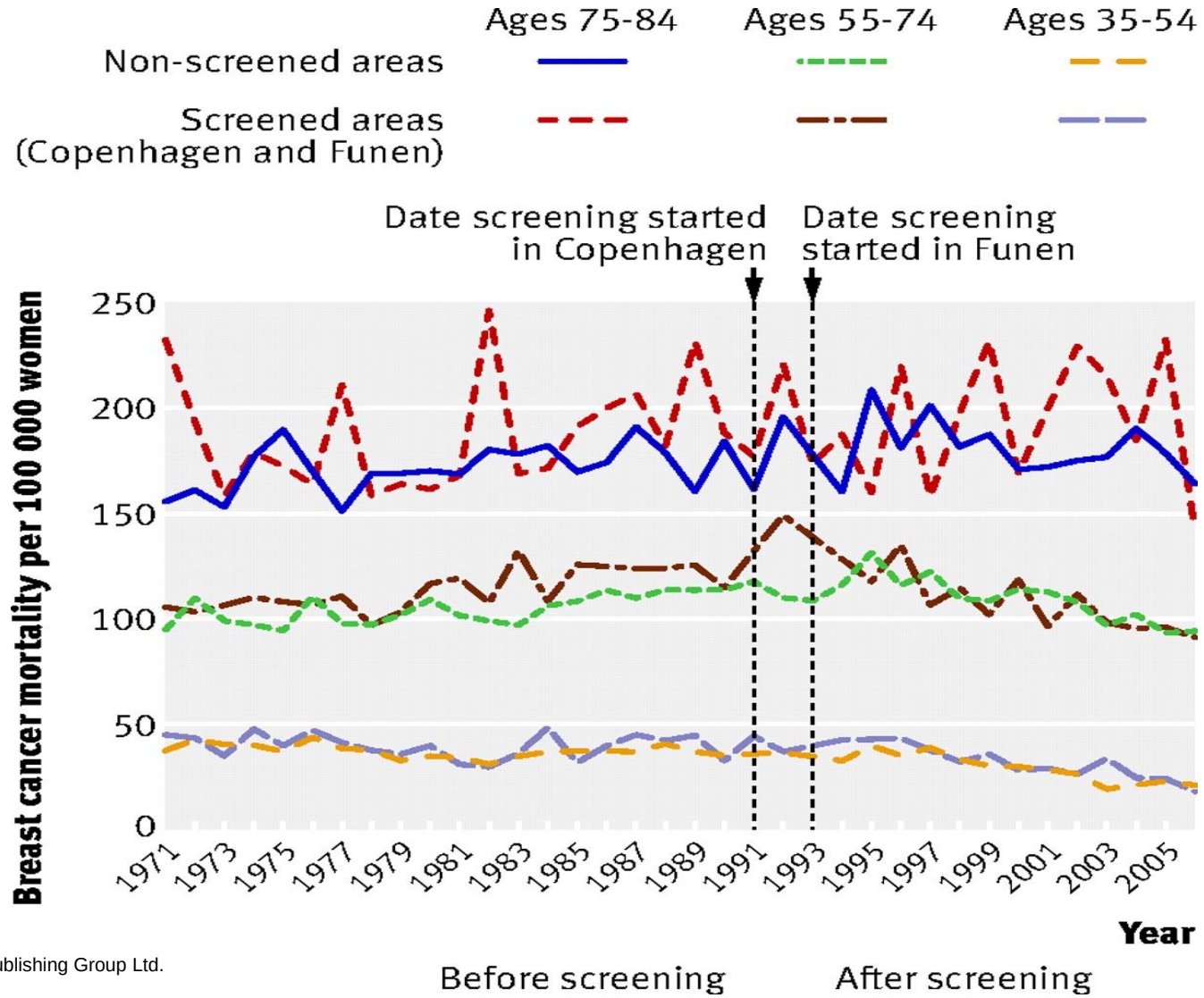
ASR per 100,000 <50 years
ASR per 100,000 50 to 69 years
ASR per 100,000 >69 years

Breast cancer mortality rates for screened and non-screened areas in Denmark



Jørgensen KJ, Zahl PH, Gøtzsche PC. BMJ 2010;340:c1241

Sundhedsstyrelsens arbejdsgruppe

- Brug for langt større åbenhed fra sundhedsmyndigheder omkring skadevirkninger og usikkerheden omkring gavn og skade
- Man bør tilstræbe at deltagelse er informeret, ikke at så mange som mulig deltager
- Aktiv tilmelding frem for aktiv framelding
- Ændringer vil møde modstand fra klinikerne, uanset evidensen
- Ændringer af screeningspraksis bør undersøges/gennemføres gennem randomisering indenfor det eksisterende program

Marmot review: Konklusioner

- *”In round terms, therefore, for each breast cancer death prevented, about three overdiagnosed cases will be identified and treated”*

- *“Given the uncertainties around the estimates, the figures quoted give a spurious impression of accuracy”*

- *“Clear communication of these harms and benefits to women is of utmost importance and goes to the heart of how a modern health system should function”*

IJC
International Journal of Cancer

Benefit-to-harm ratio of the Danish breast cancer screening programme

Anna-Belle Beau [1], Elsebeth Lynge[1], Sisse Helle Njor[2], Ilse Vejborg[3] and Søren Nymand Lophaven[1]

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[3] Department of Radiology, Copenhagen University Hospital (Rigshospitalet), DK-2100 Copenhagen, Denmark

Cancer Epidemiology

The primary aim of breast cancer screening is to reduce breast cancer mortality, but screening also has negative side-effects as overdiagnosis. To evaluate a screening programme, both benefits and harms should be considered. Published estimates of the benefit-to-harm ratio, the number of breast cancer deaths prevented divided by the number of overdiagnosed breast cancer cases, varied considerably. The objective of the study was to estimate the benefit-to-harm ratio of breast cancer screening in Denmark. The numbers of breast cancer deaths prevented and overdiagnosed cases [invasive and ductal carcinoma *in situ* (DCIS)] were estimated per 1,000 women aged 50–79, using national published estimates for breast cancer mortality and overdiagnosis, and national incidence and mortality rates. Estimations were made for both invited and screened women. Among 1,000 women invited to screening from age 50 to age 69 and followed until age 79, we estimated that 5.4 breast cancer deaths would be prevented and 2.1 cases overdiagnosed, under the observed scenario in Denmark of a breast cancer mortality reduction of 23.4% and 2.3% of the breast cancer cases being overdiagnosed. The estimated benefit-to-harm ratio was 2.6 for invited women and 2.5 for screened women. Hence, 2–3 women would be prevented from dying from breast cancer for every woman overdiagnosed with invasive breast cancer or DCIS. The difference between the previous published ratios and 2.6 for Denmark is probably more a reflection of the accuracy of the underlying estimates than of the actual screening programmes. Therefore, benefit-to-harm ratios should be used cautiously.

AARHUS
UNIVERSITY

Trust in breast cancer screening – is it justified?

Barriers for improving information and invitation to the Danish breast cancer screening programme

PhD dissertation

Eeva-Liisa Røssell Johansen

Health
Aarhus University
2023

PAPERS OF THIS DISSERTATION

This dissertation is based on the following papers:

Paper 1: Røssell EL, Lousdal ML, Viuff JH, Støvring H. Evaluating mammography screening in observational cohort designs: the importance of avoiding lead time bias. Submitted to *Cancer Epidemiology*. 2022.

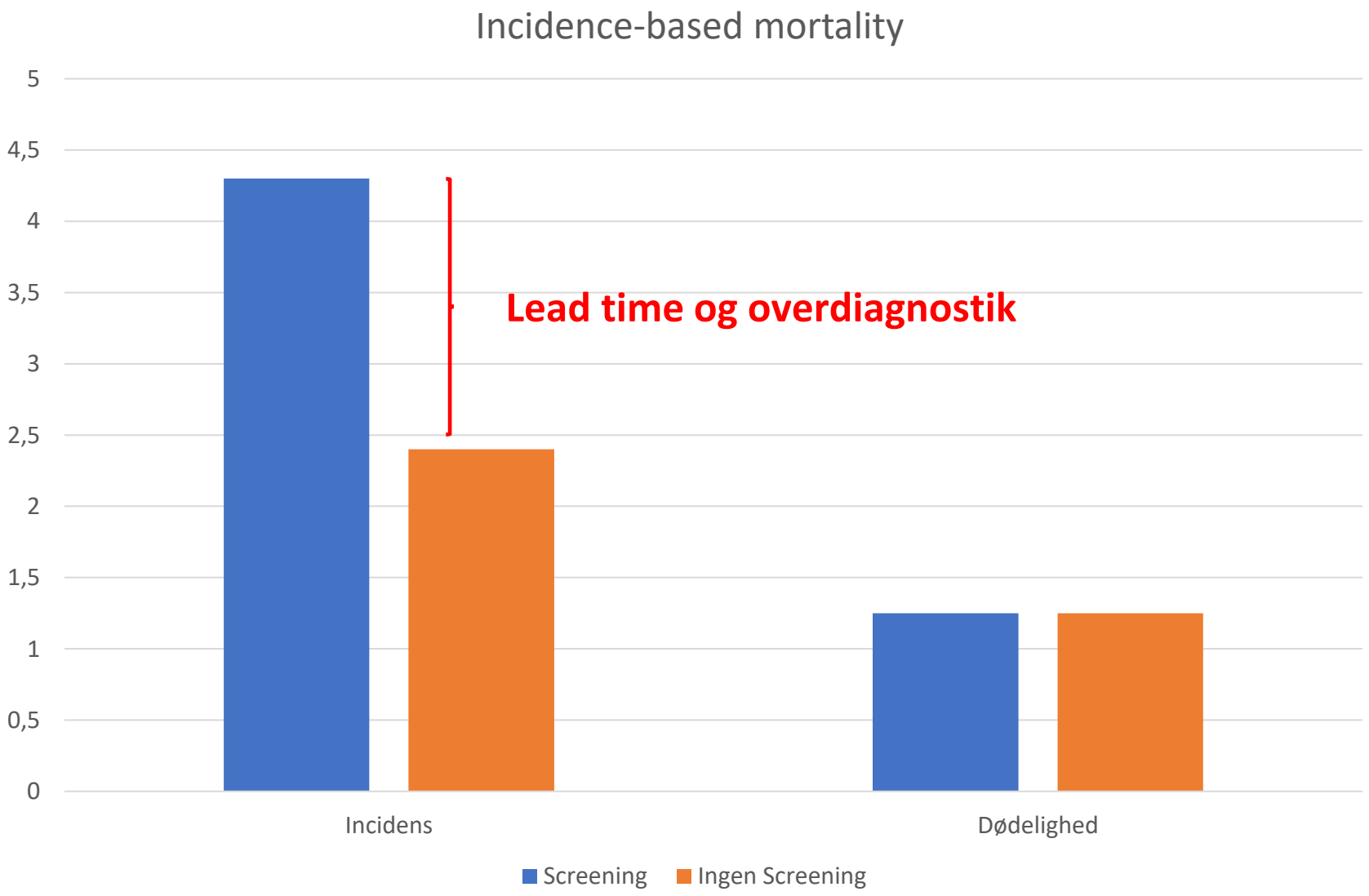
Paper 2: Røssell EL, Viuff JH, Lousdal ML, Støvring H. Investigating bias in the evaluation model used to evaluate the effect of breast cancer screening: A simulation study. Submitted to *BMC Medical Research Methodology*. 2022.

Paper 3: Røssell EL, Bornhøft LO, Lousdal ML, Støvring H. Predicting difference in mean survival time from cause-specific hazard ratios for women diagnosed with breast cancer. *Eur J Public Health*. 2021;41(4):597-601.

Paper 4: Røssell EL, Bo A, Grønborg TK, Kristiansen IS, Borgquist S, Scherer LD, Støvring H. Danish women want to participate in a hypothetical breast cancer screening with harms and no reduction in mortality: a cross-sectional survey. Accepted for publication in *Med Decis Making*. December 2022.

Paper 5: Egsgaard SD*, Røssell EL*, Sørensen JB, Støvring H. Women's health literacy and participation in breast cancer screening: a Danish population-based study combining survey and register data. Resubmitted to *Scand J Public Health* (minor revisions). 2023.
* The authors contributed equally

Paper 6: Røssell EL, Bekker HL, Borgquist S, Kristiansen IS, Schonberg MA, Støvring H. Danish women have made their decision about breast cancer screening participation prior to invitation: a cross-sectional survey of a primary barrier for informed decision-making. Prepared for submission to *Med Decis Making*.


Incidence-based mortality
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
Lead time og overdiagnostik
Incidens
Dødelighed
Screening
Ingen Screening

JAMA Patient Page

December 17, 2014

Breast Cancer Screening: Benefits and Harms

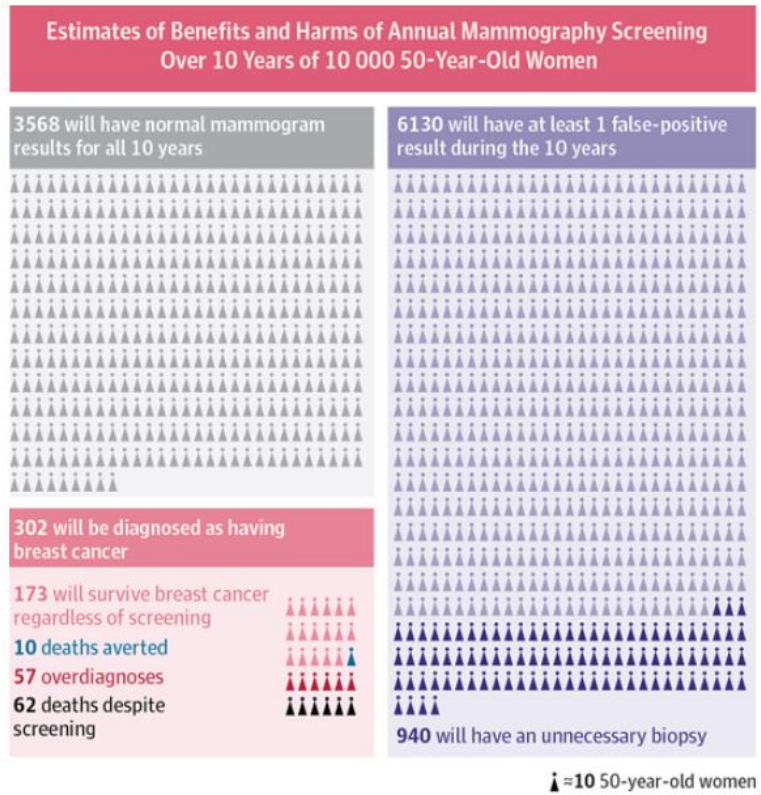
Jill Jin, MD, MPH

Article Information

JAMA. 2014;312(23):2585. doi:10.1001/jama.2014.13195

Español

Related Articles

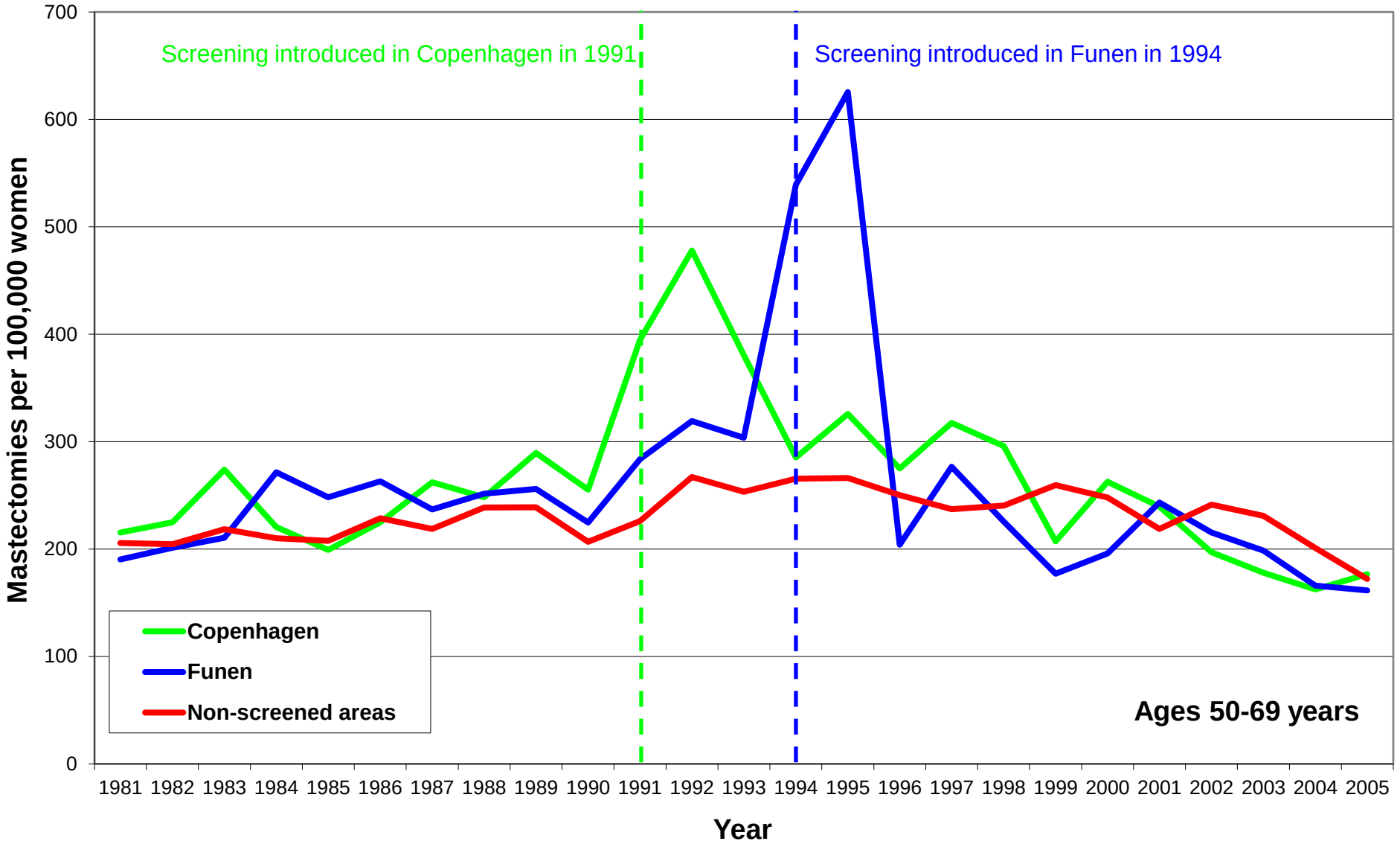


A	B
100% participation	~70% participation
4-5 rounds	2-4 rounds
2 view	1 view
2 readers	1 reader
Screening every 12 month	Screening every 24-33 month
A finds smaller average size tumors than B	
Individual randomisation	Cluster-randomisation (45)
Presents demographic data	Do not present demographic data
Consistent, transparent reporting	Inconsistent, unclear reporting
Blinded, external cause of death evaluation	No blinded cause of death evaluation
3% reduction (-26% to +27%)* 2% increase(-22% to + 33%)*	42% reduction (-55% to -3%)* 24% reduction (-39% til -5%)*

