Review: High-quality studies do not show reductions in breast cancer mortality for women screened with mammography

Gøtzsche PC, Olsen O. **Is screening for breast cancer with mammography justifiable?** Lancet. 2000 Jan 8;355:129-34.

QUESTION

Does published evidence support the finding of reduced mortality in women who are screened for breast cancer with mammography, after taking into account the methodologic strength of the studies?

DATA SOURCES

Randomized controlled trials were identified by searching the Cochrane Library with the terms breast cancer, breast neoplasms, screening, and mammography and the author names.

STUDY SELECTION

A meta-analysis from Sweden and all other randomized controlled trials were included if they studied women who were randomly allocated to screening or no screening for breast cancer with mammography.

DATA EXTRACTION

Data were extracted on randomization methods; baseline characteristics, especially prognostic factors of age, symptoms at entry, family history of breast cancer, socioeconomic status, and previous examinations for breast cancer; follow-up completeness; blinding of outcomes (all-cause mortality and mortality from breast cancer); and adverse effects associated with screening if more than 100 women reported the adverse effect. Data were extracted from the studies, or authors were contacted to provide missing information. Methodologic rigor was established by assessing the quality of randomization, baseline consistencies between screened and nonscreened groups, inconsistencies in the number of women randomized, success of follow-up, and blinding of determination of cause of death were used.

MAIN RESULTS

8 studies were identified. On the basis of the 2 predefined criteria, 2 of the studies had adequate quality (66 013 women in the screening groups and 66 105 women in the nonscreening groups), and 6 had lesser quality (182 179 women in the screening groups and 142 052 in the nonscreening groups). Data from the 2 higher-quality trials showed no reduction in mortality from breast cancer; data from the 6 lesser-quality studies showed a reduction (Table). The difference between these 2 sets of analyses was statistically significant ($P < 0.005$).

CONCLUSION

High-quality studies of screening for breast cancer with mammography show that breast cancer mortality is not reduced; lesser-quality studies show reductions in breast cancer mortality.

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Breast cancer mortality associated with screening mammography vs no mammography*

Studies	Analysis model	Weighted event rates		RRI (95% CI)
		Mammography	No mammography	
High quality ($n = 2$)	Random effects	0.3%	0.3%	4% (–16 to 27)†
				RRR (95% CI)
Lesser quality ($n = 6$)	Fixed effects	0.4%	0.5%	26% (16 to 45)

*Weighted event rates calculated from data in article. Follow-up duration not available.
†Not significant

COMMENTARY

The meta-analysis by Gøtzsche and Olsen has rekindled the often-rancorous debate about screening mammography, a debate that occurs mainly on 2 fronts: whether to screen women < 50 years of age and whether to screen at all. The meta-analysis concludes that screening with mammography is unjustified.

The meta-analysis separates the breast cancer screening trials on the basis of the methodologic quality of each trial. 2 trials are deemed to have adequate methods; the rest are not. The conclusion of the analysis is based on the negative results of the 2 "adequate" trials.

The trials were noted to be heterogeneous. Unfortunately, the authors did not report on such potential explanatory factors as age, screening modality, differences in control groups, or duration of follow-up (1, 2). For example, the Canadian studies are analyzed as a single trial, whereas they were 2 separate trials in 2 populations of women (aged 40 to 49 and 50 to 59 y at entry) that compared mammography and physical examination with 2 separate comparison groups (usual care for those < 50 and annual physical examination for those ≥ 50) (3, 4). The conclusions of meta-analyses that formally consider trial quality can depend on the trial quality-assessment methods used (5). Furthermore, the method used to ascertain quality in this trial is unvalidated and has been incorrectly applied to cluster-randomized trials, which are analyzed as if participants had been randomized individually.

Debate about the relative and absolute costs and benefits of breast cancer screening will continue because of differing values for outcomes and the gaps between current screening and treatment methods and evidence from screening trials initiated decades ago. A summary of evidence from heterogeneous trials ought to inform rational debate by providing clear insight through complete and rigorous analysis. This study has failed to do so.

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