LRCB

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Effectiveness of breast cancer screening in women under 50

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Outline

- Scientific evidence
  - *Randomised controlled trials*
  - *Service screening programmes*

- US recommendations
- Communication issues

- Benefits and harms
- Cost-effectiveness

Randomised controlled trials

Mortality reduction – RCTs

Table 1. Pooled RRs for Breast Cancer Mortality From Mammography Screening Trials for All Ages

Age	Trials Included, *n*	RR for Breast Cancer Mortality (95% CrI)	NNI to Prevent 1 Breast Cancer Death (95% CrI)
39–49 y	8*	0.85 (0.75–0.96)	1904 (929–6378)
50–59 y	6†	0.86 (0.75–0.99)	1339 (322–7455)
60–69 y	2‡	0.68 (0.54–0.87)	377 (230–1050)
70–74 y	1§	1.12 (0.73–1.72)	Not available

CrI = credible interval; NNI = number needed to invite to screening; RR = relative risk.

* Health Insurance Plan of Greater New York (27), Canadian National Breast Screening Study-1 (28), Stockholm (26), Malmö (26), Swedish Two-County trial (2 trials) (26, 31), Gothenburg trial (30), and Age trial (29).

† Canadian National Breast Screening Study-1 (28), Stockholm (26), Malmö (26), Swedish Two-County trial (2 trials) (26, 31), and Gothenburg trial (30).

‡ Malmö (26) and Swedish Two-County trial (Östergötland) (26).

§ Swedish Two-County trial (Östergötland) (26).

Nelson et al, Ann Intern Med 2009;151:727-37

New trial

UK Age Trial

- Recruitment 1991-1996
- 160,921 women aged 40-41 at entry
- Individual randomisation stratified by GP practice
- Annual screens in intervention arm in 23 units

UK Age Trial

Effect of mammographic screening from age 40 years on breast cancer mortality at 10 years' follow-up: a randomised controlled trial

Sue M Moss, Howard Cuckle, Andy Evans, Louise Johns, Michael Waller, Lynda Bobrow, for the Trial Management Group*

Summary

Findings At a mean follow-up of 10·7 years there was a reduction in breast-cancer mortality in the intervention group, in relative and absolute terms, which did not reach statistical significance (relative risk 0·83 [95% CI 0·66–1·04], p=0·11; absolute risk reduction 0·40 per 1000 women invited to screening [95% CI –0·07 to 0·87]). Mortality reduction adjusted for non-compliance in women actually screened was estimated as 24% (RR 0·76, 95% CI 0·51–1·01).

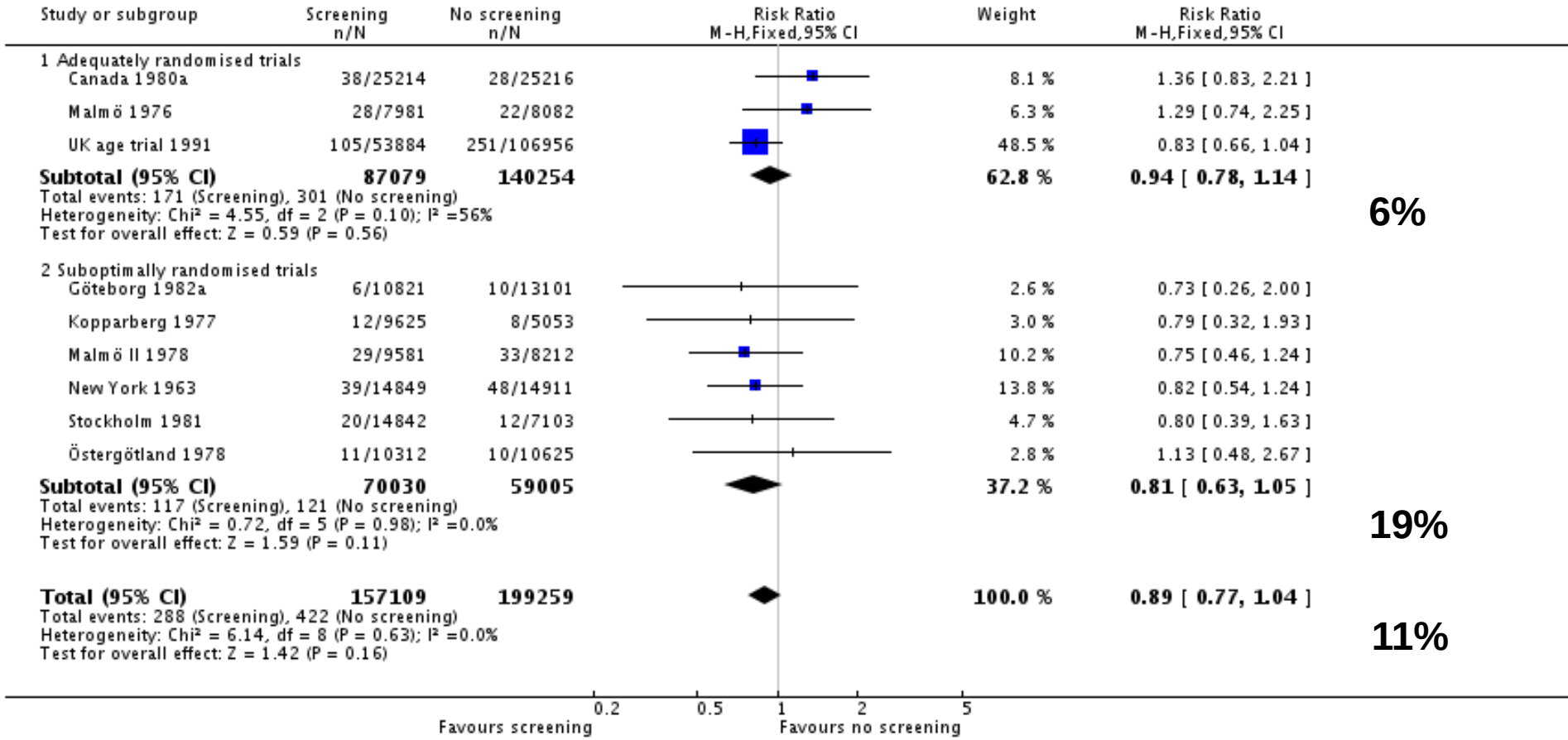
RR = 0.83 [95% CI 0.66 - 1.04]

