Cost-effectiveness analysis of anastrozole vs tamoxifen in adjuvant therapy for early stage breast cancer in the United Kingdom: the 5-year completed treatment analysis of the ATAC ('Arimidex', Tamoxifen alone or in combination) trial

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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.

CRD summary
This study investigated the cost-effectiveness of a new adjuvant hormone therapy, anastrozole, compared with tamoxifen, for hormone receptor positive women with early-stage breast cancer. The authors concluded that anastrozole was a cost-effective option in the UK. With a few exceptions, the methods were transparent and clearly reported. The conclusions reached by the authors reflected the scope of their analysis.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to assess the cost-effectiveness of the adjuvant hormone agent anastrozole compared with tamoxifen for early-stage breast cancer.

Interventions
This study compared anastrozole with tamoxifen for post-menopausal women with hormone receptor positive (HR+) early-stage breast cancer. Both drugs were administered for up to five years. The study population was a hypothetical cohort of post-menopausal women in the UK with early, invasive, operable, breast cancer who had completed primary therapy.

Location/setting
UK/out-patient care.

Methods
Analytical approach:
A Markov model was used to synthesise the published data from various sources including a key randomised controlled trial. The analysis covered a 25-year period and the authors stated that the perspective was that of the UK National Health Service (NHS).

Effectiveness data:
The clinical data for efficacy of anastrozole included the breast cancer-related deaths, event rates for recurrence, adverse events, drug withdrawal, and switching rates. The key adverse events were hip fractures, endometrial cancer, thromboembolic events, and hysterectomy rates, although other events were also reported. The efficacy data were derived primarily from a five-year trial, entitled the ‘Arimidex’, Tamoxifen alone or in combination (ATAC) trial, in 2003 (ATAC Trialists’ Group. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). The resource use data were derived from both published sources and an expert panel during 2003 to 2005.

Monetary benefit and utility valuations:
The health states were directly measured using the standard gamble approach. A cross-section of 26 representative UK patients, with early or advanced breast cancer and a mean age of 68 years, were asked to value 14 health states, by comparing these states to perfect and worst health, and then comparing perfect and worst health to death. Full descriptions of the health states were reported.
Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) and these were discounted at an annual rate of 3.5%.

Cost data:
The direct medical costs were those for the medical management during treatment, follow-up and off-treatment (due to remission or adverse events); the medical management at diagnosis and during disease recurrence; the treatment for serious adverse events, which required hospitalisation, and for non-serious adverse events; and palliative care. The resource use data were obtained from structured interviews with the expert panel and, where possible, published sources. The unit costs were obtained from the Medical Technology Assessment Program database, the British National Formulary (2003 to 2004) and NHS reference costs. All costs were discounted at 3.5% and reported in 2003 to 2004 UK pounds sterling (£).

Analysis of uncertainty:
The uncertainty was captured through the use of probabilistic sensitivity analysis, with Monte Carlo simulations. Overall uncertainty in the results was expressed as a cost-effectiveness acceptability curve. One-way sensitivity analyses were also undertaken on the key parameters. A scenario analysis was performed to assess a different duration of benefit for anastrazole.

Results
The mean QALYs for anastrazole were 9.21 per patient compared with 8.96 for tamoxifen. The mean, discounted life-years gained at 25 years, for anastrazole were 9.46 compared with 9.23 for tamoxifen. The incremental gain, for anastrazole, in life-years was 0.231, which was 0.244 QALYs.

The mean, discounted cost per patient at 25 years was £9,935 for anastrazole and £5,620 for tamoxifen. Using anastrazole incurred higher drug costs at £3,598, compared with tamoxifen at £113, which were partly offset by lower costs for the treatment of recurrence and palliative care.

Over 25 years, the incremental cost per QALY gained for anastrazole over tamoxifen was £17,656 (95% confidence interval: £10,280 to £39,325) or £18,702 per life-year gained.

The incremental cost per QALY gained at five years was £219,950, while, at 10 years, it was £47,489. There was a 90% probability that the incremental cost per QALY would be under £30,000. The sensitivity analyses found that the results were robust to changes in the key parameters and assumptions including the fracture rates, cost distributions, and probabilities. The time to recurrence was the most sensitive parameter.

Authors’ conclusions
The authors recommended that anastrazole should be considered to be an effective, well-tolerated and cost-effective adjuvant therapy for post-menopausal women with HR+ early breast cancer in the UK.

CRD commentary
Interventions:
The authors chose tamoxifen as the comparator for the newer drug anastrazole. Tamoxifen was reported to be an established adjuvant treatment option for the patient population.

Effectiveness/benefits:
The parameters were derived from published research and the most recent randomised controlled trial (the ATAC trial) for these two therapies. They were therefore likely to have high internal validity, in terms of their clinical effects. However as the full details of the ATAC trial were not presented in this paper and a full assessment of its internal validity was not possible. It is also not clear whether the ATAC trial was the only relevant clinical trial available. A systematic review of the available evidence may have been warranted. The utility values were measured directly from a small number of patients with breast cancer, and these methods and health states were clearly reported.

Costs:
The perspective was that of the NHS, and all the relevant direct medical costs appear to have been included along with
those of several important adverse events, for both the short and five-year analyses. The adverse events and resource use data were obtained from expert opinion, due to the lack of available relevant data. However, it was unclear why or how the authors selected their group of specialists. Additionally, it was not clear whether these specialists were directly involved in the ATAC trial, which could have biased the data. The issue of bias was addressed by the thorough sensitivity analyses which assessed the uncertainty of the resource and cost data estimates. The details of these analyses were clearly reported.

Analysis and results:
The authors reported a number of limitations to their study, including the time horizon, the time for expected benefits of anastrozole over 10 years, and reliance on clinical expert opinion. They also suggested improvements for data quality to populate their model. They acknowledged variations in patient characteristics and costs for different settings, when discussing their results, in comparison with two similar studies. They comprehensively evaluated the impact of data variability in the sensitivity analyses and appear to have presented their results in detail. As the quality-of-life estimates were based on a small number of women, it may have been appropriate to discuss and explicitly report how any variation in the utility scores impacted on the results.

Concluding remarks:
Despite a lack of available data, the methods of the study were appropriate and comprehensive. The conclusions reached by the authors reflected the scope of their analysis.

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Other publications of related interest
ATAC Trialists' Group. Results of the ATAC (Arimidex, Tamoxifen Alone or in Combination) trial after completion of 5 years' adjuvant treatment for breast cancer. Lancet 2005;365:60-2.

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