* Thirteen years follow-up

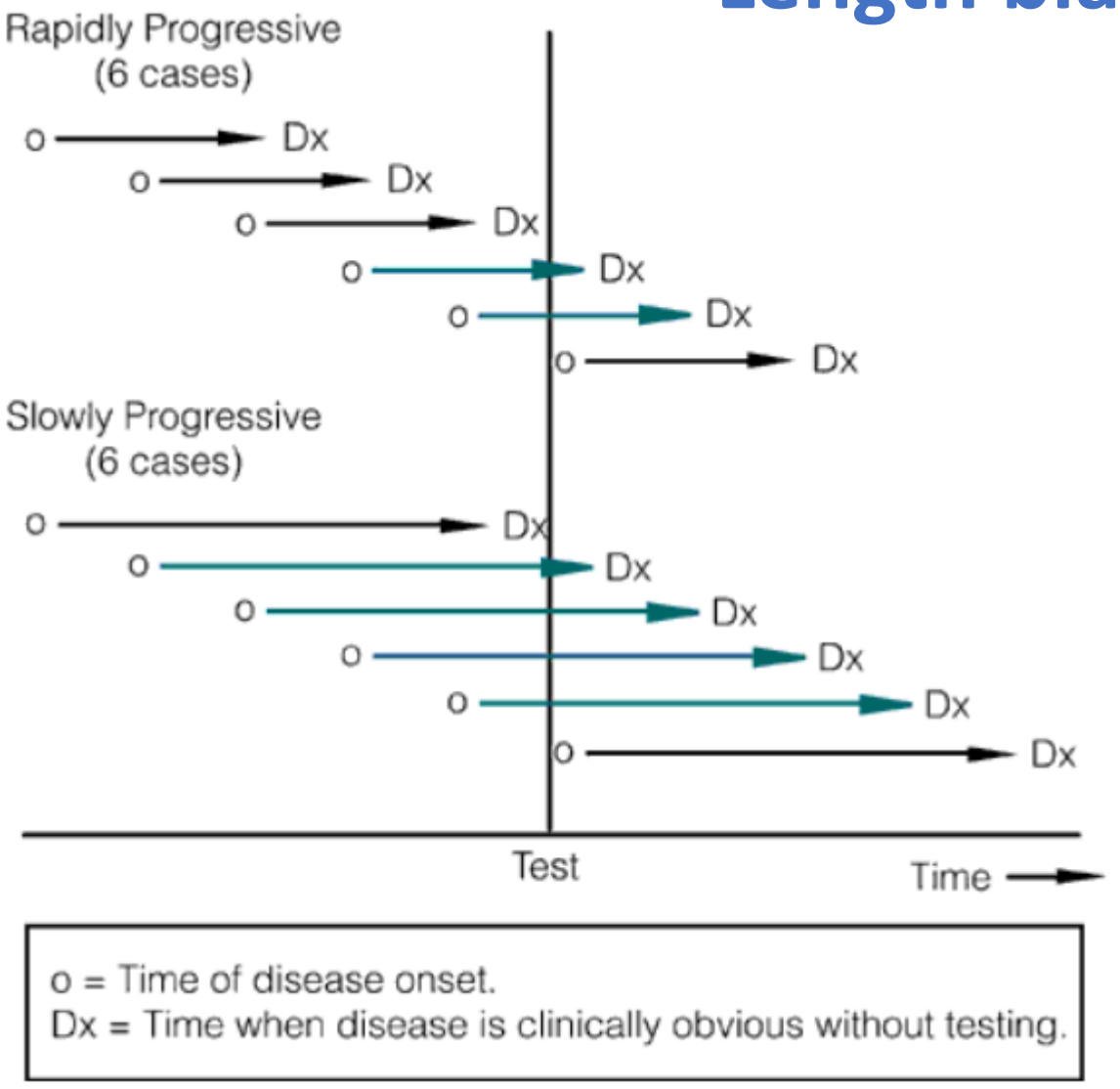
Gøtzsche PC, Nielsen M. Cochrane Database syst. Rev. 2011, Issue 1. Art. No.: CD001877.
Baines CJ. AJR Am J Roentgenol 2013;200:W96-7.

Mastectomy use in sreened and non-screened areas in Denmark

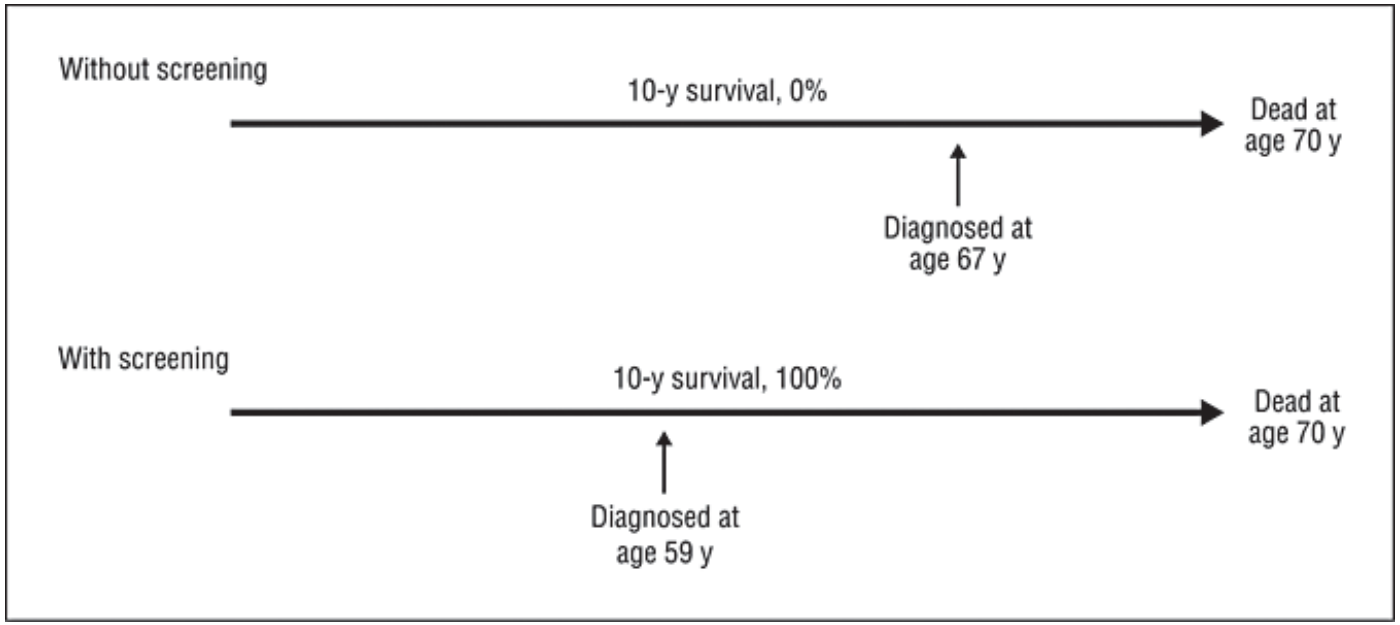


Jørgensen KJ et al. Radiology 2011; 260:621-7

Length bias


Rapidly Progressive
(6 cases)
o
Dx
Slowly Progressive
(6 cases)
Test
Time
o = Time of disease onset.
Dx = Time when disease is clinically obvious without testing.

Lead-time bias



ARCHIVES OF INTERNAL MEDICINE

Welch HG et al. Arch Intern Med 2007;167:2289-2295.

Pooled estimates for relative breast cancer mortality reductions after approximately 13 years of follow-up were similar for 2 meta-analyses of RCTs using random-effects models (UK Independent Panel,[31] relative risk [RR], 0.80; 95% CI, 0.73-0.89; and Canadian Task Force,[32] RR, 0.82; 95% CI, 0.74-0.94) and for the Cochrane analysis,[30] which used a fixed-effects model (RR, 0.81; 95% CI, 0.74-0.87).

Screening *øger* social ulighed i sundhed.

Healthy Screenee effect.

“The screenees are the healthy, well-educated, affluent, physically fit, fruit and vegetable eating, non-smokers with long-lived parents.”

J. A. Muir Gray, former Programmes Director, National Screening Commitee, UK.

A mammogram is a safe, low-dose X-ray that can detect breast cancer before there's a lump. In other words, it could save your life and your breast.

If you're a woman over 35, be sure to schedule a mammogram. Unless you're still not convinced of its importance.

In which case, you may need more than your breasts examined.

Find the time.
Have a mammogram.

AMERICAN CANCER SOCIETY®

Give yourself the chance of a lifetime.

“…one can simplify a message so much that one is lying. Too much of that has happened in breast cancer over the past 30 years...“

- Otis Brawley, MD, Chief Medical Officer, ACS

http://www.medpagetoday.com/OBGYN/BreastCancer/54228

Annals of Internal Medicine

ORIGINAL RESEARCH

Breast Cancer Screening in Denmark

A Cohort Study of Tumor Size and Overdiagnosis

Karsten Juhl Jørgensen, MD, DrMedSci; Peter C. Gøtzsche, MD, MSc; Mette Kalager, MD, PhD*; and Per-Henrik Zahl, MD, DrMedSci*

Background: Effective breast cancer screening should detect early-stage cancer and prevent advanced disease.

Objective: To assess the association between screening and the size of detected tumors and to estimate overdiagnosis (detection of tumors that would not become clinically relevant).

Design: Cohort study.

Setting: Denmark from 1980 to 2010.

Participants: Women aged 35 to 84 years.

Intervention: Screening programs offering biennial mammography for women aged 50 to 69 years beginning in different regions at different times.

Measurements: Trends in the incidence of advanced (>20 mm) and nonadvanced (≤20 mm) breast cancer tumors in screened and nonscreened women were measured. Two approaches were used to estimate the amount of overdiagnosis: comparing the incidence of advanced and nonadvanced tumors among women aged 50 to 84 years in screening and nonscreening areas; and comparing the incidence for nonadvanced tumors among women aged 35 to 49, 50 to 69, and 70 to 84 years in screening and nonscreening areas.

Results: Screening was not associated with lower incidence of advanced tumors. The incidence of nonadvanced tumors increased in the screening versus prescreening periods (incidence rate ratio, 1.49 [95% CI, 1.43 to 1.54]). The first estimation approach found that 271 invasive breast cancer tumors and 179 ductal carcinoma in situ (DCIS) lesions were overdiagnosed in 2010 (overdiagnosis rate of 24.4% [including DCIS] and 14.7% [excluding DCIS]). The second approach, which accounted for regional differences in women younger than the screening age, found that 711 invasive tumors and 180 cases of DCIS were overdiagnosed in 2010 (overdiagnosis rate of 48.3% [including DCIS] and 38.6% [excluding DCIS]).

Limitation: Regional differences complicate interpretation.

Conclusion: Breast cancer screening was not associated with a reduction in the incidence of advanced cancer. It is likely that 1 in every 3 invasive tumors and cases of DCIS diagnosed in women offered screening represent overdiagnosis (incidence increase of 48.3%).

Primary Funding Source: None.

Ann Intern Med. 2017;166:313-323. doi:10.7326/M16-0270 **Annals.org**

For author affiliations, see end of text.

This article was published at Annals.org on 10 January 2017.

* Drs. Kalager and Zahl contributed equally to this work.

Articles

Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries

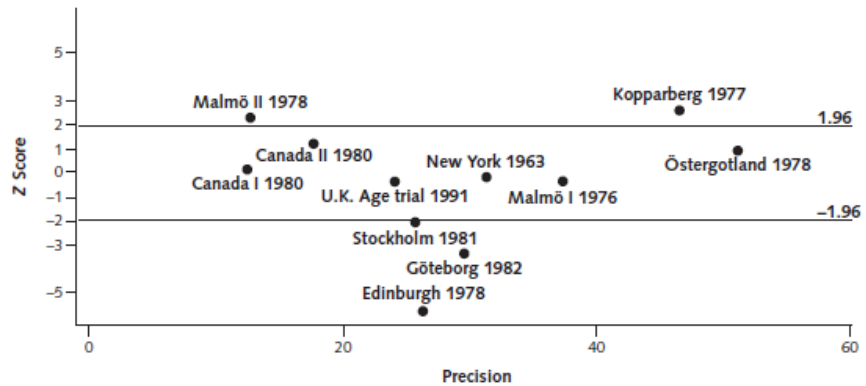
Claudia Allemani, PhD, Tomohiro Matsuda, PhD, Veronica Di Carlo, MSc, Rhea Harewood, MSc, Melissa Matz, PhD, Maja Nikšić, PhD, Audrey Bonaventure, MD, Prof Mikhail Valkov, MD, Christopher J Johnson, MPH, Prof Jacques Estève, PhD, Prof Olufemi J Ogunbiyi, MBBS, Prof Gulnar Azevedo e Silva, PhD, Wan-Qing Chen, PhD, Sultan Eser, PhD, Gerda Engholm, MSc, Charles A Stiller, MSc, Alain Monnereau, MD, Ryan R Woods, MSc, Otto Visser, PhD, Gek Hsiang Lim, MSc, Prof Joanne Aitken, PhD, Hannah K Weir, PhD, Prof Michel P Coleman, BM BCh CONCORD Working Group†

† Members are listed at the end of the Article

Current Author Addresses: Drs. Jüni and Zwahlen: Institute of Social and Preventive Medicine, University of Bern, Finkenhubelweg 11, CH-3012, Bern, Switzerland.

Author Contributions: Conception and design: P. Jüni, M. Zwahlen.
Analysis and interpretation of the data: P. Jüni, M. Zwahlen.
Drafting of the article: P. Jüni.
Critical revision of the article for important intellectual content: P. Jüni, M. Zwahlen.
Final approval of the article: P. Jüni, M. Zwahlen.
Statistical expertise: P. Jüni, M. Zwahlen.
Administrative, technical, or logistic support: P. Jüni.
Collection and assembly of data: P. Jüni, M. Zwahlen.

Appendix Figure. **Modified Galbraith plot of the estimated effects of mammography screening on deaths from causes other than breast cancer against the statistical precision of 11 screening trials.**



The Z score was calculated as ln(RR)/[SE of the ln(RR)]; statistical precision was calculated as 1/[SE of the ln(RR)]. The fixed Z score boundaries at -1.96 and 1.96, represented by the solid lines, divide the plot into areas of significant differences between the screening and control groups ($Z < -1.96$ and $Z > 1.96$, respectively) and nonsignificant differences ($-1.96 < Z < 1.96$). Three trials (Edinburgh 1978, Göteborg 1982, Stockholm 1981) are below the bounds and are associated with a significant benefit of mammography screening on deaths from other causes, whereas 2 others (Malmö II 1978 and Kopparberg 1977) are above the bounds and are associated with a significant harm from mammography screening. If the true RR equals 1, then 1 trial will be outside the boundaries with a probability of 43.1%, 2 trials with 10.2%, and 3 trials with 1.5%. The probability that 5 trials lie outside the boundaries, as is the case, is 0.01%. Data are from reference 5. RR = relative risk.

Breast screening in Denmark

- 17 year with differential access to screening
- 100,000 women aged 50 to 69 years in areas offering screening.
- 400,000 women aged 50 to 69 years in areas not offering screening.