17% reduction in bc mortality

Lancet 2006 December 9; 368: 2053-60

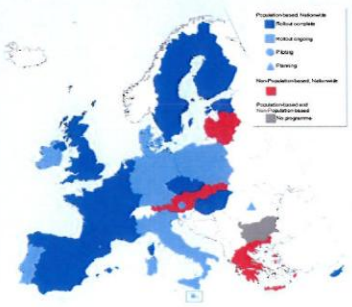
Cochrane review

Review: Screening for breast cancer with mammography
Comparison: 1 Screening with mammography versus no screening
Outcome: 3 Deaths ascribed to breast cancer, 7 years follow up, women below 50 years of age (Malmö 55)



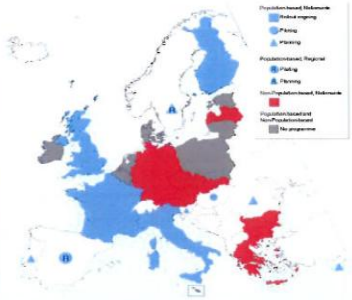
Screening in Europe

Breast Cancer Screening Programmes in the EU in 2007



Cervical Cancer Screening Programmes in the EU in 2007

Colorectal Cancer Screening Programmes in the EU in 2007



L 327/34 Official Journal of the European Union 16.12.2003

COUNCIL RECOMMENDATION
of 2 December 2003
on cancer screening
(2003/878/EC)

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 152(4), second subparagraph, thereof,

Having regard to the proposal from the Commission,

Having regard to the opinion of the European Parliament,

Whereas:

