Cost-effectiveness of MR imaging and core-needle biopsy in the preoperative work-up of suspicious breast lesions

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 compared three different treatments in women with suspicious breast lesions. The treatments were pre-operative magnetic resonance imaging (MRI), pre-operative core-needle biopsy (CNB), and excisional biopsy (EXB) without pre-operative testing.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
No explicit details of the study population were reported. The authors did, however, state that the base-case patient was a 55-year-old woman with suspicious breast lesions and without co-existent disease.

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

Dates to which data relate
The effectiveness data were taken from studies published between 1986 and 1997. The price year was 1995.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Modelling
A Markov decision-analytic model was used to compare the costs and effectiveness of MRI, CNB, and EXB without pre-operative testing, in women with a suspicious breast lesion.

Outcomes assessed in the review
The outcomes used as the input parameters for the model were divided into three categories.

The outcomes assessed for test performance were:
the sensitivity and specificity of EXB;
the sensitivity and specificity of MRI;
the sensitivity and specificity of CNB.

The probabilities of the following were assessed:
the prevalence of cancer;
the stage distribution of cancer, i.e. ductal carcinoma in situ, node-negative or node-positive;
the fraction upstaged over follow-up;
ode-negative cancer when receiving chemotherapy with major or minor side-effects, or when receiving tamoxifen therapy;
ode-positive cancer when receiving tamoxifen and chemotherapy with major or minor side-effects, or when receiving chemotherapy with major or minor side-effects;
the annual probability of first recurrence, i.e. ductal carcinoma in situ, node-negative or node-positive;
the annual probability of second recurrence;
the annual probability of third recurrence;
death after first recurrence;
death after second recurrence;
death after third recurrence;
death due to causes other then breast cancer.

The outcomes assessed for utilities were:
disutility of EXB;
disutility of MRI;
disutility of CNB;
well after local or systematic treatment;
chemotherapy with major side-effects;
chemotherapy with minor side-effects;
tamoxifen treatment;
chemotherapy with major side-effects and tamoxifen;
chemotherapy with minor side-effects and tamoxifen;
first recurrence of cancer;
second recurrence of cancer;
third recurrence of cancer;
well after first recurrence;
well after second recurrence;
well after third recurrence;
death due to cancer or other causes;
well with no cancer;
sick with no breast cancer.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
A computer search and a comprehensive review of the medical literature were undertaken. No details of the sources searched were provided.

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
Approximately 37 primary studies were included in the review.

Methods of combining primary studies
The studies were combined through the use of a meta-analysis. The mean values were reported.

Investigation of differences between primary studies
Differences between the primary data sources were discussed in the narrative.

Results of the review
The results of the outcomes used as input parameters to the model were as follows.

Test performance:
the sensitivity of EXB was 1.00 and the specificity was 1.00;
the sensitivity of MRI was 0.96 and the specificity was 0.79;
the sensitivity of CNB was 0.89 and the specificity was 0.98;

Probabilities.
The prevalence of cancer was 0.35.
Stage distribution of cancer: the probability was 0.25 for ductal carcinoma in situ, 0.47 for node-negative, and 0.28 for node-positive.

The fraction upstaged over follow-up was 0.15.

The probabilities of node-negative cancer were: 0.024 when receiving chemotherapy with major side-effects; 0.276 when receiving chemotherapy with minor side-effects; and 0.70 when receiving tamoxifen therapy.

The probabilities of node-positive cancer were: 0.056 with tamoxifen and chemotherapy with major side-effects; 0.644 with tamoxifen and chemotherapy with minor side-effects; 0.024 when receiving chemotherapy with major side-effects; and 0.276 when receiving chemotherapy with minor side-effects.

The annual probability of first recurrence was 0.011 for ductal carcinoma in situ, 0.032 for node-negative, and 0.073 for node-positive.

The annual probability of second recurrence was 0.70.

The annual probability of third recurrence was 0.90.

The probability of death after first recurrence was 0.30.

The probability of death after second recurrence was 0.50.

The probability of death after third recurrence was 0.90.

The probability of death due to causes other than breast cancer was not applicable.

