Adjuvant fluorouracil, epirubicin and cyclophosphamide in early breast cancer: is it cost-effective?
Norun J, Holtmon M

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) based on cyclophosphamide, epirubicin and fluorouracil (FEC) for the treatment of early breast cancer (BC). Fluorouracil and cyclophosphamide were given at a dose of 600 mg/m2 every 3 weeks, while epirubicin was given at a dose of 60 mg/m2 every 3 weeks.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women with early BC that needed ACT.

Setting
The setting was a hospital. The economic study was carried out in Norway.

Dates to which data relate
The effectiveness data were derived from studies published between 1998 and 2004. Dates for the resource use data were not explicitly reported. The price year was 2004.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Outcomes assessed in the review
The outcomes estimated from the literature were the effectiveness of FEC and CMF in terms of 5- and 10-year survival, life expectancy for a 50- and 60-year-old woman, and quality of life (QoL) associated with the different treatments.

Study designs and other criteria for inclusion in the review
A review of the literature was undertaken to identify primary studies on the effectiveness of the different therapies. The inclusion criteria specified English-written articles published between January 1998 and June 2004 and including the words "breast cancer" and "adjuvant". Articles dealing with metastatic, locally advanced, or male BC and studies that simply mentioned "CEF" or "FEC" without reporting any clinical study as well as meta-analyses were excluded. Most of the studies were randomised clinical trials. The number of patients included in the study, the mean age of the
sample, and tumour stage were reported for each study. Life expectancy was derived from life tables, while QoL was obtained from a study that used the EORTC QOL C-30 instrument.

**Sources searched to identify primary studies**
PubMed was searched for data on the effectiveness of ACT treatments. Of the 3,994 articles initially identified, 10 studies were finally included.

**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**
Ten primary studies were included in the review. Three more studies were used to derive other data.

**Methods of combining primary studies**
The primary estimates were not combined as the authors selected a range of estimates from among all values available from the literature.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The FEC regimen improved 5-year survival in early BC by 3 to 7% in comparison with CMF. A 5% improvement was used in the base-case.

The life expectancy for a 50-year-old woman was 28.57 years while that of a 60-year-old woman was 19.45 years.

CMF saved 2.45 life-years per patient treated.

No difference in QoL between CMF and FEC was observed.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the number of life-years gained with the new regimen over the standard approach. This was calculated by multiplying the life expectancy of a patient by the improvement in survival with FEC found in the literature. An annual discount rate of 3% was applied.

**Direct costs**
The cost analysis was conducted from a societal perspective. The direct costs were for drugs, travelling, outpatient clinic and drug administration. The unit costs and the quantities of resources used were not presented separately. The costs came from the University Hospital of North Norway, national price lists, and the Regional Health Authority of Northern Norway. Discounts obtained by regional authorities were also considered (LIS agreement). To reflect actual treatment patterns in Norway, the resource use data were based on the authors' experience at their institution. An annual discount rate of 3% was applied to the costs, which was appropriate as a 20-year timeframe was considered. The price year was 2004.
Statistical analysis of costs
Statistical analyses of the costs were not performed.

Indirect Costs
Indirect costs (i.e. productivity losses due to BC) were considered in the analysis as a societal perspective was employed. The days off work were estimated from a survey of 8 senior oncologists dealing with BC. The costs came from official statistics. The indirect costs were calculated using the friction cost method. Details of the calculation of the costs (i.e. unit costs and quantities of resources used) were reported. The price year was 2004. An annual discount rate of 3% was used. An alternative method of calculating the costs, the human capital approach, was also used.

Currency
Norwegian kroner (NOK) converted to Euros (EUR). The conversion rate was EUR 1 = NOK 8.78.

Sensitivity analysis
A univariate sensitivity analysis was carried out to assess the impact of changes in the discount rate (1, 3 and 5%) and the survival gain (3, 5 and 7%) on the estimated cost-effectiveness ratios.

Estimated benefits used in the economic analysis
Over a 20-year timeframe (corresponding to the expected survival of a 60-year-old woman), FEC led to a gain of 0.12 life-years per woman in comparison with CMF.

A 5% improvement with FEC was considered.

Cost results
Depending on cost discounts and dose intensity (DI), the total costs per woman with FEC ranged from EUR 3,278 to EUR 3,850 when using the friction cost method and from EUR 12,143 to EUR 12,715 when using the human capital approach.

The drug costs constituted between 39% and 48% of total costs.

The total cost per women with CMF was not reported.

Synthesis of costs and benefits
Incremental cost-utility ratios were calculated to combine the costs and benefits of the alternative ACT strategies.

The incremental cost per life-year gained with FEC over CMF ranged from EUR 7,150 to EUR 9,075, depending on DI.

In the sensitivity analysis, the incremental cost per life-year gained with FEC over CMF ranged from EUR 3,575 (highest survival improvement and lowest DI) to EUR 15,125 (lowest improvement in survival and highest DI).

Authors’ conclusions
The fluorouracil-epirubicin-cyclophosphamide (FEC) regimen was a cost-effective alternative to cyclophosphamide-methotrexate-fluorouracil (CMF) for the treatment of women with early BC in Norway.
The authors justified the choice of the comparators, which were appropriate for the study question. The new regimen (FEC) has taken over the role of CMF in most countries. You should decide whether they are valid interventions in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence came from published sources, which were identified through a review of the literature. Details of the conduct and methods of the review were provided, and several characteristics of the primary studies were described. Most of the studies were clinical trials, which should have ensured a high internal validity. However, the primary estimates were not combined and a single point estimate was chosen from among those available in the literature. Other data used to assess the benefits of the two ACT regimens were obtained from published studies. The impact of changing clinical data on the results of the study was only partially investigated using a univariate sensitivity analysis.

**Validity of estimate of measure of benefit**

The choice of life-years as the summary benefit measure was appropriate since the impact of the interventions on survival is a relevant dimension of health for women with early BC. The effect of the ACT regimens on QoL was not considered since published studies showed that the two treatments were equally effective.

**Validity of estimate of costs**

The cost analysis was carried out from a societal perspective, which was appropriate as productivity losses associated with early BC might be relevant. The approach used to assess the indirect costs was reported and an alternative method was also used. However, the unit costs and the quantities of resources used were not given for direct costs, which could limit the possibility of replicating the analysis in other settings. Statistical analyses of the costs were not performed, but the impact of different doses and different approaches for the cost calculations was considered. The price year was reported, which will facilitate reflation exercises in other time periods. The impact of changes in the discount rates was also investigated.

**Other issues**

The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. In general, the external validity of the study appears low and no sensitivity analyses of the costs were performed. The issue of uncertainty was not appropriately addressed as only univariate sensitivity analyses were carried out on a few parameters. The study referred to women with early BC and this was reflected in the authors' conclusions.

**Implications of the study**

The study results support the use of FEC as ACT therapy for women with early BC. Future reductions in the costs of epirubicin would make FEC more cost-effective.

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None stated.

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Other publications of related interest


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