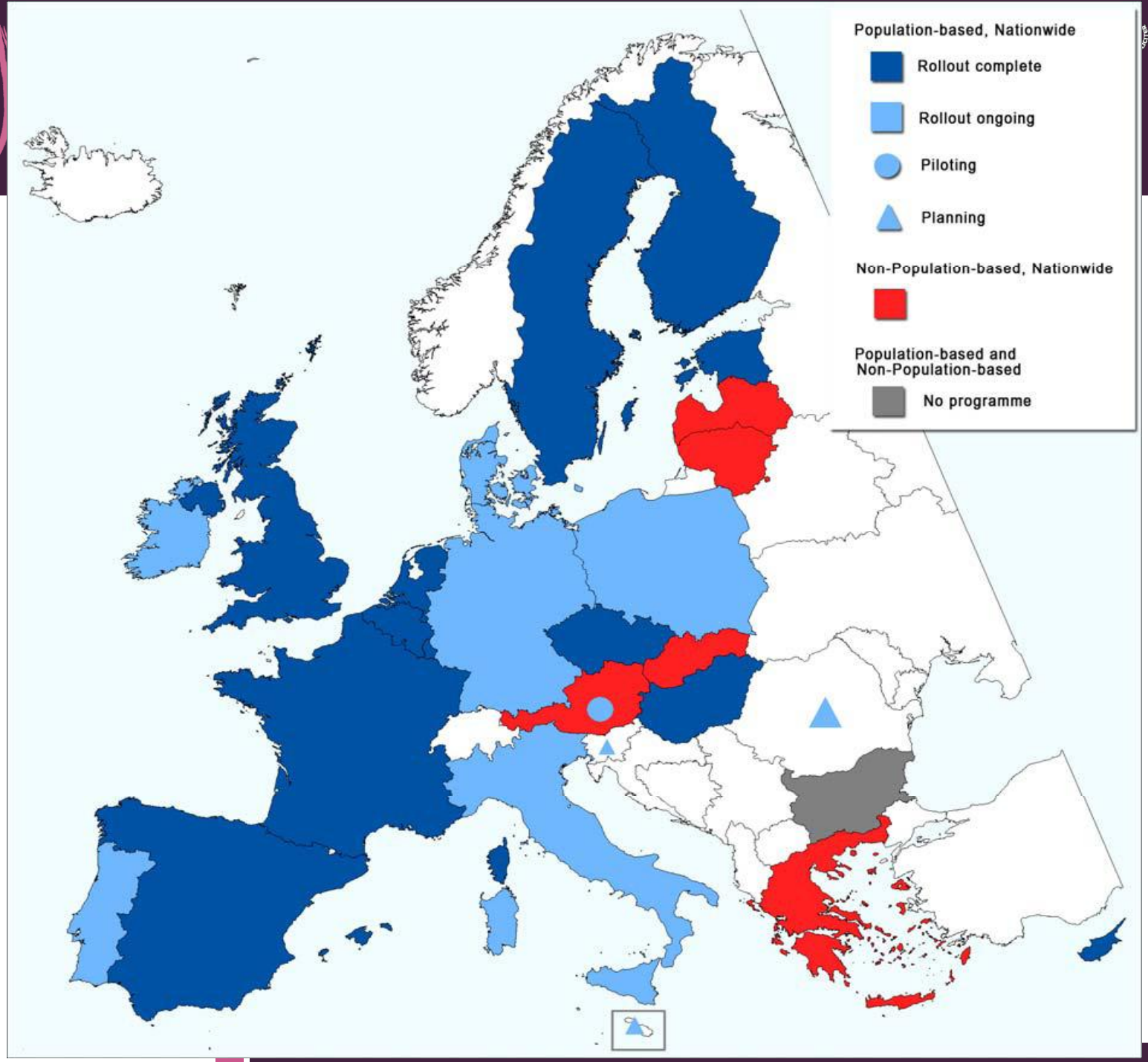
(1) Article 152 of the Treaty provides that Community action is to complement national policies and be directed towards improving public health, preventing human illness and diseases, and obviating sources of danger to human health. Such action shall cover the fight against the major health scourges, by promoting

Cancer screening in the European Union

Report on the implementation of the Council Recommendation on cancer screening

First Report

European Commission


Population-based, Nationwide
Rollout complete
Rollout ongoing
Piloting
Planning
Non-Population-based, Nationwide
Population-based and
Non-Population-based
No programme

Europe

Region/Country	*Start of programme*	*Screening test*[1]	*Age group targeted*	*Screening interval – years*	
				40-49	*50+*
Europe					
Denemark	1991	M	50-69	NVT	2
France	1989	M; KBO	50-74	NVT	2
Iceland	1987	M; KBO	40-69	2	2
Italy	2000	M	50-69	NVT	2
Luxemburg	1992	M	50-69	NVT	2
Netherlands	1989	M	50-74	NVT	2
Norway	1996	M	50-69	NVT	2
Portugal	1990	M; KBO; BZO	45-64	2	2
Spain	1990	M	45-69	2	2
Sweden	1986	M	40-74[2]	1.5	2
Switzerland	1999	M	50-69	NVT	2
United Kingdom	1988	M	50-64[3]	NVT	3

Service screening programmes

Should women under 50 be screened for breast cancer?

Despite some controversy in recent years, the majority of experts agree on the evidence for effectiveness of breast screening by mammography for women aged 50 years and above, but for those under 50 years, the picture is much less clear. However, the issue remains of importance both to policy makers and to individual women; although the incidence of breast cancer is lower at younger ages, the life years lost due to cancers diagnosed below 50 years amount to a third of all those lost due to the disease.

Moss S, Br J Cancer 2004;91:413-17

Informed Decision Making: Age of 50 Is Arbitrary and Has No Demonstrated Influence on Breast Cancer Screening in Women

OBJECTIVE. The article discusses the fact that for more than 20 years, there has been controversy concerning whether there is a benefit from mammographic screening for women ages 40–49. Based on a decision made many years ago to try to determine how menopause might influence the value of screening, the age of 50 was chosen as a surrogate for menopause. Despite the fact that there are no data to support this age as having any biologic relevance, it continues to be used as if the parameters and benefits of screening change abruptly at the age of 50.

c whether meno ause

Daniel B Kopans, MD

AJR: 185, 2005 177-182

The age of 50 years is used as a threshold for screening despite the fact that this cutoff has no biological or scientific basis

Kopans DB, Lancet Oncol 2010;11:1108-9.

A rationale for starting breast cancer screening under age 50

van Schoor et al, *Ann Oncol* 2008;19:1208-9.

