Decision analysis for the cost effectiveness of sestamibi scintimammography in minimizing unnecessary biopsies


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
Three strategies for breast cancer screening were examined:

- conventional mammography (MM) alone (strategy A);
- sestamibi scintimammography (SSMM) after indeterminate MM (strategy B); and
- SSMM after both a positive and an indeterminate MM (strategy C).

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women aged 40 years or older.

Setting
The setting was not explicitly reported, but it is likely to have been primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence came from studies published between 1984 and 2000. No dates were explicitly reported for resource use. The price year was not explicitly reported.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies, augmented with authors’ assumptions.

Modelling
A quantitative model, based on a decision tree, was constructed to compare the three screening strategies. The costs and the benefits common to both alternative strategies were not modelled. The Bayesian approach was used to obtain the explicit probabilities of each outcome measure. The structure of the tree was depicted graphically. Women between 40 and 49 years old were screened once every other year, while those of 50 years or older underwent annual screening. Under strategy A, women with positive or indeterminate results of MM were further investigated by core needle biopsy (CNB), and then excisional biopsy (EB) if required. Women with a negative MM returned for screening on the basis of
their age. Under strategy B, SSMM was performed only after an indeterminate MM and women with a negative SSMM returned for a follow-up MM after 3 months. Under strategy C, SSMM was performed on all women with both a positive or indeterminate MM, and those negative after SSMM were followed for 3 months. The time horizon of the model was lifetime.

**Outcomes assessed in the review**
The model inputs assessed in the review were the following probability values:

- pre-test likelihood of disease;
- MM sensitivity and specificity;
- SSMM sensitivity and specificity;
- CNB insufficiency rate;
- CNB sensitivity and specificity;
- EB sensitivity and specificity;
- the percentage of indeterminate MM in the initial group;
- disease prevalence in the indeterminate MM sub-group;
- the mortality and morbidity with MM, SSMM, CNB and EB;
- the distribution of cancers according to stage at time of diagnosis for local, regional or distant cancers with no delay, 3-month delay and 6-month or greater delay;
- the distribution of cancers according to stage at time of diagnosis for patients with palpable lesions;
- the mean life expectancy (LE) of a healthy woman of 61 years of age (mean age of the cohort included in the model); and
- the compliance rate.

**Study designs and other criteria for inclusion in the review**
The authors stated that the literature was searched to obtain mean values and ranges for the model inputs required in the decision model. The designs of the primary studies and the inclusion criteria were generally not mentioned. Several groups of literature reviews were conducted on the basis of the parameters considered. For the sensitivity and specificity of MM, the English literature was searched from 1983 to 1996 for studies that employed definitive diagnosis of positive mammograms by biopsy, and that reported the results in sufficient detail to allow the averaging of sensitivities and specificities between the individual studies.

**Sources searched to identify primary studies**
Not stated.

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

**Methods used to judge relevance and validity, and for extracting data**
Number of primary studies included
The effectiveness data were obtained from 15 primary studies.

Methods of combining primary studies
Estimates coming from the primary studies were combined by calculating the average value, weighted by the sample size of each study. Data for the sensitivity and specificity of SSM were not pooled due to the small sample size of the primary studies.

Investigation of differences between primary studies
Not stated.

Results of the review
The probability values used in the model were as follows:

0.24 for pre-test likelihood of disease;
83% for MM sensitivity and 92% for MM specificity;
52% for SSMM sensitivity and 93.5% for SSMM specificity;
2% for CNB insufficiency rate;
97% for CNB sensitivity and 99% for CNB specificity; and
100% for both EB sensitivity and specificity.

The percentage of indeterminate MM in the initial group was 4%.

The disease prevalence in the indeterminate MM sub-group was 0.16.

The mortality and morbidity values were 0 with all techniques.

The distribution of local cancer was 0.875 with no delay, 0.8538 with 3-month delay and 0.826 with 6-month or greater delay.

The distribution of regional cancer was 0.125 with no delay, 0.1365 with 3-month delay and 0.16 with 6-month or greater delay.

The distribution of distant cancer was 0 with no delay, 0.0097 with 3-month delay and 0.014 with 6-month or greater delay.

The distribution of local cancers for patients with palpable lesions was 87.5% with no delay, 66.3% with 3-month delay and 38.5% with 6-month or greater delay.

The distribution of regional cancers for patients with palpable lesions was 12.5% with no delay, 24% with 3-month delay and 47.5% with 6-month or greater delay.

The distribution of distant cancers for patients with palpable lesions was 0% with no delay, 9.7% with 3-month delay and 14% with 6-month or greater delay.

The mean LE of a healthy woman of 61 years of age was 22.4 years.
The compliance rate was 47%.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
Some of the assumptions were:

the indeterminate rate did not vary with the pre-test likelihood of breast cancer;

the probability of stage progression, as a result of a delayed diagnosis, was assumed to have been zero (lower bound of the range used in the sensitivity analysis);

the follow-up compliance was 100%; and

initial screening and follow-up screening were independent.

Measure of benefits used in the economic analysis
The summary benefit measure used in the economic analysis was the incremental LE gained with SSMM strategies (either strategy B or C) relative to strategy A. The LE was obtained through the decision model and no discounting was performed. Only incremental benefits were reported.

