WORKSHOP CONGIUNTO ONS - GISMa

gisma
gruppoitalianoscreening
mammografico

OSSERVATORIO
NAZIONALE
SCREENING

Torino 25 settembre 2013

Screening mammografico: conoscenza scientifica, controversie e incertezze

La comunicazione per una decisione consapevole

Eugenio Paci

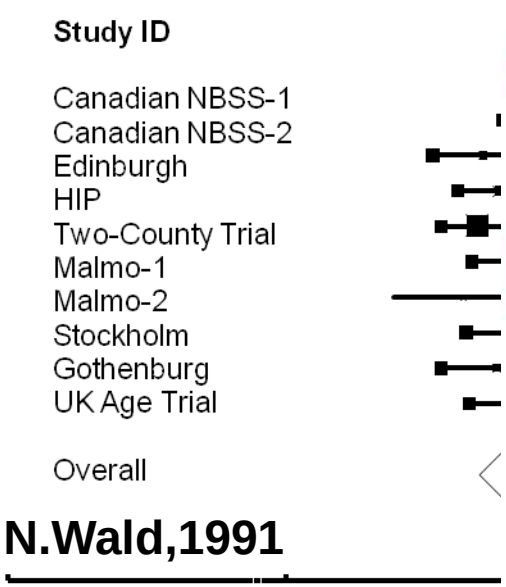
SC Epidemiologia Clinica e Descrittiva

ISTITUTO PER LO STUDIO
E LA PREVENZIONE ONCOLOGICA

SST Servizio Sanitario della Toscana

Istituto Toscano Tumori

Storia e attualità

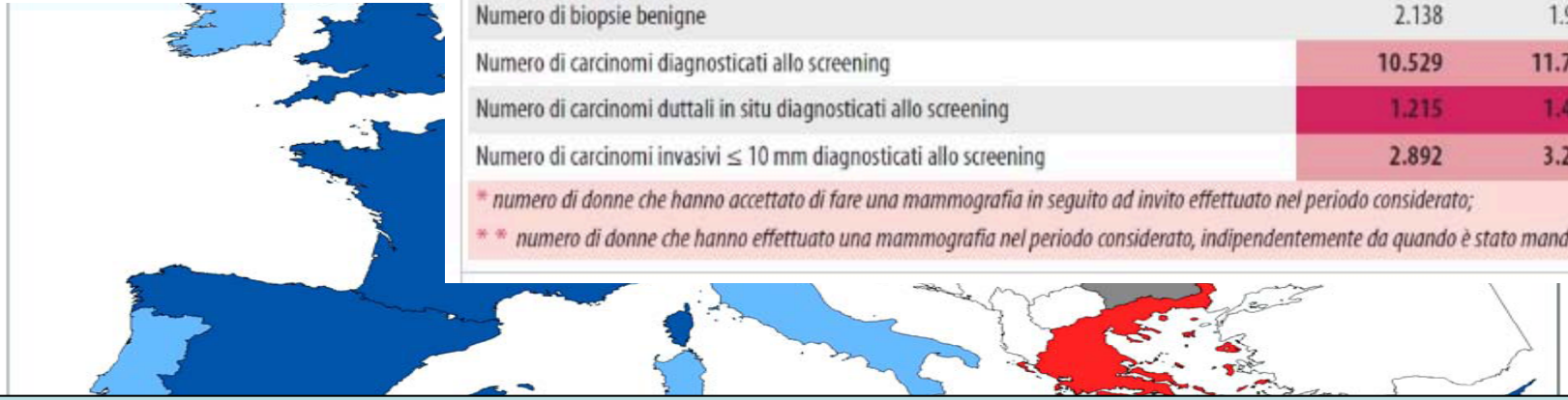


ITALIAN MONITORING CENTRE (ONS)

	2005-2006	2007-2008	2009
Numero totale di donne invitate	3.882.465	4.618.502	2.464.701
Numero di donne aderenti all'invito *	2.225.032	2.579.655	1.370.272
Adesione all'invito	57%	56%	56%
Classi di età			
50-54	54%	53%	52%
55-59	60%	59%	59%
60-64	60%	60%	60%
65-69	56%	56%	58%
Numero di donne esaminate (nel periodo considerato) * *	2.229.568	2.554.759	
Numero di donne richiamate per approfondimenti	139.617	144.049	
Percentuale di donne richiamate per approfondimenti	6,3%	5,6%	
Numero di biopsie benigne	2.138	1.964	
Numero di carcinomi diagnosticati allo screening	10.529	11.707	
Numero di carcinomi duttali in situ diagnosticati allo screening	1.215	1.421	
Numero di carcinomi invasivi ≤ 10 mm diagnosticati allo screening	2.892	3.258	

** numero di donne che hanno accettato di fare una mammografia in seguito ad invito effettuato nel periodo considerato;*

** * numero di donne che hanno effettuato una mammografia nel periodo considerato, indipendentemente da quando è stato mandato l'invito.*



26 European countries, 18 provided data for the EUNICE survey
26.9 millions of women, most 50-69 years old

Figure 3 a. Breast screening programmes in the European Union in 2007, by programme type (population-based; non-population-based; no programme or unknown) and country implementation status (population-based: nationwide or regional, rollout complete or ongoing, , piloting and/or planning; non-population-based: nationwide or regional). For definitions see the text (section 2.3).

Source: European Commission (DG SANCO, 2007); IARC (ECN and EUNICE projects, 2007)

RECOMMENDATIONS ON CANCER SCREENING IN THE EUROPEAN UNION PREPARED BY THE ADVISORY COMMITTEE ON CANCER PREVENTION

L 327/34 EN Official Journal of the European Union 16.12.2003

COUNCIL RECOMMENDATION
of 2 December 2003
on cancer screening

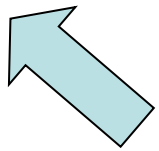
(2003/878/EC)

Screening is, however, testing of healthy people for diseases which have so far not given rise to symptoms. Aside from its beneficial effect on the disease specific mortality or incidence, screening might therefore also have some negative side effects for the screened population.

Health care providers should know all the potential benefits and risks of screening

for a given cancer site before embarking on new cancer screening programmes. For the informed public of today, it is furthermore necessary to present these benefits and risks in a way which allows the individual citizen to decide on participation in the screening programmes for her or himself.

The purpose of this document is to give recommendations on cancer screening in the European Union. These recommendations address the people, the politicians and the health administrations of the Member States, the European Commission and the European Parliament



2012 Volume 19 Suppl 1

Journal of Medical Screening

Guest Editors: Allan Hackshaw and Stephen Duffy

Review co-ordinators: E Paci, M Broeders, S Hofvind and SW Duffy

Royal Society of Medicine Press I

ORIGINAL ARTICLE

Summary of the evidence of breast cancer service screening outcomes in Europe and first estimate of the benefit and harm balance sheet

EUROSCREEN Working Group

J Med Screen 2012;**00**:1–9
DOI: 10.1258/jms.2012.012077

ORIGINAL ARTICLE

Communicating the balance sheet in breast cancer screening

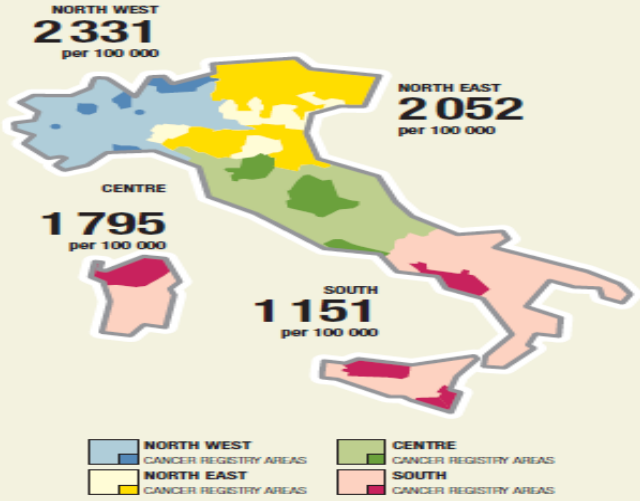
Livia Giordano, Carla Cogo, Julietta Patnick, Eugenio Paci and the Euroscreen Working Group (members listed at the end of the paper)

J Med Screen 2012;**00**:1–5
DOI: 10.1258/jms.2012.012084

Il Contesto

Tumore della mammella femminile (ICD-10 = C50)

Female breast cancer



Complete prevalence by sex, age and years since diagnosis
Pool of Cancer Registries, 01.01.2006 (proportion per 100 000)

Years since diagnosis	Age class				
	0-44	45-59	60-74	75+	All ages
♦ FEMALE					
≤ 2 years	62	453	599	558	290
≤ 5 years	121	1 054	1 444	1 330	674
≤ 10 years	153	1 724	2 551	2 487	1 147
≤ 15 years	163	2 064	3 322	3 356	1 457
≤ 20 years	164	2 202	3 851	3 995	1 651
Complete	**164**	**2 254**	**4 371**	**4 984**	**1 869**
(95%CI)	*(160 - 168)*	*(2232 - 2276)*	*(4339 - 4404)*	*(4943 - 5025)*	*(1860 - 1878)*

Complete prevalence by sex, age and macro-area
01.01.2006 (proportion per 100 000)

Macro-area	Age class				
	0-44	45-59	60-74	75+	All ages
♦ FEMALE					
North West	189	2 552	5 016	5 728	2 331
North East	170	2 432	4 716	5 340	2 052
Centre	161	2 215	3 991	4 540	1 795
South	136	1 664	3 122	3 436	1 151

POPOLAZIONE RESIDENTE IN ITALIA, 1 GENNAIO 2006

58 751 711

PERSONE CON TUMORE

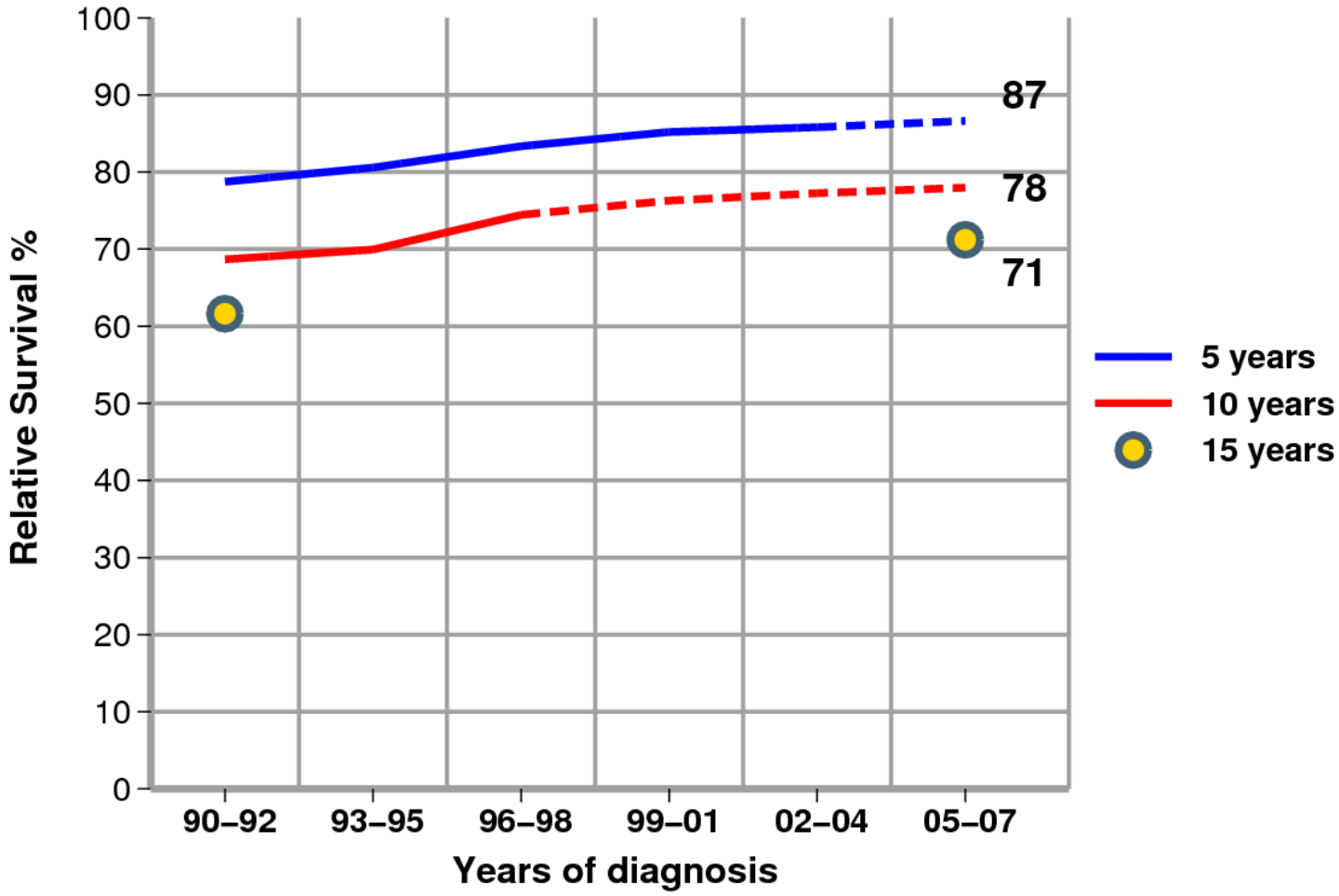
2 243 953

PERSONE CON TUMORE DELLA MAMMELLA

522 235

POOL AIRTUM 90-07

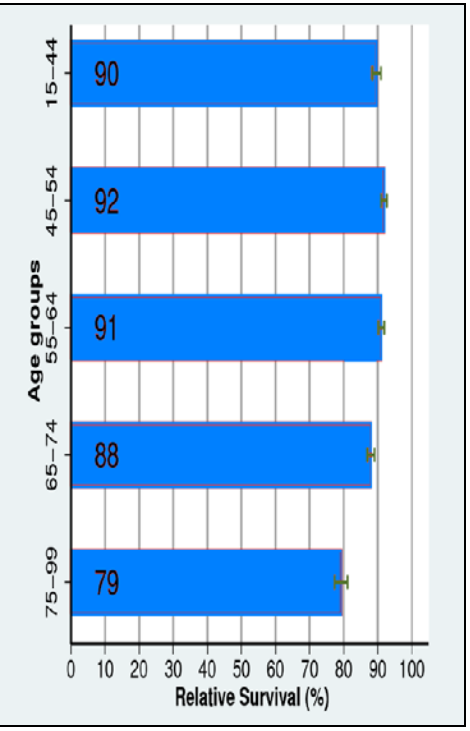
Sopravvivenza relativa a 5, 10, 15 anni dalla diagnosi standardizzata



