The cost-effectiveness of adjuvant chemotherapy for early breast cancer: a comparison of no chemotherapy and first, second, and third generation regimens for patients with differing prognoses


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 objective was to investigate the cost-effectiveness of adjuvant chemotherapy for women with early stage breast cancer. The authors concluded that different treatment strategies could be cost-effective for different types of patients. The methods were valid and the authors’ conclusions are appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to investigate the cost-effectiveness of adjuvant chemotherapy for women with early stage breast cancer.

Interventions
Four interventions were considered: no chemotherapy, and first, second, and third generation chemotherapy. First generation chemotherapy consisted of six cycles of cyclophosphamide, methotrexate, and fluorouracil (CMF). Second generation chemotherapy consisted of eight cycles of fluorouracil, epirubicin, and cyclophosphamide (FEC60) or four cycles of epirubicin followed by four cycles of CMF. Third generation chemotherapy consisted of four cycles of FEC60 followed by four cycles of docetaxel.

Location/setting
UK/secondary and tertiary care.

Methods
Analytical approach:
A short-term decision tree (six months) was used to assign patients to one of the four initial treatments. A Markov model was developed to project the longer term costs and benefits of each strategy, from month seven to 50.5 years. The authors reported that the perspective of the UK NHS was adopted.

Effectiveness data:
The effectiveness data were from a variety of sources, including trials, administrative databases, published literature, and expert opinion. The details of the model parameters and their sources were reported in online appendices, with some information in the paper. The main model parameters were estimated using individual patient data (IPD) from three UK-led pragmatic randomised controlled trials: the Adjuvant Breast Cancer (ABC) trial, the National Epirubicin Adjuvant Trial (NEAT), and the Taxotere as Adjuvant Chemotherapy Trial (TACT). All the transition probabilities, and the relative treatment effect estimates for recurrence were reported.

Monetary benefit and utility valuations:
The baseline utility value for women entering the model was assumed to be that of age-matched women in the UK general population (the population norms). The utility decrements for each health state, for women who remained recurrence free, were derived using the IPD from the three trials. The utilities and decrements were assessed using the European Quality of life (EQ-5D) tool. Health-related quality of life decrements for patients in the recurrence health states were from a comprehensive review of the literature.
Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary measure of benefit, and they were discounted at an annual rate of 3.5%.

Cost data:
The economic analysis included the initial and recurrent treatment costs, the surveillance follow-up costs, and end-of-life care for terminal breast cancer. Detailed resource use and costs were from the IPD from the three trials, for the short term. Some data were from published studies. The annual costs for each health state were from a published study, which was the only patient-level costing study for breast cancer recurrence that was identified by a comprehensive review of published literature. The price year was 2009 and the costs were reported in UK pounds sterling (£). An annual discount rate of 3.5% was applied.

Analysis of uncertainty:
A probabilistic sensitivity analysis was conducted to examine the impact of uncertainty in all the parameters simultaneously on the cost-effectiveness results. The results of this analysis were presented as the probability that a given strategy was cost-effective at different cost-effectiveness thresholds. Uncertainty was further investigated in one-way sensitivity analyses and threshold analysis.

Results
The expected costs were £14,204 for no chemotherapy, £15,076 for first generation chemotherapy, £15,246 for second generation chemotherapy, and £18,327 for third generation chemotherapy. The QALYs were 10.93 for no chemotherapy, 12.35 for first generation chemotherapy, 12.66 for second generation chemotherapy, and 12.88 for third generation chemotherapy.

The incremental cost-effectiveness ratio of third compared with second generation chemotherapy was £13,704 per QALY gained. At a willingness-to-pay of £20,000 per QALY gained, the probability that third generation chemotherapy was cost-effective was 0.72.

The subgroup analysis showed that for younger low-risk women, second generation chemotherapy tended to be the best strategy and, for some older low-risk women, no chemotherapy was cost-effective. Extensive sensitivity analysis results were presented and highlighted the importance of subpopulations in the treatment choice.

Authors’ conclusions
The authors concluded that different treatment strategies could be cost-effective for different types of patients.

CRD commentary
Interventions:
The rationale for the selection of the interventions was clear in that they were the options in use in the authors’ setting over the previous years.

Effectiveness/benefits:
The use of individual patient data from three UK trials allowed the analysis to investigate extensive subpopulations. The full details of the trials were not presented, but they were high quality sources of evidence. Further details of the analysis and other data used for the long-term model were presented in the appendices. All the parameter values and their sources were presented clearly, with a measure of their uncertainty. QALYs were an appropriate outcome measure, capturing the impact of the intervention on both quality and length of life. The quality weights were either from the trials or from the literature and were relevant to the study population. A lack of robust utility data for similar populations can be a problem, but was not for this analysis.

Costs:
The included costs reflected the stated perspective of the UK NHS. Some of the costs were presented as category totals rather than as individual items reducing the transparency of the analysis, but further details might be available in the online appendices. The source for the cost data was clearly reported and appropriate. The use of IPD for the short-term...
resource use, enhances the accuracy of the costing. The discount rate and price year were reported.

**Analysis and results:**
The data were appropriately combined in a Markov model and the details were provided, with a diagram. A full and properly conducted incremental analysis was undertaken. The impact of uncertainty was thoroughly investigated in one-way and probabilistic sensitivity analyses. The authors reported some limitations to their work, including that the results of the analysis might not be generalisable to other settings, as UK effectiveness data were used. Overall, the analysis was robust and well reported.

**Concluding remarks:**
The methods were valid and the authors' conclusions are appropriate.

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