Most countries which have implemented service screening on breast cancer invite women from age 50 [1]. With regard to younger women, findings from the UK age trial [2] showed the same trend as previous studies [3] that screening below age 50 has a positive effect on breast cancer mortality. For women screened at 40–49, Moss et al. [2] reported a breast cancer mortality reduction of 17% at 10-year follow up (relative risk 0.83, 95% confidence interval 0.66–1.04). The statistical nonsignificance of these results hampers decisions on lowering the starting age of mammographic screening. On the other hand, these results also cast doubts on the validity of age 50 as the lower age limit for breast screening.

We evaluated (surrogate) impact indicators for mortality reduction, such as screen-detected lymph node status, tumour size, and tumour stage; sensitivity of the mammographical screening test; mammographic density; and breast cancer occurrence along the continuum of age, to address the question whether breast screening should be extended to women under age 50. Our analysis thus addresses the matter of a gradual change with age in screening outcome measures instead of a sudden change, which seems to appear if data are analysed according to age dichotomised in <50 and ≥50.

Data were used from the Nijmegen breast-screening programme in The Netherlands [4]. Tumour stage II or worse represents breast cancer with either tumour size ≤2 cm and lymph node positivity or tumour size >2 cm; stage I represents breast cancer with tumour size ≤2 cm and a negative lymph node status; and ductal carcinoma *in situ* was classified as stage 0. We calculated the rate of invasive disease with lymph node positive breast cancer, the rate of invasive disease with a diameter

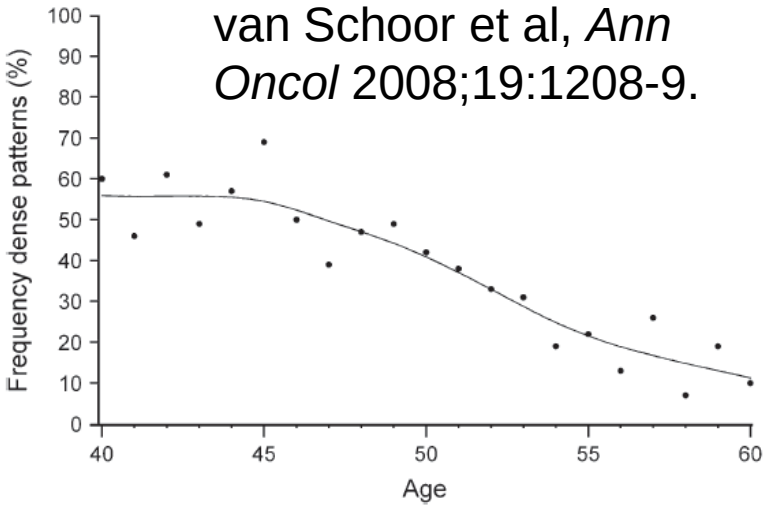


Figure 1. Proportion of women with mammographic dense breast patterns.

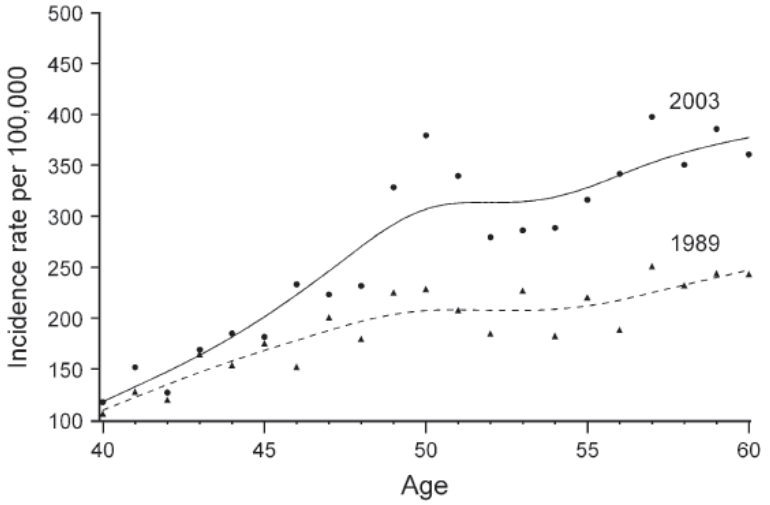


Figure 2. Breast cancer incidence rates in The Netherlands for 1989 and 2003.

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Service screening - Nijmegen

Effective biennial mammographic screening in women aged 40–49

Guido van Schoor [a,*], *Sue M. Moss* [b], *Johannes D.M. Otten* [a], *Rogier Donders* [a], *Ellen Paap* [a], *Gerard J. den Heeten* [c], *Roland Holland* [c], *Mireille J.M. Broeders* [a,c], *André L.M. Verbeek* [a,c]

Eur J Cancer 2010;46:3137-40

Service screening - Nijmegen

Table 1 – The effectiveness of mammographic screening on breast cancer mortality expressed by odds ratios, according to age at index-invitation.

Age at index-invitation	Cases	Referents	Odds ratio (95% CI)
	Screened (unscreened)	Screened (unscreened)	
40–49	50 (26)	596 (154)	0.50 (0.30–0.82)
50–59	69 (39)	350 (107)	0.54 (0.35–0.85)
60–69	53 (35)	107 (46)	0.65 (0.38–1.13)

Eur J Cancer 2010;46:3137-40.