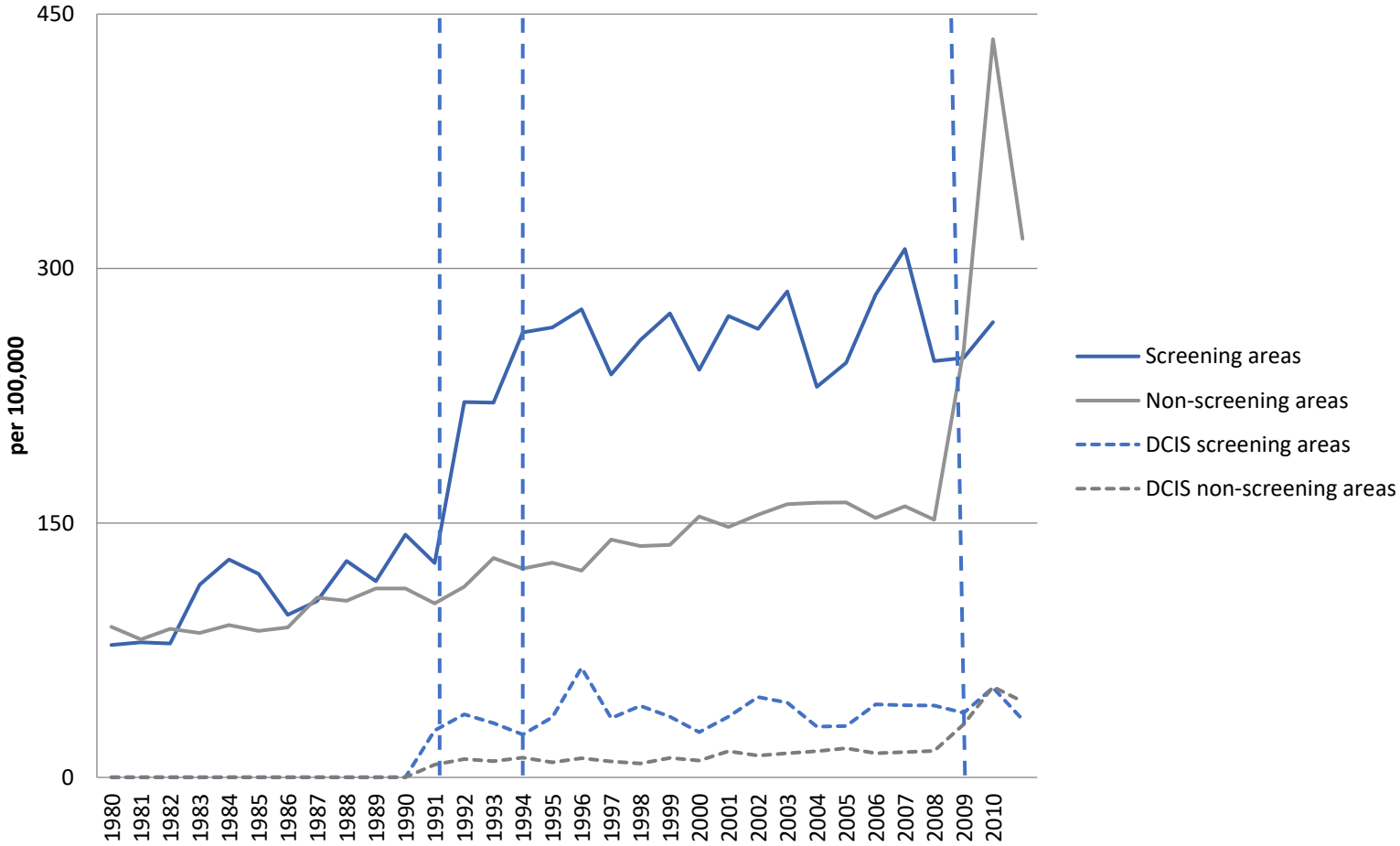
The data:

- All Danish women aged 35 to 84 years.
- Data from two independent sources; the national Danish cancer registry and a clinical database (Danish Breast Cancer Group)
- Data from 1980 to 2010
- Tumors <20mm considered non-advanced
- Tumors 20mm and above considered advanced

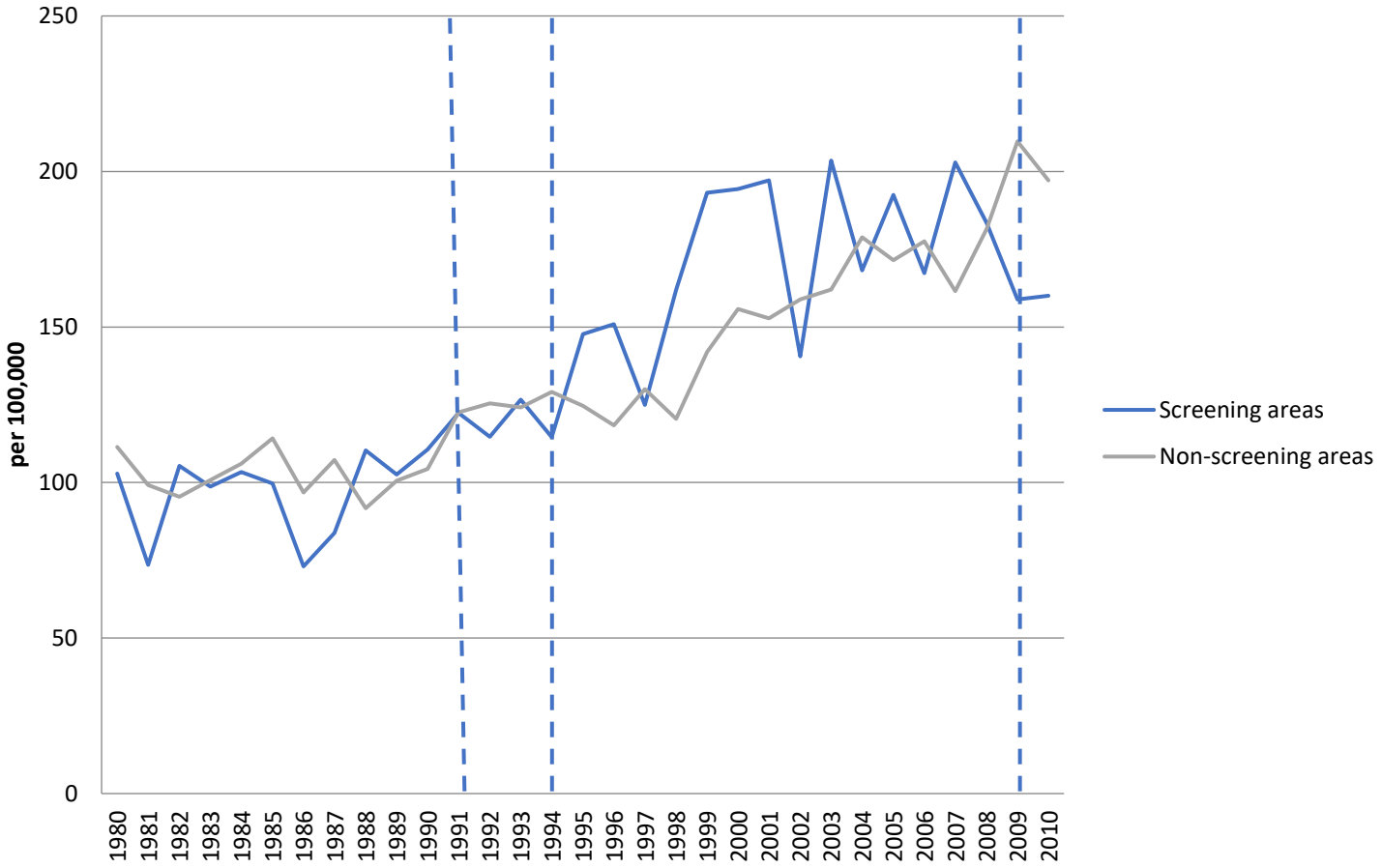
Analyses:

- **Impact on stage:** Poisson regression analyses, taking pre-screening trends and non-screened age groups into account
- **Overdiagnosis (Method 1):** compared incidence in the screening period of advanced and non-advanced cancers in the age group 50 to 84 years.
- **Overdiagnosis (Method 2):** analysed trends in incidence in the pre– and screening period for the age-groups 35-49, 50-69, and 70-84 years.

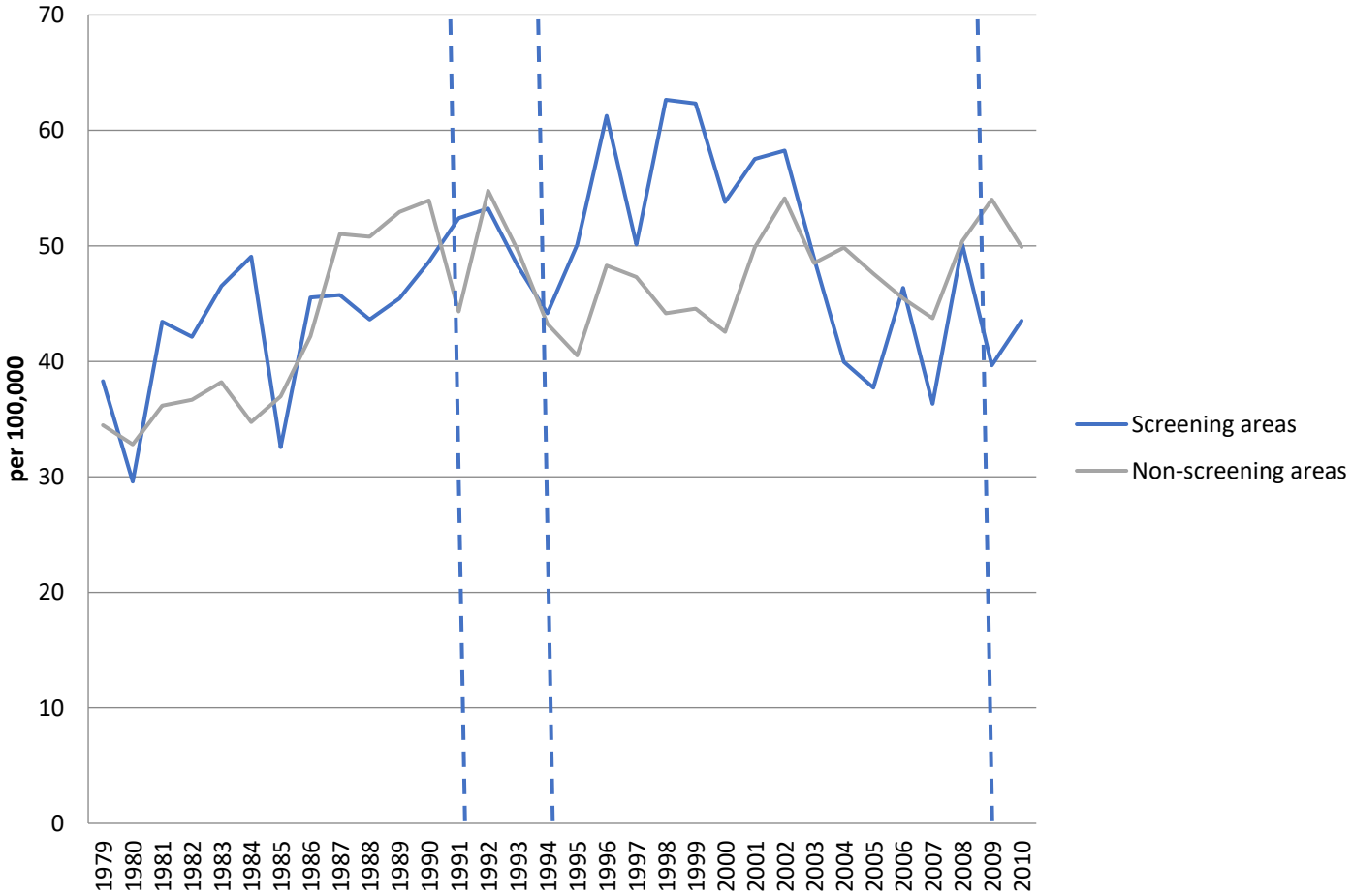
Non-advanced cancers in women aged 50 to 69 years. The dotted lines indicate screening start in Copenhagen (1991), Funen (1993-4), and the rest of Denmark (2008-9).



Non-advanced cancers in women aged 70 to 85 years. The dotted lines indicate screening start in Copenhagen (1991), Funen (1993-4), and the rest of Denmark (2008-9).



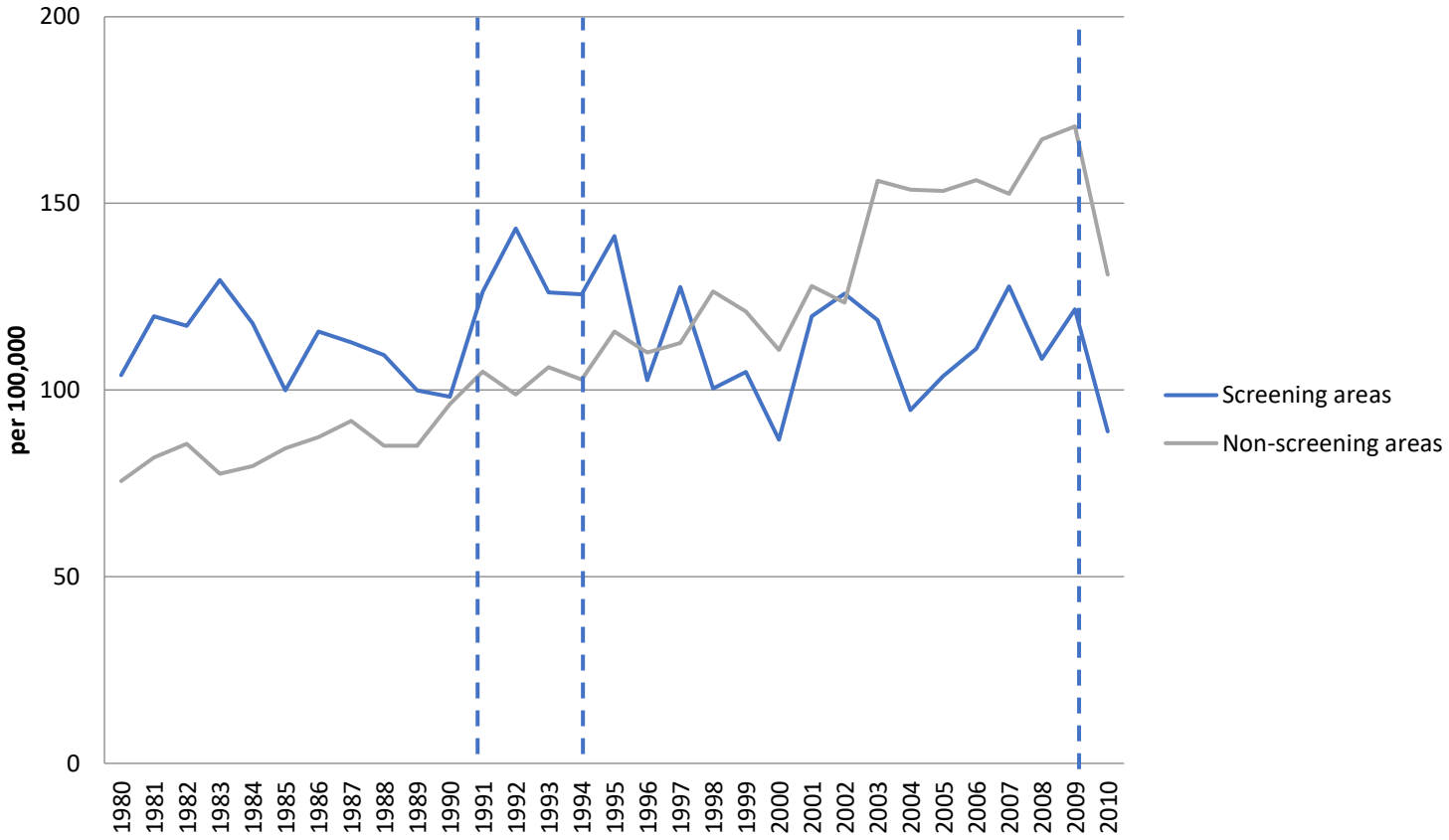
Non-advanced cancers in women aged 35 to 49 years. The dotted lines indicate screening start in Copenhagen (1991), Funen (1993-4), and the rest of Denmark (2008-9).