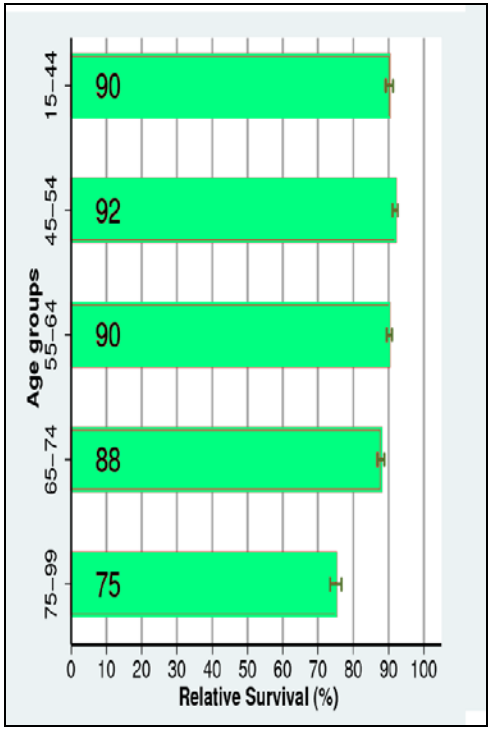
POOL AIRTUM 00-04

Sopravvivenza relativa a 5 anni dalla diagnosi per età

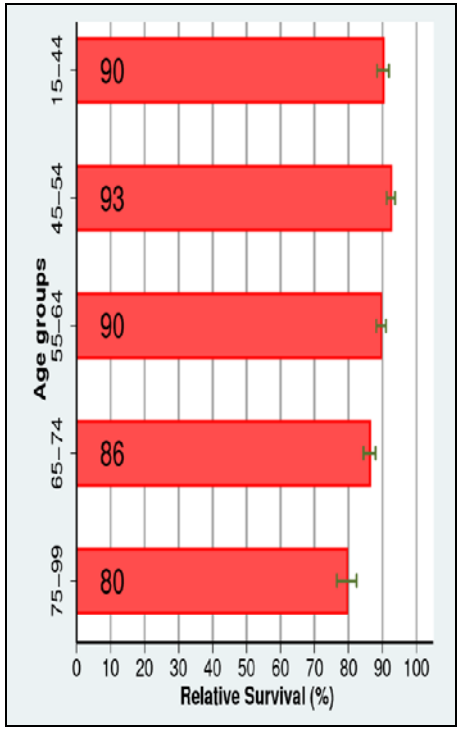
Nord-Ovest



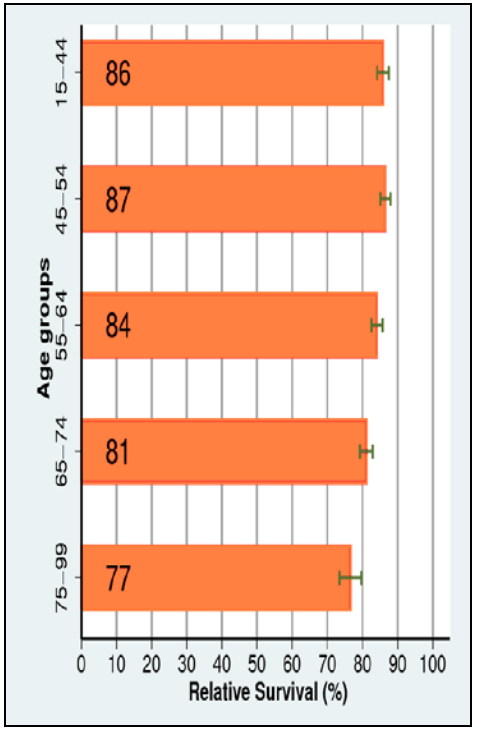
Nord-Est



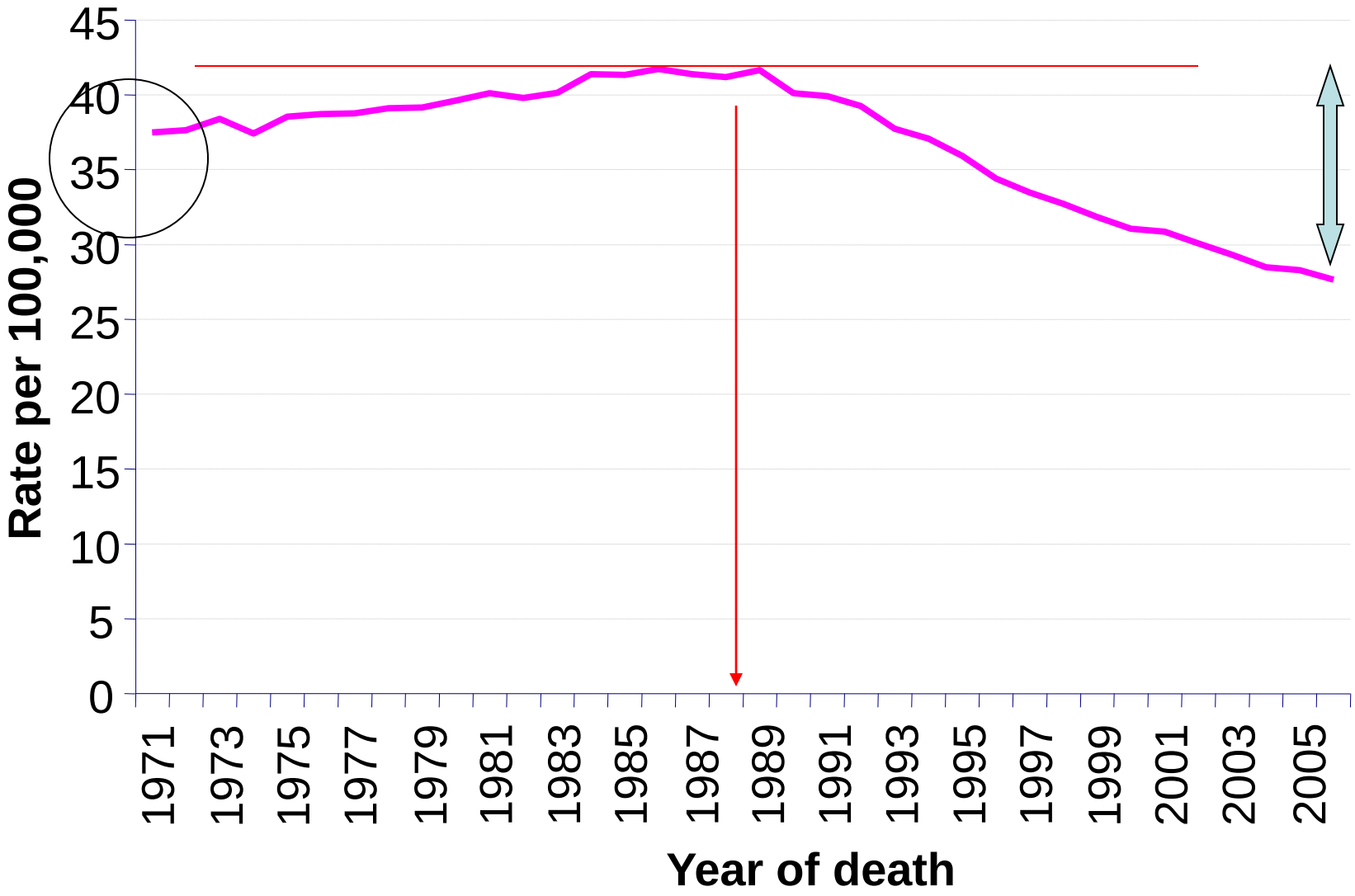
Centro



Sud



Age-standardised (European) mortality rates, breast
Breast cancer , females, UK 1971-2006



Otten et al. International Jurnal of Cancer 2008

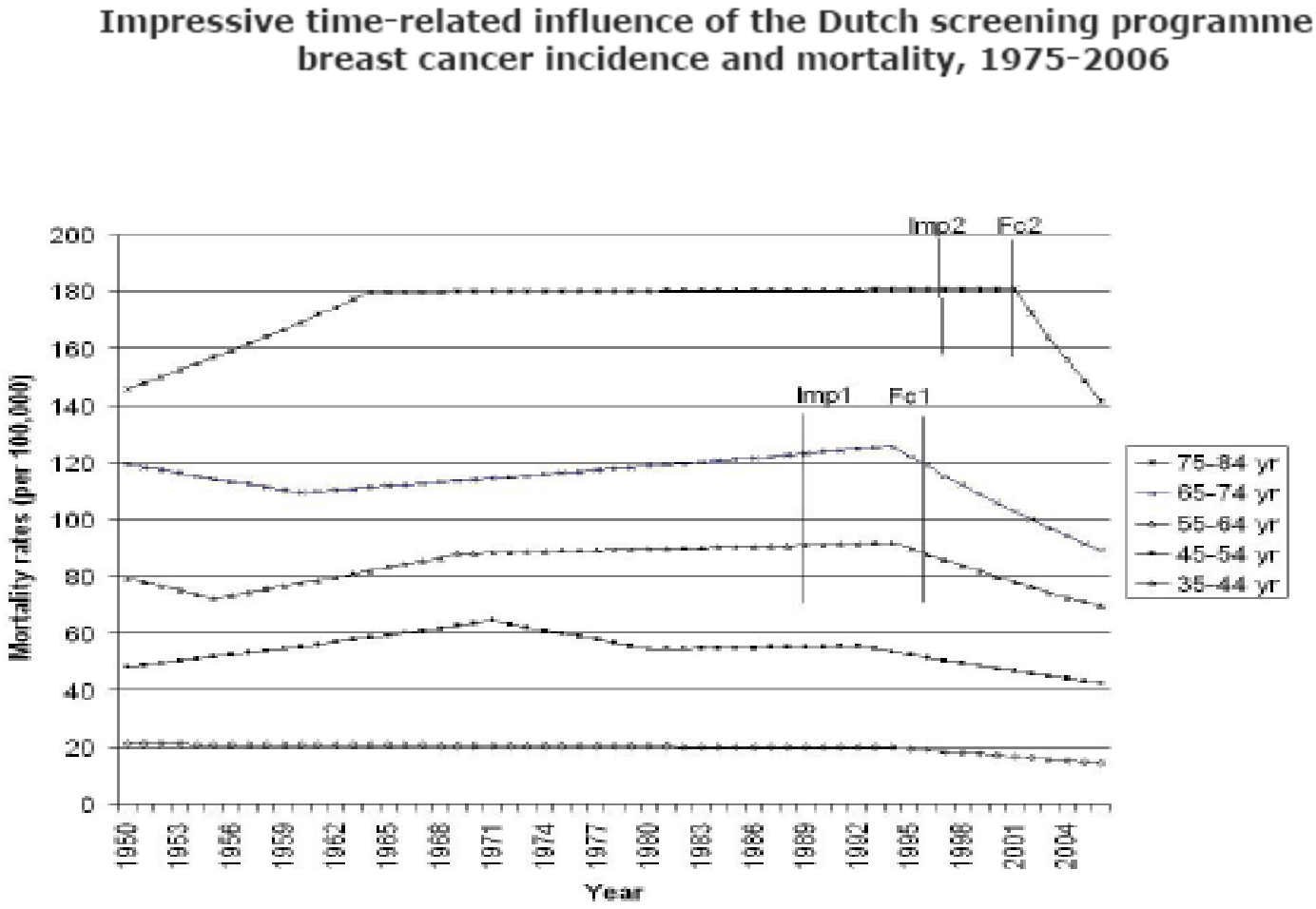
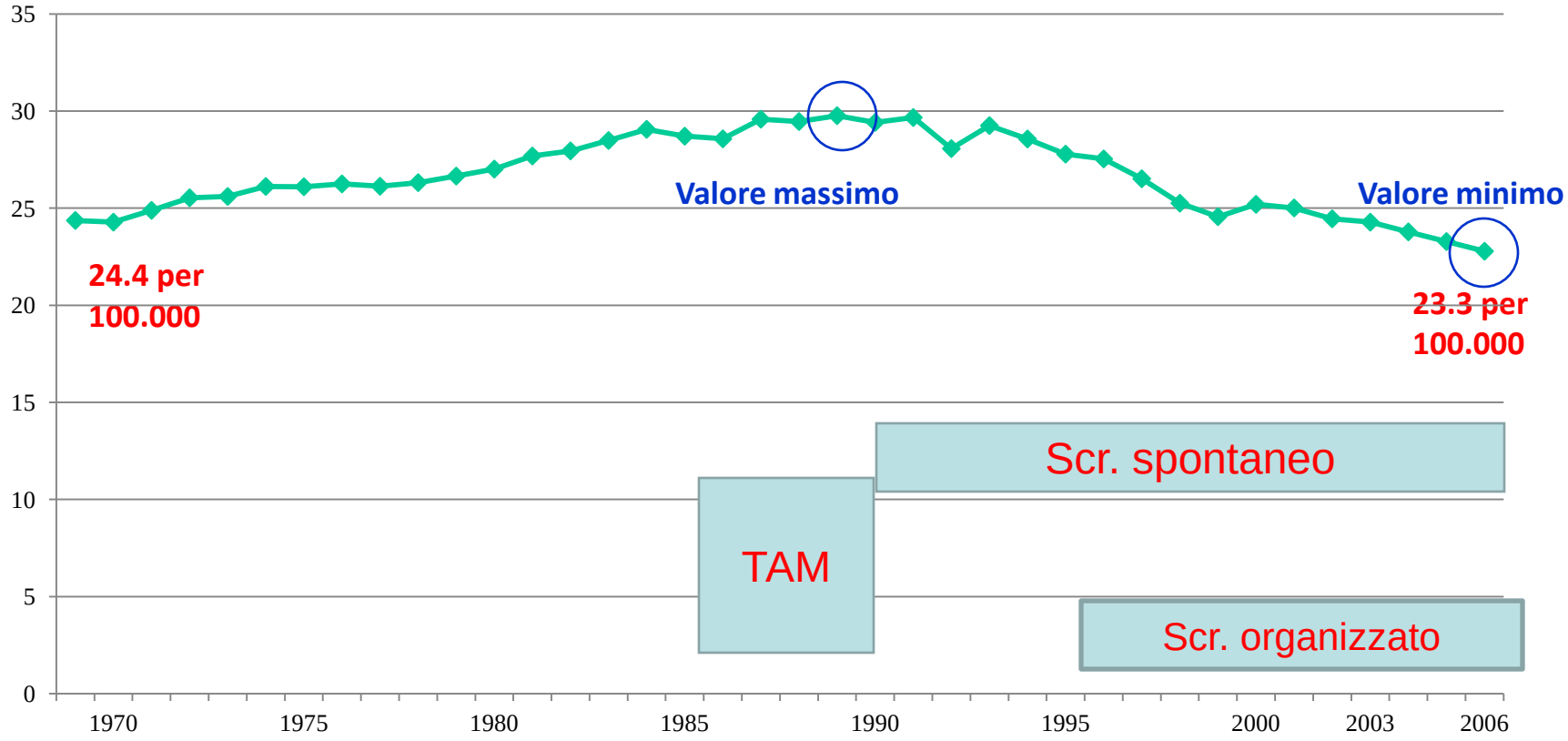


