



EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

Directorate F - Health, Consumers & Reference Materials (Ispra)
Health in Society

European Commission Initiative on Breast Cancer (ECIBC): European guidelines on breast cancer screening and diagnosis Evidence profile

Healthcare question	Should organised mammography screening vs. no mammography screening be used for early detection of breast cancer in women aged 70 to 74?
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Abbreviations	CI: Confidence interval RR: Risk ratio

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Organised mammography screening	No mammography screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer mortality (follow up: mean 20 years)												
2 ^{1,2,a}	randomised trials	not serious	not serious	not serious _{b,c}	not serious _d	none	60/7598 (0.8%)	0.9%	RR 0.77 (0.54 to 1.09)	207 fewer per 100,000 (from 414 fewer to 81 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Organised mammography screening	No mammography screening	Relative (95% CI)	Absolute (95% CI)		
								3.0% ^e		690 fewer per 100,000 (from 1,380 fewer to 270 more)		
Other cause mortality (follow up: mean 7.9 years) ^f												
2 ^{3,a}	randomised trials	not serious	not serious	serious ^b	serious ^d	none	2834/10339 (27.4%)	27.0% ^g	RR 1.01 (0.91 to 1.10)	270 more per 100,000 (from 2,430 fewer to 2,700 more)	⊕⊕○○ LOW	IMPORTANT
Stage IIA or higher (tumour size ≥ 20 mm) ^f												
1 ^{4,a}	randomised trials	not serious	not serious	very serious _{b,h}	not serious	none	389/57236 (0.7%)	1.1% ^g	RR 0.64 (0.55 to 0.73)	385 fewer per 100,000 (from 482 fewer to 289 fewer)	⊕⊕○○ LOW	IMPORTANT
Tumour size ≥ 50 mm												
1 ^{4,a}	randomised trials	not serious	not serious	very serious _{b,h}	not serious	none	62/57236 (0.1%)	0.2% ^g	RR 0.63 (0.45 to 0.89)	63 fewer per 100,000 (from 94 fewer to 19 fewer)	⊕⊕○○ LOW	IMPORTANT
Overdiagnosis (population perspective)												
2 ^{5,6,a}	randomised trials	not serious	not serious	serious ^{b,i}	not serious	none	10.1% (95% CI 8.6%-11.6%) ^j				⊕⊕⊕○ MODERATE	CRITICAL
Overdiagnosis (woman perspective)												
2 ^{5,6,a}	randomised trials	not serious	not serious	serious ^{b,i}	not serious	none	17.3% (95%CI 14.7%-20.0%) ^k				⊕⊕⊕○ MODERATE	CRITICAL
Rate of mastectomies (women ages 40-74 at inclusion)												
5 _{2,7,8,9,10}	randomised trials	not serious	not serious ^l	very serious _{b,h}	not serious	none	1542/144920 (1.1%)	0.9%	RR 1.20 (1.11 to 1.30)	180 more per 100,000 (from 99 more to 270 more)	⊕⊕○○ LOW	IMPORTANT

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Organised mammography screening	No mammography screening	Relative (95% CI)	Absolute (95% CI)		
Provision of chemotherapy (women ages 40-74 at inclusion)												
2 ^{2,9,10}	randomised trials	not serious	serious ^m	very serious ^{b,n}	serious ^d	none	252/59677 (0.4%)	0.4%	RR 0.86 (0.52 to 1.41) ^o	56 fewer per 100,000 (from 192 fewer to 164 more)	⊕○○○ VERY LOW	IMPORTANT
Quality of life (inferred from psychological effects) ^f												
54 ¹¹	observational studies	not serious	not serious ^p	not serious	not serious	none	One systematic review with 54 studies included -no meta-analysis - (Brett 2005). Mammographic screening does not appear to create anxiety in women who are given a clear result after a mammogram and subsequently placed on routine recall. Mixed results about anxiety in women recalled for further testing: several studies reported transient or long term (from 6 months to 1 year after recall) anxiety, while other studies reported no differences in anxiety levels. The nature and extent of further testing seem to determine the extent of anxiety.			⊕⊕○○ LOW	IMPORTANT	
False-positive related adverse effects (psychological distress) ^f												
24 ^{12,13}	observational studies	not serious	not serious	not serious	not serious	none	Two systematic reviews. One review included 17 studies and found that women who received a false-positive mammogram result had greater distress, fear, anxiety, and worry about breast cancer (Saltz 2010). The second review included 7 studies, the psychological distress using diseases-specific measurements, in women (age not specified) with a false-positive mammogram at 35 months after the last assessment was ; for women that needed further mammography RR=1.28 (95%CI 0.82-2.00); for women placed in early recall the RR=1.82 (95%CI 1.22-2.72); for women that needed a fine needle puncture aspiration RR=1.80 (95%CI 1.17-2.77); for women that needed a biopsy RR=2.07 (95%CI 1.22-3.52); no differences in generic measures of general anxiety and depression were observed at 6 weeks after assessment and 3 months after screening Bond (2013).			⊕⊕○○ LOW	IMPORTANT	
False-positive related adverse effects (biopsies and surgeries) ^f												
4 ¹⁴	observational studies	not serious	not serious	serious ^q	not serious	none	Results from literature review (4 studies, 390 000 women aged 50 to 69) showed an overall false-positive screening result of 19.7% in women undergoing 10 biennial screening tests (pooled risk estimate based on 3 studies; range 8 - 21%). This was related to a 2.9% pooled cumulative risk of an invasive procedure with benign outcome (range 1.8% to 6.3%; based on			⊕○○○ VERY LOW	IMPORTANT	

