Cost-effectiveness of extending screening mammography guidelines to include women 40 to 49 years of age
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Screening mammography for women 40-49 years.

Type of intervention
Screening.

Economic study type
Cost-effectiveness and cost-utility analysis.

Study population
Women of 40 years of age and older.

Setting
Primary care. The study was carried out in California, USA.

Dates to which data relate
The effectiveness data were obtained from studies published in 1995 and 1997. The resource use data were obtained from reports published in 1995 and 1997. The price year was 1995.

Source of effectiveness data
Effectiveness data were derived from a synthesis of previously completed studies.

Modelling
A Markov model using Monte Carlo methods was used in order to estimate costs and benefits in terms of additional life expectancy. Four states were incorporated into the model: healthy, development of breast cancer while remaining alive, death due to breast cancer, and death from another cause. The transition probabilities were age-and strategy-dependent. For screened women 50 to 69 years of age, the model assumed the benefit to start 5 years after the initiation of screening and continuation until age 74 years. For women beginning screening at 40 years of age, the benefit starts at the age of 50.

Outcomes assessed in the review
The outcomes assessed were a reduction in breast cancer mortality.

Study designs and other criteria for inclusion in the review
The review included English language studies reported from January 1966 to October 1993. Originally randomized controlled trials, cohort and case-control studies of the efficacy of screening mammography were candidates for inclusion into the study. From the references obtained (n=75), inclusion was determined according to the following criteria: (1) the study was an experimental study, prospective cohort study with internal controls or case-control study with population-based controls with the main outcome of breast cancer death; (2) follow-up of at least 5 years and a minimum of 10 breast cancer deaths; (3) risk ratios (RR) or odds ratios (OR) reported with a confidence interval (CI), or data presented in the paper which allowed either RR or OR and CI to be calculated; (4) RR or OR reported that was adjusted for age or based on controls that were age matched to cases. For duplicated studies, only the most recent report was included. After initial data analysis, only randomized controlled studies were included.

Sources searched to identify primary studies
MEDLINE was searched followed by a manual search of references from the bibliography of studies meeting entry criteria 1-4 and consultations with experts.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Two reviewers (two of the authors) who were not blinded to the journal, year of publication or authors of the primary studies, independently abstracted data from each article. In cases of disagreement in the results, a third author reviewed the paper in question and gave the final decision.

Number of primary studies included
Eight and nine studies were included, respectively, for the syntheses of groups (50-74 and 40-49 years of age) at the start of screening. For the former synthesis, 3 studies were associated with lengths of follow-up between 7 and 9 years after screening, whilst the other five studies had lengths of follow-up between 10 and 12 years. The latter synthesis had follow-up data available at 10 years and more after the start of screening for all 9 studies.

Methods of combining primary studies
Two meta-analyses, one for each age group, using the fixed effects model.

Investigation of differences between primary studies
The authors noted that important differences between studies existed in terms of the number of mammographic views (one or two), screening interval (either 12 or 18-33), duration of follow-up (7-9 and 10-12 years), duration of screening (3-5 and 8-10 years), and whether or not a clinical breast examination was performed in combination with mammography. Summary RR data for studies divided according to each one of these criteria, and also for studies divided into categories taking into account two criteria at a time, were analysed. The effect of study start date was also analysed by comparing RRs for studies started before 1980 and those started in 1980 and after. Tests of heterogeneity had p values above the critical value (p=0.2) established by the authors (p>0.2 for the 50-74 age group results, and p=0.4, for the 40-49 age group).

Results of the review
Mammography for women 40 to 49 years of age at the time of initial screening (performed every 18 months), led to a 16% reduction in breast cancer mortality at the age of 50 years (i.e. RR 0.84, 95% CI: 0.71- 0.99 at 10-14 years of follow-up), while the additional biennial screening of these women starting at 50 years of age and continuing until 69 years of age would make that rate 27% at the age of 55. Biennial screening for women starting at the age of 50 years and continuing until the age of 69, would translate into a 27% reduction in mortality with a delay of 5 years, at the age of 55 (i.e. RR 0.73, 95% CI: 0.63-0.84 at 7 to 9 years of follow-up).
Measure of benefits used in the economic analysis
The measure of benefits were life-years gained and quality-adjusted life-years (QALYs) gained. A model was used in estimating the benefits associated with each strategy. The quality weights were obtained from one ‘small’ Australian study. The benefits were discounted using a 3% annual rate.

Direct costs
Costs were discounted. Some quantities of resource use were not reported separately from costs (treatment of breast cancer). A model was used in the calculation of total costs. The cost of performing the screening, the cost of evaluating abnormal screening results, and the cost of breast cancer treatment were measured. The main source of cost data was the National Survey of Mammography facilities. The costs were reflated using the consumer price index for medical services. The price year was 1995.

Currency
US dollars ($).

Sensitivity analysis
One-way and multi-way analyses were performed by varying the following parameters: discount rate, mortality reduction from screening, delay in benefit, cost of mammography, screening interval, abnormal mammograms, cost of work-up at 11% abnormal rate, cost of work-up at 2% abnormal rate, utility for time after treatment, utility for metastatic disease, and stage shift due to screening.

