Cost-effectiveness of 70-gene MammaPrint signature in node-negative breast cancer
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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.

CRD summary
This study examined the cost-effectiveness of the 70-gene MammaPrint signature versus Adjuvant! Online software to determine whether women aged 60 years or younger, with early-stage breast cancer, were at high or low risk of distant metastases and to determine the most appropriate therapy. The authors concluded that 70-gene signature was likely to be cost-effective for these patients. The methods were validated, but some assumptions were needed and there was high uncertainty. Further studies are required to corroborate the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of the 70-gene MammaPrint signature compared with Adjuvant! Online software, to determine whether patients aged 60 years or younger, with early-stage breast cancer (ESBC) were at high or low risk of distant metastases, and to determine the most appropriate therapy.

Interventions
The interventions were 70-gene signature versus Adjuvant! Online. The risk estimates for Adjuvant! Online were based on the 10-year observed overall survival for women with ESBC from the Surveillance, Epidemiology, and End Results (SEER) database.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon. The authors stated that the perspective of the health care payer was adopted.

Effectiveness data:
The clinical data were from a selection of relevant sources. Most of the evidence for the accuracy of 70-gene signature, which was the key clinical input, was from a published study of 302 patients over a median of 13.6 years. The accuracy of Adjuvant! Online was based on data from the SEER database. Assumptions were made to validate the data for 70-gene accuracy for the US population. The efficacy of chemotherapy was from a published meta-analysis of randomised trials.

Monetary benefit and utility valuations:
The utility values were from two published studies.

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were the summary benefit measures. A 3% annual discount rate was applied.

Cost data:
The economic analysis included the costs of the 70-gene signature, tamoxifen citrate, adjuvant chemotherapy (medications, administration, hospitalisation, emergency department visits, and out-patient treatment of chemotherapy-)
related serious adverse events), treatment of recurrence, and terminal care due to cancer or other causes. Resource consumption and costs were based on estimates reported in the literature. Some drug costs were from the Red Book and the cost of 70-gene signature was from its manufacturer. All costs were in US dollars ($) and were discounted at an annual rate of 3%. The price year was 2007.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on all the inputs to the model, varying most of them by 50% of their base estimate. An alternative model was considered that was more representative of the US ESBC population, using key clinical data for risk classification from the SEER database.

Results
In the base case, the 70-gene signature spared 10% of patients from chemotherapy. The projected total costs were $162,140 with Adjuvant! Online and $163,580 with 70-gene signature. The life-years were 21.596 with Adjuvant! Online and 21.739 with 70-gene signature. The QALYs were 21.065 with Adjuvant! Online and 21.218 with 70-gene signature.

The incremental cost with 70-gene signature over Adjuvant! Online was $10,059 per life-year gained or $9,428 per QALY gained.

The most influential inputs were the oestrogen receptor status, the proportion of patients classified as high or low risk, and the overall survival in each risk group. Changes in these variables changed 70-gene signature from being dominant, as it was more effective and less costly, to being dominated.

For oestrogen receptor-positive women, the incremental cost with 70-gene signature was $6,167 per life-year gained or $5,908 per QALY gained. For oestrogen receptor-negative women, Adjuvant! Online was dominant. In the alternative model (US data), the incremental cost with 70-gene signature was $716 per life-year gained or $702 per QALY gained.

Authors' conclusions
The authors concluded that 70-gene signature decreased the use of chemotherapy and might increase life expectancy, making it likely to be cost-effective for determining the appropriate adjuvant chemotherapy for young women with ESBC.

CRD commentary
Interventions:
The selection of the comparators appears to have been appropriate as the two available prognostic instruments were examined. The authors stated that other treatment guidelines, such as those developed by the St Gallen International Expert Consensus, the National Cancer Comprehensive Network, and the National Cancer Institute were less likely to be cost-effective and were excluded.

Effectiveness/benefits:
The authors generally justified the sources they selected for the clinical data, but they acknowledged that the main study for 70-gene signature was a manufacturer's study and no independent studies were available. This study did not include patients representative of the population analysed and some assumptions had to be made. The other data sources were appropriate, as they were either large databases or meta-analyses of clinical trials. The authors stated that their assumptions were generally conservative against the 70-gene signature. Both life-years gained and QALYs were used as benefit measures and they were both valid and allow comparisons with other disease areas. No details of the sources for the utility weights were given and it is unclear whether these were appropriate for the study population.

Costs:
The cost categories were appropriate to the study perspective, but limited information was given on their sources and the accounting system used in these studies. Some unit costs were presented, but others were reported as category totals. Little information on the resource quantities was given and no details of the published studies that supplied most of the cost items were given. The price year and discounting were reported. The cost estimates were treated deterministically.
Analysis and results:
The results were extensively presented for both the base case and the alternative scenario. An appropriate incremental approach was used to synthesise the costs and benefits of the two strategies. The uncertainty was investigated, using deterministic methods that varied the individual inputs one at a time rather than simultaneously. A clear description of the model was provided and it appears to have been very simple with only three health states. The subgroup analysis showed that 70-gene signature was likely to be cost-effective for women who were oestrogen receptor positive, but not for those who were negative, where it was dominated. The patients’ characteristics appear to be fundamental in assessing the value for money of each strategy. This study was specific to the US context and it would be difficult to transfer the results to other settings.

Concluding remarks:
The methods were validated, but some assumptions were needed and there was high uncertainty. Further studies are required to corroborate the authors’ conclusions.

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