Figure 2. Age-adjusted (European standard population) breast cancer mortality rates per 100,000 women aged 35-84 in the Netherlands. Coverage population 50-69 years: Start implementation in 1989 (Imp1); percentage of targeted women annually invited: 11% ('90), 26% ('91), 48% ('92), 69% ('93), 77% ('94), 88% ('95) to full capacity in '96 (Fc1) Coverage population 70-74 years: Start implementation in 1997 (Imp2); percentage of targeted women annually invited: 26% ('98), 86% ('99), 91% ('00) to full capacity in '01 (Fc2)

254x180mm (96 x 96 DPI)

Tassi standardizzati di mortalità per tumore della mammella

(Italia 0-99 anni) –ISS ISTAT IMPATTO



Tassi standardizzati * 100.000 - Popolazione standard: Europa

La copertura dello screening: il problema dell'analisi dei trend geografici

(100% è l'incidenza 50-74 anni nella popolazione)

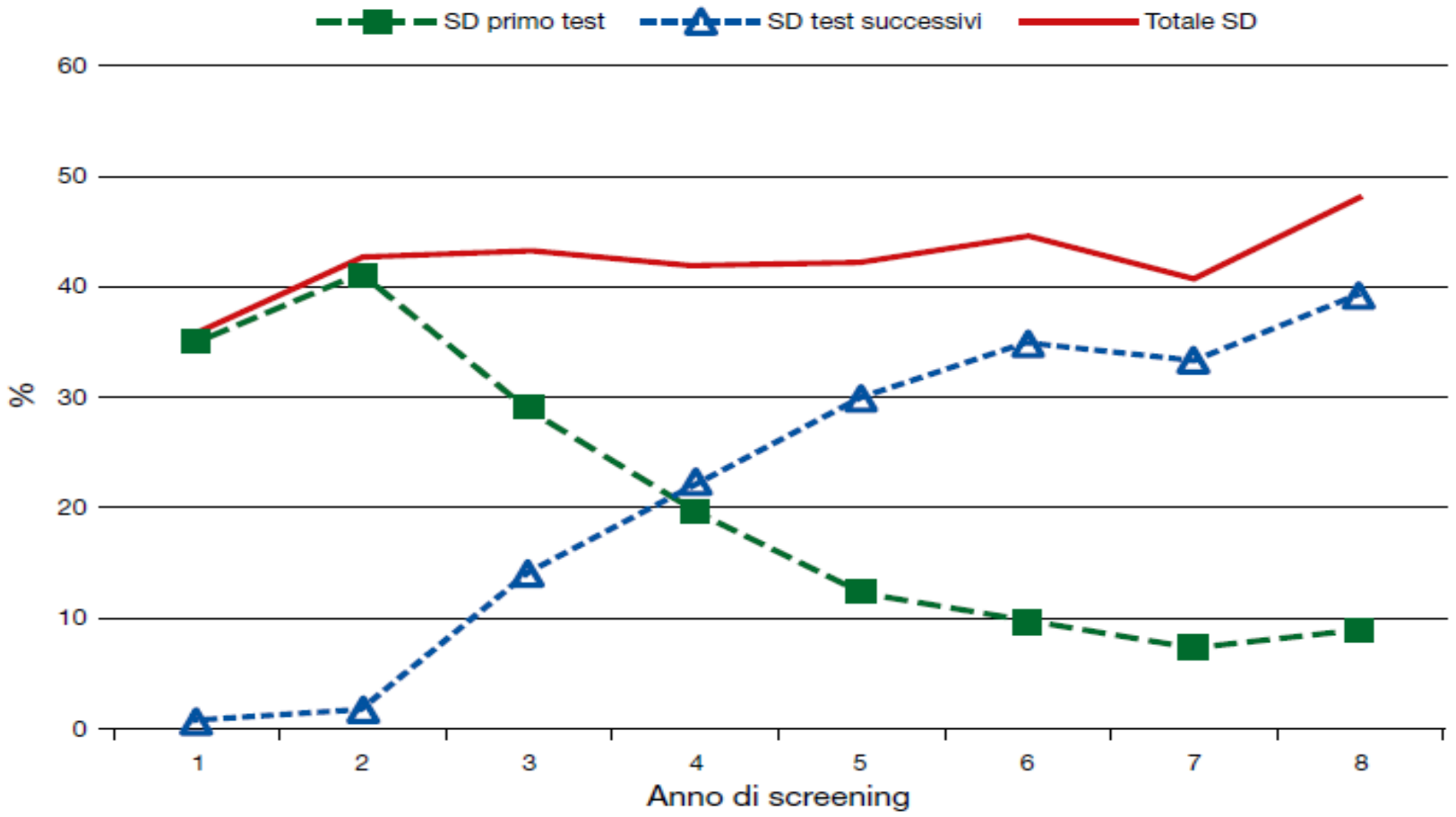
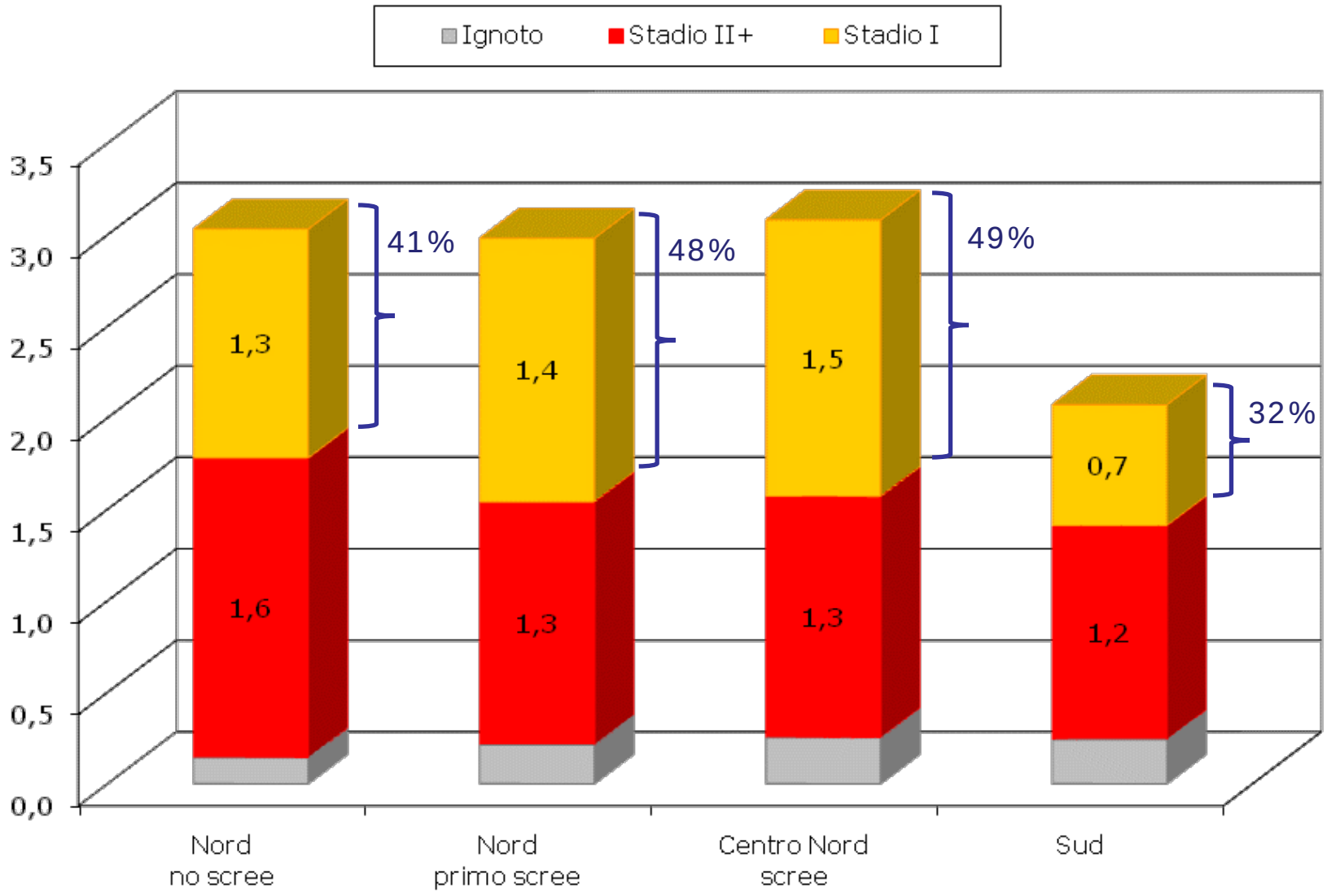


Figura 3. Proporzione (%) di cancri incidenti screen-detected (SD) al primo test e ai test successivi per anno di screening.

Tassi di incidenza per stadio del tumore e per ripartizione. Età 50-69 anni.



Lo screening spontaneo e lo screening organizzato

- Lo screening organizzato aggiunge il suo impatto a quello dello screening spontaneo , forse con diversa sensibilità , specificità, sovradiagnosi e efficacia
- Lo screening spontaneo è raramente valutato, ma è ipotizzabile un effetto sull'incidenza e mortalità negli anni 90.
- La riduzione di mortalità osservata dal 1990 in Italia per area geografica non può essere attribuita ai programmi di screening che si sono estesi progressivamente e si aggiungono all'impatto dei trattamenti e dello screening spontaneo.