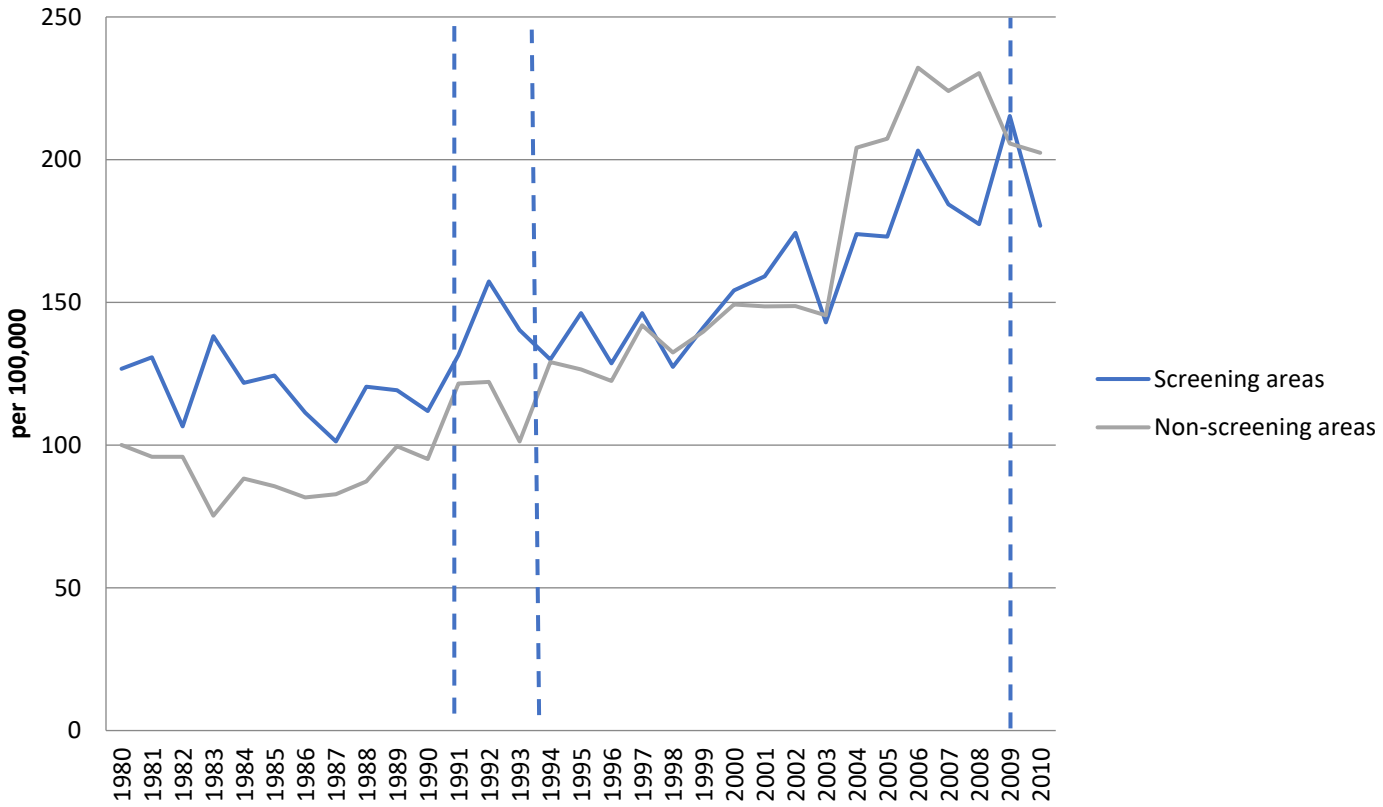
Impact of screening on non-advanced breast cancer incidence.

- Clearly visible and sustained increase in the screened age group; hazard ratio 1.50 (95% CI 1.45 to 1.55) compared to before screening.
- No visible reduction in previously screened women above the screening age.
- Comparable incidence and trends between regions in women below the screening age.

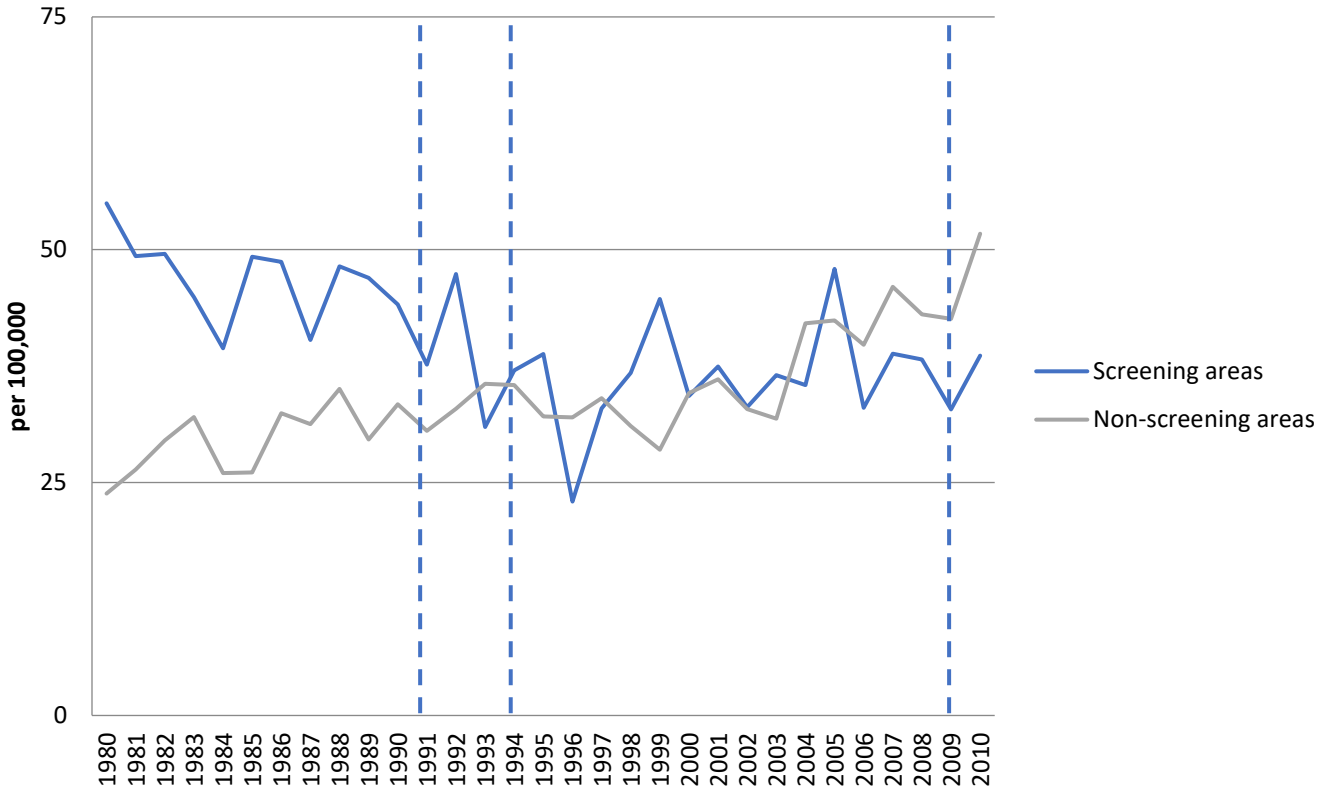
Advanced cancers in women aged 50 to 69 years. The dotted lines indicate screening start in Copenhagen (1991), Funen (1993-4), and the rest of Denmark (2008-9).



Advanced cancers in women aged 70 to 85 years. The dotted lines indicate screening start in Copenhagen (1991), Funen (1993-4), and the rest of Denmark (2008-9).



Advanced cancers in women aged 35 to 49 years. The dotted lines indicate screening start in Copenhagen (1991), Funen (1993-4), and the rest of Denmark (2008-9).



Impact of screening on advanced breast cancer incidence.

- Regional differences unrelated to screening complicate interpretation.
- Most change between regions occured prior to screening.
- No clear difference between screened and non-screened areas when comparing screened and non-screened age groups.

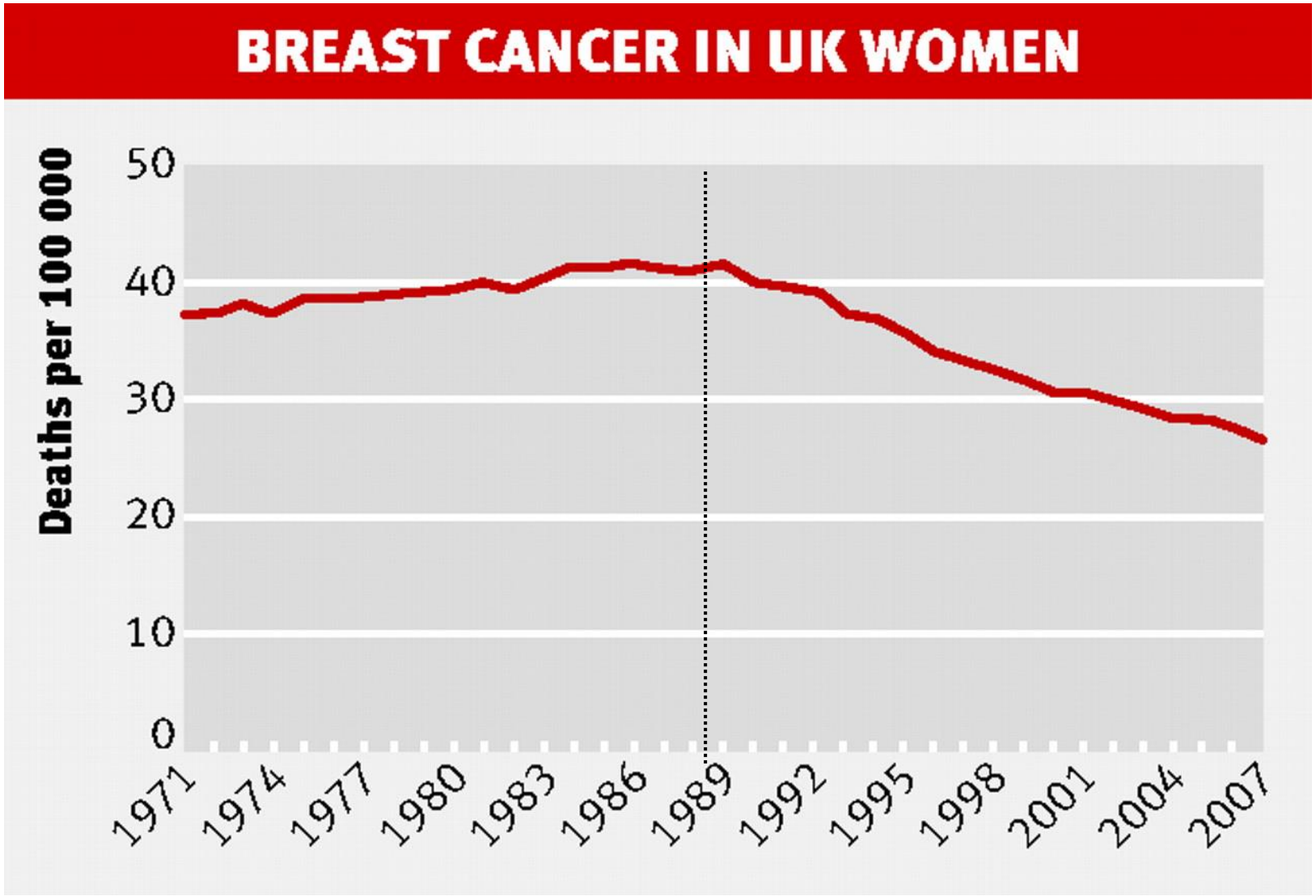
Estimates of overdiagnosis

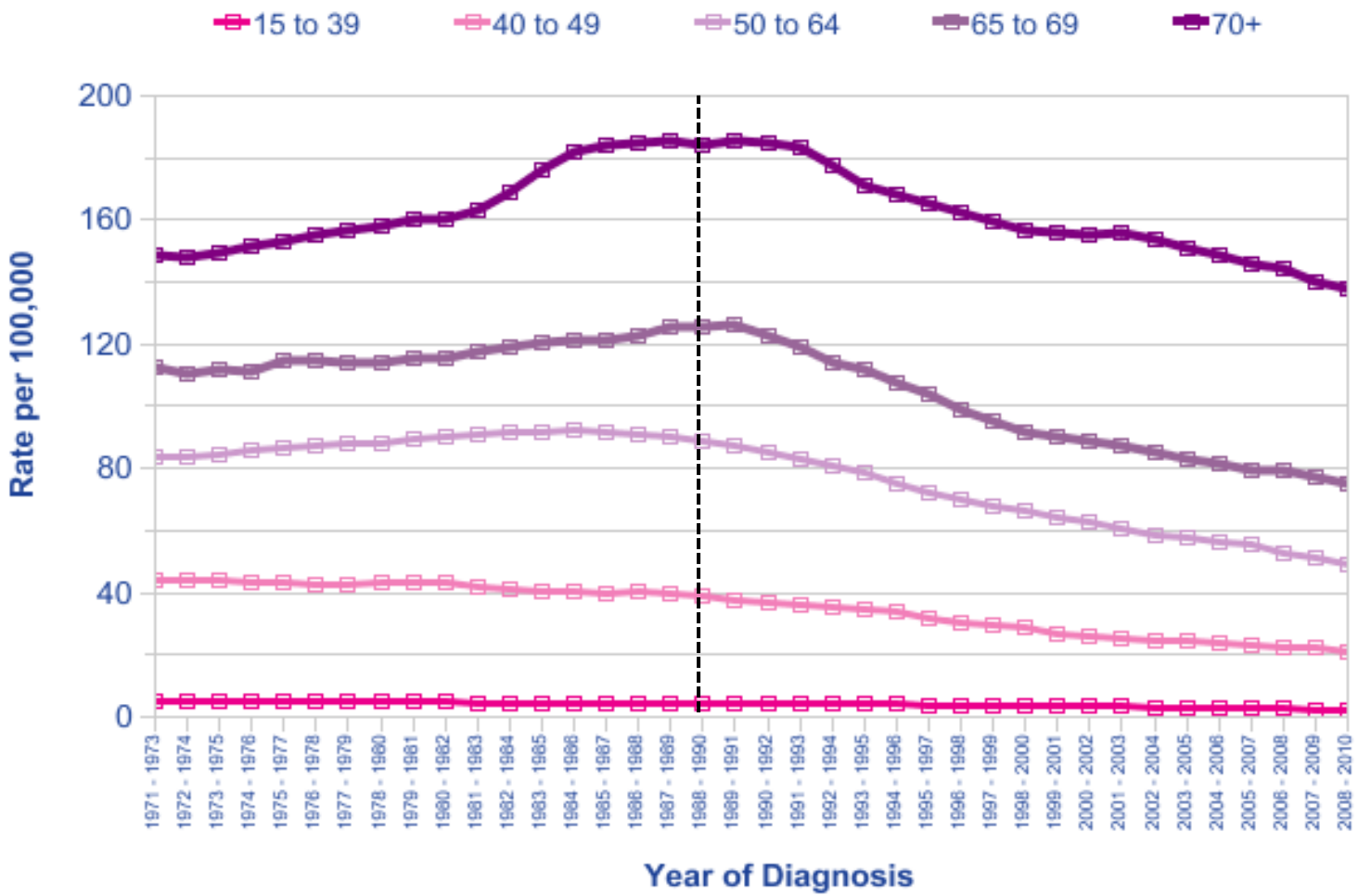
Method 1: Incidence difference for the age group 50 to 69, subtracting any reduction in women aged 70 to 84 years: **24.4%** including DCIS, **14.7%** for invasive cancers only.

Method 2: Taking trends in the pre-screening period and in women below the screening age into account, screening increased the risk of a breast cancer diagnisis by **45%** in the invited age group, including DCIS.

Conclusions

- Clear increase in non-advanced breast cancers with screening.
- No clear effect of screening on advanced breast cancers.
- Incidence of advanced breast cancers influenced by factors other than screening.
- Observational studies that do not consider the pre-screening period and non-screened age groups may provide misleading results




15 to 39
40 to 49
50 to 64
65 to 69
70+
Rate per 100,000
200
160
120
80
40
0
1971 - 1973
1972 - 1974
1973 - 1975
1974 - 1976
1975 - 1977
1976 - 1978
1977 - 1979
1978 - 1980
1979 - 1981
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2008 - 2010
Year of Diagnosis

“Between the late 1980s and 2008-2010, breast cancer mortality rates fell by 50% in the 15-39 age group, by 47% in the 40-49 age group, 45% in the 50-64 age group, 40% in the 65-69 age group and by 26% in women aged over 70 years.”[1]

1: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/breast/mortality/uk-breast-cancer-mortality-statistics

Observational studies of screening effects should include data from the pre-screening era, and for non-screened age groups.

