The impact of population-based screening with mammography on breast cancer mortality : issues in mortality trends evaluation

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Trend studies of mammographic screening

- Studies of trends in breast cancer mortality rates in a population as a whole in relation to the introduction and/or extent of mammographic screening

- usually based on aggregated data obtained from routine sources

Hierarchy of epidemiological evidence

- randomised controlled trials
- cohort studies
- case control studies
- ecologic studies

Comparison of RCTs and trend studies

RCTs	Trend studies
only include deaths from breast cancer in women diagnosed after invitation to screening ('refined' mortality)	effect of screening diluted due to use of unrefined mortality
measure exposure of all women from date of randomisation (effectively first invitation)	implementation of screening usually phased over several years
have an appropriate contemporaneous comparison group (the control arm)	difficult to identify appropriate comparison group

Possible comparison groups for ecological studies

- age groups outside age range invited for screening
- same region/country before introduction of screening
  'local historical'
- geographic areas with no organised screening
  (concurrent and / or historical)

Sources of bias in ecologic studies

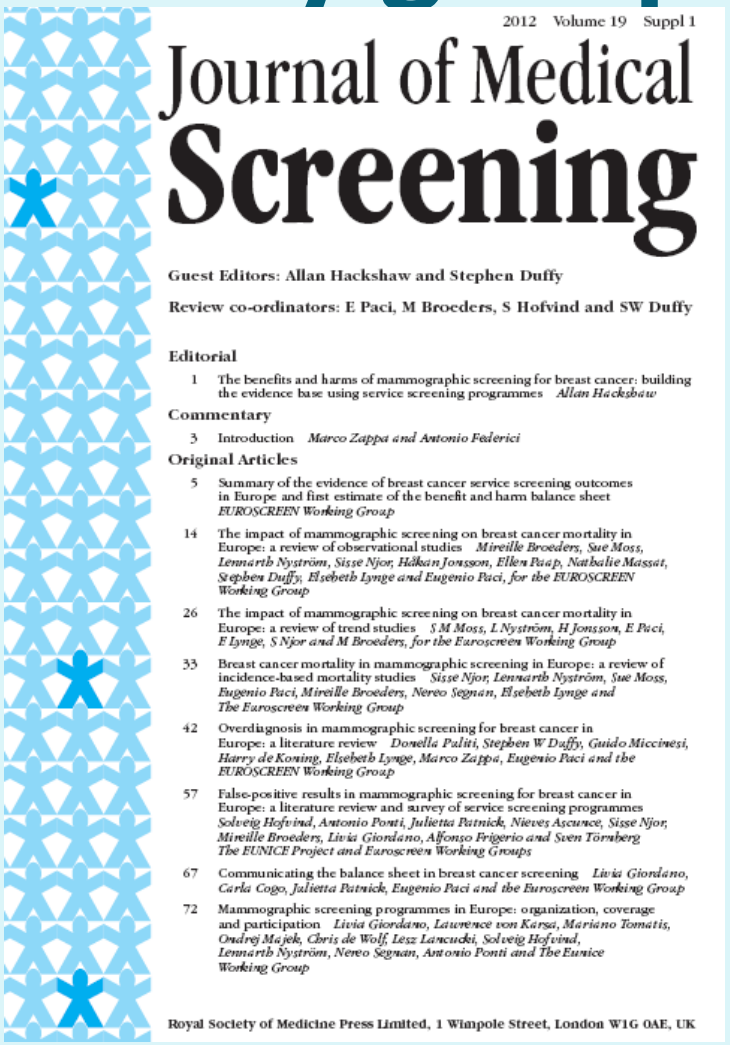
- differential changes in treatment effectiveness between time periods/regions
- 'contamination' – opportunistic screening before introduction of programme and / or outside invited age range
- differences in underlying risk of BC between regions, time periods and age-groups

Other influences on breast cancer mortality trends

- ‘halo effect’ of screening programme
- changes in cause of death coding

EUROSCREEN mortality group

- Denmark
  - Elsebeth Lynge
  - Sisse Njor
- Italy
  - Eugenio Paci
  - Nereo Segnan
- Sweden
  - Håkan Jonsson
  - Lennarth Nyström
- The Netherlands
  - Mireille Broeders
  - Ellen Paap
- UK
  - Stephen Duffy
  - Natalie Massat
  - Sue Moss



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

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Review of published papers

Objective : to estimate the effectiveness of service-screening programmes with mammography in West-Europe

- Studies included – study design:
  - trend studies (n=17)
  - incidence-based mortality studies (n=20)
  - case-control studies (n=8)

Trend studies (Moss et al, JMS 2012)

- *Only descriptions* of the trend in BCM
  - in relation to the timing of the introduction of organised screening (n=5)
- Included a more detailed *analysis*
  - with the aim of *quantifying* the impact of screening on BCM (n=12)
  - Poisson regression with or without age-cohort modelling
  - Joinpoint regression to identify 'break points' at which changes in mortality trends occurred