Protagonisti della controversia

- Cochrane group e altri 2001-2013
- UK independent panel 2012
- EUROSCREEN 2012

- Un quadro a parte gli studi americani, in particolare Welch,2012

Independent UK Panel, The Lancet 2012

The benefits and harms of breast cancer screening

An assessment by the Independent UK Panel on Breast Cancer Screening

Simon Thompson
University of Cambridge, UK

IBSR

The Controversy

Benefits:

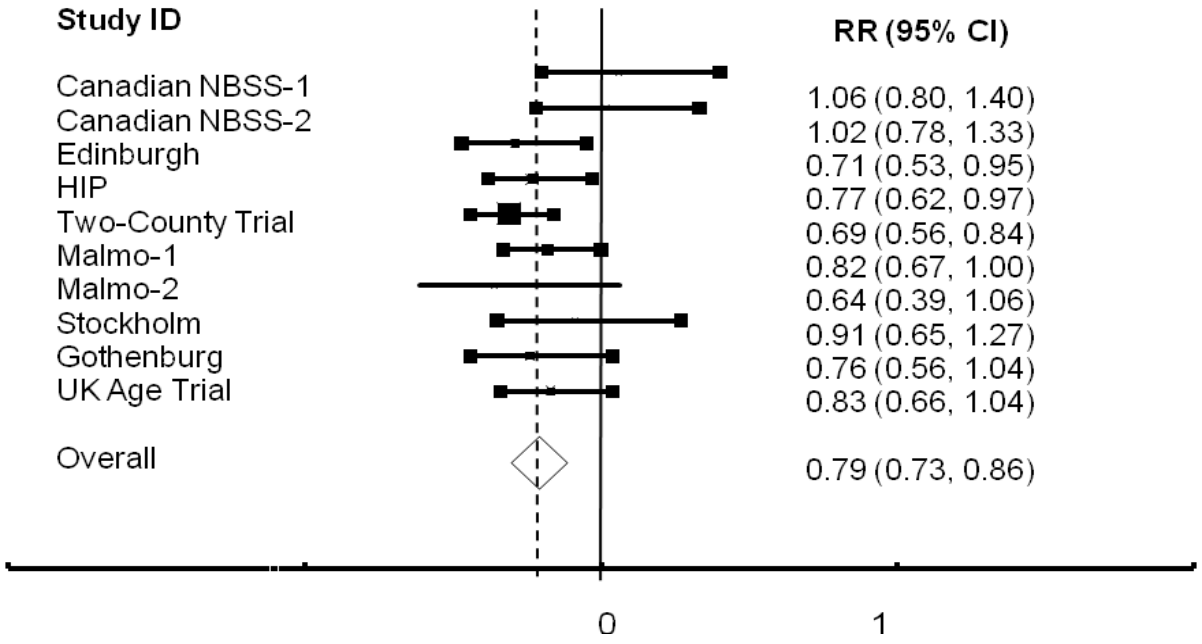
- magnitude of the reduction in breast cancer mortality
- relevance of the original trials
- interpretation of observational data
- relevance with reduced mortality from changes in treatment

Harms:

- Overdiagnosis
- DCIS
- Psychological consequences of screening
- Information given to women invited for screening

IBSR

Wald,1991


Study ID
RR (95% CI)
Canadian NBSS-1
1.06 (0.80, 1.40)
Canadian NBSS-2
1.02 (0.78, 1.33)
Edinburgh
0.71 (0.53, 0.95)
HIP
0.77 (0.62, 0.97)
Two-County Trial
0.69 (0.56, 0.84)
Malmo-1
0.82 (0.67, 1.00)
Malmo-2
0.64 (0.39, 1.06)
Stockholm
0.91 (0.65, 1.27)
Gothenburg
0.76 (0.56, 1.04)
UK Age Trial
0.83 (0.66, 1.04)
Overall
0.79 (0.73, 0.86)
0
1

Breast cancer mortality – meta-analysis

- Overall relative risk (invited vs. controls) is 0.80 (95% CI 0.73 to 0.89)
- 20% reduction in breast cancer mortality
- Some heterogeneity
- Not dissimilar to other meta-analyses

- External biases
  - Screening frequency, screening duration, age group
  - Screening technology, current treatments
- How much uncertainty?
- More contemporary estimates of relative risk?

IBSR

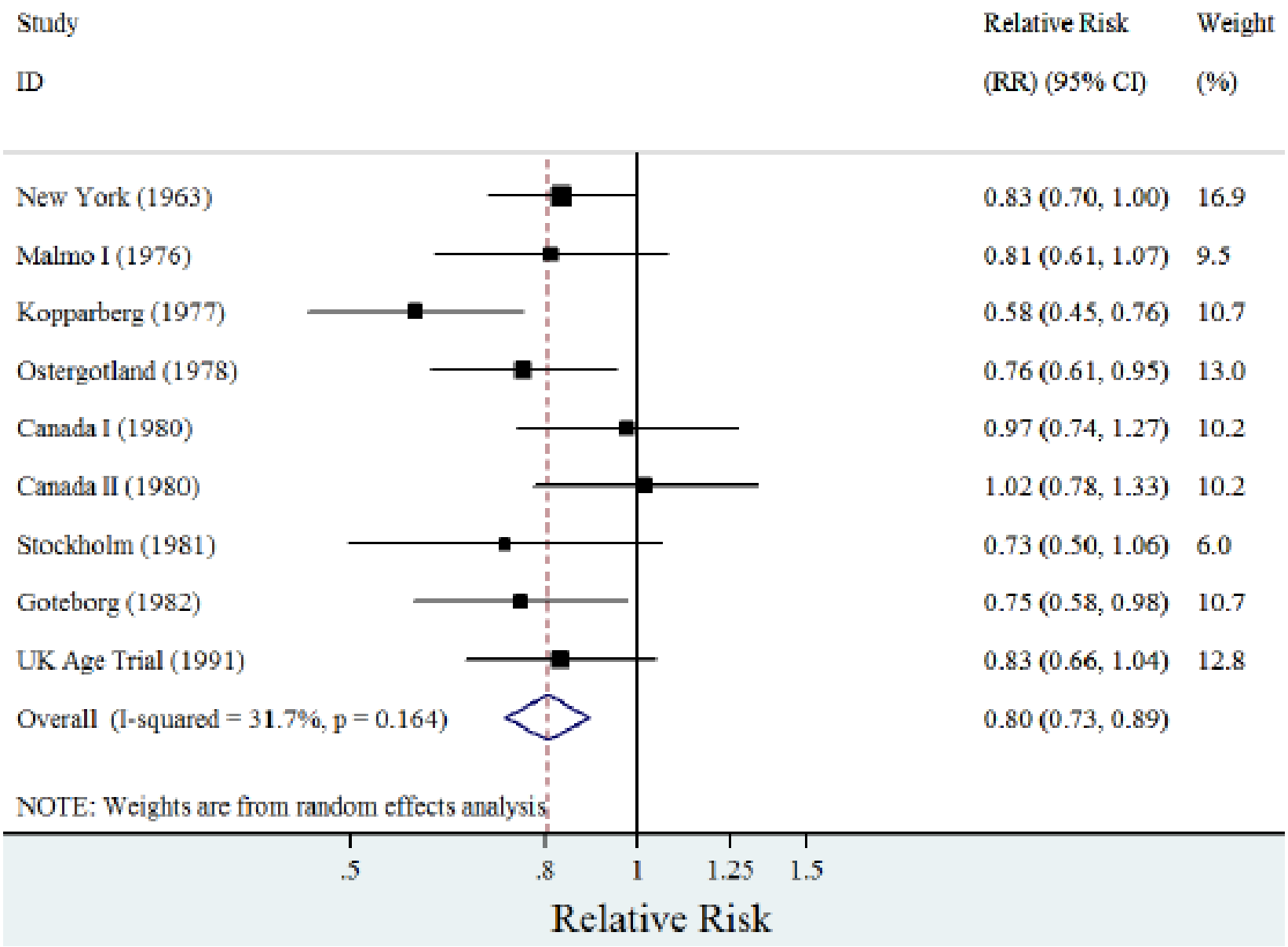


Figure 3.1 Meta-analysis of the breast cancer screening trials: relative risk (RR) of breast cancer mortality after 13 years of follow-up. Adapted from the Cochrane Review (Gøtzsche 2011).

Screening for breast cancer with mammography

Olsen O, Gøtzsche PC

This review should be cited as: Olsen O, Gøtzsche PC. Screening for breast cancer with mammography (Cochrane Review). In: The Cochrane Library, Issue 4, 2001. Oxford: Update Software.

A substantive amendment to this systematic review was last made on 28 August 2001. Cochrane reviews are regularly checked and updated if necessary.

- Background: Mammographic screening for breast cancer is controversial, as reflected in greatly varying national policies.
- Objectives: To assess the effect of screening for breast cancer with mammography on mortality and morbidity.
- **Main results: Seven completed and eligible trials involving half a million women were identified. The two best trials provided medium−quality data and, when combined, yield a relative risk for overall mortality of 1.00 (95% CI 0.96−1.05) after 13 years. However, the trials are underpowered for all−cause mortality, and confidence intervals include a possible worthwhile effect as well as a possible detrimental effect. If data from all eligible trials (excluding flawed studies) are considered then the relative risk for overall mortality after 13 years is 1.01 (95% CI 0.99−1.03).**
- **The best trials failed to show a significant reduction in breast cancer mortality with a relative risk of 0.97 (95% CI 0.82−1.14). If data from all eligible trials (excluding flawed studies) are considered then the relative risk for breast cancer mortality after 13 years is 0.80 (95% CI 0.71−0.89). However, breast cancer mortality is considered to be an unreliable outcome and biased in favour of screening. Flaws are due to differential exclusion of women with breast cancer from analysis and differential misclassification of cause of death ■**

2012 Volume 19 Suppl 1

Journal of Medical Screening

Guest Editors: Allan Hackshaw and Stephen Duffy

Review co-ordinators: E Paci, M Broeders, S Hofvind and SW Duffy

Royal Society of Medicine Press I

ORIGINAL ARTICLE

Riduzione di mortalità per causa specifica tumore della mammella

EUROSCREEN Working Group

J Med Screen 2012;**00**:1–9
DOI: 10.1258/jms.2012.012077

ORIGINAL ARTICLE

Communicating the balance sheet in breast cancer screening

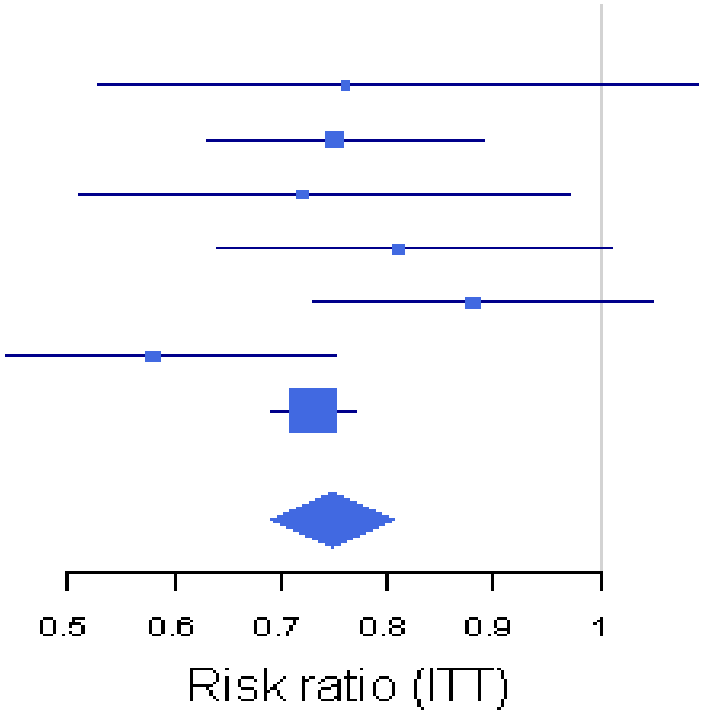
Livia Giordano, Carla Cogo, Julietta Patnick, Eugenio Paci and the Euroscreen Working Group (members listed at the end of the paper)

J Med Screen 2012;**00**:1–5
DOI: 10.1258/jms.2012.012084

IBM studies: *women invited vs not invited*

25% reduction

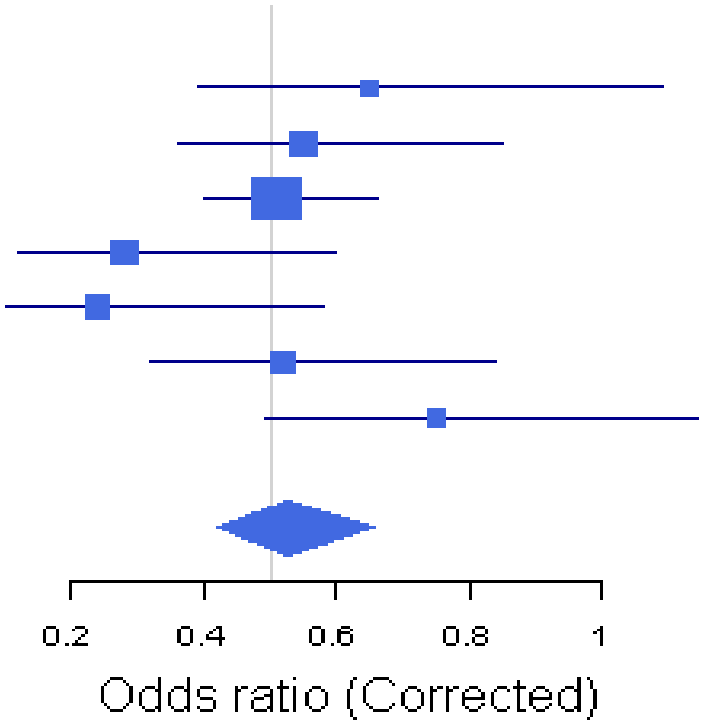
Study	RR	Lower	Upper
Hakama 1997	0.76	0.53	1.09
Olsen 2005	0.75	0.63	0.89
Sarkeala 2008	0.72	0.51	0.97
Paci 2002	0.81	0.64	1.01
Kalager 2010	0.88	0.73	1.05
Ascunce 2007	0.58	0.44	0.75
SOSSEG 2006	0.73	0.69	0.77
Summary (Random)	**0.75**	**0.69**	**0.81**



