Economic evaluation of genomic test-directed chemotherapy for early-stage lymph node-positive 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 assessed the cost-effectiveness of genomic test-directed chemotherapy versus chemotherapy alone in patients with early-stage breast cancer. The authors concluded that, although genomic test-directed treatment was cost-effective, there was substantial uncertainty surrounding the results and that further research collecting long-term outcomes was needed. The quality of the study methods was good, with adequate reporting. The results were reported in full. Given the scope of the analysis, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The study objective was to assess the cost-effectiveness of genomic test-directed chemotherapy versus chemotherapy alone for patients with oestrogen receptor-positive, lymph node-positive early-stage breast cancer.

Interventions
Genomic test-directed chemotherapy (using the Oncotype DX 21-gene assay) was compared with chemotherapy alone (standard care) in patients with lymph node-positive, oestrogen receptor-positive early-stage breast cancer

Location/setting
UK/In-patient secondary care.

Methods
Analytical approach:
The model structure was developed by clinical experts, health economists, and medical statisticians. It was based on a previously published model (Hall, et al. 2011, see ‘Other Publications of Related Interest’ below for bibliographic details). The model had two parts. The first part was a decision tree; patients were allocated a to standard care group where they all received chemotherapy or to a test where patients were allocated to high-risk or low risk recurrence groups. The low-risk group was spared chemotherapy. The second part was a state-transition model that was used to calculate costs and benefits associated with the two interventions for a hypothetical cohort of women. The time horizon was the lifetime of the patient. The authors reported that the perspective of the UK NHS was adopted.

Effectiveness data:
Clinical and effectiveness data were derived from a number of different sources including previously published trials and studies, UK national statistics, and expert opinion. The main clinical effectiveness measure used in the model was the proportion of patients assigned by the genomic test to high-risk and low-risk groups, and cancer recurrence for each of these groups; this information came from the Southwest Oncology Group (SWOG) 8814 trial (Albain, et al. 2010, see ‘Other Publications of Related Interest’ below for bibliographic details).

Monetary benefit and utility valuations:
Quality of life utility values were mostly taken from a Swedish study that used the EQ-5D (European Quality of life at 5 dimensions) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure. They were discounted at an annual rate of 3.5%.

Cost data:
The direct costs included were treatment of recurrences and distant recurrences, terminal care, cancer treatment, outpatient care, genomic testing with Oncotype DX test, and chemotherapy-related toxicities treatment (including gut perforation, bleeding, thrombosis, allergic reactions and hypertension). Resource use was taken from published studies and National Institute for Health and Clinical Excellence (NICE) guidelines. Unit costs were from the UK NHS reference costs. Drug costs were from the British National Formulary. All costs were reported in UK £. The price year was 2011. Future costs were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
A probabilistic analysis was conducted by varying all the uncertain model parameter inputs simultaneously in a Monte Carlo simulation (with 10,000 simulations). A one-way sensitivity analysis was also conducted. A value-of-information analysis was undertaken to provide a framework for setting priorities for further research.

Results
For patients who received Oncotype DX-directed chemotherapy, the QALYs gained were 10.32 and the cost per patient was £23,130.

For patients who received standard care (chemotherapy alone), the QALYs gained were 10.16 and the cost per patient was £22,270.

Costs and benefits were combined using an incremental cost-utility ratio (the additional cost per QALY gained). When compared with standard care, the incremental cost-utility ratio of Oncotype DX-directed chemotherapy was £5,529 per QALY gained.

Results of the probabilistic sensitivity analysis showed that a £30,000 per QALY threshold, the probability that Oncotype DX-directed chemotherapy was cost-effective was 0.61; at a £20,000 per QALY threshold, the probability that it was cost effective was 0.58.

Results of the value-of-information analysis showed that the overall maximum expected healthcare resource lost as a consequence of uncertainty in cost-effectiveness was in excess of £2,000 million.

Authors' conclusions
The authors concluded that although genomic test-directed chemotherapy was cost-effective, there was substantial uncertainty surrounding the results and that further research collecting long-term outcome data was needed.

CRD commentary
Interventions:
The interventions were clearly reported. The comparator (standard chemotherapy) was relevant to the study setting.

Effectiveness/benefits:
Clinical and effectiveness data were derived from a number of different sources including national statistics, published studies and trials, and expert opinion. The authors did not report how published studies were identified or if a systematic review of the literature was undertaken. As a result, it was not possible to determine if all the relevant information was included. However, the main estimates of effectiveness were derived from clinical trials published recently in high-impact peer reviewed journals. Most of the effectiveness data were from randomised controlled trials, so it was likely that these estimates were internally valid. QALYs were an appropriate benefit measure, which captured the impact of the interventions on quality of life and survival. The details of the derivation of the utility values would have been useful to fully assess their validity.

Costs:
For the explicitly stated UK NHS perspective, all relevant cost categories and costs appear to have been included. The sources for unit costs and resource use were adequately reported; they appeared to be appropriate to the study setting.
Unit costs and resource quantities were presented separately, which enhanced generalisability. The price year, time horizon, and annual discount rate were all reported. The impact of variations in key cost inputs was tested in sensitivity analysis.

Analysis and results:
All cost and outcome information were synthesised using a state-transition model. Details of the model structure were reported in detail; a diagram was provided. An incremental approach was appropriately conducted to synthesise the costs and benefits of the alternative strategies. Model uncertainty was exhaustively tested using a series of one-way and probabilistic sensitivity analyses, and a value-of-information analysis; these findings were clearly reported and discussed. The authors acknowledged the limitations of their study, reporting they had only included Oncotype DX and had not considered other alternative tests.

Concluding remarks:
The quality of the study methods was good, with adequate reporting. The results were reported in full. Given the scope of the analysis, the authors’ conclusions appear to be valid.

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MeSH
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