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Service screening - Sweden

Original Article

Effectiveness of Population-Based Service Screening With Mammography for Women Ages 40 to 49 Years

Evaluation of the Swedish Mammography Screening in Young Women (SCRY) Cohort

Barbro Numan Hellquist, MSc[1]; Stephen W. Duffy, MSc[2]; Shahin Abdsaleh, MD, PhD[3]; Lena Björneld, RN[4]; Pál Bordás, MD[5]; László Tabár, MD, PhD[6]; Bedrich Viták, MD, PhD[7]; Sophia Zackrisson, MD, PhD[8]; Lennarth Nyström, PhD[9]; and Håkan Jonsson, PhD[1]

Cancer 2011;117:714–22

40-44	17% bc mortality reduction	RR = 0.83 (0.59-0.78)
45-49	32% bc mortality reduction	RR = 0.68 (0.54-0.75)

US Preventive Services Task Force recommendation

2009

In Reversal, Panel Urges Mammograms at 50, Not 40

By GINA KOLATA
Published: November 16, 2009

Most women should start regular breast cancer screening at age 50, not 40, according to new guidelines released Monday by an influential group that provides guidance to doctors, insurance companies and policy makers.

Enlarge This Image

Scott Dalton for The New York Times

The new recommendations, which do not apply to a small group of women with unusual risk factors for breast cancer, reverse longstanding guidelines and are aimed at reducing harm from overtreatment, the group says. It also says women age 50 to 74 should have mammograms less frequently — every two years, rather than every year. And it said doctors should stop teaching women to examine their breasts on a regular basis


SO, HELP ME HERE, DOC. THE GOVERNMENT EXPERTS AND INSURANCE FOLKS SAY I SHOULD GET A MAMMOGRAM AFTER 50 INSTEAD OF AFTER 40, AND A PAP SMEAR EVERY THREE YEARS AFTER 30 INSTEAD OF EVERY OTHER YEAR AFTER 30.
MY QUESTION IS ... WHERE EXACTLY DO YOU AND I FIT INTO THIS PICTURE?
www.penroseonpolitics.wordpress.com
PENROSE
11-24-09

