A model-based comparison of breast cancer screening strategies: mammograms and clinical breast examinations

Shen Y, Parmigiani G

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
The study evaluated a total of 48 screening strategies for breast cancer. Each strategy was determined by the combination of an age range (40 - 79, 45 - 79 and 50 - 79 years), an interval between examinations (0.5, 1, 1.5 and 2 years), and whether mammography and clinical breast examination (CBE) were given at every exam or at every two exams. The strategies were compared with no screening for breast cancer.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a birth cohort of 100,000 women.

Setting
The study setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1979 and 2003. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a review of published studies.

Modelling
A decision analysis based on a micro-simulation model was used. For all women who developed breast cancer during their lifetime, the authors simulated their natural histories. This included the age at onset of the preclinical disease, the preclinical durations (via tumour growth rates), the age at onset of the clinical disease, and the subsequent survival time depending on age and tumour characteristics at detection.

For more information on the model, the authors referred the readers to Parmigiani (2002), Parmigiani et al. (1999) and Shen et al. (in press) (see ‘Other Publications of Related Interest’ below for bibliographic details).

Outcomes assessed in the review
The outcomes assessed were:
the age-specific incidence of clinical breast cancer;
the distribution of preclinical breast cancer duration;
the sojourn time;
the sensitivity of CBE and mammography;
the death rate due to breast cancer; and
dead from other causes.

Study designs and other criteria for inclusion in the review
The authors reported that the effectiveness data were derived from population level data, randomised breast cancer screening trials, and data from large clinical trials evaluating standard treatments for breast cancer.

Sources searched to identify primary studies
Not reported.

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

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Over 17 primary studies were included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
The authors did not report whether any differences between the primary studies were investigated.

Results of the review
The results of the review were not reported in this paper. The authors referred the reader to Parmigiani et al. (1999) for more information on the survival model, and to Shen et al. (in press) for more information on specific extensions made for the present analysis.

Methods used to derive estimates of effectiveness
The authors used a deconvolution approach to derive the age-specific incidence of preclinical disease, given the age-specific incidence of clinical breast cancer and the distribution of preclinical duration. The authors generalised an exponential distribution for preclinical duration to incorporate age effect and uncertainties.

Estimates of effectiveness and key assumptions
The sensitivity of each screening modality was assumed to depend on tumour size and age at the time of test via a logit model. To assess the overall sensitivity of a screening policy using both mammography and CBE, the authors assumed that the two modalities were independent.

The estimates of outcomes were reported in Parmigiani et al. 2002 (see 'Other Publications of Related Interest' below for bibliographic details) and Shen et al. (in press).

**Measure of benefits used in the economic analysis**

The measure of benefits used was the quality-adjusted life-year (QALY). For more information on the quality adjustments undertaken in the model, the authors referred the reader to Parmigiani et al. (1999).

**Direct costs**

The authors adopted a public health perspective. The direct medical costs included in the analysis were for the examinations (i.e. mammography and CBE test costs). The authors did not explicitly consider the costs of false-positive exams, possible over-diagnosis, and the downstream financial consequences of early detection. They also did not report the sources from which the unit costs for the screening tests were derived. All the quantities of resources used were derived from the model. Discounting was not reported, although it would appear to be necessary as the costs of the screening programme could be incurred over future years (0.5-, 1- or 2-year intervals). The study reported the marginal costs. The price year was not reported.

**Statistical analysis of costs**

The costs were treated as point estimates (i.e. the data were deterministic).

**Indirect Costs**

The indirect costs were not included.

**Currency**

US dollars ($).

**Sensitivity analysis**

The authors performed sensitivity analyses by using different age-specific preclinical breast cancer duration distributions. The two cost scenarios considered were CBE at $100 and mammography at $200 or $150. Therefore, the authors investigated the effect of varying the cost ratio between CBE and mammography from 1.5 to 2.

**Estimated benefits used in the economic analysis**

The authors compared a total of 48 screening interventions. They estimated the marginal (or incremental) benefits of the screening strategy over those of no screening. The marginal benefit was reported for 18 alternatives of breast cancer screening, based on the combination of age at start (40 or 50 years), interval between examination (6 months, 1 year or 2 years), and whether mammography and CBE were given at every exam or at every two exams.

For each screening interval and starting age, giving mammography and CBE at every exam had the highest marginal benefit (i.e. additional QALYs) over no screening. This ranged from 0.055 additional QALYs when women started screening at age 50 and the interval of examination was every 2 years, to 0.221 additional QALYs when women started screening at age 40 and the interval of examination was every 6 months.

