The efficacy and cost-effectiveness of adjuvant therapy of early breast cancer in pre-menopausal women

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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
Adjuvant tamoxifen with or without chemotherapy for early breast cancer in pre-menopausal women.

Type of intervention
Secondary prevention.

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

Study population
Women aged 45 years with early breast cancer, eligible for trials of alternative cancer treatments included in the review of effectiveness evidence.

Setting
The setting was not specifically stated, but presumably was a hospital oncology or gynaecology department. The economic study was conducted in the United States.

Dates to which data relate
The systematic review by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) from which this analysis derived effectiveness data was published in 1992. The dates of the trials included in the review were not specified. The dates of resource data collection were not specified in this paper. Financial costs were at 1989 US prices.

Source of effectiveness data
Systematic review by the EBCTCG, published in the Lancet, 1992

Clinical conclusions
In premenopausal early-stage breast cancer, chemotherapy resulted in substantial clinical benefits. Tamoxifen alone led to clinical benefits only in ER+ cancer. Combined therapy was clinically effective for all women but particularly beneficial for women with ER+ cancer.

Modelling
The cost utility analysis was based on a decision analysis, for which methods for deriving death rates, costs and quality of life were described in a separately published paper (Hillner, 1991). A Markov model with nine possible health states was used to estimate cumulative outcomes over time.
Outcomes assessed in the review
Life years gained, probabilities of baseline occurrence of each of nine health states, recurrence of cancer and percentage of women with disease free survival were estimated.

Study designs and other criteria for inclusion in the review
Randomised controlled trials, otherwise not specified (see Hillner 1991).

Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
The number of trials was not stated. Data were combined for 75,000 women taking part.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
Unadjusted life-years gained were not reported. The baseline percentage of women with disease free survival at 5 years was given for four groups:

for axillary node negative, oestrogen receptor positive (N-,ER+): 77.4%;
for axillary node negative, oestrogen receptor negative (N-,ER-): 67%;
for axillary node positive, oestrogen receptor positive (N+,ER+): 47.6%
for axillary node positive, oestrogen receptor negative (N+,ER-): 44.1%

Relative reductions in recurrence rate were reported as follows:

Chemotherapy: 0.37 (range 0.3-0.5)
Tamoxifen alone, oestrogen receptor positive: 0.19 (range 0.05-0.35)
Tamoxifen alone, oestrogen receptor negative: 0.03 (range 0.00-0.19)
Combined therapy, oestrogen receptor positive: 0.44 (range 0.38-0.56)
Combined therapy, oestrogen receptor negative: 0.39 (range 0.37-0.44)
Measure of benefits used in the economic analysis
Quality adjusted life years gained. Life years gained were estimated from a Markov model with five year survival rates and recurrence rates were derived from a review of trials. Quality of life in different health states was based on clinical opinion, derived from 'focus groups of oncology professionals'.

Direct costs
Future costs were discounted at 5% per annum. Quantities of resource use were not reported separately. Costs of health services included medication, outpatient treatment, costs of adjuvant therapy, costs of terminal care. The methods for estimating costs were not clear, but were derived from outpatient charges and Medicare data.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analysis was included, to test the effects on the results of variation in data, discounting, quality of life adjustment, and to estimate the generalisability of results for women with different types of early breast cancer. Multiple one-way, two-way and threshold analyses were used.

Estimated benefits used in the economic analysis
Depending on cancer type, quality adjusted months gained varied between 0.17 and 3.49 in the case of Tamoxifen treatment vs no treatment; between 4.09 and 10.70 in the case of chemotherapy vs no treatment and varied between 0.20 and 2.11 in the case of combined treatment versus chemotherapy.

Cost results
Chemotherapy cost $6,000 per case treated. Tamoxifen cost $1,000 per case treated, but reduced to $500 if generic drugs were used. Details of the costs per case with different treatments were not reported.

Synthesis of costs and benefits
Costs per quality adjusted life year gained were estimated with discounting of both costs and benefits. The analysis was incremental. Costs per QALY gained ($) were:

11,400(N-,ER+), 214,000(N-,ER-) 4,330(N+,ER+) and 57,800(N+,ER-) for Tamoxifen treatment vs no treatment;

11,370(N-,ER+), 4,970(N-,ER-), 9,230(N+,ER+) and 4,890(N+,ER-) for chemotherapy vs no treatment;

33,100(N-,ER+), 186,200(N-,ER-), 14,750(N+,ER+) and 80,700(N+,ER-) for combined therapy.

The model was sensitive to relative efficacy. If the effects of Tamoxifen and chemotherapy were assumed to be additive, combined therapy was more cost-effective than chemotherapy alone. Exclusion of quality of life adjustment, and discounting at 0%, did not alter the ranking of cost-effectiveness.

Authors' conclusions
For ER+ women, Tamoxifen alone added 3.5 to 5.2 quality adjusted months compared with no adjuvant therapy. The incremental CE of Tamoxifen was within acceptable limits in this group, but the combined strategy was always less cost effective than chemotherapy alone. Combined therapy for ER+ cancer added benefit at a cost within accepted limits. In ER- women, the incremental cost effectiveness of combined therapy compared with chemotherapy was always more than $80,000 per QALY gained, and would be higher if Tamoxifen had a negative effect on quality of life.
CRD Commentary
Very little detail was provided about the methods for estimation of costs and effectiveness. The reader is referred to other published papers. The results table did not specify whether the ranges in parentheses were confidence intervals or at what level of significance. It was difficult, on the basis of this paper alone, to judge the reliability of the results. The authors stated that a societal viewpoint was adopted, but it was not clear what this meant, since they measured neither patients' costs nor indirect costs.

Implications of the study
Tamoxifen has been demonstrated to prolong life of women with early breast cancer. This study suggests that chemotherapy alone is a more cost-effective treatment than Tamoxifen alone for oestrogen receptor negative disease. Priority in the use of Tamoxifen should be for women with oestrogen receptor positive disease. Further research is needed on the costs of care and follow up, and on quality of life for women experiencing Tamoxifen treatment with or without chemotherapy.

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Other publications of related interest

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