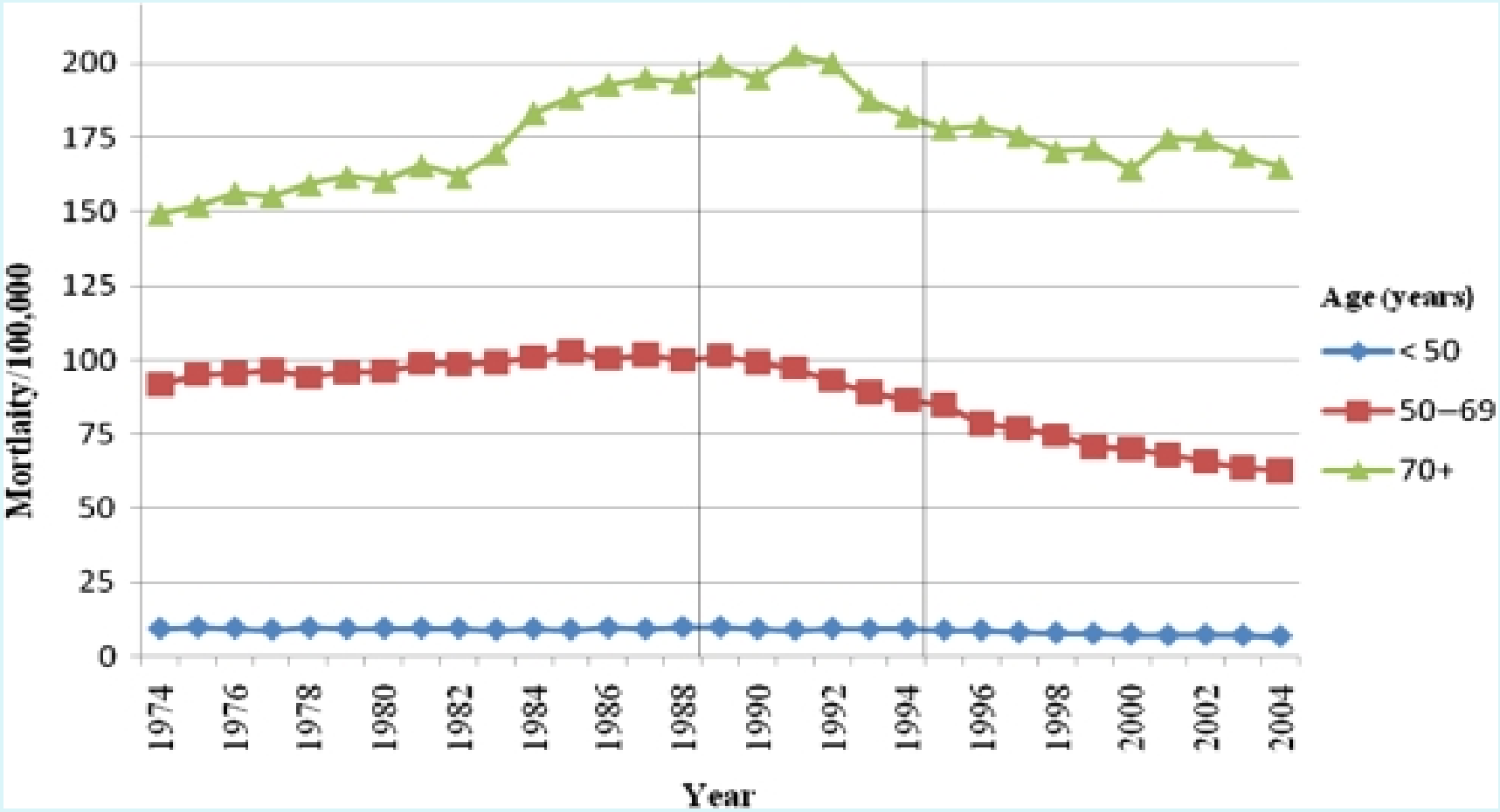
Table 2 Summary of trend studies that give a quantified estimate of the effect of screening