CC-studies: *women screened vs not screened*

48% reduction

Study	OR	Lower	Upper
Gabe 2007	0.65	0.39	1.09
Puliti 2008	0.55	0.36	0.85
Otto 2011	0.51	0.4	0.66
Van Schoor 2011	0.28	0.12	0.6
Paap 2010	0.24	0.1	0.58
Allgood 2008	0.52	0.32	0.84
Fielder 2004	0.75	0.49	1.14
Summary (Random)	**0.52**	**0.42**	**0.65**



	EUROSCREEN Working Group (2012)		UK Independent Review, 2012
Status in regard to screening	**Screened**	**Invited**	**Invited**
Measure of mortality reduction (data source)	**38% - 48% (European observational studies)**	**25% - 31% (European observational studies)**	**20% (randomised controlled trials)**

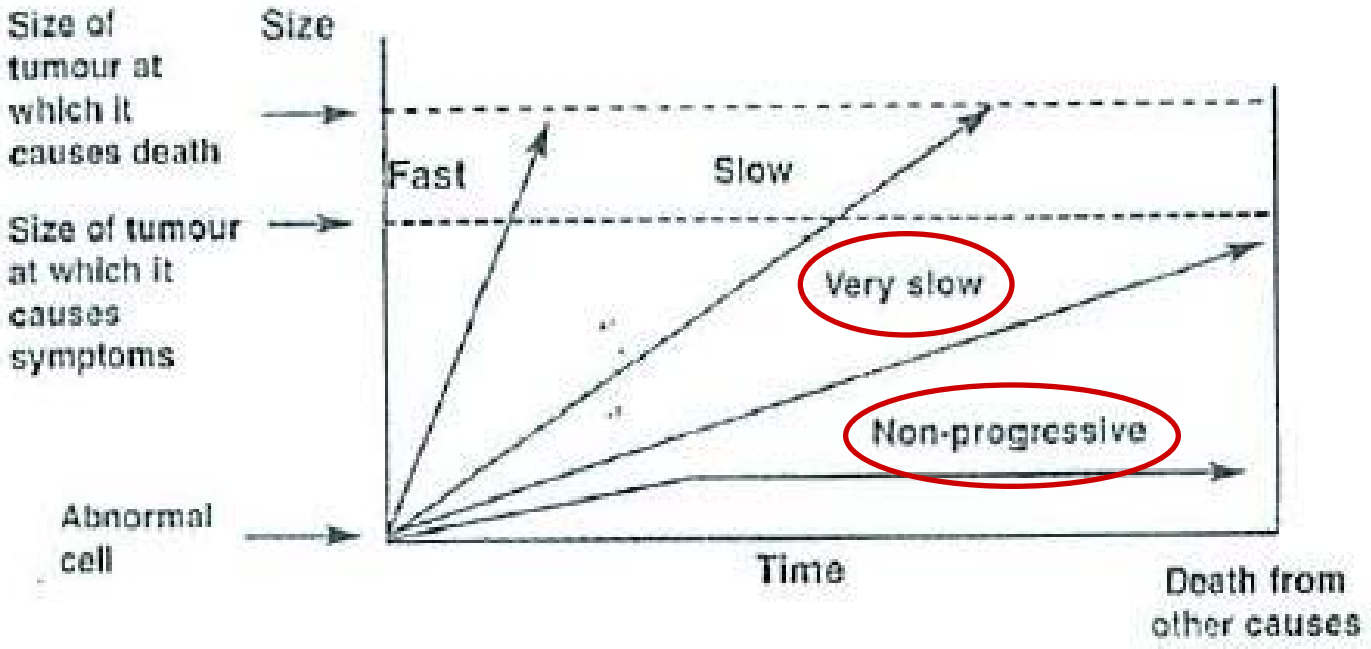
EUROSCREEN WG -2012 conclusioni

- **Le stime dei risultati di mortalità per le donne invitate sono comparabili con quelle ottenute dai trial randomizzati**
- **I disegni dello studio che sono considerati validi derivano dalla valutazione dei dati individuali, prospettici**
- **E' giudizio degli autori che larga parte della controversia sullo screening sia attribuibile (in particolare nella stima della sovradiagnosi) a problemi metodologici**
- **Il pieno impatto delo screening organizzato deve essere ancora stimato e questo è solo un risultato iniziale**

I rischi dello screening

Sovradiagnosi e falsi positivi

Growth rates of cancers (IARC, 2002)



The diagnosis of these cancers (very slow and non-progressive), that Morrison (1992) have called "pseudodisease", is overdiagnosis.

SOVRADIAGNOSI

- **La proporzione di casi di cancro (in situ e invasivi) confermati istologicamente , diagnosticati a seguito di un episodio di screening e che non sarebbero giunti all'attenzione clinica se la mammografia di screening non fosse stato eseguita.**

- **Da Paci&Duffy, BCR, 2005**

The benefits and harms of breast cancer screening

An assessment by the Independent UK Panel on Breast Cancer Screening

Simon Thompson

University of Cambridge, UK

IBSR

The benefits and harms of breast cancer screening

An assessment by the Independent UK Panel on Breast Cancer Screening

Simon Thompson
University of Cambridge, UK

IBSR

Overdiagnosis

- Definition: Detection of cancers on screening that would not have been found in the woman's lifetime were it not for the screening test
- Does it occur, and if so how common is it?
- Essentially, occurs if woman dies before the end of the lead time for her cancer
- Neither a woman nor her doctor will ever know whether a breast cancer found represents overdiagnosis

IBSR

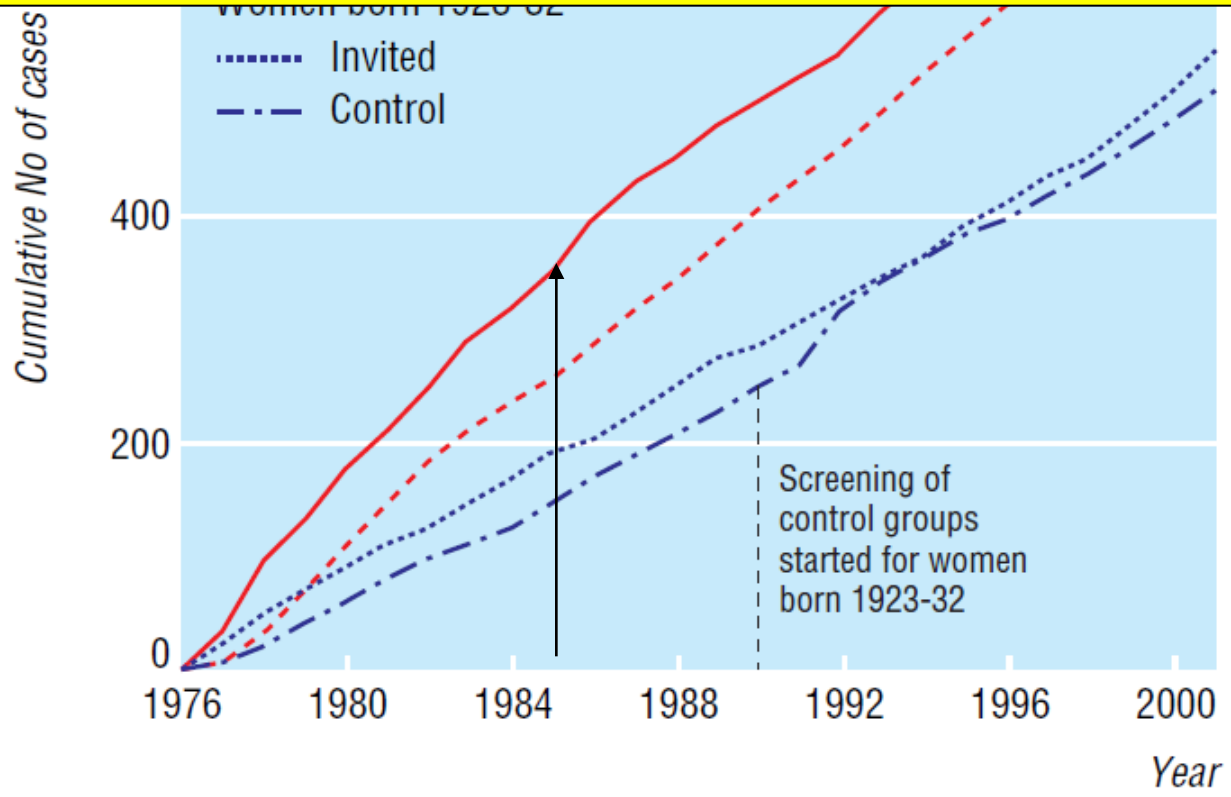
How to estimate overdiagnosis

- RCT of women invited to screening for 20 years aged 50-70 compared with an uninvited control group
- Follow-up to death
- Any excess of breast cancers in the invited group would represent overdiagnosis
- Such a study does not exist

Fig 2 Cumulative number of all breast cancer cases (in situ and invasive) per year and group for total follow-up of women born during 1908-22 (unscreened control group) and 1923-32 (controls groups invited to screening from 1990 onwards)

Randomised control trial: red control group unscreened

Estimate of the excess of incidence /overdiagnosis after 15 years since the screening cycle end: about 10%



What is the best measure?

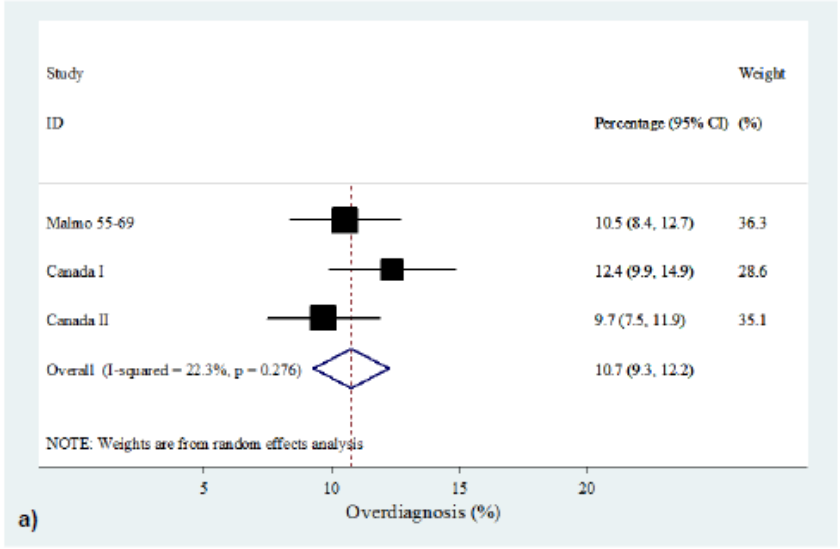
The Benefits and Harms of Breast Cancer Screening:

An Independent Review

Lancet , 2012

A. Excess cancers as a proportion of cancers diagnosed over whole follow up period in unscreened women
B. Excess cancers as a proportion of cancers diagnosed over whole follow up period in women invited for screening
C. Excess cancers as a proportion of cancers diagnosed during screening period in women invited for screening
D. Excess cancers as a proportion of cancers detected at screening in women invited for screening

Measure A is the traditional measure used in the Malmo Trial, and in reviews as Jorgensen, 2009 and EUROSCREEN , 2012



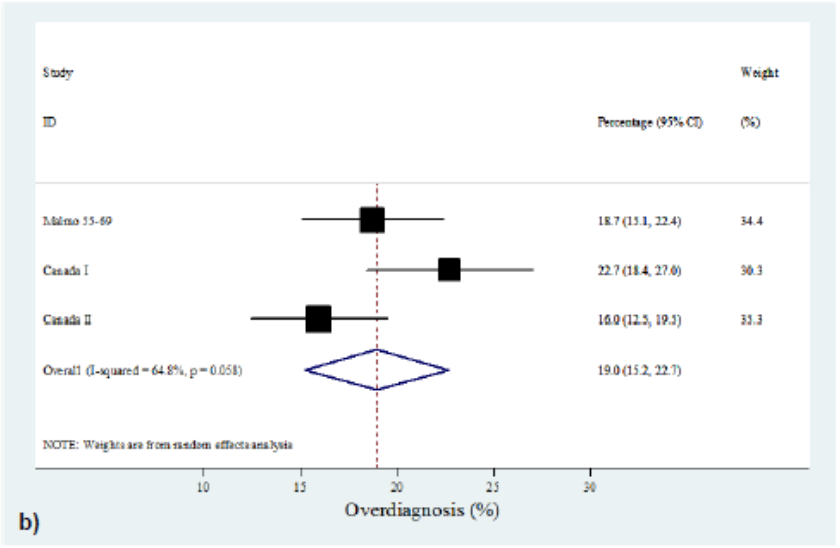


Figure 4.3 Meta-analysis of estimates of overdiagnosis: (a) excess cancers as a proportion of cancers diagnosed over whole follow up period in women invited for screening, (b): excess cancers as a proportion of cancers diagnosed during screening period in women invited for screening

