Assessing the real-world cost-effectiveness of adjuvant trastuzumab in HER-2/neu 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 adjuvant trastuzumab in the treatment of women with human epidermal growth factor receptor 2 (HER-2)/neu positive breast cancer. The authors concluded that 12-months adjuvant trastuzumab chemotherapy appeared to be cost-effective in a Canadian setting. There were some limitations in the level of reporting of the study methods and results, so the authors’ conclusions should be considered with a degree of caution.

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

Study objective
The study assessed the cost-effectiveness of adjuvant trastuzumab in the treatment of HER-2/neu positive breast cancer.

Interventions
Twelve-month adjuvant trastuzumab was compared with standard chemotherapy.

Location/setting
Canada/hospital inpatient and outpatient care.

Methods
Analytical approach:
A Markov model with a three-month cycle length was developed to synthesise the cost and outcome data. The time horizon was 28-years. The model followed a hypothetical cohort of one thousand 50-year old women with early HER-2/neu-positive breast cancer, who had successfully completed a surgical resection of disease. The authors stated that the perspective of the health care payer was adopted.

Effectiveness data:
The effectiveness data came from a number of published studies: Transition probabilities (such as disease progression) were from clinical trials; and estimates of survival came from a phase II trial. Various assumptions were made to extrapolate survival effects after the trial follow-up period (of five years). National mortality rates (Canadian) were used to estimate gender and age specific death rates. Survival was the main measure of clinical effectiveness.

Monetary benefit and utility valuations:
Utilities values came from published studies. The study providing utilities for each Markov state was a systematic review of health utilities in cancer.

Measure of benefit:
The summary measures of benefit were quality-adjusted life-years (QALY) and life years. Future benefits were discounted at an annual rate of 5%.

Cost data:
Breast cancer treatment costs included those associated with chemotherapy, radiotherapy, diagnostics, complications and drugs. Resource use and cost data came from a variety of sources: diagnostic and complications costs were from
previously published studies; the cost of trastuzumab was calculated using British Columbia Cancer Agency (BCCA) pharmacy data. The authors reported that the costs were adjusted for inflation and were presented in Canadian dollars (CAD). Future costs were discounted at an annual rate of 5%.

Analysis of uncertainty:
Monte Carlo simulation (using 10,000 model iterations) was used to examine uncertainty in model outputs. The results were presented using a cost-effectiveness acceptability curve for various willingness-to-pay thresholds and plotted on a cost-effectiveness plane. One-way and two-way sensitivity analyses were carried out on key model inputs including the rate of relapse and the cost of trastuzumab-based chemotherapy.

Results
Treatment with adjuvant trastuzumab resulted in a gain of 1.38 QALYs or 1.17 life years at an additional cost of CAD 18,133 per patient. The incremental cost per QALY gained was CAD 13,095; the incremental cost per life year gained was CAD 15,492.

The one-way sensitivity analysis showed the results to be sensitive to the discount rate. The probabilistic sensitivity analysis produced an interquartile range of CAD 10,900 to CAD 32,030 per QALY gained.

Authors' conclusions
The authors concluded that 12-months adjuvant trastuzumab chemotherapy for women with HER-2/neu positive breast cancer appeared to be cost-effective in a Canadian setting.

CRD commentary
Interventions:
The details of the interventions were brief, but the authors referred to a supplemental online appendix (available on registration). The choice of interventions was appropriate with the proposed strategy compared with usual care (standard chemotherapy).

Effectiveness/benefits:
Details of the methods used to identify and select the studies from which the effectiveness data came were not described, which made it difficult to ascertain whether the most up-to-date and relevant studies were included; however, details of some of the studies were reported and they appeared to have a high degree of internal validity (phase II and III clinical trials). Utility values came from a systematic review of health utilities in cancer, so should be a valid source of evidence. Life years and QALYs were appropriate measures of benefit that captured the impact of the treatment options on length and quality of life, as well as being generalisable to other interventions.

Costs:
The study perspective was clearly reported. It appeared that the relevant costs were included. There were some limitations to the cost analysis; most of the costs were presented as category totals rather than individual items; the sources of some of the resource data were unclear; and the price year was not reported. These factors reduced the transparency of the cost analysis. Details of the discount rate were reported.

Analysis and results:
It was unclear whether an incremental approach was adopted in the analysis: whether the additional cost and benefit of the trastuzumab intervention (compared with usual care) was considered; or whether the results referred to the overall cost and outcomes of the trastuzumab intervention. The costs and outcomes associated with each intervention were not reported separately, which reduced the transparency of the analysis. Valid approaches were used to investigate uncertainty. The authors reported some limitations of their analysis including the reliance on clinical trial data for some model probabilities.

Concluding remarks:
There were some limitations in the level of reporting of the study methods and results, so the authors’ conclusions should be considered with a degree of caution.
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