The Benefits and Harms of Breast Cancer Screening:

An Independent Review

Authors:
The Independent UK Panel on Breast Cancer Screening

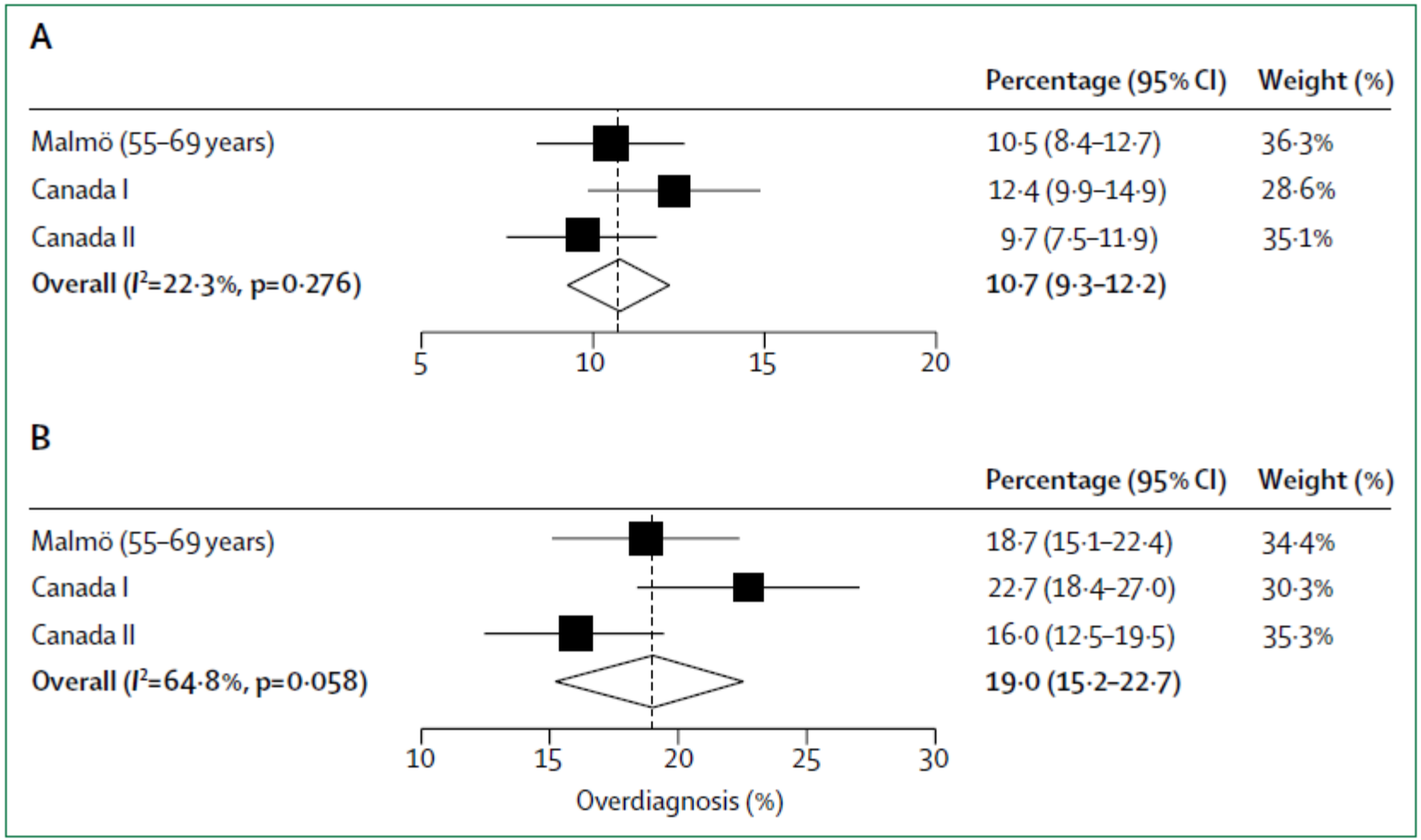
IBSR
Independent Breast Screening Review

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

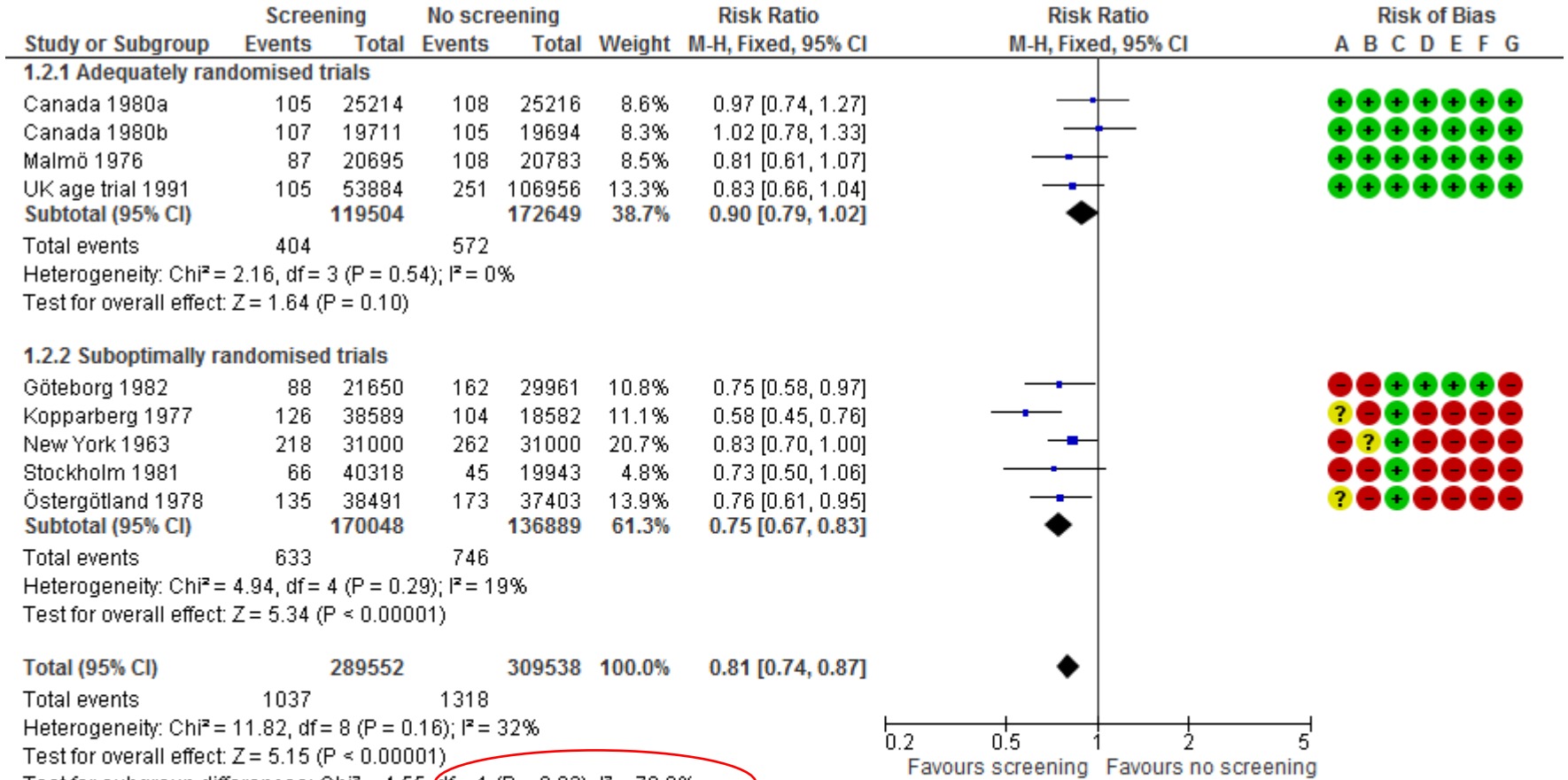
October 2012

Main results:

1 woman avoids a breast cancer death for every 3 overdiagnosed; 1 300 and 4 000 women per year, respectively, in the UK.



A: Excess cancers as a proportion of cancers diagnosed over long-term follow- up.
B: Excess cancers as a proportion of cancers diagnosed during the screening period.



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

BMJ

BMJ 2011;343:d4411 doi: 10.1136/bmj.d4411

RESEARCH

Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database

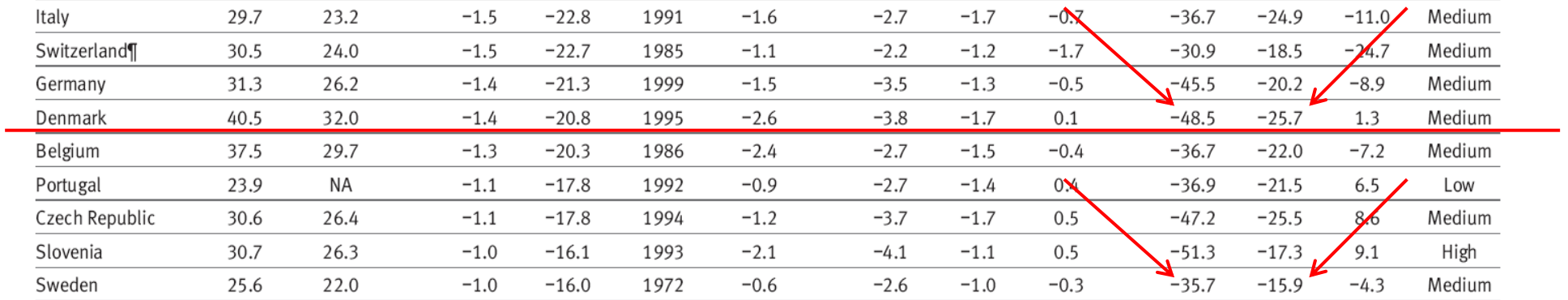
Philippe Autier *research director*[1], Mathieu Boniol *senior statistician*[1], Anna Gavin *director*[2], Lars J Vatten *professor*[3]

[1]International Prevention Research Institute, 95 Cours Lafayette, 69006 Lyon, France; [2]Northern Ireland Cancer Registry, Belfast, Northern Ireland, UK; [3]Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway

Conclusions The contrast between the time differences in implementation of mammography screening and the similarity in reductions in mortality between the country pairs suggest that screening did not play a direct part in the reductions in breast cancer mortality.

Table 1 | Changes in breast cancer mortality between 1989 and 2006 in European countries ranked according to overall decline in mortality

	Mean mortality*		Mortality change for all ages (%)				Mortality change 1989-2006 by age group (%)						
			For 1989-2006				Annual change			Overall change			
Country	1987-9	2004-6†	Annual	Overall	Year for start of decline‡	Annual change 1999-2006	<50	50-69	≥70	<50	50-69	≥70	Quality of data on cause of death§
Iceland	33.1	23.5	−3.4	−44.5	1995	1.1	−8.1	−2.5	−3.1	−76.3	−35.0	−41.5	High
England and Wales	41.9	28.1	−2.5	−34.9	1989	−2.0	−3.2	−3.0	−1.5	−42.1	−40.1	−22.6	High
Luxembourg	36.3	22.9	−2.4	−34.1	1988	−2.8	−5.3	−2.5	−1.3	−60.0	−34.9	−19.9	Medium
Scotland	39.3	29.0	−2.1	−29.9	1990	−1.4	−2.9	−2.7	−0.7	−39.1	−37.2	−11.9	High
Northern Ireland	37.0	28.1	−2.0	−29.2	1991	−1.2	−3.8	−2.6	0.0	−48.2	−36.2	−0.7	High
Austria	31.8	24.5	−1.8	−26.8	1990	−1.6	−4.0	−1.7	−1.1	−50.3	−25.3	−16.9	Medium
Spain	23.7	18.9	−1.8	−26.8	1992	−2.2	−3.4	−2.1	−0.3	−44.7	−30.3	−4.6	Medium
Ireland	40.3	30.5	−1.8	−26.4	1991	−2.3	−3.2	−1.9	−1.0	−42.7	−27.2	−15.7	High
Netherlands	39.0	30.1	−1.7	−25.1	1993	−2.7	−1.7	−1.9	−1.4	−25.3	−27.8	−20.9	Medium
Norway	27.4	21.5	−1.6	−24.3	1995	−2.2	−2.5	−1.5	−1.4	−35.2	−22.6	−20.8	Medium
Italy	29.7	23.2	−1.5	−22.8	1991	−1.6	−2.7	−1.7	−0.7	−36.7	−24.9	−11.0	Medium
Switzerland¶	30.5	24.0	−1.5	−22.7	1985	−1.1	−2.2	−1.2	−1.7	−30.9	−18.5	−24.7	Medium
Germany	31.3	26.2	−1.4	−21.3	1999	−1.5	−3.5	−1.3	−0.5	−45.5	−20.2	−8.9	Medium
Denmark	40.5	32.0	−1.4	−20.8	1995	−2.6	−3.8	−1.7	0.1	−48.5	−25.7	1.3	Medium
Belgium	37.5	29.7	−1.3	−20.3	1986	−2.4	−2.7	−1.5	−0.4	−36.7	−22.0	−7.2	Medium
Portugal	23.9	NA	−1.1	−17.8	1992	−0.9	−2.7	−1.4	0.4	−36.9	−21.5	6.5	Low
Czech Republic	30.6	26.4	−1.1	−17.8	1994	−1.2	−3.7	−1.7	0.5	−47.2	−25.5	8.6	Medium
Slovenia	30.7	26.3	−1.0	−16.1	1993	−2.1	−4.1	−1.1	0.5	−51.3	−17.3	9.1	High
Sweden	25.6	22.0	−1.0	−16.0	1972	−0.6	−2.6	−1.0	−0.3	−35.7	−15.9	−4.3	Medium
Finland	24.5	21.4	−0.7	−11.7	1990	−1.5	−2.3	−0.7	0.0	−32.6	−10.8	0.1	High
Hungary	32.4	29.0	−0.7	−11.4	1994	−3.1	−2.4	−0.5	−0.1	−34.4	−8.3	−2.4	High
France	28.5	25.6	−0.7	−10.7	1994	−1.4	−0.9	−0.9	−0.1	−14.3	−14.9	−1.6	Medium
Poland	21.5	21.1	−0.4	−5.9	None	−0.1	−2.5	−0.3	0.8	−34.5	−4.3	14.6	Low
Slovakia	23.6	23.4	−0.1	−1.5	2000	−3.2	−2.1	−0.1	1.1	−30.7	−1.9	20.5	High



Autier P et al. BMJ 2010; 341:c3620

Evidence from Norway

- **Kalager et al.** (NEJM 2010):

  10% (CI: 0.78 to 1.04)

  average 6.6 years of follow-up
- **Olsen et al.** (Int J Cancer 2012):

  11% (CI: 0.77 to 1.12)

  ”up to 13 years of follow-up”

Annals of Oncology Advance Access published January 20, 2011

review

Annals of Oncology
doi:10.1093/annonc/mdq633

Advanced breast cancer incidence following population-based mammographic screening

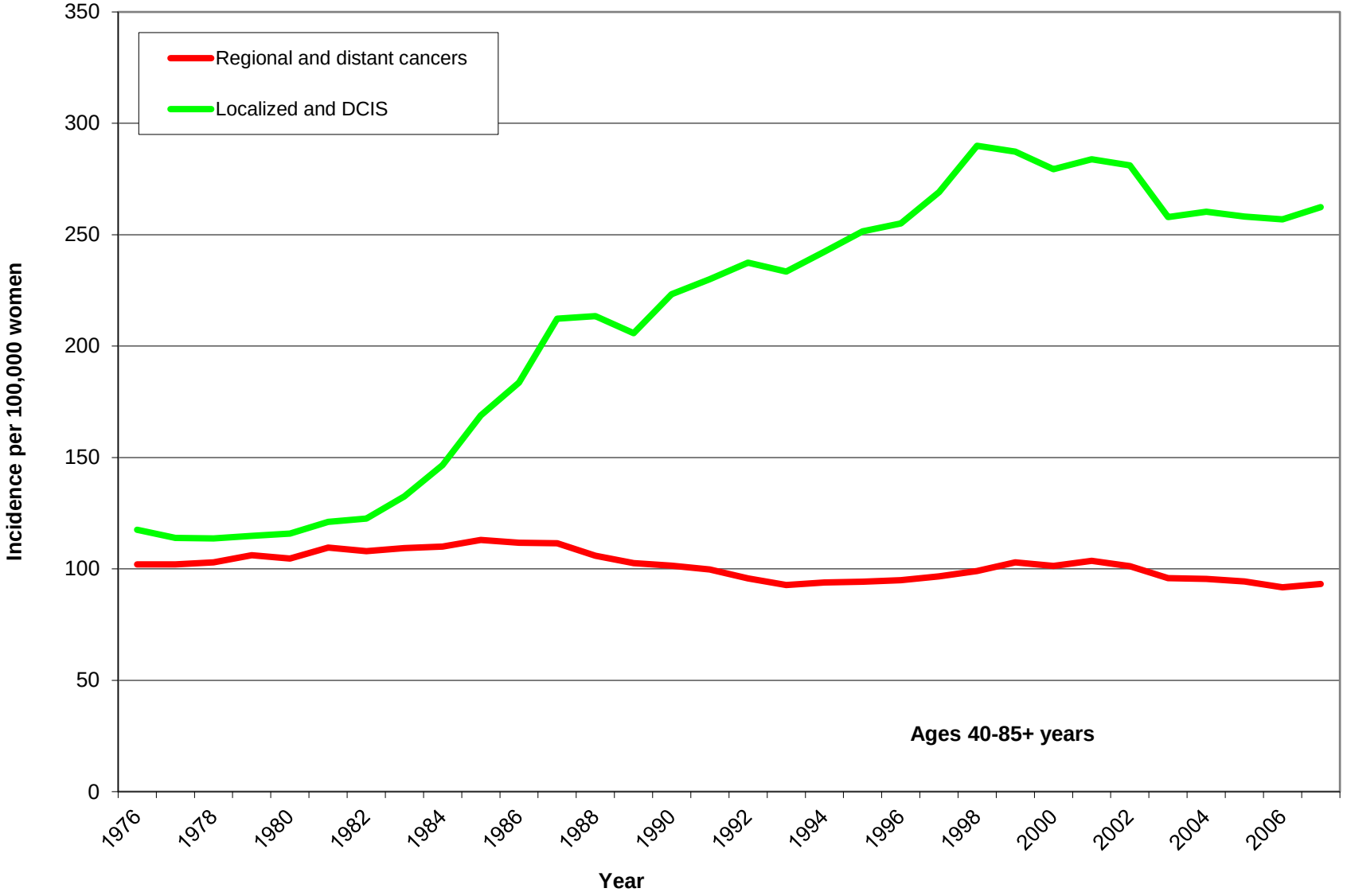
P. Autier[1]*, M. Boniol[1], R. Middleton[2], J.-F. Doré[3], C. Héry[3], T. Zheng[4] & A. Gavin[2]

[1]Department of Epidemiology and Biostatistics, International Prevention Research Institute (iPRI), Lyon, France; [2]Direction and Data Department, Northern Ireland Cancer Registry (NICR), Queens University Belfast, Belfast, UK; [3]Unit of Molecular Epidemiology, INSERM U 590, Lyon, France; [4]Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, USA

Received 22 September 2010; accepted 24 September 2010

Conclusions: In areas with widespread sustained mammographic screening, trends in advanced breast cancer incidence do not support a substantial role for screening in the decrease in mortality.

