Cost-effectiveness of anastrozole compared to tamoxifen in hormone receptor-positive early breast cancer: analysis based on the ATAC trial

Moeremans K, Annemans L

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
The authors compared anastrozole and tamoxifen, both alone and in combination. Dosages and further details were not provided.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised female patients with hormone receptor-positive early breast cancer. No inclusion or exclusion criteria were reported, but these might have been determined by the criteria noted in the parent study (Howell et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details).

Setting
The setting was outpatient care. The economic study was carried out in Belgium.

Dates to which data relate
The effectiveness data were taken from studies published between 2001 and 2005. The resource use data were derived from information available in the original ATAC trial published in 2005. The unit cost-related data were obtained from a range of published sources, one of which was dated 2003.

Source of effectiveness data
The authors derived 6-monthly transition probabilities from the clinical study. The probabilities of locoregional, distant and contralateral relapse when treated with tamoxifen, and the probabilities of locoregional, distant and contralateral relapse when treated with Arimidex, were estimated from the ATAC trial. The probability of death due to other causes was estimated. The probabilities of distant disease progression following locoregional disease recurrence for patients developing locoregional recurrence within 5 years of the primary diagnosis and after 5 years were estimated separately. The probability of metastatic relapse after distant disease development and the mortality rate following distant disease were also estimated.

Modelling
The authors used a Markov state transition model to depict breast cancer-related health states. Such health states were primary treatment, metastatic disease, locoregional recurrence and death. The probabilities of locoregional, contralateral and distant disease recurrence, and death were used to model the movement of patients between health
states. A 20-year time horizon with 6-month time periods was used. The model was validated beyond available study data by comparing 10-year modelled outcomes with the 10-year tamoxifen outcomes reported by the Early Breast Cancer Trialists Collaborative Group.

**Sources searched to identify primary studies**
The majority of the clinical data was taken from the ATAC trial, but all-cause mortality was derived from the National Institute of Statistics. Further disease progression following locoregional, distant disease recurrence and mortality following distant disease were based on published studies (only references were provided). The probability of metastatic relapse after distant disease development was based on a large trial related to hormonal therapy in metastatic breast cancer.

**Methods used to judge relevance and validity, and for extracting data**
No details of any search strategy or inclusion criteria employed were reported. It therefore seems likely that the authors selected references specifically to match the requirements of their model. The primary data, which do not appear to have been combined, were used to inform specific parameter estimates.

**Measure of benefits used in the economic analysis**
The primary measures of benefit were the life-years (LYs) and quality-adjusted life-years (QALYs). Utility values applicable to each disease state were obtained from a published source (Karnon et al. 2003, see 'Other Publications of Related Interest' below for bibliographic details). The LYs were estimated directly from the Markov model and then combined with utility values in order to estimate the QALYs.

**Direct costs**
The economic analysis was carried out from the perspective of the Belgian health care system. It aimed to estimate the appropriate health care costs for each recognised disease state in the Markov model. Resource use was multiplied by local unit costs per resource item. Hormonal therapy consumption was taken from the ATAC study. The source of the drug prices was unclear although the authors reported the pack size and price. The costs of adverse events were reported to have been taken from the literature but specific sources were not described. The costs of breast cancer recurrence were taken from a retrospective chart review that was updated and validated in 2001, but it was unclear whether this related to the ATAC population or to an alternative population. A price year was not reported, and there was no report that discounting was carried out.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
Productivity costs were not relevant to the perspective adopted, but it was unclear from the report whether or not they were included in the analysis.

**Currency**
Euros (EUR).

**Sensitivity analysis**
The authors used multiple sensitivity analyses to investigate parameter uncertainty in the risk reduction for disease progression by anastrozole and the costs of disease progression. The time horizon was also varied.
Estimated benefits used in the economic analysis
After 20 years, patients treated with anastrozole gained 0.353 LYs and 0.378 QALYs compared with those treated with tamoxifen. The estimated total benefits were not reported.

