Should the elderly receive chemotherapy for node-negative breast cancer? A cost-effectiveness analysis examining total and active life-expectancy outcomes

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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 chemotherapy in elderly women with breast cancer.

Type of intervention
Treatment.

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

Study population
Hypothetical cohorts of postmenopausal women from ages 60 to 80 years with a diagnosis of primary breast cancer.

Setting
Acute hospital. The economic study was carried out in the USA.

Dates to which data relate
The data on the effectiveness of adjuvant chemotherapy were based on the results of a meta-analysis published in 1992 and other studies published between 1983 and 1992. No distinction was made between resource use data and prices. Cost data related to 1989, 1991 and 1992. The fiscal year was 1990.

Source of effectiveness data
The evidence for the final outcomes of adjuvant chemotherapy was based on a review of the literature and assumptions made by the authors.

Modelling
A Markov model was used to estimate the costs and benefits associated with treatment strategies.

Outcomes assessed in the review
The outcomes assessed were as follows: the utility values attributed to health states; loss in active life expectancy; annual probability of first recurrence and annual relative reduction in recurrence due to adjuvant chemotherapy.

Study designs and other criteria for inclusion in the review
The meta-analysis on which the effectiveness data were based, analysed the available data from published clinical trials in 2,048 node negative women. Two randomised studies were used as references alongside a number of other studies.
and reports, the designs of which were not specified.

**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**
A total of 7 studies and reports were included.

**Methods of combining primary studies**
Not reported.

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

**Results of the review**
The utility values attributed to the health states were: well (1), minor toxicity with chemotherapy (0.9), major toxicity with chemotherapy (0.8), first recurrence (0.7), and dead (0). Annual loss in active life expectancy for individuals between 65 and 69 years old was 7%, between 80 and 84 was 16%, and beyond 84 was 34%. The annual recurrence risk was 5% (range: 3 - 10%) or 23% at 5 years. The annual relative reduction in recurrence with adjuvant chemotherapy was taken to be 20% (range: 10 - 40%).

**Methods used to derive estimates of effectiveness**
A series of assumptions were made by the authors.

**Estimates of effectiveness and key assumptions**
It was assumed that chemotherapy would only affect the probability of a first recurrence of breast cancer; six cycles of standard cyclophosphamide, methotrexate, and fluorouracil (CMF) were given to the patients; severe comorbidity (such as renal failure) making chemotherapy particularly unsafe was absent in the patient cohort; and equal distribution of the chemotherapy effectiveness (5-year effectiveness period) across all 5 years.

**Measure of benefits used in the economic analysis**
Life years gained, quality-adjusted life years (QALYs) and active life expectancy were used as the benefit measures in the economic analysis. The basic method of valuation of health states was reported to have been previously published but was not stated here.

**Direct costs**
Costs and quantities of resources were not separately identified. Costs (1990) were discounted. The costs in the last year of life were an estimate based on two published estimates. Costs to the health service of chemotherapy, major and
minor toxicity were based on charge data from the study institution and Medicare data. The perspective adopted in the cost analysis was reported to be that of society. Charge data were used to estimate the costs. The date of the price data was 1990.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
A set of one-way and multi-way sensitivity analyses were performed on the parameters of the model. An analysis of extremes (worst- and best-case scenarios) was also carried out.

**Estimated benefits used in the economic analysis**
The average survival benefit for a 60 year old was 5.5 months and for an 80 year old woman was 2.5 months. The quality-adjusted benefit of adjuvant chemotherapy for women with breast cancer at various ages was calculated to be 2.8 months (aged 60), 2.8 months (aged 65), 2.2 months (aged 70 years), 1.8 months (aged 75 years) and 1.4 months (aged 80 years). When active life expectancy was the outcome measure the average gain fell to 1.3 months for a 65 year old and 0.4 months for an 80 year old. The model was run until every person died or reached the age of 95. The side-effects of treatment were considered. The discount rate was 5% (range:0 - 10%).

**Cost results**
The discount rate was 5%. Chemotherapy, if given, was costed at $6,000, minor toxicity at $1,500 and major toxicity at $10,000. Total costs of breast cancer treatments were not reported. The model was run until every person died or reached the age of 95.

**Synthesis of costs and benefits**
Incremental cost-utility/effectiveness ratios were calculated. Using conventional survival as the outcome measure the costs per life year were $14,910 for a 60 year old woman and $24,400 for a 75 year old. The costs per QALY were $28,200 (aged 60), $31,300 (aged 65), $36,300 (aged 70), $44,400 (aged 75) and $57,100 (aged 80). Using active life expectancy the costs per QALY of adjuvant chemotherapy in elderly women with breast cancer increased to $59,300 (aged 65), $75,000 (aged 70), $96,000 (aged 75) and $212,500 (aged 80). Both costs and benefits (years accrued in the future) were discounted at 5%. The sensitive parameters were the rate of major toxicity, the risk of chemotherapy related death, the effectiveness of chemotherapy and the rate of minor toxicity. The sensitivity analysis of single and multiple variables did not have a major impact on the result.

**Authors’ conclusions**
There is a small survival benefit for adjuvant chemotherapy in elderly patients with node-negative breast cancer. The use of active life expectancy as the primary outcome reduces the benefits and adds to the cost. If active life expectancy is accepted as a relevant outcome then withholding chemotherapy for patients aged over 70 is a reasonable approach.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator is clear.

**Validity of estimate of measure of benefit**
The internal validity of the estimates of the benefit measure can not be guaranteed due to lack of both a comprehensive
literature review and quality assessment of the primary studies included in the review.

Validity of estimate of costs
Quantities were not reported separately from the costs and insufficient details of methods of cost estimation were provided. Charge data were used to estimate the true costs. The study lacked a prospective cost analysis.

Other issues
The analysis of extremes and single and multi-way sensitivity analyses were performed, and, although the results were not presented in their entirety, the authors did comment on the impact of these analyses.

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Bibliographic details

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Other publications of related interest
Hillner B E, Smith T J. Efficacy and cost-effectiveness of adjuvant chemotherapy in women with node negative breast cancer. A decision-analysis model. New England Journal of Medicine 1991;324:160-168. This article contains the model, health states, costs and results in younger populations, to which this paper refers.

Indexing Status
Subject indexing assigned by NLM

MeSH
Age Factors; Aged; Aged, 80 and over; Antineoplastic Agents /economics /therapeutic use; Breast Neoplasms /drug therapy /economics /mortality /pathology; Chemotherapy. Adjuvant /economics; Cost-Benefit Analysis; Decision Support Techniques; Female; Humans; Lymphatic Metastasis; Middle Aged; Quality of Life; Survival Rate; Treatment Outcome

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