Stage-related breast cancer incidence in the USA.



http://seer.cancer.gov/

Annals of Internal Medicine | ORIGINAL RESEARCH

Overdiagnosis of Invasive Breast Cancer Due to Mammography Screening: Results From the Norwegian Screening Program

Mette Kalager, MD; Hans-Olov Adami, MD, PhD; Michael Bretthauer, MD, PhD; and Rulla M. Tamimi, ScD

Background: Precise quantification of overdiagnosis of breast cancer (defined as the percentage of cases of cancer that would not have become clinically apparent in a woman's lifetime without screening) due to mammography screening has been hampered by lack of valid comparison groups that identify incidence trends attributable to screening versus those due to temporal trends in incidence.

Objective: To estimate the percentage of overdiagnosis of breast cancer attributable to mammography screening.

Design: Comparison of invasive breast cancer incidence with and without screening.

Setting: A nationwide mammography screening program in Norway (inviting women aged 50 to 69 years), gradually implemented from 1996 to 2005.

Participants: The Norwegian female population.

Measurements: Concomitant incidence of invasive breast cancer from 1996 to 2005 in counties where the screening program was implemented compared with that in counties where the program was not yet implemented. To adjust for changes in temporal trends in breast cancer incidence, incidence rates during the preceding decade were also examined. The percentage of overdiagnosis was calculated by accounting for the expected decrease in incidence following cessation of screening after age 69 years (approach 1) and by comparing incidence in the current screening group with incidence among women 2 and 5 years older in the historical screening groups, accounting for average lead time (approach 2).

Results: A total of 39 888 patients with invasive breast cancer were included, 7793 of whom were diagnosed after the screening program started. The estimated rate of overdiagnosis attributable to the program was 18% to 25% ($P < 0.001$) for approach 1 and 15% to 20% ($P < 0.001$) for approach 2. Thus, 15% to 25% of cases of cancer are overdiagnosed, translating to 6 to 10 women overdiagnosed for every 2500 women invited.

Limitation: The study was registry-based.

Conclusion: Mammography screening entails a substantial amount of overdiagnosis.

Primary Funding Source: Norwegian Research Council and Frontier Science.

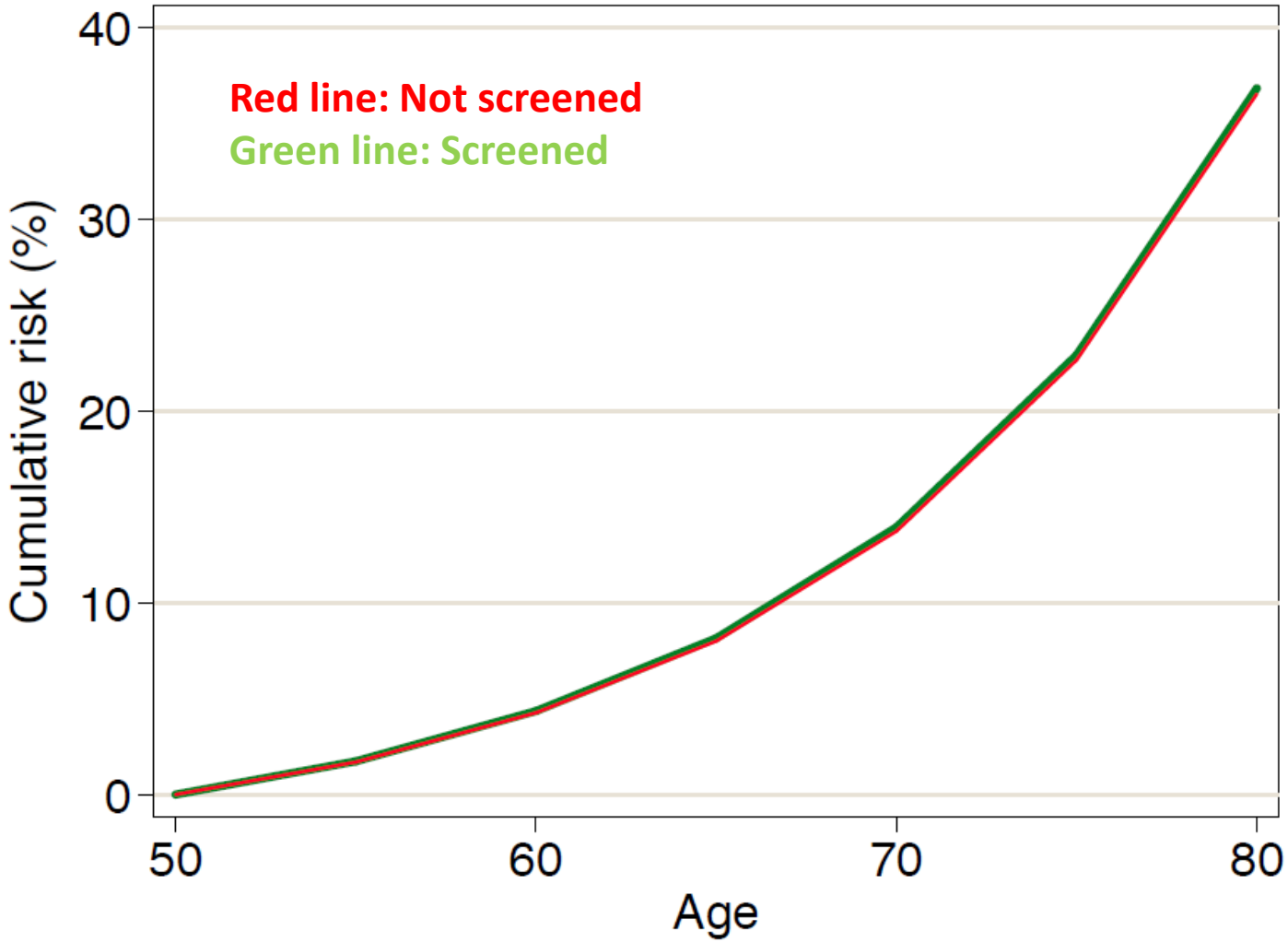
Ann Intern Med. 2012;156:491-499. www.annals.org
For author affiliations, see end of text.

A few quotes

- *”When we reviewed the available evidence and contemplated its implications in detail (…) we became increasingly concerned.”*
- *”We would be in favour of mammography screening if [benefits were large]. Unfortunately, they are not, and we believe women need to be told so.”*
- *”From an ethical perspective, a public health program that does not clearly produce more benefits than harms is hard to justify.”*

Biller-Adorno and Jüni, New Engl J Med 2014.

Total mortaliy (breast screening)



Pharoah P, Professor of Cancer Epidemiology, Univ. of Cambridge.

thebmj

BMJ 2015;350:h2175 doi: 10.1136/bmj.h2175 (Published 5 May 2015)

OBSERVATIONS

THE ART OF RISK COMMUNICATION

Towards a paradigm shift in cancer screening: informed citizens instead of greater participation

Germany aims to stop nudging the public on screening

Gerd Gigerenzer *director, Harding Centre for Risk Literacy and Centre for Adaptive Behaviour and Cognition, Max Planck Institute for Human Development, Berlin, Germany*

Policy on screening people for cancer poses a dilemma: should we aim for higher participation rates or for better informed citizens? The dilemma is that both cannot be had. A focus on informing citizens risks lowering participation rates, because

Turning the tables in screening

But Germany's National Cancer Plan, which was initiated by the government in 2008 and coordinates screening and treatment, is now turning the tables. It was announced at a workshop in February 2015 that, on the basis of a 2013 law on improving the detection of cancer,[5] "the goal of informed participatory decision making is now ranked higher than the goal of a maximum participation rate in cancer screening."[6] To change policy so clearly and publicly is unprecedented and represents a potential paradigm shift in screening. Its implementation will require fundamental changes. In my view, these include the following.

Evidence based information

All screening pamphlets and websites aimed at the public need

Use of a decision aid including information on overdetection to support informed choice about breast cancer screening: a randomised controlled trial

Jolyn Hersch, Alexandra Barratt, Jesse Jansen, Les Irwig, Kevin McGeechan, Gemma Jacklyn, Hazel Thornton, Haryana Dhillon, Nehmat Houssami, Kirsten McCaffery

Summary

Background Mammography screening can reduce breast cancer mortality. However, most women are unaware that inconsequential disease can also be detected by screening, leading to overdiagnosis and overtreatment. We aimed to investigate whether including information about overdetection of breast cancer in a decision aid would help women aged around 50 years to make an informed choice about breast screening.

Methods We did a community-based, parallel-group, randomised controlled trial in New South Wales, Australia, using a random cohort of women aged 48–50 years. Recruitment to the study was done by telephone; women were eligible if they had not had mammography in the past 2 years and did not have a personal or strong family history of breast cancer. With a computer program, we randomly assigned 879 participants to either the intervention decision aid (comprising evidence-based explanatory and quantitative information on overdetection, breast cancer mortality reduction, and false positives) or a control decision aid (including information on breast cancer mortality reduction and false positives). Participants and interviewers were masked to group assignment. The primary outcome was informed choice (defined as adequate knowledge and consistency between attitudes and screening intentions), which we assessed by telephone interview about 3 weeks after random allocation. The primary outcome was analysed in all women who completed the relevant follow-up interview questions fully. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12613001035718.

Findings Between January, 2014, and July, 2014, 440 women were allocated to the intervention group and 439 were assigned to the control group. 21 women in the intervention group and 20 controls were lost to follow-up; a further ten women assigned to the intervention and 11 controls did not answer all questions on attitudes. Therefore, 409 women in the intervention group and 408 controls were analysed for the primary outcome. 99 (24%) of 409 women in the intervention group made an informed choice compared with 63 (15%) of 408 in the control group (difference 9%, 95% CI 3–14; p=0·0017). Compared with controls, more women in the intervention group met the threshold for adequate overall knowledge (122/419 [29%] *vs* 71/419 [17%]; difference 12%, 95% CI 6–18; p<0·0001), fewer women expressed positive attitudes towards screening (282/409 [69%] *vs* 340/408 [83%]; 14%, 9–20; p<0·0001), and fewer women intended to be screened (308/419 [74%] *vs* 363/419 [87%]; 13%, 8–19; p<0·0001). When conceptual knowledge alone was considered, 203 (50%) of 409 women in the intervention group made an informed choice compared with 79 (19%) of 408 in the control group (p<0·0001).

Interpretation Information on overdetection of breast cancer provided within a decision aid increased the number of women making an informed choice about breast screening. Becoming better informed might mean women are less likely to choose screening.

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February 18, 2015
http://dx.doi.org/10.1016/S0140-6736(15)60123-4

See Online/Comment
http://dx.doi.org/10.1016/S0140-6736(15)60258-6

Screening & Test Evaluation Program (STEP) (J Hersch MApplSc, J Jansen PhD, Prof L Irwig MBBCh, Prof N Houssami MBBS, Prof K McCaffery PhD), **Centre for Medical Psychology & Evidence-based Decision-making (CeMPED)** (J Hersch, J Jansen, Prof K McCaffery, Prof A Barratt MBBS, K McGeechan PhD, H Dhillon PhD), **School of Public Health** (G Jacklyn MPH), **and Central Clinical School** (H Dhillon), **The University of Sydney, Sydney, NSW 2006, Australia; and Department of Health Sciences, University of Leicester; Leicester, UK** (H Thornton Hon DSc)

Correspondence to:
Prof Kirsten McCaffery, School of Public Health, The University of Sydney, Sydney, NSW 2006, Australia
kirsten.mccaffery@sydney.edu.au

Annals of Internal Medicine | ORIGINAL RESEARCH

Aggregate Cost of Mammography Screening in the United States: Comparison of Current Practice and Advocated Guidelines

Cristina O'Donoghue, MD, MPH; Martin Eklund, PhD; Elissa M. Ozanne, PhD; and Laura J. Esserman, MD, MBA

Background: Controversy exists over how often and at what age mammography screening should be implemented. Given that evidence supports less frequent screening, the cost differences among advocated screening policies should be better understood.

Objective: To estimate the aggregate cost of mammography screening in the United States in 2010 and compare the costs of policy recommendations by professional organizations.

Design: A model was developed to estimate the cost of mammography screening in 2010 and 3 screening strategies: annual (ages 40 to 84 years), biennial (ages 50 to 69 years), and U.S. Preventive Services Task Force (USPSTF) guidelines (biennial for those aged 50 to 74 years and personalized based on risk for those younger than 50 years and based on comorbid conditions for those 75 years and older).

Setting: United States.

Patients: Women aged 40 to 85 years.

Intervention: Mammography annually, biennially, or following USPSTF guidelines.

Measurements: Cost of screening per year, using Medicare reimbursements.

Results: The estimated cost of mammography screening in the United States in 2010 was $7.8 billion, with approximately 70% of women screened. The simulated cost of screening 85% of women was $10.1 billion, $2.6 billion, and $3.5 billion for annual, biennial, and USPSTF guidelines, respectively. The largest drivers of cost (in order) were screening frequency, percentage of women screened, cost of mammography, percentage of women screened with digital mammography, and percentage of mammography recalls.

Limitation: Cost estimates and assumptions used in the model were conservative.

Conclusion: The cost of mammography varies by at least $8 billion per year on the basis of screening strategy. The USPSTF guidelines are based on the scientific evidence to date to maximize patient benefit and minimize harm but also result in far more effective use of resources.

Primary Funding Source: University of California and the Safeway Foundation.

Ann Intern Med. 2014;160:145-153. www.annals.org

For author affiliations, see end of text.

Breast screening controversy continues

”At what stage must we seriously consider whether this screening is a good use of £96m of the NHS budget?”

Fiona Godlee, Editor’s Choice, BMJ.

BMJ 2013;346:f477.