Reference and study area	Service screening programme: Start	Service screening programme: 100% coverage	Service screening programme: Age group invited	Time period studied	Age range studied	Method	Comparison /reference group	Reduction in breast cancer mortality
Jørgensen *et al.*[7] Copenhagen & Funen, Denmark	1991, 1993		50–69	1971–2006	35–84	Poisson	Rest of Denmark 55–74 *v.* other age groups	1977–2006: 1% (95% CI: 1–4) reduction per yr v. 2% (95% CI 1–3) in non-screening areas
Barchielli and Paci[8] Florence, Italy	(1970) 1990	1995 (72%)	50–69	1970–1997	25+	Poisson	Florence *v.* rest of Tuscany	Similar reduction in both areas
Gorini *et al.*[9] Florence, Italy	1970 (ES), 1990 (LS)		(40) 50–69, 50–69	1985–2000	35+	Log linear regression	Early (ES) *v.* late starting (LS) areas	1985–2000: 30% reduction in age standardised rate; 41% (95% CI: 21–56) in ES *v.* 11% (95% CI: 0–21) in LS
Otto *et al.*[10] Netherlands	1989	1997	50–69	1980–2001	55–74	Poisson	Before/after: Clustered by start date	1989–2001: 1.7% (95% CI 1.0–2.4) reduction per yr after start of screening
Otten *et al.*[11] Netherlands	1989	1997	50–69	1975–2006	35–85	Joinpoint	Before/after in age group 55–74	1994–2006: 2.3% per yr (95% CI: 1.6–3.0) −2.8% per yr (95% CI: 2.2–3.4) reduction
Ascunce *et al.*[12] Navarre, Spain	1990		45–65	1975–2004	30+	Joinpoint	Before/after: 50–69 *v.* other age groups	1987/9–2002/4: 36% reduction (95% CI: 21–48) all ages Change-point 1995 1995–2004: 9.0% reduction pa 50–69y, no significant trend in other age groups
Pons-Vigues *et al.*[13] Barcelona, Spain	1995	2004	50–69	1984–2004	50–74	Poisson	Before/after: Grouped by start date	1995–2004: 5% (95% CI: 1–8) reduction per yr *v.* 1% (95% CI: 1–2%) before start
Cabanes *et al.*[14] Spain	1990–99	2001	(45) 50–64	1980–2006	25+	Joinpoint	Trends in age groups 25–44, 45–64, 65+	Change-point 1993 Reduction per yr (95% CI) 1993–2006 by age group: 4.0% (3.5–4.4) 25–44yr; 3.1% (2.9–3.4) 45–64 yr; 1.3% (0.9–1.7) 65+ yr
Haukka *et al.*[15] Sweden (9 counties)	1980–1990		40–69	1974–2003	40–69, 70–79	Poisson regression	Screening effect allowing for lead time and secular trend. Grouped by start date	16% reduction (40–69 yr) (95% CI 9–22) 11% reduction (70–79 yr) (95% CI 2–20) After start of screening
Blanks *et al.*[16] England & Wales, UK	1988	1993	50–64	1969–1998	40–79	Poisson/APC	Observed *v.* expected in 55–69 *v.* other age groups	Reduction in 1998 of 6.4% (21.3% ages 55–69 *v.* 14.9 other age groups) Range 5.4–11.8%
Duffy *et al.*[17] England, UK	1988	1993	50–64 (69)	1974–2004	All ages	Poisson	Before/after 50–69 *v.* other age groups	1995–2004 *v.* 1974–1988: 28% reduction (95% CI: 26–30)
Autier *et al.*[18]					40–79	Joinpoint	50–69 yr	1989–2006: % change age-standardized rate
N. Ireland	1990	1993	50–6	1980–2006			N Ireland *v.* Rep. of Ireland	36.7 *v.* 27.7
Sweden	1986	1990 (90%)	(40)–69 (74)	1980–2006			Sweden *v.* Norway	28.0 *v.* 21.4
Netherlands	1989	1997	50–69 (74)	1980–2006			Netherlands *v.* Belgium	16.0 *v.* 22.8

Problems with selected studies

- inadequate follow up (< 10 years from year complete coverage of screening was achieved)
- inclusion of early years after introduction of screening
- not restricted to appropriate age range
- fail to consider rates/trends prior to start of screening

Breast cancer mortality in England 1974–2004



Duffy et al JMS 2010

Duffy et al JMS 2010

- compared with other age groups there was a highly significant 28% reduction in breast cancer mortality in the age group invited to screening in 1995-2004 vs 1974-1988
- includes age group 50-54
- ignores possible different trends between age groups

- “we have deliberately derived simple age-specific estimates from the English incidence and mortality rates. More complex age–period–cohort analyses might yield different estimates ”

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]

Autier et al concluded:

‘The contrast between the time differences in implementation of mammography screening and the similarity in reductions in mortality between the country pairs suggests that screening did not play a direct part in the reductions in BCM’

Autier et al BMJ 2011

- differences between neighbouring countries
- declines in mortality occurring prior to introduction of screening
- conclusions based on mean rate for all ages (% change 1989 vs 2006)
- e.g. NI vs Rep of Ireland -29.6% vs -26.7%

  age group 50-69 -36.7% vs -27.7%

- ignores opportunistic screening in Norway before start of programme

Summary of Euroscreen review of trend studies

For studies with adequate follow-up:

- 1-9% reduction in BCM per year in post-screening period
- 28-36% reduction in BCM in post vs. pre-screening period

No pooled estimates:

- due to differences in methodology, comparisons and outcome measures

Moss et al JMS 2010

Grimes & Schulz : “Descriptive studies: what they can and cannot do” (Lancet 2002)

“Descriptive studies have both strengths and weaknesses. Often, the data are already available and thus inexpensive and efficient to use. Furthermore, few ethical difficulties exist. However, descriptive studies have important limitations. Temporal associations between putative causes and effects might be unclear. A dangerous pitfall is that the investigators might draw causal inferences when none is possible”

Conclusions

- trend studies are an ‘obvious’ approach to evaluation of population screening
- numerous sources of bias
- interpret with caution
- need for more rigorous individual based studies