Cost-effectiveness of breast MR imaging and screen-film mammography for screening BRCA1 gene mutation carriers

Lee JM, McMahon PM, Kong CY, Kopans DB, Ryan PD, Ozanne EM, Halpern EF, Gazelle GS

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.

CRD summary

This study examined the cost-effectiveness of screening for breast cancer, using magnetic resonance imaging (MRI), screen-film mammography, or both, for women with mutations of the breast cancer gene BRCA1. The authors concluded that annual mammography and MRI detected breast cancer at smaller sizes and earlier stages than mammography or MRI alone and was likely to be cost-effective. The methods were valid and the uncertainty was assessed, but the data sources were not well described. The conclusions appear to be robust.

Type of economic evaluation

Cost-utility analysis

Study objective

This study examined the cost-effectiveness of screening for breast cancer by magnetic resonance imaging (MRI), screen-film mammography, or both, for women with mutations of the breast cancer gene BRCA1.

Interventions

The three strategies were: annual screen-film mammography; annual MRI; and annual MRI and mammography. Clinical surveillance without screening was the background strategy.

Location/setting

USA/out-patient.

Methods

Analytical approach:

The analysis was based on a Markov model, with a lifetime horizon and a hypothetical cohort of 500,000 25-year-old women with the BRCA1 mutation. The authors stated that a societal perspective was adopted.

Effectiveness data:

The clinical data were identified by a critical review of the medical literature and publicly available databases. Calibration was required for some of the clinical inputs. The key input was the accuracy (sensitivity and specificity) of the diagnostic strategies. These data were from a prospective multicentre cohort study of women with an increased risk of breast cancer. Some assumptions were required.

Monetary benefit and utility valuations:

The utility values were from the literature and they were reported in detail in an online appendix.

Measure of benefit:

Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3%. Other model outcomes, for example the number of false positives for each strategy, were reported.

Cost data:

The economic analysis included four main categories: breast cancer diagnosis, treatment (drugs and other health care resources depending on stage and type), health care for women without breast cancer, and patient time. A list of cost items was given in the appendix with details of most of the unit costs. The costs of screening and diagnosis were from

Medicare reimbursement data. Other costs were from official sources and estimates in the literature. All costs were in US dollars ($) and the price year was 2007. A 3% annual discount rate was applied.

Analysis of uncertainty:
A Monte Carlo simulation was used to assess the first-order uncertainty. Threshold analyses were conducted to assess the impact of varying the model parameters on the results. The parameters varied, over plausible ranges, were mutation penetrance, diagnostic test performance, costs of screening and diagnosis, annual discount rate, and quality-of-life weights. Multivariate analyses were carried out to examine the diagnostic test performance. Alternative scenarios were considered to assess the impact of changes in other model inputs.

Results

The number of false positives that required biopsy investigation was higher with the combined screening than with the single options. The projected costs were $96,042 with clinical surveillance, $100,336 with mammography, $108,641 with MRI, and $110,973 with both. The QALYs were 44.21 with surveillance, 44.46 with mammography, 44.50 with MRI, and 44.62 with both mammography and MRI.

MRI was excluded because of extended dominance, where it was less cost-effective than a more effective option. The incremental cost per QALY gained was $16,751 with mammography over surveillance and $69,125 with both over mammography.

The sensitivity analysis showed that the most influential inputs for the cost-effectiveness of mammography plus MRI were the MRI cost and mutation penetrance. When the mutation penetrance was over 71% or the MRI cost was more than $960 (base case $577), mammography plus MRI had an incremental cost-effectiveness ratio over $100,000 per QALY, compared with mammography. In general, the ratio remained within the range $50,000 to $100,000 per QALY with all other variations.

Authors' conclusions

The authors concluded that annual mammography and MRI detected breast cancer at smaller sizes and earlier stages than either screening alone and was likely to be cost-effective.

CRD commentary

Interventions:
The selection of the comparators was appropriate as mammography and MRI together was compared against each one individually. The background option of surveillance was appropriate.

Effectiveness/benefits:
The authors provided limited information on the derivation and assessment of the clinical inputs, especially the designs of the studies they were from. The test accuracy was from a prospective multicentre cohort study. The details of the other sources were available in another publication (Lee et al 2008, see 'Other publications of related interest' below for bibliographic details) which makes it difficult to judge the validity of the clinical inputs, but extensive sensitivity analyses were carried out on most of these parameters. The key details of the calibrations used to fit some inputs into the model were presented in the appendix. The approach used to derive the utility values for the QALYs was not described. Some intermediate and long-term outcomes of the model were reported and QALYs were appropriately selected as the main benefit measure, given the impact of the disease on both survival and quality of life.

Costs:
The cost categories were consistent with a broad perspective. A breakdown of cost categories and the unit costs were presented in the appendix. The sources appear to have been representative of the authors' context. The price year and discounting were clearly stated. The economic estimates were varied in the sensitivity analyses, to assess the impact of alternative assumptions on the cost-effectiveness results.

Analysis and results:
The authors used an appropriate incremental approach to synthesise the costs and benefits and the expected values were clearly presented. The uncertainty was satisfactorily investigated for non-dominated strategies and the most relevant

findings were clearly illustrated. An extensive description of the decision model was provided in the appendix. The results appear to have been specific to the authors' context and might not be transferable to other contexts.

Concluding remarks:
The methods were valid and various aspects of uncertainty were considered, but the data sources were not extensively presented. The authors' conclusions appear to be robust.

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Bibliographic details

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Other publications of related interest

Lee JM, Kopans DB, McMahon PM, et al. Breast cancer screening in BRCA1 mutation carriers: effectiveness of MR imaging--Markov Monte Carlo decision analysis. Radiology 2008; 246 (3): 763-771.

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