Cost results
The cumulative 20-year breast cancer costs were EUR 37,827 in the anastrozole group and EUR 36,332 in the tamoxifen group. Therefore, the incremental cost of anastrozole was EUR 1,495.

Synthesis of costs and benefits
Anastrozole had an incremental cost-effectiveness ratio of EUR 4,233 per LY and EUR 3,958 per QALY gained.

A sensitivity analysis exploring the use of a small pack of Arimidex showed costs of EUR 9,263 per LY gained and EUR 8,662 per QALY gained.

The results were reported to be robust to variations in the costs and progression rates, but varied with the time horizon.

Authors' conclusions
The "cost-effectiveness of adjuvant treatment is time horizon dependent due to different timings of treatment costs and benefits". "Anastrozole lies within acceptable cost-effectiveness benchmarks if long term (9 - 12 years) outcomes are taken into account."

CRD COMMENTARY - Selection of comparators
The authors compared anastrozole and tamoxifen. These comparators were chosen in order to facilitate extrapolation of the outcomes of the ATAC trial beyond the studied timeframe. Readers should consider whether these drugs are relevant comparators within their own setting.

Validity of estimate of measure of effectiveness
Although it was clear that the authors specifically selected a model from the literature on which to base their analysis, it would have been useful had they considered the wider literature in order to demonstrate that this model and the initial analysis were the best quality and/or most applicable analysis available at the time. Where the original analysis was supplemented with data from other sources, the authors could have reviewed the available data more widely to demonstrate the validity of their new inputs.

Validity of estimate of measure of benefit
The utility estimates were taken from a published source and, as the authors did not provide the reader with more detail of the methods of estimation or patient sample used to obtain these estimates, the reader is referred to the original source to assess the quality of the utility inputs. Both LYs and QALYs gained provide a generic measure of health benefit that is comparable across a very wide range of health-related technologies. However, given the long time horizon of the analysis, it is worth noting that the authors chose not to discount, in order to reflect the individual's time preference.

Validity of estimate of costs
Although the perspective of the Belgian health care system was identified, it was not possible to assess whether the actual analysis reflected this given the lack of details presented. For instance, it was unclear whether physicians' time was accounted for in the analysis, or whether health care-related overhead costs were considered when treating adverse events. It was also unclear as to which population or sample the costs of breast cancer recurrence related, thus it was not possible to determine whether they applied directly to the sample used within this study. No price year was reported and discounting does not appear to have been used, which means it is not possible to be sure which year these results apply to, or whether any time preference was included. Given these considerations, readers should exercise caution when...
interpreting the results and considering their applicability to a different setting. The analysis would have been improved by better reporting practices.

**Other issues**
The authors were unable to compare their results with those of other studies, although it was unclear whether this might have been the first study to explore results over such a long time horizon. Ten-year predicted results were compared in order to validate the Markov model, and this validation process improves confidence in the overall results. The issue of generalisability was not explicitly addressed and, as noted already, readers should be careful if attempting to generalise the results to their own setting. The base-case results were well presented and easy to interpret, although the results of sensitivity analysis could have been reported in more detail. The conclusions were an accurate reflection of the results presented and the scope of the study, applying well to the relevant patient population. No limitations were discussed.

**Implications of the study**
The authors did not recommend any changes to policy or practice following on from their study, nor did they suggest areas for further work.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
17010076

**DOI**
10.1111/j.1525-1438.2006.00699.x

**Other publications of related interest**
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antineoplastic Agents, Hormonal /economics /therapeutic use; Breast Neoplasms /drug therapy /economics /secondary; Canada; Chemotherapy, Adjuvant; Cost-Benefit Analysis; Disease-Free Survival; Female; Humans; Neoplasm Recurrence, Local /drug therapy /economics; Nitriles /economics /therapeutic use; Quality-Adjusted Life Years; Receptors, Estrogen /metabolism; Receptors, Progesterone /metabolism; Sensitivity and Specificity; Survival Rate;