Cost effectiveness of adjuvant trastuzumab in human epidermal growth factor receptor 2-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
The aim of the study was to assess the cost-effectiveness of 12-month adjuvant trastuzumab therapy in women with high-risk epidermal growth factor receptor 2 (HER2)-positive early breast cancer. The authors concluded that, in the longer term, adjuvant trastuzumab is a cost-effective therapy for women with early breast cancer. Despite some limitations with data transparency, the methods of the study appear appropriate and comprehensive. The authors' conclusions reflect the scope of the analysis.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim of the study was to assess the cost-effectiveness of 12-month adjuvant trastuzumab therapy in women with high-risk epidermal growth factor receptor 2 (HER2)-positive early breast cancer.

Interventions
Standard chemotherapy (doxorubicin, cyclophosphamide plus paclitaxel) was compared with standard chemotherapy followed by weekly trastuzumab (2 mg/kg per week). A hypothetical cohort of women had a median age of 50 years, HER2-positive early breast cancer and weighed 60 kg.

Location/setting
Italy/USA. Outpatient care.

Methods
Analytical approach:
A Markov model was used to synthesise data from a combined report of the National Surgical Adjuvant Breast and Bowel Project-B31 and the North Central Cancer Treatment Group N9831 randomised clinical trials (Romond et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details). Full details are not reported in this paper. These trials were selected for having the longest follow-up periods of existing trials evaluating trastuzumab. The analysis was over a 15-year period and the authors stated the study perspective to be that of the Italian and US health care systems.

Effectiveness data:
The clinical estimates included the rate of relapse, disease-free time, metastatic disease, deaths and the adverse side-effect of cardiac dysfunction. Evidence of the clinical estimates was abstracted from meta-analyses, randomised clinical trials and a longitudinal cohort study.

Monetary benefit and utility valuations:
Utility weights were assigned to the health states and derived from three published articles, of which two were of women with early breast cancer. The utility methods were not reported.

Measure of benefit:
The two measures of benefit used were the life-years gained and quality-adjusted life-years (QALYs). Discounting was applied at a rate of 3%.
Cost data:  
The direct costs were included in the analysis. The cost categories comprised the cost of the drugs, local relapse, metastatic disease (extra chemotherapy lines and palliative care), short-term care of cardiac dysfunction, cardiac monitoring and follow-up of disease-free patients. The unit costs were presented and referenced. Data on resources used and valuations were derived from published sources in each of the respective countries. The cost of therapies for relapse reflected local treatments in Italy. Discounting was performed at a rate of 3%. Prices were given in US dollars ($) and euros (EUR). No price year was stated. No other adjustments to the prices were reported.

Analysis of uncertainty:  
Parameter uncertainty was handled using probabilistic and multi-way sensitivity analyses of the main variables. Full details of the data distributions assigned and methods used were reported. Cost-effectiveness acceptability curves were plotted.

Results  
Adjuvant trastuzumab produced 9.22 discounted QALYs and standard therapy 8.03 QALYs. For the Italian health system, adjuvant trastuzumab cost EUR 54,058 compared with EUR 36,522 (discounted) for standard therapy alone, while in the US setting, adjuvant trastuzumab cost $77,947 and standard therapy alone $55,562 (discounted).

The incremental cost-utility ratio was EUR 14,861 ($18,970) per QALY gained for adjuvant trastuzumab.

Sensitivity analyses showed adjuvant trastuzumab to be less cost-effective in older women and also if a shorter time horizon of 7 to 8 years was applied. The results of the probability sensitivity analysis indicated a 91% probability that trastuzumab would be cost-effective at a threshold of EUR 20,000 per QALY gained.

Authors' conclusions  
The authors concluded that, in the longer term, adjuvant trastuzumab is a cost-effective therapy for women with early breast cancer.

CRD commentary  
Interventions:  
The two adjuvant therapy options, including dosages, were described clearly. It is unclear whether other anthracycline-based chemotherapy agents might have also been relevant comparators.

Effectiveness/benefits:  
The effectiveness data were mainly derived from clinical trials and the authors justified their selection of these studies. The utility values used in the model, and their sources, were reported clearly but no details provided on the methods of utility measurement. It is therefore not possible to assess the validity of these values without recourse to the referenced studies. The results were reported clearly.

Costs:  
Direct medical costs were included in the analysis and would appear appropriate for the perspective taken, including the important side-effect of cardiac dysfunction. The sources of resource use and the unit costs were clear. However, the author did not state the price year, nor whether any inflationary or other cost adjustments were performed, and this hinders any reflation exercises. Differences in resource use in the Italian system compared with other health care settings, and the likely impact on the results, were discussed briefly.

Analysis and results:  
The cost and effect analyses were appropriate and comprehensive. The results and sensitivity analyses were fully reported and illustrated. The impact of uncertainty on the base findings were discussed with regard to trastuzumab having lower cost-effectiveness if the time horizon of the analysis is shortened and the age of the cohort is higher (>70 years). Generalisability of the results and limitations of the economic model were identified and discussed, including some data imperfections, the relative case-mix of HER2-positive patients and their impact on model outcomes.

Concluding remarks:
Despite some limitations with data transparency, the methods of the study appear appropriate and comprehensive. The authors' conclusions reflect the scope of the analysis.

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**Bibliographic details**

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

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