Warner, NEJM 2011

Table 4. Guidelines for Breast-Cancer Screening.*

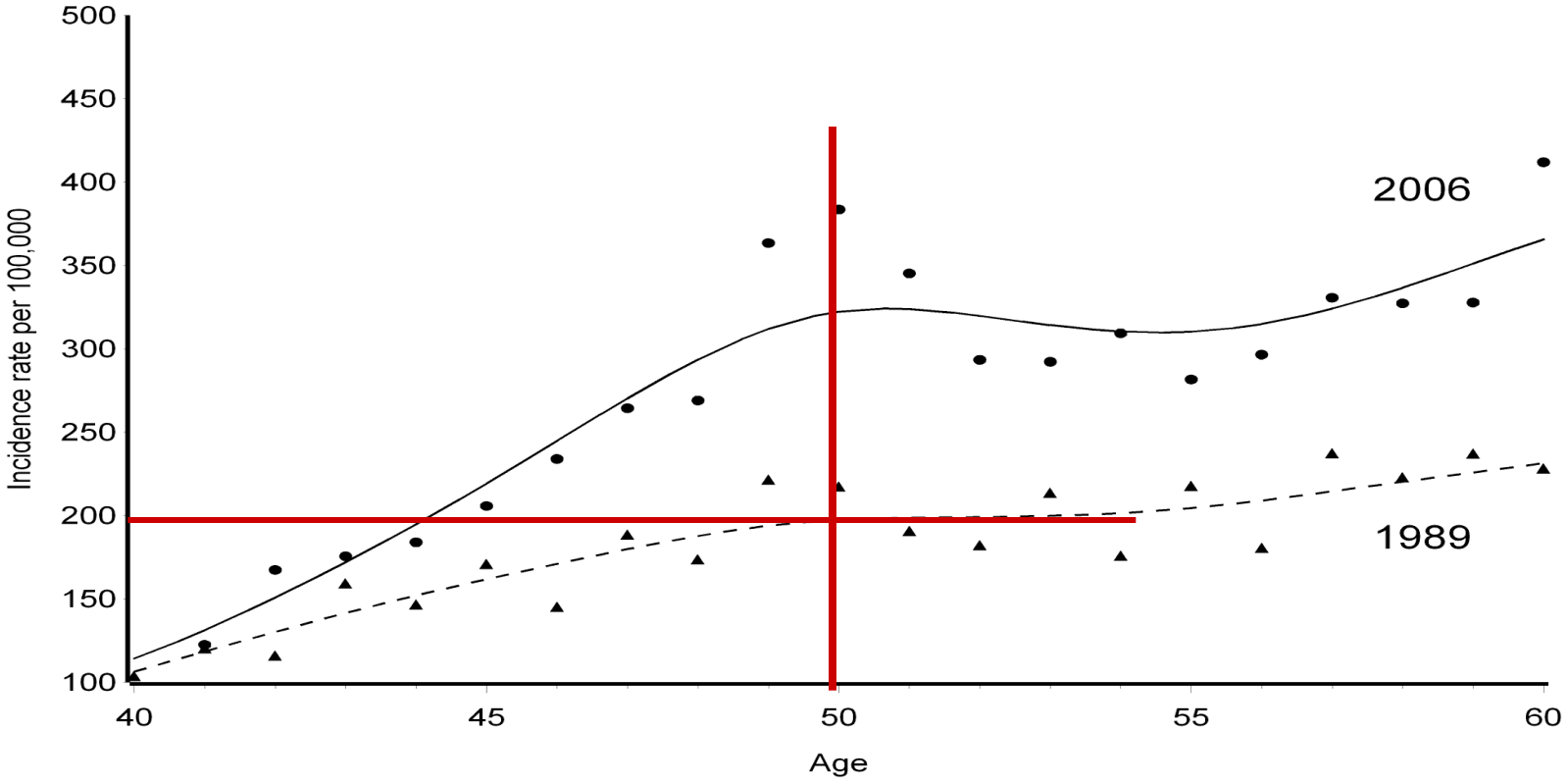
Organization	Year Guidelines Issued	Mammography	Clinical Breast Examination	Breast Self-Examination
USPSTF	2009	Age 50–74 yr, every 2 yr; age 40–49 yr and age ≥75 yr, individualize the decision (every 2 yr, if performed)	Insufficient evidence for recommendation	Not recommended
American Cancer Society	2010	Age ≥40 yr, annually†	Age 20–39 yr, every 3 yr Age ≥40 yr, annually	Optional, ≥20 yr of age
National Comprehensive Cancer Network	2011	Age ≥40 yr, annually†	Age 20–39 yr, every 1–3 yr Age ≥40 yr, annually	Optional, ≥20 yr of age
National Cancer Institute	2010	Age ≥40 yr, every 1–2 yr†	Age and frequency not stated	Optional
American College of Physicians	2007	Age 50–74 yr, every 1–2 yr‡; age 40–49 yr, individualize the decision (every 1–2 yr, if performed)	Not stated	Not stated
American College of Obstetricians and Gynecologists	2003	Age 40–49 yr, every 1–2 yr; age ≥50 yr, annually†	Age ≥20 yr, annually	Optional
American College of Radiology	2008	Age ≥40 yr, annually†	Not stated	Not stated
Canadian Task Force on Preventive Health Care	1998–2001	Age 50–69 yr, every 1–2 yr; age 40–49 yr, individualize the decision (every 1–2 yr, if performed)	Every 1–3 yr, with periodic health examinations, for ages <40 and >70 yr	Not recommended for women 40–69 yr of age Optional, ≥70 yr of age
National Health Service, United Kingdom	2011	Age 47–73 yr, every 3 yr	Not stated	Not stated

* USPSTF denotes U.S. Preventive Services Task Force.
† No upper age limit was specified.
‡ These recommendations have not been updated since 1989.

Screening in the Netherlands

Should we change our lower age limit?

New diagnoses breast cancer



European Journal of Cancer
Issue 18, 2010
By Helen Saul

Breast screening 'should be considered' in younger women

Biennial mammographic screening may halve the risk of dying from breast cancer among women aged 40-49, according to a study in the Netherlands. Researchers say in a forthcoming issue of *EJC (doi:10.1016/j.ejca.2010.09.041)* that their work 'adds convincing evidence of the effectiveness of biennial mammographic screening in women aged 40 to 49.'

The study included 272 breast cancer deaths; 1360 referents aged 40-69 were sampled from the population invited for screening.
The odds ratio (OR) for dying of breast cancer was calculated in screened versus unscreened women.

In women aged 40-49, the effect of screening was OR = 0.50, similar to that among those aged 50-59 (OR = 0.54) or 60-69 (OR = 0.65).

370.021 ondertekeningen

Borstkankeronderzoek vervroegen

Borstkankeronderzoek vindt pas vanaf 50 jaar standaard plaats.
Vele vrouwen van ver onder de 50 jaar worden echter geconfronteerd met deze ziekte, die vaak door vervroegd onderzoek veel eerder ontdekt had kunnen worden.
Natuurlijk is en blijft zelfonderzoek heel belangrijk, maar een mammografie of ander passend onderzoek laat meer zien dan een zelfonderzoek.

Wij pleiten er dus voor om het borstonderzoek door middel van een bij de leeftijd passend onderzoek tegelijk te laten starten en plaatsvinden met het maken van een uitstrijkje, dus vanaf 30-jarige leeftijd.