In contrast, for each screening interval and starting age, giving mammography every two exams and CBE at every exam had the lowest marginal benefit over no screening. This ranged from 0.050 additional QALYs when women started screening at age 50 and the interval of examination was every 2 years, to 0.195 additional QALYs when women started
screening at age 40 and the interval of examination was every 6 months.

**Cost results**
The authors compared a total of 48 screening interventions. They estimated the marginal (or incremental) costs of the screening strategy over those of no screening. The marginal cost was reported for 18 alternatives of breast cancer screening.

For each screening interval and starting age, giving mammography every two exams and CBE at every exam had the lowest marginal cost over no screening. This ranged from an additional $2,400 when women started screening at age 50 and the interval of examination was every 2 years, to an additional $13,100 when women started screening at age 40 and the interval of examination was every 6 months.

In contrast, for each screening interval and starting age, giving mammography and CBE at every exam had the highest marginal cost over no screening. This ranged from an additional $3,700 when women started screening at age 50 and the interval of examination was every 2 years, to an additional $19,700 when women started screening at age 40 and the interval of examination was every 6 months.

**Synthesis of costs and benefits**
The costs and benefits were combined using an incremental cost-utility ratio (i.e. the additional cost per QALY saved). For each screening interval and starting age, giving mammography every two exams and CBE at every exam had the lowest marginal cost per QALY saved. This ranged from $48,600 per QALY saved when women started screening at age 50 and the interval of examination was 2 years, to $67,200 per QALY saved when women started screening at age 40 and the interval of examination was 6 months.

In contrast, giving both mammography and CBE at every exam had the highest marginal cost per QALY saved. This ranged from $66,900 per QALY saved when women started screening at age 50 and the interval of examination was 2 years, to $89,200 per QALY saved when women started screening at age 40 and the interval of examination was 6 months.

The results of the sensitivity analysis showed that varying the age-specific preclinical duration distributions did not alter the relative cost-effectiveness of the policies. The authors also reported that using a cost ratio of 2 between the costs of mammography and CBE increased the overall costs for each strategy, especially the strategies with relatively short screening intervals. However, such a change did not alter the relative cost-effectiveness of the policies.

**Authors’ conclusions**
A biennial mammography coupled with an annual clinical breast examination (CBE) was the most cost-effective screening strategy for breast cancer.

**CRD COMMENTARY - Selection of comparators**
No justification was given for using no screening as the comparator. However, it would appear that this strategy has been used to evaluate the active value of the other 48 screening options. More importantly, the authors failed to compare the costs and outcomes of screening using both CBE and mammography with screening using mammography only, which is current practice in many European countries. You should decide if the comparator represents current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not report that a systematic review of the literature had been undertaken to identify relevant research and minimise biases. However, the study presented here was published as a short communication paper, consequently the authors had limited space in which to present their methods and results. The authors therefore referred the reader to other sources for more background information. This made it difficult to judge, on the basis of this paper, the overall
quality of the study.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. The authors used health utility (QALYs) as a measure of benefit in the economic analysis. The utility values were derived from the literature, but no specific details on the method used to derive them were reported in the current study. This makes it difficult to comment on the quality of the estimates used. Although discounting of the benefits would appear to have been relevant, the authors did not report if future benefits were discounted.

**Validity of estimate of costs**
The cost analysis was performed from a public health perspective. The authors only included the costs of actual screening for breast cancer. They did not consider other relevant costs, such as those associated with the consequences of early detection, over-diagnosis and false-positive exams. It is unclear if the overall impact of these omissions would have biased the results in favour or against the screening interventions. The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results. The sources from which the unit costs were derived were not reported. The authors undertook limited sensitivity analyses of the costs by varying the cost ratio between mammography and CBE. Discounting appears to have been relevant, as part of the screening costs were incurred in the future, but the authors did not report discounting of future costs. The price year was not reported, which will hamper any future inflation exercises.

**Other issues**
The authors reported that their analysis was the first to evaluate the costs and utility of the combined use of mammography with CBE in the early detection of breast cancer. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported no limitations to their study. However, one limitation of the study was that there were very few details of the methods used to assess the outcomes and costs. This made it difficult to judge, solely on the basis of this paper, the overall quality of the study.

**Implications of the study**
The authors recommended that, in European countries where common practice is to screen women aged over 50 years with a mammography every other year, a clinical breast examination would be helpful during the year in which they do not have their regular mammography.

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**Bibliographic details**

**Other publications of related interest**


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