Cost-effectiveness of extended adjuvant letrozole therapy after 5 years of adjuvant tamoxifen therapy in postmenopausal women with early-stage breast cancer

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
This study compared the costs and effects of extended adjuvant letrozole therapy with no letrozole therapy, in postmenopausal women, with early-stage breast cancer, who had successfully completed five years of adjuvant tamoxifen therapy. The authors concluded that the cost-effectiveness of extended letrozole therapy for this population was within the range of other generally accepted medical interventions in the USA. The methods were appropriate and comprehensively reported and, overall, the authors' conclusions appear to be reasonable.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The purpose was to compare the costs and effects of adjuvant letrozole therapy with no adjuvant letrozole therapy in postmenopausal women, with early-stage breast cancer and receptor-positive tumours, who had successfully completed about five years of adjuvant tamoxifen.

Interventions
Extended adjuvant therapy with 2.5mg per day of letrozole was compared with no extended letrozole therapy. The women, in the hypothetical cohort, were postmenopausal with early-stage breast cancer and receptor-positive tumours. They had successfully completed about five years of adjuvant tamoxifen and were assumed to have a mean age of 62 years. Half of the cohort were node positive and disease-free at the start of letrozole therapy.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A Markov model was developed to synthesise published and unpublished data estimates for a 30-year time frame. The authors stated that the perspective was that of the US health care system.

Effectiveness data:
The effectiveness data were derived from a combination of published literature, but the key source for the main clinical effect parameter was a single randomised controlled trial (Goss, et al. 2003, and Goss, et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details). The clinical outcomes were disease recurrence including distant metastases, disease-free survival, treatment-related adverse events (osteoporosis and hip fractures), and deaths. Several assumptions were made to derive the model parameters and these were clearly reported and supported with references where relevant.

Monetary benefit and utility valuations:
The utilities were based on the results of published studies, where preferences were elicited from US women with early-stage breast cancer, who had received adjuvant therapy and were disease free (Sorensen, et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details). The chained standard gamble technique was used to generate the utility scores. The change in utility score for women who developed osteoporosis was assumed to be nil.
Measure of benefit:
The two measures of benefit used were quality-adjusted life-years (QALYs) and life-years (LYs) saved. These were discounted at an annual rate of 3%.

Cost data:
The direct medical costs were those for tumour recurrences, surveillance, adverse events, and pharmaceuticals. The prices were derived from various sources including clinical charges, published studies based on Medicare claims, wholesale drug acquisitions, and Medicare reimbursements. These prices were adjusted to 2004 US dollars ($) using the US Consumer Price Index and adjusted downwards using a cost-to-charge multiplier of 0.5. All costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
One-way sensitivity analyses investigated the effects of changes in key parameters, including costs, from 50 to 150% of their base values, in addition to different time horizons, different ages at the start of therapy, and positive and negative nodal status. A probabilistic sensitivity analysis was also used and the results were presented in cost-effectiveness plane and acceptability curve graphs.

Results
The total mean costs for the extended letrozole group were $55,254 compared with $45,555 for no extended therapy. Letrozole drug acquisition accounted for the majority of this cost difference, but higher costs also occurred for osteoporosis treatment and hip fractures in the letrozole therapy group.

Disease recurrences occurred in 17.6% of women with extended letrozole compared with 22% of women with no letrozole therapy. Disease-free survival was extended by approximately 10 months per patient after letrozole therapy, while LYs and QALYs increased by approximately six months (undiscounted).

The incremental cost-effectiveness ratios (ICERs) were $30,270 per LY gained, and $28,728 per QALY gained for extended letrozole therapy.

These results were sensitive to different model time frames, the age at initiation of therapy, node status, and relative risk and probability of recurrence at baseline. The cost-effectiveness ratios were more favourable for younger women, node positive patients, and time horizons greater than 20 years.

Probabilistic sensitivity analyses revealed that the ICER credible interval was $18,169 to $62,289 per QALY gained and that ICERs were less than $50,000 per QALY gained in more than 94% of simulations.

Authors’ conclusions
The authors concluded that the cost-effectiveness of extended letrozole therapy for this population was within the range of other generally accepted medical interventions in the USA.

CRD commentary
Interventions:
The profile of the intended patient population and both the interventions were clearly described. Letrozole therapy was also supported for use as an aromatase inhibitor by the American Society of Clinical Oncology.

Effectiveness/benefits:
The effectiveness data were derived from various published studies that appear to have been of high quality. However the methods used to identify and select these particular studies were not stated. It is therefore not possible to ascertain if the best available evidence was used to populate the model. The derivation of utilities from a published study involved patient preferences, rather than preferences from the general population. The use of patients’ preferences can bias the utilities, which can bias the QALY results, however the sensitivity analyses addressed this uncertainty.

Costs:
The costs appear to reflect those applicable to the health system perspective. The costing methods were reported in
detail and the data sources and references were clearly documented. All costs were adjusted for inflation and charges and the methods used were clearly presented.

Analysis and results:
An illustration of the model structure was presented and a thorough description of the health states and possible transitions between them was given. The health outcomes and net costs were synthesised into cost-effectiveness ratios. The validity of the decision analytic model structure was not discussed although it was graphically presented and it was an updated and improved version of a previous model published by the same authors (Karnon, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). The model distributions that were assigned for the probabilistic sensitivity analyses were assumed because there was no data available for them. The authors do not appear to have investigated whether varying these distributions impacted on the results. The authors identified and discussed a number of limitations to their study.

Concluding remarks:
The study methods and limitations were comprehensive and transparently reported. The authors’ conclusions appear to be a fair assessment of the analysis undertaken.

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Other publications of related interest


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Adult; Age Factors; Aged; Aged, 80 and over; Antineoplastic Agents, Hormonal /administration & dosage /adverse effects /economics; Antineoplastic Combined Chemotherapy Protocols /adverse effects /economics /therapeutic use; Aromatase Inhibitors /administration & dosage /adverse effects /economics; Breast Neoplasms /drug therapy /economics /pathology; Chemotherepy, Adjuvant /economics; Cohort Studies; Cost-Benefit Analysis; Decision Support Techniques; Disease Progression; Female; Humans; Markov Chains; Middle Aged; Neoplasm Metastasis /drug therapy; Neoplasm Recurrence, Local /drug therapy; Neoplasm Staging; Nitriles /administration & dosage /adverse effects /economics; Postmenopause /drug effects; Quality-Adjusted Life Years; Tamoxifen /administration & dosage /adverse effects /economics; Time Factors; Triazoles /administration & dosage /adverse effects /economics; United States
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