PETITIE

Wij

Nederlandse vrouwen, jonger, maar ook ouder dan 50 jaar

370.106 persons signed the petition

constateren

dat borstonderzoek pas vanaf 50-jarige leeftijd standaard bij iedere Nederlandse vrouw wordt uitgevoerd. Naar onze mening is dit veel te laat, omdat borstkanker helaas ook steeds vaker wordt vastgesteld bij vrouwen jonger dan 50 jaar.

en verzoeken

tot vervroeging van de standaard onderzoeksleeftijd en gelijkstelling van deze leeftijd aan de leeftijd voor het bevolkingsonderzoek naar baarmoederhalskanker

D66 wil borstonderzoek ook voor jonge vrouwen mogelijk maken

dinsdag 19 januari 2010 19:21

0 stemmen

Den Haag - Vrouwen moeten zich voortaan op jongere leeftijd kunnen laten screenen op borstkanker om zo de kans dat ze daaraan overlijden verder terug te dringen. Een meerderheid van de Tweede Kamer steunde dinsdag een voorstel van D66-Tweede Kamerlid Fatma Koser Kaya daartoe.

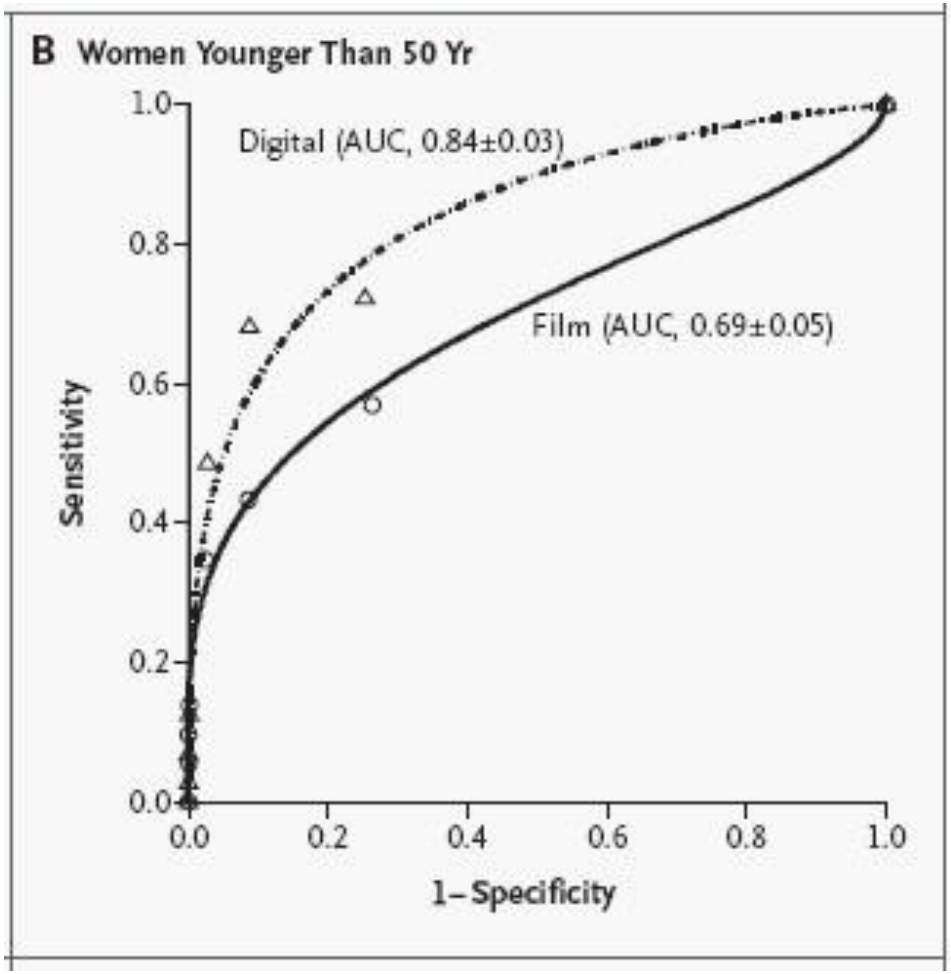
Koser Kaya: 'Onderzoek wijst uit dat door screening de sterfte aan borstkanker onder vrouwen afneemt. Immers, door vroegtijdige opsporing kunnen patiënten eerder worden behandeld, waardoor de genezingskans groter is. Vrouwen kunnen zich nu pas vanaf 50 jaar laten screenen. Als we die leeftijd verlagen, kunnen we er mogelijk voor zorgen dat nog minder vrouwen sterven aan borstkanker.'

De regering moet op verzoek van Koser Kaya ook komen met voorstellen om doorverwijzing en snelheid van handelen bij jonge vrouwen met borstkanker mogelijk te maken.

BUT

this is all based on film-screen mammography….

DMIST-trial



Pisano et al, Radiology 2008;246:376-83.