Informed choice in screening needs more than information

In *The Lancet*, Jolyn Hersch and colleagues report on a randomised controlled trial of two decision aids for women approaching the target age for starting breast screening (age 48–50 years): an intervention decision aid that included information about the most severe harm of breast cancer screening (overdiagnosis); and a control decision aid that did not have this information.[1] The aim of the trial was to see if including information on overdiagnosis would help women make an informed choice about breast screening. We could argue that to do a trial in which half of the participants are not given information about the harms of an intervention is ethically unacceptable. However, most breast screening programmes do not include information about overdiagnosis or other relevant harms of screening in their invitations,[2] which is why this study is so important. Of 409 women who received information about overdiagnosis in their decision aid, 99 (24%) were judged to have made an informed choice, the

Balanced comprehensive information is important from an ethical perspective; however, it might not have a substantial effect on the ability of women to make truly informed choices. In the study by Hersch and colleagues,[1] a woman was judged to have made an informed choice if she had sufficient knowledge and made a decision consistent with her personal preferences and values. We agree this definition of informed choice is useful in a research context, but it assumes that information speaking to people's intellect is easily integrated into understanding of risk. Yet research suggests that our understanding of risk relies mainly on emotions and that cognitive comprehension has little effect on decision making.[5,6] Furthermore, if emotionally charged messages have formed our perception of a particular risk, which is certainly the case for breast cancer, subsequent information is unlikely to change our understanding of that risk nor our attitudes or behaviour.[6] Therefore, emotional factors are likely

Science Photo Library

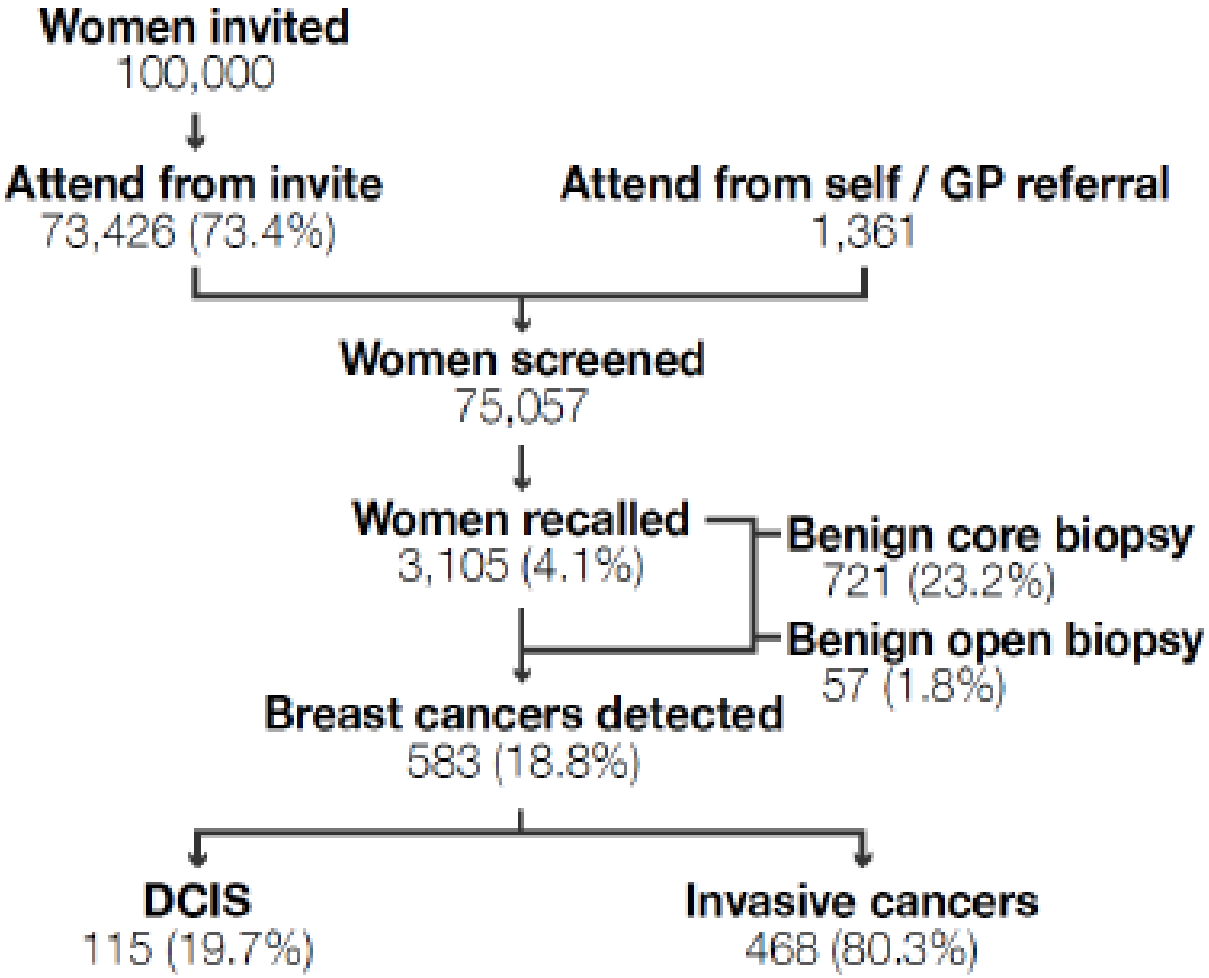
Published Online
February 18, 2015
http://dx.doi.org/10.1016/S0140-6736(15)60258-6

See Online/Articles
http://dx.doi.org/10.1016/S0140-6736(15)60123-4

Tumour size and breast screening

- Average tumour size in Denmark was reduced from 33 mm in 1978-9 to 24 mm in 1988-9.
- Average size reduction in the trials was 5 mm.

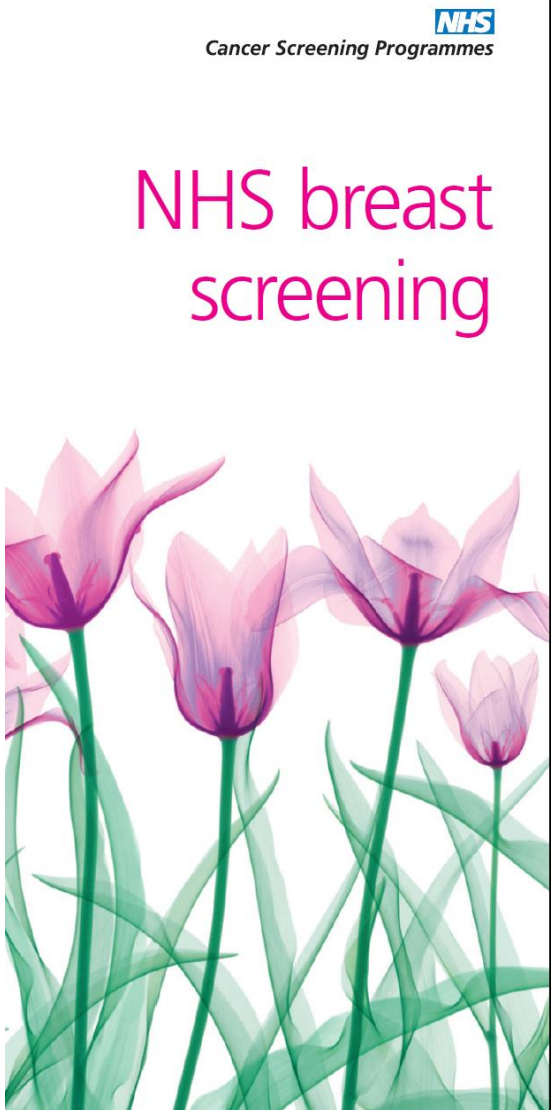
Rostgaard et al. *Acta Oncol* 2010;49:313-21


Women invited
100,000
Attend from invite
73,426 (73.4%)
Attend from self / GP referral
1,361
Women screened
75,057
Women recalled
3,105 (4.1%)
Benign core biopsy
721 (23.2%)
Benign open biopsy
57 (1.8%)
Breast cancers detected
583 (18.8%)
DCIS
115 (19.7%)
Invasive cancers
468 (80.3%)

2.7 million women invited in 2009[1].

- False positives: 65,094
- Benign core biopsies: 19,467
- Benign open biopsies: 1,539
- False negatives: ~33% of cases in a screened population were not detected
- Direct cost: £ 96 million

1: NHS Breast Screening Programme: Annual Review 2011.



"Designed to ensure that women are told what screening can and cannot achieve, the leaflet includes an explanation about false positive and false negative results […]".

"This means that women should be able to make a genuinely informed choice based on an understanding about why they are attending for screening".

http://www.cancerscreening.nhs.uk/breastscreen/publications/ia-02.html

NHS
Cancer Screening Programmes

NHS breast screening

Some statistics you might find helpful

- Breast cancer is the most common cancer in women. There are around 46,000 cases a year in the UK. Eight out of 10 breast cancers are found in women aged 50 and over.
- About 12,000 women die of breast cancer each year in the UK.
- For every 400 women screened regularly for 10 years, one less will die from breast cancer. This means that around 1,400 women are prevented from dying from breast cancer each year in England.

http://www.cancerscreening.nhs.uk/breastscreen/publications/ia-02.html

NHS
Cancer Screening Programmes

NHS breast screening

What are the benefits of breast screening?

- Regular screening prevents deaths from breast cancer.
- If a breast cancer is found early, you are less likely to have a mastectomy (your breast removed) or chemotherapy.

What are the downsides of being screened?

- Having a mammogram means your breasts are exposed to a small amount of radiation.
- Screening can find cancers which are treated but which may not otherwise have been found during your lifetime.

http://www.cancerscreening.nhs.uk/breastscreen/publications/ia-02.html

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

Mette Kalager, M.D., Marvin Zelen, Ph.D., Frøydis Langmark, M.D., and Hans-Olov Adami, M.D., Ph.D.

RESULTS

We analyzed data from 40,075 women with breast cancer. The rate of death was reduced by 7.2 deaths per 100,000 person-years in the screening group as compared with the historical screening group (rate ratio, 0.72; 95% confidence interval [CI], 0.63 to 0.81) and by 4.8 deaths per 100,000 person-years in the nonscreening group as compared with the historical nonscreening group (rate ratio, 0.82; 95% CI, 0.71 to 0.93; $P<0.001$ for both comparisons), for a relative reduction in mortality of 10% in the screening group ($P=0.13$). Thus, the difference in the reduction in mortality between the current and historical groups that could be attributed to screening alone was 2.4 deaths per 100,000 person-years, or a third of the total reduction of 7.2 deaths.

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.)

Why does vehement opposition to screening come from Denmark, which has one of Europe's highest breast cancer mortality rates?

Denmark still has one of the highest breast cancer mortality rates in Europe, similar to that of Serbia. On the other hand, Finland and Sweden have among the lowest breast cancer mortality rates in Europe, although all the Nordic countries use identical breast cancer treatment guidelines. The health care systems among these countries are similar in most other aspects as well, except that Finland and Sweden introduced nationwide screening more than two decades ago. The implementation of organized nationwide screening should dramatically decrease breast cancer mortality throughout Denmark, as has already happened in Sweden and Finland.

Dean P, Tabár L, Yen MF. BMJ 2010 Rapid Response

“The 10-year fatality of screen-detected tumours is 50% lower than that of symptomatic tumours”

Steven Duffy, Professor of Statistics, St. Barts & the London Medical and Dental Schools. NHS BSP Annual Review 2008.

Nyhedscenter

Nyheder
- 2013
- 2012
- 2011
- 2010
- 2009
- 2008
- 2007
- 2006
- 2005
- 2004
- 2003
- 2002
- 2001
- 2000
- Alle nyheder

Nyheder på Widget
Abonnement
Nyhedsbreve
Sundhedsfaglig kommentar

Lavere overlevelse for danske kvinder med brystkræft

01. marts 2013

Kvinder i Danmark og Storbritannien har haft en lavere overlevelse efter brystkræft, end kvinder i Australien, Canada, Norge og Sverige i perioden 2000-2007. Det viser et nyt videnskabeligt studie, som offentliggøres i dag i British Journal of Cancer. Studiet er udført af International Cancer Benchmarking Partnership, som Sundhedsstyrelsen deltager i og har medfinancieret.

Tre-års overlevelsen for danske kvinder var 89 procent, hvilket var på niveau med Storbritannien, men lavere end i de andre fire lande, der lå på 91-94 procent. Studiet undersøgte, om forskellene mellem landene kunne forklares ved forskelle i sygdomsstadie på diagnosetidspunktet, og fandt at kun 30 procent af danske kvinder blev diagnosticeret i tidligt sygdomsstadie (stadium I), sammenlignet med 42-45 procent i de andre fem lande.

Ifølge forskerne kan en medvirkende forklaring på den lavere overlevelse blandt danske kvinder være, at kvinderne bliver diagnosticeret i senere stadier, formentlig på grund af at Danmark, som det eneste land i undersøgelsen, ikke havde udrullet et nationalt screeningsprogram for brystkræft før 2007.

Kvaliteten af behandlingen kan også forklare noget af forskellen mellem landene, men studiet peger på, at det først er fremmeste er tilfældet for Storbritannien, hvor den specifikke overlevelse for de enkelte sygdomsstadier generelt lå lavere end de øvrige seks lande.

Studiet er baseret på data fra 257.362 kvinder, der fik diagnosticeret brystkræft i årene 2000-2007, for danske kvinders vedkommende dog kun data for fire-års perioden 2004-2007.

Link

Link til artiklen i British Journal of Cancer

Fakta om screening for brystkræft

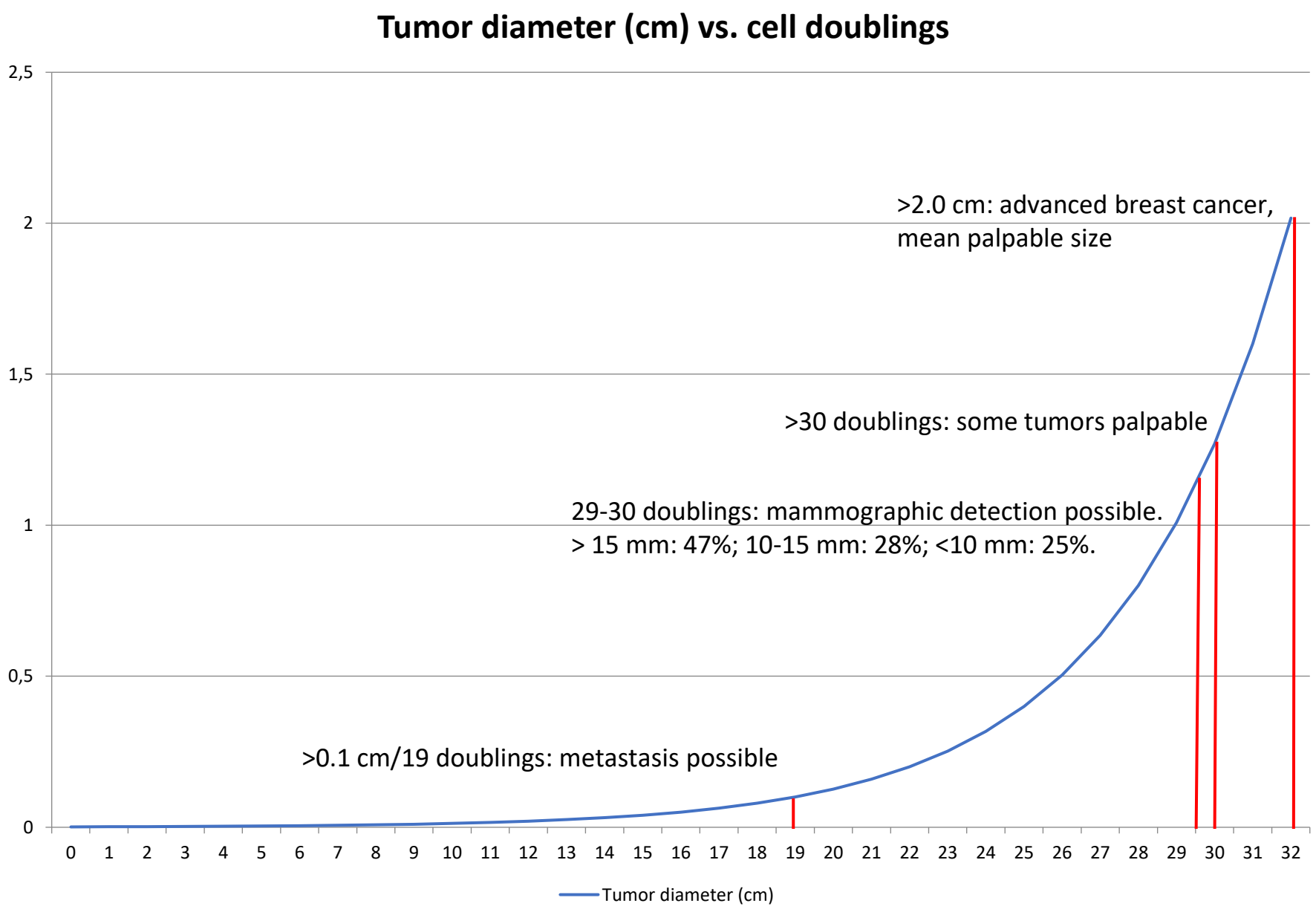
Screening for brystkræft med mammografi har siden 2009 været tilbudt til alle kvinder i Danmark i aldersgruppen 50-69 år. Mammografi er en standardiseret røntgenundersøgelse af brysterne, som tilbydes hvert andet år til kvinder uden symptomer. Mammografiscreening nedsætter ikke risikoen for brystkræft, men kan afsløre kræft i tidligere faser, det vil sige på et tidspunkt, hvor kvinden ikke har symptomer, og hvor risikoen for, at sygdommen har spredt sig, er mindre. Derved øges muligheden for helbredelse.

Kvaliteten af behandlingen følges blandt andet af en landsdækkende klinisk kvalitetsdatabase for brystkræft. Kræftbehandlingen i Danmark har fået et løft med indførelse af pakkeforløb, der har været med til at skabe hurtigere og veltilrettelagte forløb for en række patienter.

