Cost-effectiveness of letrozole versus tamoxifen as initial adjuvant therapy in postmenopausal women with hormone-receptor positive early breast cancer from a Canadian perspective

Delea T E, El-Ouagari K, Karnon J, Sofrygin O

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 study determined the cost-effectiveness of two initial adjuvant therapies, tamoxifen and letrozole, in postmenopausal women with hormone receptor-positive early breast cancer in the Canadian setting. The authors concluded that letrozole was a cost-effectiveness treatment from the perspective of the health care system. The quality of the study methodology was good in terms of the methods and presentation of the results, although information on the sources of the economic data was not extensive.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective of the study was to determine the cost-effectiveness of two initial adjuvant therapies, tamoxifen and letrozole, in postmenopausal women aged 60 years with hormone receptor-positive (HR+) early breast cancer (BC) in the Canadian setting.

Interventions
Tamoxifen and letrozole were given for 5 years as adjuvant therapy to postmenopausal women with HR+ operable invasive BC who have completed primary surgical therapy.

Location/setting
Canada/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a Markov model, which was developed to simulate the clinical and economic impact of the two therapies. The time horizon of the analysis was 30 years. The authors stated that the analysis was carried out from the perspective of the Canadian health care system.

Effectiveness data:
The clinical estimates appear to have been derived from a selection of known relevant studies. Key clinical estimates on treatment effect for the two therapies under analysis were derived from the Breast International Group 1-98, an ongoing, international, randomised, double-blind four-arm clinical trial. Another source of key data on BC to estimate transition probabilities among health states was a meta-analysis by the Early Breast Cancer Trialists' Collaborative Group. Rates of adverse events and other complications were based on data from the US Surveillance Epidemiology and End Results programme. A key assumption was made about a carryover effect of the adjuvant therapies after treatment discontinuation, on the basis of published evidence.

Monetary benefit and utility valuations:
The utility estimates were based largely on a study of US women with BC. This study used a chained standard-gamble technique. Other utility valuations were based on a longitudinal cohort study or on authors’ assumptions.

Measure of benefit:
The summary benefit measure was the expected number of quality-adjusted life-years (QALYs). These were estimated using the decision model. Other model outputs, such as life-years (LYs) and recurrences prevented, were also reported. The benefits were discounted at an annual rate of 5%.

Cost data:
The analysis included the costs of adjuvant hormonal therapy (letrozole or tamoxifen), treatment of BC events (depending on the stage of cancer) and adverse events (endometrial cancer, thromboembolism, cardiac events, fractures, arthralgia and hypercholesterolaemia). Basically, the cost and resource use data were derived from published studies, which reflected the costs of managing BC in Canada. Prices of medications were based on wholesale acquisition costs. Details on the other sources of resource use and unit costs were not reported. An annual discount rate of 5% was applied to the long-term costs. The price year was 2005. The costs were in Canadian dollars (CAD).

Analysis of uncertainty:
A deterministic sensitivity analysis was undertaken by varying probabilities and costs across their 95% confidence intervals, if available, or from 50 to 150% of the base-case values. Alternative assumptions about patient age, model timeframe, carryover effect of therapy and discount rates were also considered. A probabilistic sensitivity analysis was carried out by assigning probabilistic distributions to all model inputs in order to generate CIs for the costs and benefits, as well as cost-effectiveness acceptability curves.

Results
Under base-case assumptions, letrozole resulted in a gain of 0.368 LYs and 0.343 QALYs in comparison with tamoxifen.

The additional cost of letrozole was CAD 8,110. This resulted in an incremental cost per QALY gained of CAD 23,662 (95% CI: 15,667 to 52,014).

The deterministic sensitivity analysis showed that the model results were quite sensitive to variations in the relative risk of BC events and the age of therapy initiation, although the incremental cost per QALY gained for letrozole over tamoxifen almost always remained below CAD 50,000. In fact, the probabilistic sensitivity analysis suggested that letrozole was the preferred option in 97% of simulations at a willingness-to-pay of CAD 50,000 per QALY gained.

Authors' conclusions
The authors concluded that initial adjuvant therapy with letrozole in postmenopausal women with HR+ BC was a cost-effective alternative to tamoxifen in the Canadian setting, especially in younger women.

CRD commentary
Interventions:
The authors did not provide an explicit justification for their choice of the comparators. However, letrozole, a new aromatase inhibitor, appears to have been appropriately compared against tamoxifen, which represented the standard of care for this specific patient population. The comparison was based on recent data from a randomised controlled trial, and this may also explain the choice of the therapies included.

Effectiveness/benefits:
The authors did not report the details of a systematic review of the literature, thus the primary studies might have been identified selectively. The bulk of the evidence came from two main sources (a large international clinical trial and a meta-analysis). Both represent valid sources of data, which should have ensured the validity of the clinical estimates. The key assumption on a potential carryover effect of treatment relied upon published evidence from multiple sources. The authors acknowledged that this was an uncertain estimate, but the cost-effectiveness of letrozole did not change under different assumptions about treatment effectiveness. The authors discussed the selection of data derived from published sources, the design of which was described in part. The use of both LYs and QALYs represents a further strength of the analysis.

Costs:
The analysis of the costs appears to have been carried out in accordance with the authors' stated perspective. The price
year was reported and the use of a discount rate was appropriate. Moreover, the option of no discounting was
investigated. However, a breakdown of the cost categories was not given and the sources used to derive the main cost
categories were not described in detail. This may limit the reproducibility of the study in other contexts.

Analysis and results:
The results of both the base-case and sensitivity analyses were presented clearly. The issue of uncertainty was
satisfactorily addressed in the sensitivity analysis and acceptability curves were shown. Extensive details of the decision
model were reported. The authors noted that the use of simplifying assumptions may represent a limitation of the
analysis.

Concluding remarks:
The analysis was presented clearly in terms of the methods and results, although the provision of more information on
the economic side of the study would have been helpful. The authors’ conclusions appear valid and robust.

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Other publications of related interest

Delea TE, Karnin J, Smith RE, et al. Cost-effectiveness of extended adjuvant letrozole therapy after 5 years of adjuvant

Indexing Status
Subject indexing assigned by NLM

MeSH
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Chemotherapy, Adjuvant /economics; Cost-Benefit Analysis; Drug Costs; Female; Humans; Markov Chains;
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