Direct costs
A 5% annual discount rate was applied because the costs were incurred over more than 2 years. The unit costs were reported, but details of the resources used were provided for a limited number of items only. The health services included in the economic evaluation were MM, SSMM, CNB, EB and the treatment of local, regional and distant cancer (initial work-up, systemic treatment, follow-up and terminal care). The cost of the screening tests incorporated both technical and professional components. The cost/resource boundary adopted appears to have been that of the health care service. Two alternative sources of actual costs were used, Medicare reimbursement rates versus physician charges. The total costs associated with each screening strategy were derived using modelling. Resource use was based on authors' assumptions and some probability values, which were estimated in the review of the effectiveness evidence. The price year was not reported.

Statistical analysis of costs
Statistical tests of the costs or quantities were not conducted.

Indirect Costs
The indirect costs were not included in the economic analysis, even though they were relevant given the perspective reported by the authors.

Currency
US dollars ($).

Sensitivity analysis
One-way and two-way sensitivity analyses, to deal with the issue of uncertainty in the use of probability and cost estimates, were conducted. All the model inputs were varied over ranges observed in the literature. Particular attention was given to variations in the costs of cancer treatment.
Estimated benefits used in the economic analysis
In the base-case, compared with strategy A, strategy B resulted in a loss of 0.000178 life-years and strategy B in a loss of 0.000222 life-years.

Cost results
In the base-case, compared with strategy A, strategy B resulted in cost-savings of $9 per patient and strategy C in cost-savings of $20.

Using physician charges, the cost-savings relative to strategy A would be $25 with strategy B and $52 with strategy C.

The reduction in unnecessary biopsies was 750,063 with strategy B and 1,557,915 with strategy C.

If strategy B replaced strategy A, the overall yearly cost-savings to the US health care system (cohort of 21 million women) would range from $189 million to $525 million. If strategy C was used instead of strategy A, the overall cost-savings would be between $420 million and $1,092 million per year.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and benefits of the SSMM strategies relative to strategy A.

Compared with strategy A, the ICER (cost of achieving an additional life-year) was $50.562 with strategy B and $90,090 with strategy C.

Using physician charges rather than Medicare rates, the ICER would be $140,449 with strategy B and $234,234 with strategy C.

The estimated ICERs were fairly robust despite the input variations carried out in the sensitivity analysis.

SSMM sensitivity and specificity had the greatest impact on the results of the analysis.

Under several assumptions and when using Medicare rates, the SSMM strategies cost less than strategy A.

Authors' conclusions
The use of sestamibi scintimammography (MMSS)-based screening reduced costs and avoided unnecessary biopsies among healthy women older than 40 years of age. However, this was obtained at the expense of small reductions in life expectancy (LE) in comparison with conventional screening using mammography (MM) alone.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparator. MM appears to have represented the standard approach for breast cancer screening among healthy women. Following MM, CNB was used to confirm the results of a positive MM. It was selected from other biopsy techniques because it offered high specificity and sensitivity values at the lowest cost, compared with other available procedures. In terms of the choice of the interventions under study, the authors stated that other nuclear medicine techniques were available (i.e. thallium-201 or MDP), but SSMM was the most widely used and reliable tool for breast cancer detection. You should decide whether they represent valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness involved several reviews of the literature. A review was conducted for each model input. Estimates coming from the primary studies were pooled, weighting by the size of the sample. However, the methods and conduct of the review were described only for one review. Further, the authors did not describe the design of the
primary studies nor discuss their validity. Differences between the studies were not commented on and some assumptions were made. The uncertainty surrounding all assumptions and input values was investigated in the sensitivity analysis.

**Validity of estimate of measure of benefit**
LE was selected as the summary benefit measure in the economic evaluation and appears to have been appropriate. The use of LE allows comparisons to be made with the benefits of other screening programmes. The LE was obtained through the decision model. Discounting was not conducted, although its applicability to benefits represents a controversial issue. The total benefits gained with each strategy were not reported since only incremental figures were provided.

**Validity of estimate of costs**
The authors stated that a societal perspective was adopted, but it appears that only the costs relevant to the health service have been included. The costs common to the three strategies were not considered. The unit costs were reported but the price year was not, thus making reflation in other settings difficult. Two sources of costs were considered in the analysis. It would have been interesting to have included the indirect costs. Discounting was conducted appropriately. As with benefits, the total expenses were not reported and only differences in the costs were provided. The source of the resource use data was unclear. The costs were specific to the study setting, but extensive sensitivity analyses were conducted. The authors acknowledged that there is no Medicare reimbursement rate for SSMM, thus its cost was derived from other sources.

**Other issues**
The authors did compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. However, the external validity of the analysis was enhanced by the sensitivity analyses, the results of which were reported in detail. The authors also noted that the MM classification might vary across medical centres and that SSMM may not be readily available in all settings. Some limitations of the analysis, such as the use of assumptions, were highlighted. It was also noted that the study did not differentiate between palpable and non-palpable lesions detected in the screening population.

**Implications of the study**
The authors noted that future studies should incorporate quality of life issues in their evaluation. The approach used in the analysis may be useful for evaluating other imaging modalities, such as MDP SSMM and FDG breast positron emission tomography.

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