The utility values were as follows:

for disutility of EXB, 0.00;
for disutility of MRI, 0.00;
for disutility of CNB, 0.00;
for well after local or systematic treatment, 1.00;
for chemotherapy with major side-effects, 0.80;
for chemotherapy with minor side-effects, 0.90;
for tamoxifen treatment, 0.99;
for chemotherapy with major side-effects and tamoxifen, 0.79;
for chemotherapy with minor side-effects and tamoxifen, 0.89;
for the first recurrence of cancer, 0.70;
for the second recurrence of cancer, 0.50;
for the third recurrence of cancer, 0.30;
for well after first recurrence, 0.85;
for well after second recurrence, 0.55;
for well after third recurrence, 0.55;
for death due to cancer or other causes, 0.00;
for well with no cancer, 1.00;
for sick with no breast cancer, 0.50.

**Measure of benefits used in the economic analysis**
The measure of benefit was the number of quality-adjusted life-years (QALYs). The utility values used to weight life expectancy were derived from the review of the literature. The methods used to generate the utility values were not reported.

**Direct costs**
The resource use and the unit costs were not reported separately. The following direct costs were included in the analysis:

- excisional biopsy, $3,574;
- MRI, $703;
- CNB, $615;
- initial local treatment for cancer, $12,918;
- chemotherapy with major side-effects, $20,972;
- chemotherapy with minor side-effects, $8,171;
- tamoxifen treatment, $1,108;
- first recurrence, $8,675;
- second or third recurrence, $12,076;
- mammography and office visit, $90;
- routine follow-up, $252;
- death after first recurrence, $37,650;
- death after second or third recurrence, $15,060;
- death from non-cancer causes, $24,144;
- well with no cancer, $125;
- sick due to non-breast cancer causes, $10,000.

The cost estimates were mainly obtained from the medical literature published between 1988 and 1995, and from the 1995 Medicare Resource-based Relative Value Scale. The authors combined multiple sources of data by estimating the mean costs. Discounting was undertaken at a rate of 3% per year. The price year was 1995. All of the costs were adjusted to 1995 US dollars using the inflation-adjusted Consumer Price Index for medical services.
Statistical analysis of costs
No statistical analysis of costs was conducted.

Indirect Costs
No indirect costs were included in the analysis.

Currency
US dollars ($). No currency conversions were reported.

Sensitivity analysis
A one-way sensitivity analysis was performed for each parameter of the model using a clinically plausible range of values. The authors stated that multivariate analyses were performed where appropriate. The effect of these changes on the outcomes, costs and cost-effectiveness was identified. Threshold values were subsequently calculated for the sensitive variables.

Estimated benefits used in the economic analysis
The differences in the predicted life expectancies among patients who underwent EXB, pre-operative MRI, and pre-operative CNB were minimal. The lifetime expected QALYs from testing were 17.409 for EXB, 17.205 for MRI and 17.398 for CNB. The incremental differences were reported in quality-adjusted days rather than years. For EXB versus MRI, the difference was 1.5 quality-adjusted days. For EXB versus CNB, the difference was 4.0 quality-adjusted days.

Side-effects arising from the therapy were also included in the analysis. It was assumed that false positive results would be detected by subsequent EXB, and that there would be no adverse events as a result. The authors assumed that a false negative result would lead to a 6-month delay in diagnosis. It was unclear whether differences in the outcome were likely or were included in the analysis.

Cost results
The lifetime treatment cost per patient was $31,438 for EXB, $29,072 for MRI and $28,573 for CNB. The incremental costs were $2,366 for EXB versus MRI, and $2,865 for EXB versus CNB. The costs of side-effects due to therapy, and additional tests due to false positive test results, were included in the analysis.

Synthesis of costs and benefits
The costs and benefits were synthesised by calculating an incremental cost-effectiveness ratio (cost per QALY gained). The cost per QALY was $576,258 when using EXB instead of MRI, $253,540 when using EXB instead of CNB, and $69,446 when choosing MRI instead of CNB.

The one-way sensitivity analyses, which used wide-ranging estimates, indicated that the results were insensitive to changes in the values of most variables.

The two-way sensitivity analysis across a range of sensitivity and specificity for both MRI and CNB, revealed that the maximum gain in life expectancy from choosing EXB over pre-operative testing was 0.10 years (37 days). The authors stated that the incremental cost-effectiveness ratio of EXB relative to MRI or CNB was always above $100,000 for all combinations of sensitivity and specificity for pre-operative testing.

