Adjuvant cyclophosphamide, methotrexate, fluorouracil (CMF) in breast cancer: is it cost-effective

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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.

Health technology
The use of adjuvant chemotherapy (ACT), consisting of cyclophosphamide, methotrexate and fluorouracil (CMF), for the treatment of breast cancer was considered.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The author studied a hypothetical population of women, aged 50 years, with breast cancer.

Setting
The setting was secondary care. The economic study was carried out in the Department of Oncology, University Hospital of Tromso, Tromso, Norway.

Dates to which data relate
The effectiveness data were derived from studies published between 1986 and 1998. The resource use data related to 1998. The price years were 1996 and 1998.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies.

Modelling
A model was used to estimate the benefits and costs of ACT with CMF. However, the author did not report the type of model employed.

Outcomes assessed in the review
The outcomes obtained from the literature and included as inputs in the model were the years gained per 100 women during the first 10 years of treatment, and improvement in survival among 10-year survivors. The quality of life (measured on a scale from 0 to 1) for 6 months during therapy and for the rest of life was considered. The life expectancy for 60-year-old Norwegian women was also included as a parameter of the model.
Study designs and other criteria for inclusion in the review
The only criteria reported by the author were articles on ACT in breast cancer.

Sources searched to identify primary studies
MEDLINE was searched between 1986 and 1998.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
A total of 778 articles citing the words "breast cancer" and "adjuvant chemotherapy" were initially included in the review.

Methods of combining primary studies
Sub-groups were identified from the initial studies identified. The author used data from three included studies for effectiveness (Fisher et al.) and quality of life (Resing K, et al. and Norum J, et al. (see Other Publications of Related Interest).

Investigation of differences between primary studies
Not investigated.

Results of the review
The following values were included as parameters of the model:

51 years gained per 100 women during the first 10 years of treatment;
an improvement of 8.5% for survival among 10-year survivors; and
a life expectancy of 22.8 years for 60-year-old Norwegian women.

In terms of quality of life, the author considered a decrease of 0.33 (0 - 1 scales) for 6 months during therapy, and a quality of life of 0.86 following adjuvant CMF lasting for the rest of life.

Measure of benefits used in the economic analysis
The measures of benefits used were the life-years gained and the quality-adjusted life-years (QALYs).

Direct costs
The cost/resource boundary adopted was that of society. The broad expenditure areas included were drugs, administration and travel costs. The resource use data came from the University Hospital of Tromso, while the price data came from the National Health Administration and the Norwegian Price List. A discount rate of 5% was used. The quantities and the costs were reported separately. The price year was 1998.
Statistical analysis of costs
The cost data were treated deterministically.

Indirect Costs
The human capital approach and the friction cost methods were used to measure productivity losses. The data came from Norway Statistics. The travel costs were obtained from a published study. A discount rate of 5% was used. The price year was 1996.

Currency
UK pounds sterling (£). The conversion rate was Norwegian kroner 12 = 1.

Sensitivity analysis
Variability in the data was investigated. One-way sensitivity analyses were performed on drug prices (use of brand-name products instead of generic products) and life expectancy.

Estimated benefits used in the economic analysis
The benefits were not reported separately in the paper, but are reflected in the synthesis of costs and benefits (see Synthesis of Costs and Benefits).

Cost results
The author reported undiscounted total costs for ACT with CMF of 2,365 (friction cost approach) and 6,253 (human capital approach).

Synthesis of costs and benefits
Incremental cost-effectiveness and cost-utility analyses were performed. The undiscounted incremental cost per life-year saved was 965 with the friction cost method and 2,552 with the human capital approach. When considering the effect of a 5% discount rate on both the benefits and costs, the results were estimated to be 2,170 and 5,737, respectively.

The undiscounted incremental cost per QALY was 1,218 with the friction cost method and 3,220 with the human capital approach. When considering the effect of a 5% discount rate on both the QALYs and costs, the results were reported to be 2,973 and 7,860, respectively.

Authors’ conclusions
When considering two cut-offs from the literature (12,000 and 24,000), adjuvant chemotherapy (ACT) with cyclophosphamide, methotrexate and fluorouracil (CMF) would appear to be cost-effective for the treatment of patients with breast cancer.

CRD COMMENTARY - Selection of comparators
The comparator was not explicitly stated. The author chose a “no-treatment” comparator for the CMF chemotherapy. This allowed the active value of the treatment to be determined, but it did not include an active agent such as tamoxifen as an alternative.

Validity of estimate of measure of effectiveness
Although the author searched MEDLINE for relevant literature, a full systematic review was not undertaken. This is common practice in modelling studies, but it does not always ensure that the best data available are used in the model.
The author appears to have used data from the available studies selectively and did not consider the impact of differences between the studies identified when estimating the effectiveness. However, to compensate for this limitation, a sensitivity analysis was undertaken to explore the impact of variability in the estimates.

**Validity of estimate of measure of benefit**

The QALYs and life-years gained were used for the economic analysis. However, these data might have been obtained from the available studies selectively, as it was unclear whether other studies reporting the parameters of interest were found in the review.

**Validity of estimate of costs**

A good feature of the study was the chosen perspective (society). Relevant cost categories were included for this perspective, but side effects leading to hospitalisation were not considered. The resource use data came from the hospital, while the price data came from the Norwegian Price List. The resource quantities and the costs were reported separately, as were dates for the prices.

**Other issues**

The author compared the findings with those of published studies, although only a limited number of the results obtained were presented. In addition, no justification for why these particular results had been selected for comparison was provided. The author reported three main limitations to the study. First, all women were assumed to be 50 years of age. Second, the costs in additional years, such as follow-up visits, hospitalisation and terminal care, were not included in the model. Finally, the quality of life data were obtained from different CMF regimens. Thus, the results of this study should be treated with some caution.

**Implications of the study**

The study suggested that, when new adjuvant regimens are introduced in the future, cost-effectiveness analyses should be undertaken before initiating any new form of general systematic therapy. The results of this piece of research may be used as a benchmark for future comparisons.

**Source of funding**

None stated.

**Bibliographic details**


**PubMedID**

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**Other publications of related interest**


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Subject indexing assigned by NLM

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