Information om brystkræftscreening på Sundhedsstyrelsens hjemmeside

Kontakt

Enhedschef
Søren Brostrøm
Sundhedsstyrelsen
Telefon: 72 22 78 67


Tumor diameter (cm) vs. cell doublings
2,5
2
1,5
1
0,5
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32
>2.0 cm: advanced breast cancer, mean palpable size
>30 doublings: some tumors palpable
29-30 doublings: mammographic detection possible.
> 15 mm: 47%; 10-15 mm: 28%; <10 mm: 25%.
>0.1 cm/19 doublings: metastasis possible
Tumor diameter (cm)

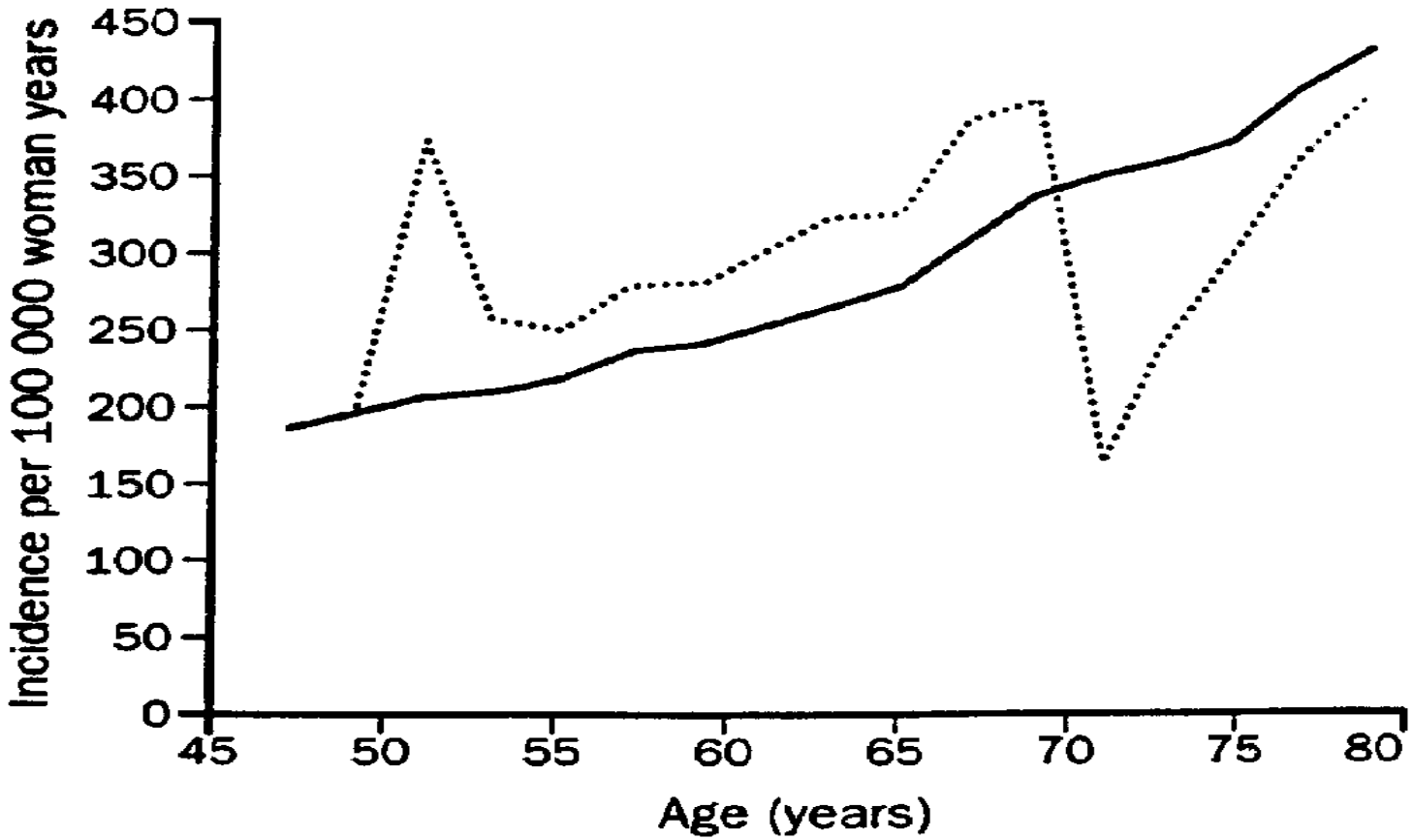
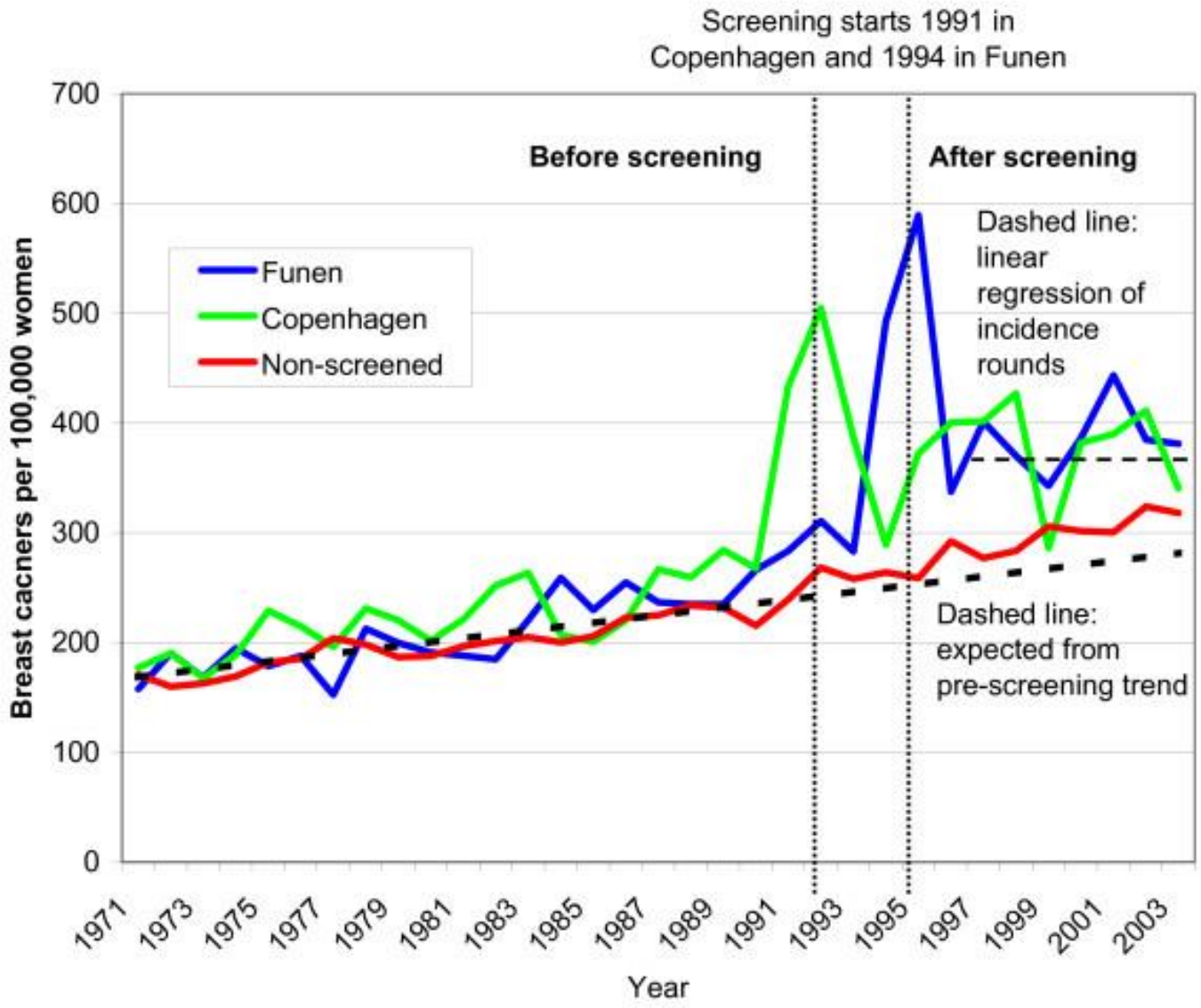


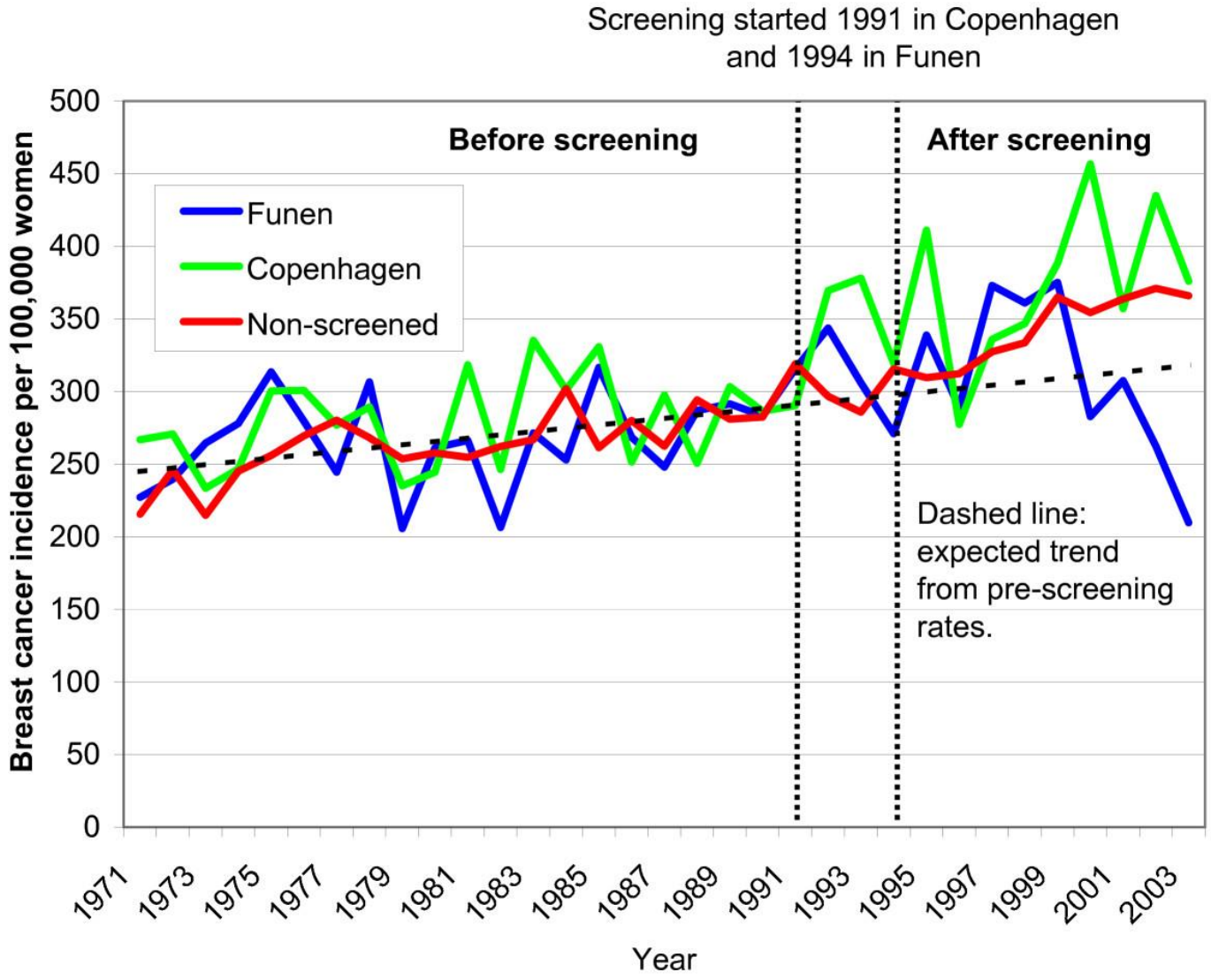
Figure: **Expected breast cancer incidence in 2-year age categories**

Solid line = not screened, dotted line = screened.

Boer et al. Lancet 1994; 343: 979.



Jørgensen KJ, Zahl PH, Gøtzsche PC. BMC Women's Health 2009 **9**:36


Screening started 1991 in Copenhagen
and 1994 in Funen
Before screening
After screening
Funen
Copenhagen
Non-screened
Dashed line:
expected trend
from pre-screening
rates.
Breast cancer incidence per 100,000 women
500
450
400
350
300
250
200
150
100
50
0
1971
1973
1975
1977
1979
1981
1983
1985
1987
1989
1991
1993
1995
1997
1999
2001
2003
Year

Flexible sigmoidoscopy versus faecal occult blood testing for colorectal cancer screening in asymptomatic individuals (Review)

Holme Ø, Bretthauer M, Fretheim A, Odgaard-Jensen J, Hoff G

THE COCHRANE COLLABORATION®

- Reduced incidence carries great weight
- Mechanism of effect differs fundamentally between programmes
- Which screening programmes we use is as much about timing and politics as about science and the benefit/harm balance

New UK leaflet - improvements

- Clearly states that there is a choice
- Clear presentation of the most important harm
- No direct encouragement to attend
- No indication that breast screening reduce the risk of mastectomy

New UK leaflet – pending improvements

- Remaining harms must also be clearly presented using absolute numbers
- The importance and long-term consequences of false positive findings must be clearly stated
- Harms are not risks
- Pre-assigned appointments must be abandonned

Conclusions on Marmot-report:

- The benefit was overestimated and not based on an observed effect in the UK, but extrapolations.
- The major harm is clearly visible in UK statistics, but was underestimated.
- Improved treatment is the major cause of observed reductions in breast cancer mortality in the UK.
- An improvement in all cause or all cancer mortality has never been demonstrated.

How was the benefit estimated?

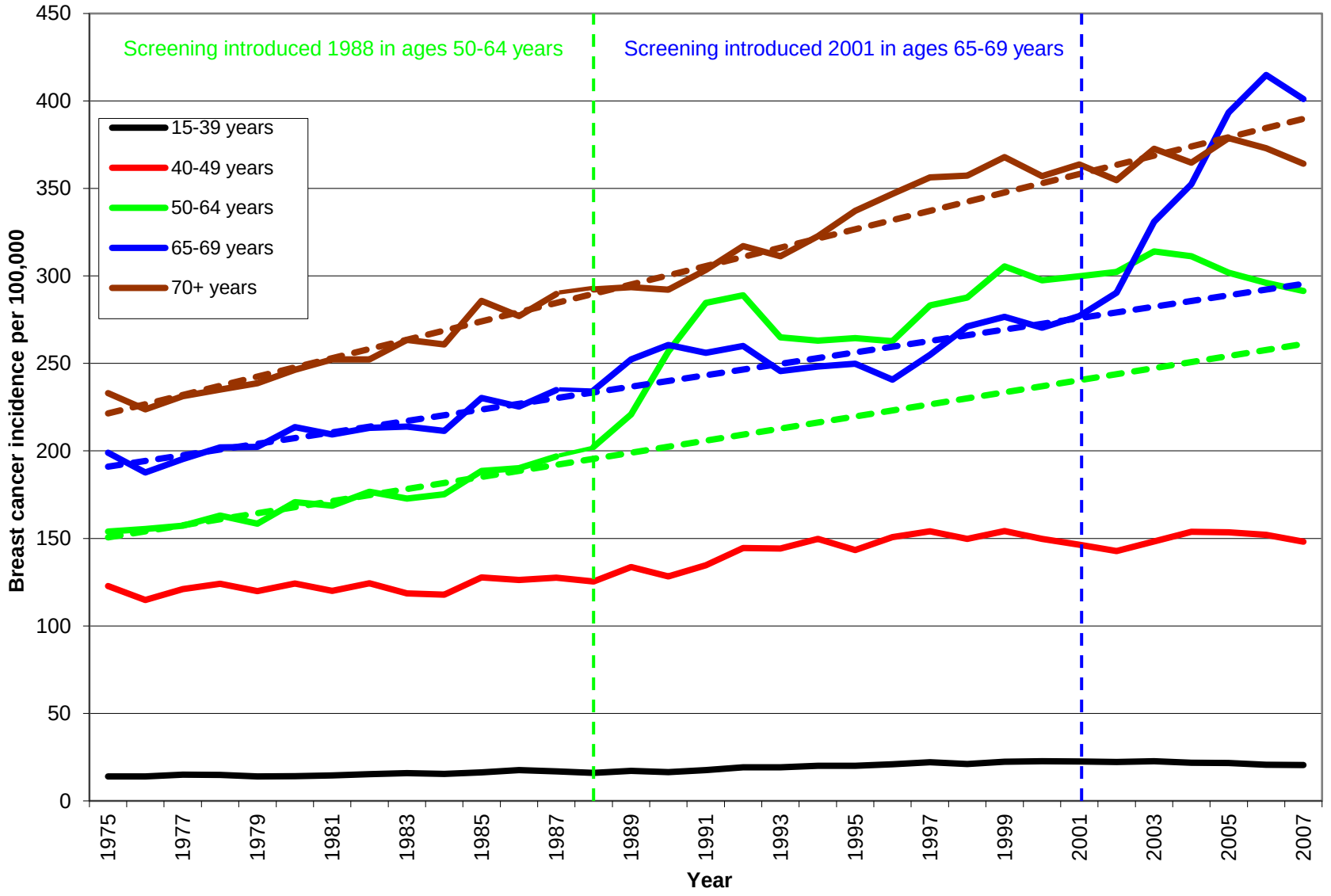
- ***Assumption 1:*** The randomised trials are equally reliable.
- ***Assumption 2:*** The effect can be extrapolated as unchanged 8-17 years beyond trial duration.
- ***Assumption 3:*** Identical effect today as then.
- ***Assumption 4:*** The effect remains unchanged 10 years beyond the screening age.
- ***Calculation:*** 20% fewer breast cancer deaths today than without screening in the age group 55-79 years (5843[1]) = 1461 fewer breast cancer deaths.

1: Average no. breast cancer deaths per year 2008-10: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/breast/mortality/uk-breast-cancer-mortality-statistics

How was overdiagnosis estimated?

- Modelling based on observed invasive breast cancer incidence in the UK.
- 2250 linear and Poisson regression models applied to data from 1975-2004 with various assumptions.
- Most model results estimated ~3000 overdiagnosed invasive breast cancers per year.
- 50-69 years: 23,297 invasive, 3,931 CIS. 19% ODX = 5,920 cases per year in the UK.[1]

1: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/breast/incidence/



Jørgensen KJ, Keen J, Gøtzsche PC. Radiology 2011; 260: 621-627