IBSR
Independent Breast Screening Review

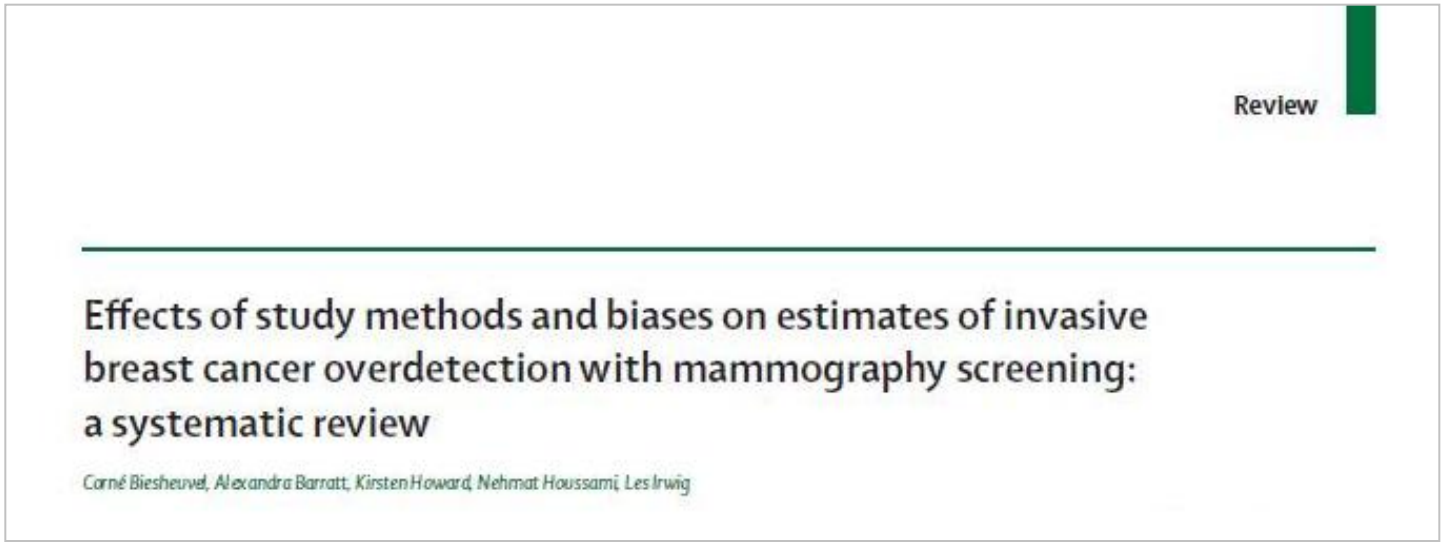
A report jointly commissioned by Cancer Research UK and the Department of Health (England).

October 2012

Measure B : 10.7%

Measure C: 19%

STUDY METHODS TO ESTIMATE OVERDETECTION:



Review

Effects of study methods and biases on estimates of invasive breast cancer overdetection with mammography screening: a systematic review

Carné Biesheuvel, Alexandra Barratt, Kirsten Howard, Nehmat Houssami, Les Irwig

"The theoretically most robust method to estimate overdetection is the cumulative-incidence approach with data from a randomised controlled trial, in which there is more than several years of follow-up after screening stops, and the control group is never screened."

"If there is little or no follow-up after the last screen, there will be lead-time bias that should be adjusted for statistical methods, otherwise the estimate of overdetection will be too high." (adjusted for lead-time method)

Lancet oncology, 2007

BMJ

RESEARCH

Overdiagnosis in publicly organised mammography screening programmes: systematic review of incidence trends

Karsten Juhl Jørgensen, researcher Peter C Gøtzsche, director

The Nordic Cochrane Centre, Rigshospitalet, Dept 3343, Blegdamsvej 9, DK-2100 Copenhagen, Denmark
Correspondence to: KJ Jørgensen kj@cochrane.dk

Cite this as: BMJ 2009;339:b2587
doi:10.1136/bmj.b2587

ABSTRACT

Objective To estimate the extent of overdiagnosis (the detection of cancers that will not cause death or symptoms) in publicly organised screening programmes.

Design Syste
incidence of
introduction

Data sources
authors.

Review meth
of breast can
size, screenin
which were cl
Linear regres
incidence bef
and in older,
was used to e

Results Incid
before screen
been fully imp
non-screened
Kingdom; Ma
Australia; Sw
implementati
excluded and
incidence an
older, previou
estimated at
Data from thr
the women e
reduction wa
was compens

Conclusions
was closely r
little of this i
incidence of
One in three
offered organ

cancers, which would not have been identified clinically in someone's remaining lifetime, is called overdiagnosis and can only be harmful to those who experience it.[1] As it is not possible to distinguish

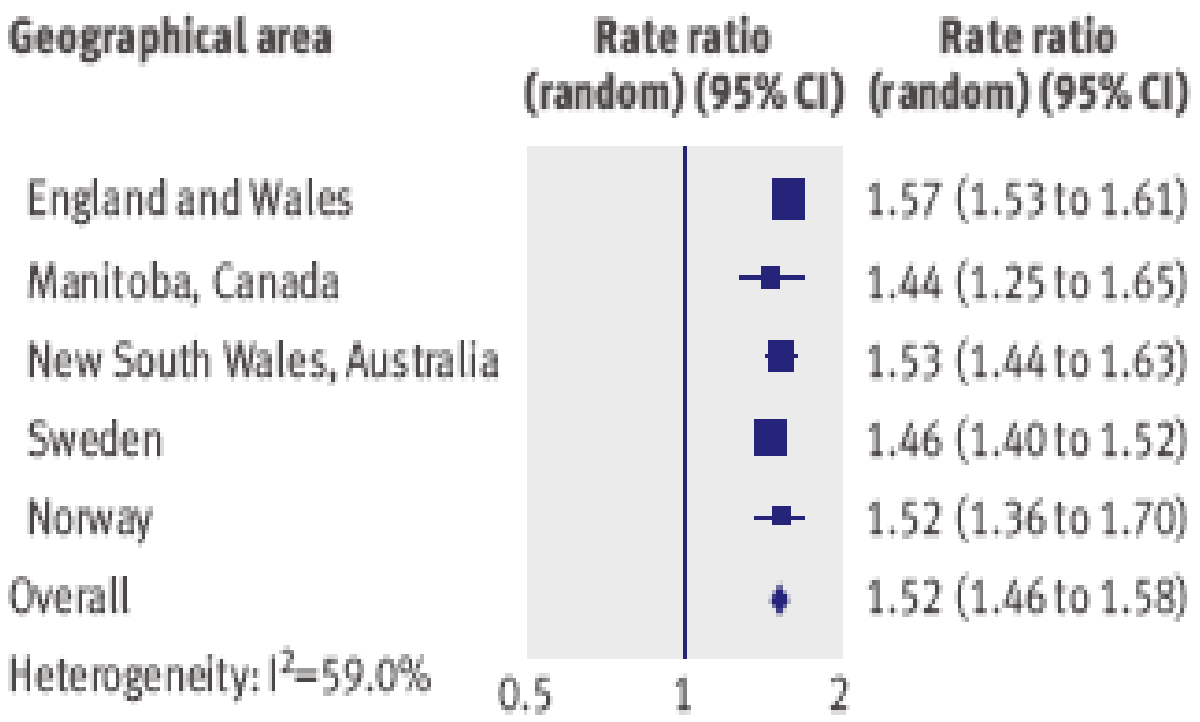


Fig 8 | Meta-analysis of overdiagnosis of breast cancer (including carcinoma in situ) in publicly available mammography screening programmes

EUROPEAN JOURNAL OF CANCER 45 (2009) 3166–3171

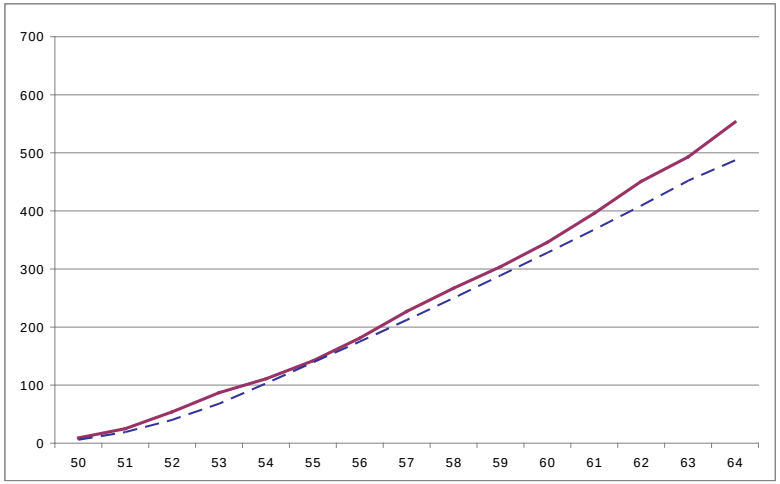
available at www.sciencedirect.com

ScienceDirect

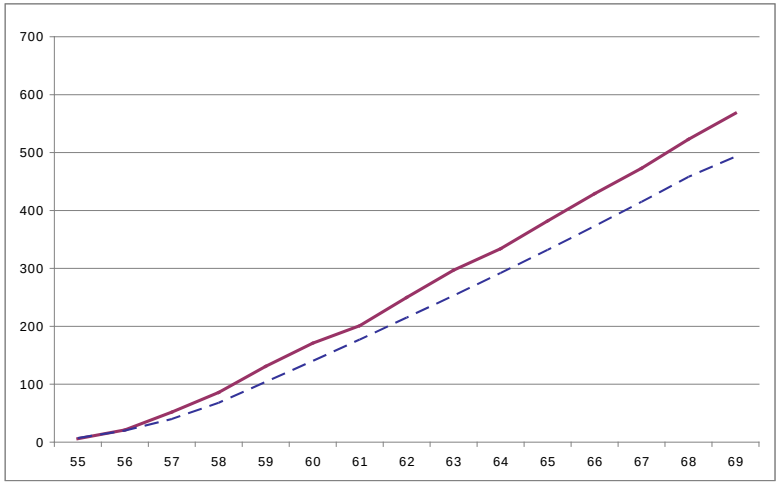
journal homepage: www.ejconline.com

An estimate of overdiagnosis 15 years after the start of mammographic screening in Florence

