Adjuvant chemotherapy for breast cancer: a cost-utility analysis of FEC-D vs. FEC 100

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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 investigated the cost-effectiveness of a new adjuvant chemotherapy regimen of 5-fluorouracil, epirubicin, and cyclophosphamide-docetaxel (FEC-D), compared with 5-fluorouracil, epirubicin, and cyclophosphamide-100, in women with node-positive breast cancer. The authors concluded that FEC-D was a cost-effective regimen producing comparable cost-utility ratios to other adopted breast cancer strategies. With a few exceptions, the methods were transparent and clearly reported. The conclusions reached by the authors reflected the scope of their analysis.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to assess the costs and effects of the adjuvant regimen of 5-fluorouracil, epirubicin, and cyclophosphamide-docetaxel (FEC-D) for women with node-positive breast cancer. A hypothetical cohort of women, who had node-positive breast cancer, a median age of 50 years, and an average body surface area of 1.7 m², was assessed.

Interventions
FEC-D was compared with 5-fluorouracil, epirubicin, and cyclophosphamide (FEC-100). FEC-100 comprised 5-fluorouracil at 500 mg/m², epirubicin at 100 mg/m², and cyclophosphamide at 500 mg/m² intravenously administered on day one of every 21-day cycle, for six cycles. The FEC-D regimen was similar for three cycles, which were followed by three cycles of docetaxel at 100 mg/m² intravenously on day one.

Location/setting
Canada/out-patient care.

Methods
Analytical approach:
A Markov state transition model was used to capture the costs and benefits associated with changes of health states. Published data were synthesised from various sources including one key randomised controlled trial (Roche, et al. 2003, 2004, 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). The full details of this trial were not reported in this paper. The analysis was carried out over a 10-year period, and the authors stated that the perspective was that of the Canadian health care system.

Effectiveness data:
The clinical estimates included time free of disease, the recurrence rate, and deaths. Canadian life tables were used to determine the disease-free survival rates. Hazard rates comparing the two treatments were obtained from the randomised controlled trial (Roche, et al. 2004, 2006).

Monetary benefit and utility valuations:
The utility weights were assigned to the health states and derived from an online published registry (Tufts – New England Medical Center, see ‘Other Publications of Related Interest’ below for bibliographic details).

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) and discounting was applied at an annual rate of 3%.
Cost data:
The direct costs were those for drug acquisition, local relapse, distant relapse, supportive medications, laboratory tests, health resource utilisation, management of febrile neutropenic complications, and growth factor support. The unit costs were presented and referenced. The data on resources used and their valuations were derived from published sources relevant to the population. Discounting was performed at an annual rate of 3%. The costs were inflated using the Canadian Consumer Price Index (health care component) and presented in 2006 Canadian dollars (CAD).

Analysis of uncertainty:
Parameter uncertainty was addressed using one-way sensitivity analyses on the main parameters as well as scenario analyses of pre- versus post-menopausal women and younger (under 50 years) versus older women. The sensitivity analysis results were presented using tornado diagrams.

Results
For the Canadian health system, discounted costs were CAD 11,914 for adjuvant FEC-D and CAD 8,370 for FEC-100. The incremental costs were CAD 3,544 for FEC-D and the incremental discounted QALYs gained were 0.156 over FEC-100 per patient.

Over the 10-year period, the incremental cost-utility ratio was CAD 14,612 per QALY gained for FEC-D over FEC-100.

The sensitivity analyses showed that the base-case results were stable to wide variations in the input estimates. The results varied most when the baseline recurrence risk at 10 years was lowered to 25%, which increased the ratio to CAD 37,793 per QALY gained. Lower and more favourable cost-utility ratios were found for post-menopausal and older women.

Authors’ conclusions
The authors concluded that FEC-D was a cost-effective adjuvant therapy for women with node-positive breast cancer, and that it was comparable to other recently adopted breast cancer treatments.

CRD commentary
Interventions:
The two adjuvant therapies were clearly described including their dosages and frequency. FEC-D had been shown to be efficacious in clinical trials and was adopted as standard care from 2007, superseding FEC-100, so FEC-100 appears to have been an appropriate comparator. However, earlier regimens, such as FEC-50, may still have been in widespread use and might also have been analysed.

Effectiveness/benefits:
The effectiveness data were mostly derived from clinical trials and the trials selected appear to have been those published most recently. It is not clear if this was the only or the best evidence available. The utility values and their sources were clearly reported, but no details were provided on the methods of utility measurement and the utility tools used. An assessment of the validity of these values is therefore not possible without recourse to these referenced studies. The resulting QALYs for each regimen were not separately reported, which may have been useful for comparison with the QALYs for other regimens.

Costs:
Direct medical costs were included and appear to have been appropriate for the perspective. They included the costs of the important side-effect of febrile neutropenia and growth factor. The sources of the resource use and unit costs and the cost adjustment methods were clearly presented. The cost estimates were relevant to the population.

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 was discussed in detail. The generalisability of the results was discussed. Comparisons were made with other findings for adjuvant therapies within the breast cancer literature and the authors concluded that their results were very cost-effective in this context. Limitations of the model...
were identified and discussed, including the lack of evidence on the probability distributions, which were used to justify the absence of a more comprehensive multivariable sensitivity analysis.

Concluding remarks:
Despite some limitations with data transparency, the methods appear to have been appropriate and comprehensive. The conclusions reached by the authors reflected the scope of their analysis.

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