The choice between MRI and CNB was extremely sensitive to the estimates of their test performance. Five series of sensitivity and specificity data for CNB were compared with three series of data for MRI. The authors stated that the incremental cost-effectiveness ratio for MRI ranged from $69,446 per QALY in the base-case to being dominated by CNB. The choice between MRI and CNB was also sensitive to the estimates of breast cancer prevalence and risk. MRI became preferable as the risk of cancer increased. The cost per QALY of MRI ranged from $710,019 if used for
minimally suspicious lesions with a risk of 0.05, to $12,506 if used for highly suspicious lesions with a risk of 0.75.

The efficacy and cost-effectiveness were very sensitive to patient preference regarding EXB. The authors stated that when a patient's disutility was greater than or equal to 0.005 years (2 days), MRI became the option that yielded the most QALYs. However, as a patient's disutility for EXB increased above 0.058 years (21 days), the optimal strategy changed again and CNB was preferred.

**Authors' conclusions**

The results of the study showed that pre-operative testing was a cost-effective alternative to excisional biopsy (EXB). However, the choice between magnetic resonance imaging (MRI) and core-needle biopsy (CNB) was highly dependent on the accuracy of each test and on the patient's preference.

**CRD COMMENTARY - Selection of comparators**

The choice of the comparator was justified on the grounds that it represented the standard management option for suspected cases of breast cancer in the authors' setting. You should decide if this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**

The authors did not report the methods used for the literature review or whether a systematic search or review of the literature had been undertaken. The effectiveness data from the multiple sources were combined using a meta-analysis. The analytical model used for the meta-analysis was not reported, and neither were the criteria used to select the methodology. The criteria used to assess the validity and relevance of the data, and to extract the data, were also not reported. Thus, it was not possible to assess whether the authors used the data from the available studies selectively. The differences between the primary studies were discussed, but the authors did not state whether these were taken into account when estimating the individual input parameters for the model.

**Validity of estimate of measure of benefit**

The benefits were estimated using a Markov decision-analytic model. The authors described the model structure, their assumptions, and the rationale for these assumptions, in detail. However, they did not report whether the model structure and sequence of events were validated in terms of representing current practice, consistency and reliability. The methods used to estimate the utility values in the primary studies were not reported.

**Validity of estimate of costs**

The authors did not report the perspective of the analysis. It was therefore not possible to assess whether all the costs relevant to that perspective were included. Although some costs were omitted, these were unlikely to have affected the authors' conclusions. The costs and quantities were not reported separately. No statistical analysis of the quantities or prices was undertaken. However, a sensitivity analysis of each parameter of the model was performed over a clinically plausible range of values. Discounting was undertaken at a rate of 3% per annum. No currency conversions were reported.

**Other issues**

The authors made appropriate comparisons of their findings with those from other studies, and addressed the issue of generalisability to other settings. The authors used a value of $100,000 per QALY as the threshold above which interventions were not considered to be value for money. Lower thresholds have been reported, for example, $50,000 per QALY and 20,000 per QALY. You should consider what cost per QALY is considered reasonable in your own setting, and interpret the results and conclusions of the study accordingly.

As the authors reported, the main limitation of their study was that more precise estimates of diagnostic test performance are required before clear conclusions can be made concerning the most cost-effective pre-operative test.
However, the authors also stated that, because their sensitivity analysis indicated that even large differences in test performance had a very small impact on efficacy, it is likely that patient preferences will play a significant role in the choice between the pre-operative tests. The authors reported that the importance of exploring individual patient preferences was underscored in their study. The authors used deterministic base-case and sensitivity analyses using point estimates for each variable. This approach gives a range of possible estimates of outcomes and costs, but no information about the likelihood that they will occur. Given the quantity of data reported by the authors, a probabilistic sensitivity analysis could have been conducted to assess the level of uncertainty in the results due to uncertainty in the data used.

**Implications of the study**
The results of the study showed that pre-operative testing was a cost-effective alternative to EXB. However, the authors also stated that the choice between MRI and CNB was highly dependent on the accuracy of each test and on the patient's preference. The authors propose that, until more precise estimates of MRI and CNB test performance characteristics are available, individual patient preferences should be a major factor in deciding which pre-operative test should be used.

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