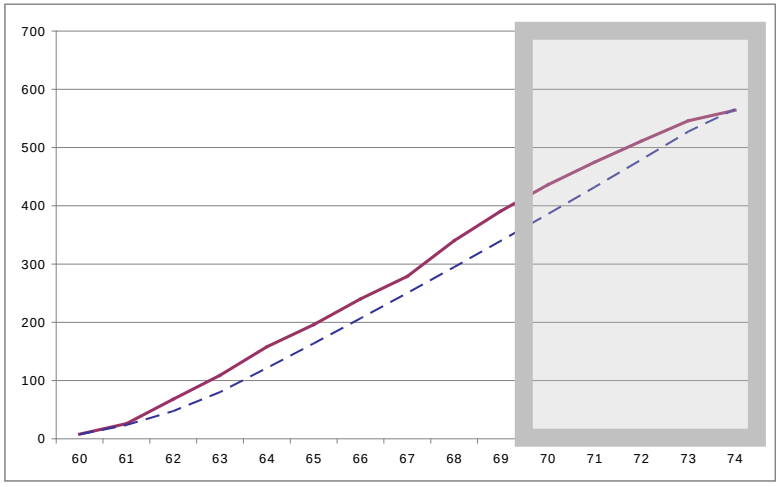
a) 50- 54 years



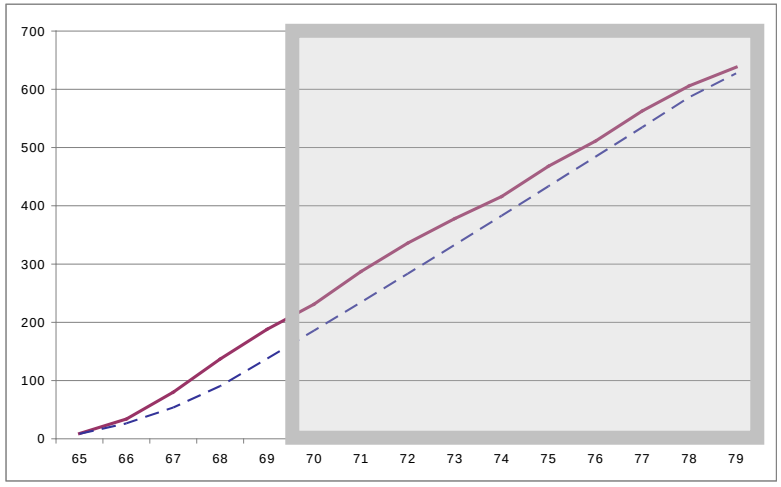
b) 55-59 years



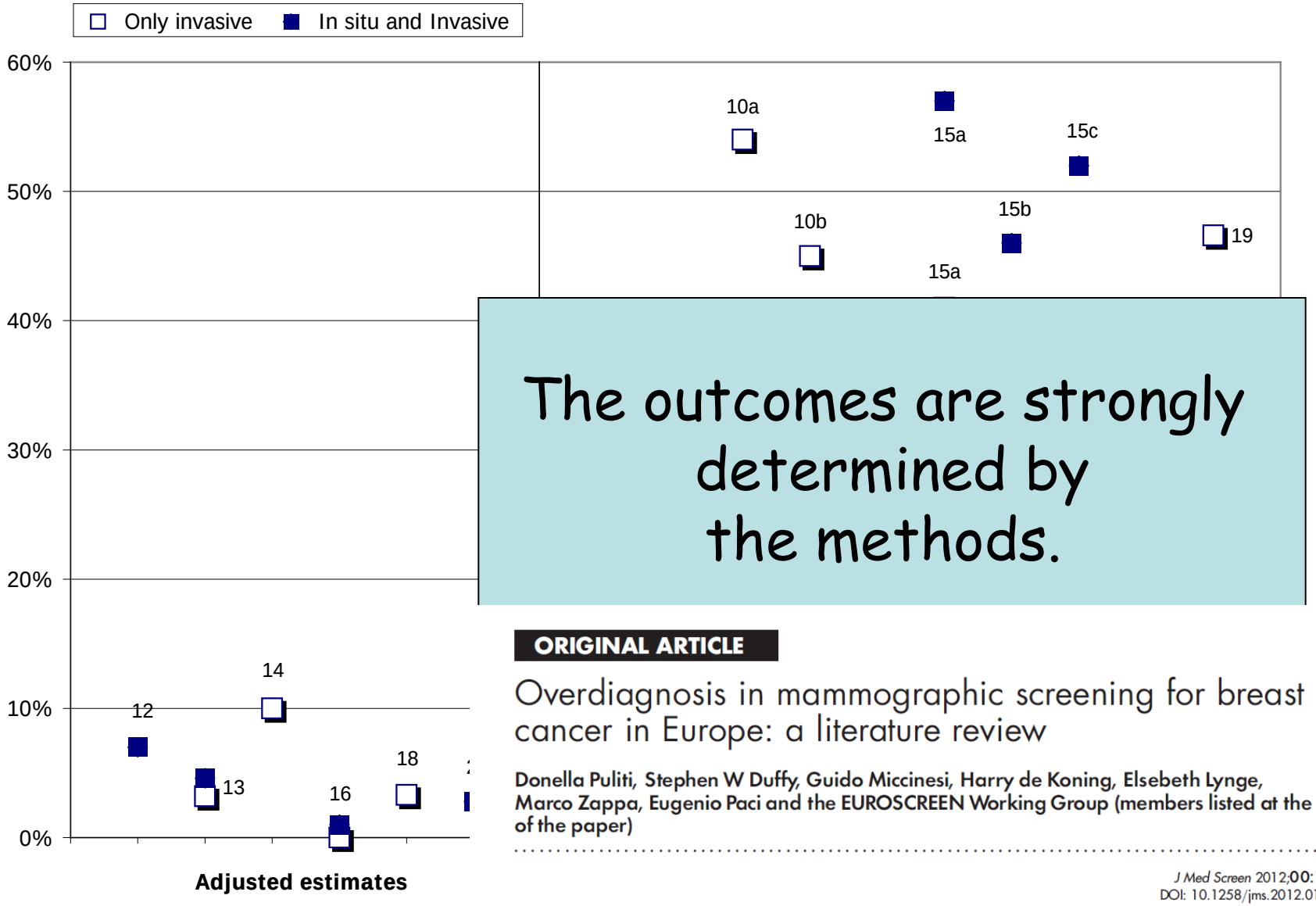
c) 60-64 years



d) 65-69 years



STUDI OSSERVAZIONALI
OVERDIAGNOSIS ESTIMATES CLASSIFIED ACCORDING TO THE PRESENCE/ABSENCE OF BOTH THE ADJUSTMENTS



The outcomes are strongly determined by the methods.

ORIGINAL ARTICLE

Overdiagnosis in mammographic screening for breast cancer in Europe: a literature review

Donella Puliti, Stephen W Duffy, Guido Miccinesi, Harry de Koning, Elsebeth Lynge, Marco Zappa, Eugenio Paci and the EUROSCREEN Working Group (members listed at the end of the paper)

J Med Screen 2012;**00**:1–15
DOI: 10.1258/jms.2012.012082

Breast screening: the facts—or maybe not

Peter Gøtzsche and colleagues argue that women are still not given enough, or correct, information about the harms of screening

Summary from evidence based leaflet

- It may be reasonable to attend for breast cancer screening with mammography, but it may also be reasonable not to attend because screening has both benefits and harms
- If 2000 women are screened regularly for 10 years, one will benefit from the screening, as she will avoid dying from breast cancer
- At the same time, 10 healthy women will, as a consequence, become cancer patients and will be treated unnecessarily. These women will have either a part of their breast or the whole breast removed, and they will often receive radiotherapy and sometimes chemotherapy
- Furthermore, about 200 healthy women will experience a false alarm. The psychological strain until one knows whether it was cancer, and even afterwards, can be severe

	EUROSCREEN Working Group (2012)		UK Independent Review, 2012
Status in regard to screening	**Screened**	**Invited**	**Invited**
Measure of mortality reduction (data source)	**38% - 48% (European observational studies)**	**25% - 31% (European observational studies)**	**20% (randomised controlled trials)**
Measure of overdiagnosis (data source)	**6.5% (European observational studies)**	**4.7% (European observational studies)**	**19% * (randomised controlled trials)**

Overtreatment versus Overdiagnosis

- **Tutte donne che hanno un tumore della mammella sovradiagnosticato sono sovratrattate, ma oggi un clinico non è in grado di dire chi è sovradiagnosticato. La sovradiagnosi è un costrutto epidmiologico.**
- **Molti casi di carcinomi in situ e precoci possono essere sovratrattati o trattati in maniera non proporzionata. Le procedure diagnostiche sono spesso aggressive anche nei casi precoci.**
- **I programmi di screening hanno avuto un rilevante impatto nel favorire il lavro di gruppo, facilitare l'uso di approcci diagnostici meno aggressivi e diminuire la frequenza di screening in paragona con lo screening spontaneo.Questi tumori screen detected , nei programmi maturi, sono intorno al 50% dei casi di popolazione.**

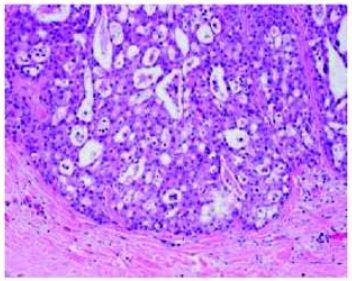
Better knowledge of the relationship between tumour characteristics and screening

Basal-like and Triple-Negative Breast Cancers

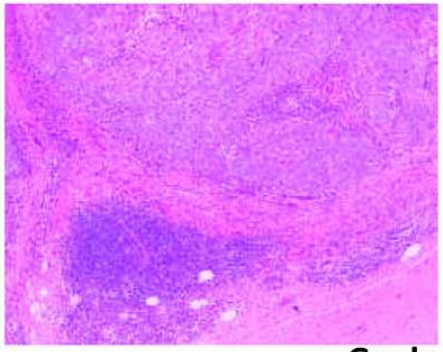
Low-grade tumors

High-grade tumors

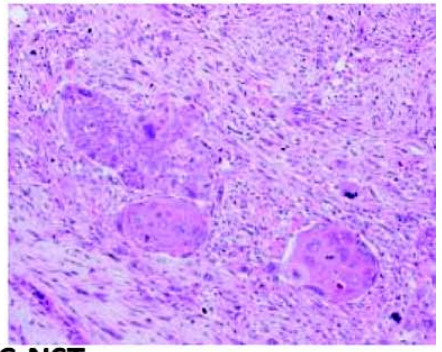
Secretory carcinoma



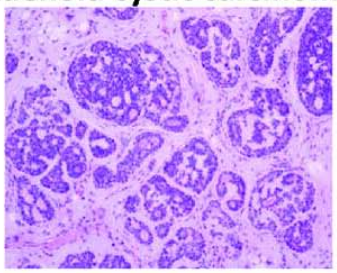
Medullary breast cancer



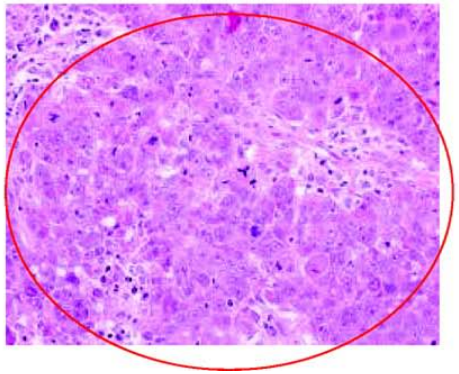
Metaplastic breast cancer



Adenoid cystic carcinoma



Grade 3 – IDC-NST



Hudis C A , Gianni L The Oncologist 2011;16:1-11

The Oncologist

Swedish Two-County Trial: Impact of Mammographic Screening on Breast Cancer Mortality during 3 Decades[1]

László Tabár, MD

Radiology

Purpose: To estimate the long-term (29-year) effect of mammographic

There was a highly significant reduction in breast cancer mortality in women invited to screening according to both local end point committee data (relative risk [RR] = 0.69; 95% confidence interval: 0.56, 0.84; $P < .0001$) and consensus data (RR = 0.73; 95% confidence interval: 0.59, 0.89; $P = .002$). At 29 years of follow-up, the number of women needed to undergo screening for 7 years to prevent one breast cancer death
519 according to con
cancer deaths would
screening) after the fi

Invitation to mammo
significant decrease in
uation of the full imp
mates of absolute be
requires follow-up ti
observed number of
creases with increasi

Radiology

Is Mammographic Screening Justifiable Considering Its Substantial Overdiagnosis Rate and Minor Effect on Mortality?

Karsten Juhl Jørgensen, MD
John D. Keen, MD, MBA
Peter C. Gøtzsche, MD

Proponents of mammographic screening generally say that the benefit is large and established beyond

There have been substantial advances in treatment since most of the trials were performed, and these advances must

REVIEW

The Breast Screening Programme and misinforming the public

Peter C Gøtzsche • Karsten Juhl Jørgensen
The Nordic Cochrane Centre, Copenhagen, Denmark
Correspondence to: Peter C Gøtzsche. Email: pcg@cochrane.dk

DECLARATIONS

Summary

Balance Sheet

IL BILANCIO SUGLI SCREENING. UNA NARRAZIONE SUI BENEFICI E I DANNI CORRELATI ALLO SCREENING

- **Consideriamo una piccola città in Europa, in cui risiedono 1000 donne di età compresa tra 50 e 51 anni. Se queste donne vengono tenute sotto osservazione per i successivi 30 anni in assenza di un programma di screening mammografico attivo, ci si aspetta di riscontrare 67 casi di tumore al seno che porterà al decesso 30 pazienti.**
-

- Consideriamo ora un'altra città, uguale alla precedente ma dotata di un programma di screening mammografico conforme alle linee guida europee che invita in maniera regolare le mille donne tra i 50 e i 51 anni a eseguire una mammografia ogni due anni per un periodo di 20 anni. Se l'adesione di questa popolazione target è totale, le stime indicano che l'incidenza dei decessi dovrebbe essere tra 21 e 23 casi in un periodo di 30 anni (contro i 30 dell'esempio precedente).

Per molte donne

- La maggior parte delle donne che partecipano al programma avranno referti mammografici negativi e il vantaggio consisterà nella conferma delle loro buone condizioni di salute. D’altra parte gli aspetti negativi possono solo riferirsi al possibile disagio e all’ansia a breve termine per l’esecuzione dell’esame. Invece nel caso in cui l’esito sia positivo, i disagi sono accompagnati al beneficio di ottenere una diagnosi precoce.

Sovradiagnosi e screening

- Le sovradiagnosi sono dovute alla rilevazione da parte dei programmi di screening di tumori poco aggressivi e in fase di sviluppo precoce, per esempio, in situ, e di tumori invasivi in fase di sviluppo molto precoce. Le conoscenze attuali impediscono di distinguere tra i tumori che diventeranno aggressivi e quelli che non costituiscono una minaccia per la vita. Per questo motivo, la ricerca volta all'identificazione di indicatori e alla definizione di protocolli in grado di ridurre l'impatto del trattamento del cancro al seno è, e deve restare, tra le priorità.

Cosa è la sovradiagnosi

- Il problema della sovradiagnosi rappresenta sicuramente un danno significativo perché comporta una diagnosi di tumore al seno senza una controparte di benefici (se chi la riceve non avesse partecipato al programma di screening, non avrebbe dovuto sottoporsi a ulteriori accertamenti e trattamenti). Secondo le nostre stime 4 donne tra le 1000 partecipanti al programma di screening incorreranno in una sovradiagnosi, un dato che si aggiunge ai 67 casi di tumore diagnosticati tra le donne della città dove non esiste di un programma di screening mammografico

I falsi positivi

- Un altro potenziale danno per le donne sottoposte a screening è l'identificazione di un "falso positivo", ovvero di un'anomalia sospetta che non viene confermata dai successivi esami di approfondimento. Si trattava di un falso allarme. Seppure la rilevazione di un sospetto non sia equivalente a una diagnosi positiva, si parla comunque di "falso positivo" a causa delle indagini necessarie per verificarne l'esatta natura.
  Quando si rende necessaria una valutazione successiva al primo test, nella maggior parte delle volte si tratta di un secondo esame mammografico o di un'ecografia, in alcuni casi, tuttavia, sono necessari ulteriori esami clinici del seno che possono comportare anche interventi invasivi, come la biopsia, per ottenere i tessuti necessari per l'esame istopatologico.