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Organised mammography screening	No mammography screening	Relative (95% CI)	Absolute (95% CI)		
							2 studies) and 0.9% risk of undergoing surgical intervention with benign outcome (based on 1 study) (Hofvind 2012). Cross-sectional data from the EUNICE Project (women aged 50 to 69): 17 countries, 20 screening programmes, 1.7 million initial screens, 5.9 million subsequent screens; showed that 2.2% and 1.1% of all screening examinations resulted in needle biopsy among women without breast cancer (initial and subsequent screens, respectively). In addition, 0.19% and 0.07% of all screening examinations resulted in surgical interventions among women without breast cancer (initial and subsequent screens, respectively).					

Explanations

- The reference listed in the evidence profiles correspond to the specific publications used to extract crude data for estimating the outcomes' effect sizes. Additional reference describing the characteristics of the included studies can be found in the document's main text of this systematic review.
- Trials were conducted more than 20 years ago. Currently, women have higher adherence to breast cancer screening while quality control of screening and breast cancer care have improved.
- Despite concerns about indirectness from the trials, including the fact that the population age range of 40 to 74 is broader than the age range in this question, after considering evidence from contemporary non-randomised studies (Broeders 2012) the GDG did not downgrade the quality of evidence for indirectness.
- For the mortality related outcomes, the GDG decided not to downgrade for imprecision because the relative effect is consistent with those in other age groups and that lends support that the estimate of the effect is close to what is reported here. This decision is also reinforced by the fact that, if the indirect evidence from the 50-69 age stratum were considered here, the certainty of the evidence for this outcome would also have been rated as 'moderate', as a result of downgrading that evidence from 'high' to 'moderate' by one level for indirectness and using it here.
- UK cancer registry data indicate a higher estimate, of 3% over 20 years.
- The GDG changed the importance of the outcome from 'critical' to 'important' because the members felt this outcome influenced neither the direction nor the strength of the recommendation.
- Median or mean of the control group of the included studies unless otherwise specified.
- Analysis includes women aged 40-74 years, however only about 13% of women were ≥ 70 years.
- Indirect data from women aged 50 to 69.
- Estimate from a meta-analysis of 2 trials including women aged 50 to 69 (CNBSS-2 and Malmo I) in which women in the control group were not offered mammography screening at the end of the trial. Excess cancers as a proportion of cancers diagnosed over whole follow-up period in women invited for screening (population perspective). Independent UK Panel on Breast Cancer Screening (2012).
- Estimate from a meta-analysis of 2 trials (CNBSS-2 and Malmo I) in which women in the control group were not offered mammography screening at the end of the trial. Excess cancers as a proportion of cancers diagnosed during screening period in women invited for screening (woman perspective).

- l. Some studies were sub-optimally randomised and had non-blinded assessment of cause of death; however analysis restricted to low risk of bias trials provided a similar risk estimate.
- m. Unexplained inconsistency with statistical heterogeneity ($I^2 = 71\%$, $p = 0.06$).
- n. Chemotherapy protocols and their indications have significantly changed (e.g. node status was not determined in earlier studies).
- o. Same assumptions as in younger women can be made about lead time. This may be an even bigger issue in older women and it is influenced by life expectancy.
- p. Unexplained inconsistency for variability in anxiety in the group of women recalled for further testing.
- q. Studies included women aged 50 to 69. The estimates are likely lower within the stratum of women aged 70 and older.

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