Europe

Studie (publicatie)	Periode	Leeftijd	Onderzoeken	Verwijscijfer (%) analoog	Verwijscijfer (%) digitaal	Detectiecijfer (%) analoog	Detectiecijfer (%) digitaal
Helsingborg, Zweden	2000-05	46-74	Vervolg	1,4	1,0	0,31	0,49
Florence, Italië	2004-05	50-69	Eerste Vervolg	7,8 3,4	7,5 4,2	0,82 0,55	0,74 0,72
Vestfold, Noorwegen	2004-05	50-69	Eerste	4,2	4,1	0,65	0,77
Londen, Ver. Koninkrijk	2006-07	50-70	Eerste + vervolg	4,4	4,8	0,65	0,68
Barcelona, Spanje (Sala, 2009)	2002-07	50-69	Eerste Vervolg	11,5 3,6	11,1 2,4	0,4 0,4	1,1 0,2
Utrecht, Nederland (Karssemeijer, 2009)	2003-08	50-75	Eerste Vervolg	2,3 1,2	4,4 1,7	0,62 0,49	0,77 0,55

Table 2

Logistic Regression Model for Cancer Detection*

Variable	Cancer		Crude OR†	Adjusted OR*
	No	Yes		
Technology				
SFM	170421	770	1.040 (0.911, 1.187)	1.048 (0.847, 1.298)
Full-field DM	71337	310	1.000	1.000
Women's screening mammogram				
1	89908	472	1.196 (1.003, 1.426)	1.579 (1.233, 2.022)
2	65942	242	0.836 (0.687, 1.018)	1.194 (0.937, 1.522)
3	47184	196	0.946 (0.770, 1.163)	1.215 (0.959, 1.539)
≥4	38724	170	1.000	1.000
Age at screening (y)				
45–49	22220	70	0.561 (0.426, 0.739)	0.440 (0.324, 0.597)
50–54	64882	247	0.678 (0.561, 0.820)	0.554 (0.451, 0.680)
55–59	62729	244	0.693 (0.573, 0.838)	0.614 (0.506, 0.747)
60–64	58250	330	1.009 (0.844, 1.208)	0.897 (0.746, 1.079)
65–69	33677	189	1.000	1.000
Radiology unit screening round				
1st	43207	267	1.373 (1.177, 1.601)	1.053 (0.806, 1.377)
2nd	53895	204	0.841 (0.711, 0.994)	0.753 (0.583, 0.972)
3rd	51347	189	0.818 (0.689, 0.971)	0.738 (0.585, 0.931)
≥4th	93309	420	1.000	1.000

* Model adjusted according to variables in the Table and program. Each mammogram has been considered an independent observation.

† Data in parentheses are 95% CIs.

Sala et al, Radiology 2011

Conclusions

Screening with digital mammography

- Diagnostic performance at least equal
- Reduction in mortality not yet known

Decision on screening younger women

- Breast cancer burden
- Questions:
    - Balance benefits and harms
    - Radiation risk
    - Cost-effectiveness

Benefits and harms by starting ages

		Potential Benefits (vs. no screening)			Potential Harms	
Strategy	**Average Screens/ 1000**	**% Mortality Reduction**	**Deaths Averted/ 1000**	**Life Years Gained per 1000**	**# False positives/ 1000**	**# extra biopsies/ 1000**
Biennial						
B 40-69	**13865**	**16%**	**6.1**	**120**	**1250**	**88**
B 45-69	**11771**	**17%**	**6.2**	**116**	**1050**	**74**
B 50-69	**8944**	**15%**	**5.4**	**99**	**780**	**55**
B 55-69	**6941**	**13%**	**4.9**	**80**	**590**	**41**
B 60-69	**4246**	**9%**	**3.4**	**52**	**340**	**24**
Annual						
A 40-69	**27583**	**22%**	**8.3**	**164**	**2250**	**158**
A 45-69	**22623**	**22%**	**8.0**	**152**	**1800**	**126**
A 50-69	**17759**	**20%**	**7.3**	**132**	**1350**	**95**
A 55-69	**13003**	**16%**	**6.1**	**102**	**950**	**67**
A 60-69	**8406**	**12%**	**4.6**	**69**	**600**	**42**

Mandelblatt et al, Ann Intern Med 2009

Population-based mammography screening below age 50: balancing radiation-induced *vs* prevented breast cancer deaths

R de Gelder*[,1], G Draisma[1], EAM Heijnsdijk[1] and HJ de Koning[1]

[1]*Erasmus MC, Department of Public Health, P.O. box 2040, 3000 CA, Rotterdam, The Netherlands*

Yaffe & Mainprize, Radiology 2011

"The risk of radiation-induced breast cancer should not be a deterrent from mammographic screening of women over the age of 40 years"

Personalizing Mammography by Breast Density and Other Risk Factors for Breast Cancer: Analysis of Health Benefits and Cost-Effectiveness

John T. Schousboe, MD, PhD; Karla Kerlikowske, MD, MS; Andrew Loh, BA; and Steven R. Cummings, MD

Ann Intern Med 2011;155:10-20.

Stratifying women according to their risk of breast cancer – will personalised screening become the new paradigm?

Thank you for your attention!