Conseguenze di un falso positivo

- Le conseguenze negative psicologiche legate a questo percorso di accertamento sono state studiate e descrivono solo un impatto nel breve periodo, riconducibile all'ansia. In alcuni Paesi europei, la percentuale totale di donne che durante i 20 anni di partecipazione al programma di screening mammografico incorrono in una diagnosi di falso positivo, è stata stimata nel 17% per follow-up non invasivi e nel 3% per follow-up invasivi.
  Poiché questi falsi allarmi sono inevitabili in ogni processo di screening, le linee guida europee tra i parametri di qualità fissano la percentuale massima accettabile di donne sottoposte allo screening che devono essere richiamate per una valutazione successiva (tasso di richiamo) e raccomanda la possibilità di consultazione degli indicatori di performance da parte della popolazione invitata.

Altri danni possibili

- Questo studio non prende in considerazione gli effetti a lungo termine come i rischi da radiazione, che sono tuttora molto controversi perché basati su estrapolazioni e quindi di significato incerto. In ogni caso questo tipo di rischio è valutato comunque come molto inferiore ai benefici dello screening.

Essential components of the Decision Making Scenario

Components	Value	Comments and communicative implications
Number of women	1000	The average number of women for 1 year birth cohort in asmall city at 50
Age at the start of the risk period (years)	50	Recommended starting age for service screening in Europe
Status in regard to screening	Screened	The outcomes in terms of benefits and harms to screened women are informative to invited women who are making the decision whether or not to attend
Number of screening mammograms expected in the screening period	10 (every 2 years)	Recommended number for service screening in Europe
Age span for screening (years)	50 to 69	Recommended age range for service screening in Europe
Age at the end of follow up (years)	79	The outcomes in terms of benefits and harms refer to the period from 50 to 79 years.

EUROSCREEN Working Group

Balance sheet for 1000 women aged 50-51 years, screened biennially until 69 years and followed until 79 years

Balance sheet	
Benefits	**Harms**
7-9 women's lives are saved (out of 30 deaths expected in the absence of screening)	4 women are overdiagnosed (out of 67 cancers expected in the absence of screening)
	170 women have at least one recall with no-invasive assessment giving a negative result
	30 women have at least one recall with invasive assessment giving a negative result

Comparison of the balance sheets of the EUROSCREEN Working group and UK Independent Review (Modified)

	EUROSCREEN Working Group 2012		UK Independent Review, 2012
Status in regard to screening	Screened	Invited	Invited
Expected preventable BC deaths from 50 to 79 years , brea st cancer diagnosed in ages 50 -69	19 out 30	19 out 30	19 out 30
N° lives saved	7-9	5-6	4
Expected BC cases from 50 to 79 years	67	67	67
N° overdiagnosed cases	4	3	7- 13 *
N° overdiagnosed cases for every life saved	0.4 – 0.6	0.5 – 0.6	3

*Measure of overdiagnosis estimated using screening period incident breast cancer cases in the Malmo trial

BMJ 2009

Breast screening: the facts— or maybe not

Peter Gøtzsche and colleagues argue that women are still not given enough, or correct, information about the harms of screening

10 years

Summary from evidence based leaflet

- It may be reasonable to attend for breast cancer screening with mammography, but it may also be reasonable not to attend because screening has both
- If 2000 women are screened regularly for 10 years, o will avoid dying from breast cancer
- At the same time, 10 healthy women will a will be treated unnecessarily. The breast removed, and they will often
- Furthermore, about 200 healthy women will experience a false alarm. The psychological strain until one knows whether it was cancer, and even afterwards, can be severe

0.5 life saved per 1000 screened women

5 overdiagnosed breast cancer cases per 1000

Balance Sheet

ORIGINAL ARTICLE

Communicating the balance sheet in breast cancer screening

Livia Giordano, Carla Cogo, Julietta Patnick, Eugenio Paci and the Euroscreen Working Group (members listed at the end of the paper)

J Med Screen 2012;00:1–5
DOI: 10.1258/jms.2012.012084

THE BALANCE SHEET: A TOOL FOR MORE TRANSPARENT INFORMATION

In the past, public information about cancer screening has been accused sometimes of overemphasizing the benefits, underestimating harms and understating scientific controversies, though there has been a public health objective to achieve high attendance rates.[1–3] In recent years, there has been debate about the issues and potential conflicts associated with providing information on mammographic screening. Information must reflect the fact that screening would not be offered if it were not considered sufficiently beneficial. However, there is a need to enable those invited to screening to make an informed choice. Health professionals have started to reflect on what 'good quality information' means in practical terms and invited women have taken a more active role in their decisions about screening.[3–5] Such changes have been consistent with other processes since the late 1980s: the abandonment of the paternalistic model of medical information, and citizens' demand for greater involvement in health, environmental and civil rights issues.[6,7]

Transparency about benefits and harms is a key principle for producing good quality information – a maxim that should hold true for any kind of information, in all activities of human interaction. Most European screening programmes are moving in this direction, making efforts to improve the way they communicate with the public. European guidelines for quality assurance in breast, cervical and colorectal cancer screening contain specific recommendations that aim to help professionals to understand the complexities of screening communications and to develop more effective information strategies[8–10], and in recent times, information materials have been revised and updated.[11]

In cancer screening, the communication of quantitative information for, *inter alia*, individual risk, mortality and survival data and overdiagnosis is particularly complex, and to this end the screening balance sheet, as a tool that conveys simple estimates based on the best available evidence, is key both for women who must make decisions about screening and for professionals who must communicate screening strategy.[12]

THE BALANCE SHEET BACKGROUND

In this supplement, evidence from European service screening programmes is collated on the effect of mammographic screening on breast cancer mortality, overdiagnosis and false-positive results, and synthesized into a balance sheet.[13] This should help screening professionals to deliver

IMPACT WORKING GROUP

E. Paci, D. Puliti, M. Zappa, G. Miccinesi, P. Falini, E. Crocetti, G. Manneschi, Clinical and Descriptive Epidemiology Unit – ISPO – Cancer Prevention and Research Institute;

Torino: N. Segnan, A. Ponti, L. Giorc
R. Zanetti, S. Patriarca, S. Rosso; Re
A. Sapino; Università di Torino, AOU
Varese: S. Pisani, M.L. Gambino, L. E
P. Contiero, G. Tagliabue, L. Preto, D
Sondrio: R. Tessandori, M.L. Annulli
Sondrio.
Trento: S. Piffer, S. Franchini, M.A
M. Pellegrini, Senologia – Screening

Grazie a tutti gli operatori
che hanno collaborato allo screening mammografico
e a tutte le donne che hanno aderito al nostro invito.

Veneto: M. Zorzi, S. Baracco, C. Fedato, S. Guzzinati, A.R. Fiore, M. Baracco, A.. Dal Cin, D. Monetti, A. Rosano, S. Ciatto, Registro Tumori del Veneto, IOV IRCCS; Padova. A. Molino, Università di Verona; Verona. F. Caumo, Azienda ULSS 20; Verona. M. Pieno, M. Bovo, Azienda ULSS 9, Treviso. L. Gallo, A. Stomeo, Azienda ULSS 18, Rovigo
Friuli Venezia Giulia: D. Serraino, L. Dal Maso, M. de Dottori, A. De Paoli, A. Zucchetto, O. Forgiarini, E. De Santis, L. Zanier, Epidemiologia e Biostatistica, IRCCS Centro di Riferimento Oncologico, Aviano (PN).
Regione Emilia-Romagna: C. Naldoni, A..C. Finarelli, P. Sassoli de' Bianchi, Screening Programme - Emilia-Romagna Region Health Dept; Bologna.
Bologna: N. Collina, C. Petrucci, V. Perlangeli, Breast specialized Cancer Registry AUSL Bologna
A. Pasquini, P. Baldazzi, M. Manfredi, G. Saguatti: Breast Cancer Screening Programme AUSL Bologna;
Ferrara: S. Ferretti, Cancer Registry; Ferrara. G.P. Baraldi, G. Benea, Breast Cancer Screening Programme AUSL Ferrara.
Modena: M. Federico, C. Cirilli, Cancer Registry; Modena. E. Gallo, R.. Negri, Breast Cancer Screening Programme AUSL Modena.
Parma: V. De Lisi, P. Sgargi, M. Michiara Cancer Registry; Parma. G.M. Conti, Breast Cancer Screening Programme AUSL Parma
Reggio Emilia: L. Mangone, N. Borciani, Cancer Registry; Reggio Emilia. C.A. Mori, A. Cattani, L. Paterlini, C. Campari Breast Cancer Screening Programme AUSL Reggio Emilia.
Romagna: F. Falcini, A. Ravaioli, R. Vattiato, A. Colamartini, P. Sanna, Romagna Cancer Registry and Breast Cancer Screening Programme; Forlì. M. Serafini, B. Vitali, P. Bravetti, Breast Cancer Screening Programme AUSL Ravenna; D. Canuti, C. Fabbri, G. Monticelli, Breast Cancer Screening Programme AUSL Rimini; C. Imolesi, M. Palazzi, N. Bertozzi, Marina Faedi, Breast Cancer Screening Programme AUSL Cesena.
Perugia: F. Stracci, F. La Rosa Registro Tumori Umbro; Perugia. M. Petrella, I. Fusco Moffa, Unità di Epidemiologia ASL2; Perugia.
Napoli: M. Fusco, Registro Tumori Regione Campania c/o ASL NA4. C. Maione, Servizio Materno Infantile ASL NA4.
Catania: M. Castaing, G. Benedetto, M. Fidelbo, G. Sciacchitano, E. Vasquez, S. Cordio, S. Sciacca, Università degli Studi di Catania, Dipartimento "G.F. Ingrassia", Registro Tumori Integrato CT-ME-SR-EN.
Palermo: A. Traina, M. Zarcone, Dept. of Oncology ARNAS Ascoli; Palermo.
Ragusa: R. Tumino, Registro Tumori e Anatomia Patologica Distretto Ospedaliero 1, ASP 7 Ragusa. A. Sigona, Registro Tumori, ASP 7 Ragusa C. Iacono, G. La Perna, Progetto Oncoibla - U.O. di Oncologia, Distretto Ospedaliero 1, ASP 7 Ragusa
Siracusa: A. Madeddu, M.L. Contrino, F. Tisano, Registro Tumori Integrato CT-ME-SR, Sez Siracusa.
Trapani: P. Candela, T. Scuderi, Dipartimento di Prevenzione – Servizio Epidemiologia e Malattie Infettive ASP Trapani.


Galleria degli Uffizi

J Cancer Res Clin Oncol (2013) 139:181–185
DOI 10.1007/s00432-012-1304-1

ORIGINAL PAPER

Biological characteristics of interval cancers: a role for biomarkers in the breast cancer screening

A. Caldarella · D. Puliti · E. Crocetti · S. Bianchi · V. Vezzosi · P. Apicella · M. Biancalani · A. Giannini · C. Urso · F. Zolfanelli · E. Paci

Abstract

Introduction In a population-based screening program, a percentage of tumors remain undetected; these tumors comprise a heterogeneous group, and they are more likely to have adverse prognostic features. The aim of this study was to identify differences in biological characteristics of screen-detected versus interval breast cancers in a population-based screening program according to molecular subtypes.

Materials and methods We analyzed the population-based data from a long-running screening program in the area of Florence. Data on screening history and on age, *T* and *N* status, grade, histotype, hormonal status and Ki-67 and HER2 expression were retrieved. Subtypes of breast cancer were defined on the expression of ER, PR, Ki-67 and HER2: luminal A if ER/PR+, HER2− and Ki67 <14 %, luminal B (HER2 negative) if ER/PR+, HER2− and Ki67 ≥14 %, luminal B (HER2 positive) if ER/PR+ and HER2+, triple negative if ER/PR−and HER2−, HER2 positive if ER/PR− and HER2+. Association between molecular subtypes and mode of detection will be evaluated by a logistic regression model adjusted for the potential confounding variables.

Results Information about biomarkers was known for 277 cases, 211 screening-detected and 66 interval cancers. Among interval cases, the triple-negative cancers were more represented than luminal A (OR = 3.52; CI, 1.112–11.13; $p = 0.0319$), while the proportion of HER2+ was quite similar (OR = 1.57; $p = 0.4709$).

Conclusion Although made on a small number of cases, our results suggest a difference in distribution of molecular subtypes according to mode detection, confirming the results of earlier studies.

A. Caldarella (✉) · D. Puliti · E. Crocetti · E. Paci
Clinical and Descriptive Epidemiology Unit, Institute for Study and Cancer Prevention (ISPO), Via delle Oblate 2, 50141 Florence, Italy
e-mail: a.caldarella@ispo.toscana.it