Estimated benefits used in the economic analysis
The total number of life-years saved with the biennial screening option for women 50 to 69 years of age was 329, relative to no-screening. The option involving screening every 18-months for women 40 to 49 years of age plus biennial screening starting at age 50 years until 69 years of age saved 64 years, relative to the former option. The corresponding figures in QALYs saved were 324 and 61, respectively, for both comparisons.

Cost results
Using a 3% discount rate, the total cost for the no-screening option was $27.03 million, with the biennial screening option for women 50 to 69 years of age alone being $34.07 million. The option involving every-18-month screening for 40 to 49-year-old women plus biennial screening for 50 to 69-year-old women had a corresponding figure of $40.83 million.

Synthesis of costs and benefits
The cost per year of life saved and the cost per QALY gained, both in 1995 prices at a 3% discount rate used for costs and benefits, were the outcome measures used to synthesize costs and benefits associated with each strategy. The corresponding figures for the comparisons of (a) the biennial screening programme for 50 to 69-year-olds with respect to no-screening and (b) the every-18-month screening for women 40 to 49 years of age plus biennial screening starting at 50 years (until 69 years of age) relative to the biennial option alone were (a) $21,400 and $21,700, and (b) $105,000 and $111,800, respectively, for the cost per life-year saved and cost per QALY saved. The most important parameters found in the sensitivity analyses were, in order of importance: the discount rate, mortality reduction from screening, delay in benefit, cost of mammography (a cost of $45 or less would make the cost-effectiveness ratio of the intervention decrease to $50,000 or less), and screening interval. The multi-way Monte Carlo analyses (all parameters varied) yielded 95% of iterations within the ranges for the cost-effectiveness ratios of $7,200 and $109,100, for the screening of 50 to 69 year-olds, and $43,000 and $1,624,400, for the incremental cost-effectiveness of screening 40 to 49 year-olds.
Authors' conclusions
Screening mammography is relatively cost-ineffective among women 40 to 49 years of age because mammography is less efficacious and the incidence of breast cancer is low in this age group.

CRD COMMENTARY - Selection of comparators
The comparator used in the study has been previously found to be a cost-effective screening option to reduce breast cancer mortality, that is screening (base case, every two years) of presumed healthy women aged 50 to 69 years. This strategy was in turn compared with the do-nothing option (no-screening).

Validity of estimate of measure of benefit
The model did not account for carcinoma in situ and this simplification would need further investigation to assess whether the estimate of measure of benefit is valid. The estimates of reduction in breast-cancer mortality are likely to be valid because an adequate methodology was used in their estimation (meta-analyses based on a comprehensive review of the literature, entry criteria - which included only RCTs, analysis of differences between studies -test for homogeneity, and analysis of uncertainty in the estimates). Although some criticism has been stressed for the analysis of results by subgroups (i.e. women 40-49 years of age) from primary studies designed for wider populations (i.e. women 40 to 74 years), the corresponding argument has been opposed in terms of the advantages of meta-analysis (pooling of sample data to obtain more precise estimates of effects (see Kerlikowske, 1997)). Either way, Kerlikowske (1997) concludes that there is no compelling scientific evidence supporting mass mammography screening for women aged 40 to 49 years.

Validity of estimate of costs
Some resource quantities were not reported separately from costs, thus affecting the reproducibility of the analysis. Apart from this, adequate details of cost estimation were given, which revealed some data to be of poor quality. The exclusion of carcinoma in situ from the model meant that the associated costs were omitted from the analysis. The sensitivity analysis performed analysed the robustness of the results given the potential bias just discussed.

Other issues
The conclusions reached by the authors were justified on the evidence of results of the sensitivity analyses. However, provided the model used in the present study is clinically adequate, the generalisability to other countries would depend on the prevalence and incidence rates of breast cancer among different age groups and, also, on the relative prices of treatment of breast cancer and mammography screening. The effectiveness results were compared with previous studies which used unreasonable assumptions of no delay in the effect of screening on breast cancer mortality, while one of them calculated average cost effectiveness of screening women 40 to 49-years-old, instead of calculating incremental cost-effectiveness relative to screening in 50 to 69-year-old women as this study did. The results were not presented selectively.

Implications of the study
This study offers evidence supporting the hypothesis that mammography screening of 40 to 49-year-old women, in addition to screening of 50 to 69-year-old women, is not cost-effective.

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**Other publications of related interest**


Kerlikowske K. Efficacy of screening mammography among women aged 40 to 49 years and 50 to 69 years: comparison of relative and absolute benefit. Monographs of the National Cancer Institute 1997;22:79-86.

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Age Factors; Aged; Breast Neoplasms /epidemiology /prevention & control; Cost-Benefit Analysis; Female; Humans; Life Expectancy; Mammography /economics; Markov Chains; Mass Screening /economics; Middle Aged; Monte Carlo Method; Randomized Controlled Trials as Topic; Sensitivity and Specificity

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