The benefits and costs of tamoxifen for breast cancer prevention
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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
The use of tamoxifen therapy for 5 years, relative to placebo, for the prevention of breast cancer.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised women with a high risk of breast cancer. The cohort of women that was simulated in the model had the same baseline distribution as those enrolled in the NSA BP-1 trial (see Other Publications of Related Interest).

Setting
The setting was primary care. The economic study was conducted in New South Wales, Australia.

Dates to which data relate
The effectiveness evidence was taken from three studies published in 1998 (see Other Publications of Related Interest). The costs and prices were in 1997/98 Australian dollars.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Modelling
A Markov model was used to evaluate the costs and benefits of the different technologies in three different alternatives. In the first alternative, using a 5-year prevention model, the duration of risk reduction for breast cancer and the increases in risk for endometrial cancer, cataract and pulmonary embolism were set at 5 years, with no effect thereafter. In the second alternative, this duration of risk reduction and increase in risk for endometrial cancer were extended to 10 years. In the third alternative, 5 years of tamoxifen only delayed the appearance of breast cancer rather than reducing the incidence of breast cancer.

Outcomes assessed in the review
The main outcomes assessed in the review were:

the annual rates and risk ratios (tamoxifen/placebo) of breast cancer, endometrial cancer, stroke and myocardial
the percentage of case fatality within 1 year due to stroke, acute myocardial infarction and endometrial cancer; and conditional mortality with breast cancer.

**Study designs and other criteria for inclusion in the review**
RCTs offering comparative data on tamoxifen and placebo were included.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Three RCTs and one meta-analysis were included in the review.

**Methods of combining primary studies**
The meta-analysis techniques were reported elsewhere (see Other Publications of Related Interest).

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

**Results of the review**
The annual rate of breast cancer was 0.00676 (range tested: 0.00332 - 0.01), of endometrial cancer 0.00091 (range tested: 0 - 0.00091), of stroke 0.00092, and of myocardial infarction 0.00107.

The risk ratio (tamoxifen/placebo) was 0.58 (range tested: 0.45 - 0.70) for breast cancer, 2.62 (range tested: 1.40 - 4.90) for endometrial cancer, 1 (range tested: 0.93 - 2.77) for stroke, and 1 (range tested: 0.65 - 1.92) for myocardial infarction.

Twenty-four per cent (range tested: 20 - 28) of case fatalities within 1 year were due to stroke, 40% (range tested: 35 - 45) to acute myocardial infarction, and 7.7% (range tested: 6.4 - 9.2) to endometrial cancer.

Conditional mortality with breast cancer was 0.0295 (range tested: 0.0178 - 0.0400) plus age-specific non-breast-cancer death rate.

**Measure of benefits used in the economic analysis**
The measures of benefit were the life-years gained and the quality-adjusted life-years (QALYs) gained. A utility weight for breast cancer was applied for each year following a diagnosis of cancer. The ranges for the sensitivity analysis were chosen from clinician-based standard gamble method and patient-based healthy-years equivalent, time trade-off-based method studies. The benefits were discounted at a rate of 5%.
Direct costs
The estimation of the costs was derived using modelling. The cost data were obtained from published literature. Only health service medical costs were included. The cost of breast cancer treatment was modelled using cost relativities (see Other Publications of Related Interest): an initial reference treatment phase (IRTP), an annual maintenance phase (40% of IRTP), and a final 12 months' treatment phase for terminal care (costing double of IRTP). The IRTP was an estimate of an average cost of the initial treatment phase according to early breast cancer treatment patterns in Australia (see Other Publications of Related Interest). The cost of hospitalisations for acute health states (e.g. pulmonary embolism) was derived using the average cost weights of Australian National Diagnosis-Related Groups. The quantities and the costs were not analysed separately. The cost of tamoxifen was taken from the Pharmaceutical Benefit Scheme list and the cost of monitoring for endometrial cancer from the Medicare Schedule. All of the costs were in 1997/98 Australian dollars. Discounting was relevant, as the costs were incurred in more than 2 years, and was carried out at a rate of 5%.

Statistical analysis of costs
The costs were treated deterministically. However, the cost of tamoxifen was varied in the sensitivity analysis from half to twice its Australian price. No statistical tests for the costs were carried out.

Indirect Costs
No indirect costs were reported.

Currency
Australian dollars (Aus$).

Sensitivity analysis
One-way, multi-way and Monte Carlo simulation sensitivity analyses were carried out. The one-way sensitivity analysis investigated the risk reduction effect of treatment, duration of tamoxifen benefits, discount rate, cost of tamoxifen, and the relative risk for myocardial infarction, stroke and others. The multi-way sensitivity analysis was performed on the parameters most important in determining the effects of tamoxifen on reducing the risk of breast cancer and increasing the rates of endometrial cancer and pulmonary embolism (baseline risk, relative risk ratio, mortality rates). One thousand Monte Carlo simulations, based on random sampling from evidence-based distributions of relative risks and mortality for all beneficial and detrimental health state effects, were used to construct distributions of incremental costs per life-year saved (LYS). Ninety-five per cent CIs and cost-effectiveness acceptability curves were constructed.

Estimated benefits used in the economic analysis
The incremental life-years and QALYs were used in the economic analysis.

The incremental life-years of tamoxifen compared to placebo were 0.0505 for the 5-year prevention model, 0.0801 for the 10-year prevention model and 0.0141 for the delay model. The corresponding incremental QALYs of tamoxifen compared to placebo were 0.0574 (5-year prevention), 0.0939 (10-year prevention) and 0.0131 (delay), respectively.

Cost results
The total cost for the placebo strategy was Aus$5,872. For the tamoxifen model, the costs were Aus$8,065 for 5-year prevention, Aus$7,690 for 10-year prevention and Aus$8,480 for the delay alternative.

The annual discount rate for the base-case was 5%.

The incremental costs of tamoxifen compared to placebo were Aus$2,193 for 5-year prevention, Aus$1,817 for 10-year prevention and Aus$2,607 for the delay alternatives.

No statistical analysis of the costs was presented.
Synthesis of costs and benefits
The costs and benefits were combined using the incremental cost per LYS and the incremental cost per QALY saved.

The incremental cost per LYS of tamoxifen over placebo was Aus$43,466 in the 5-year prevention model, Aus$22,697 in the 10-year prevention model and Aus$189,349 in the delay model.

The incremental cost per QALY gained was Aus$38,271 (95% confidence interval, CI: 26,000 - 89,000) for 5-year prevention, Aus$19,354 (95% CI: 13,000 - 42,000) for 10-year prevention and Aus$199,149 (95% CI: 120,000 - dominated by placebo) for the delay model.

Moreover, cost-effectiveness acceptability curves showed that, at Aus$50,000 per QALY, the probability of the tamoxifen strategy being optimal was 98% for 5-year prevention, 79% for 10-year prevention and 0% for the delay alternative.

Authors’ conclusions
Tamoxifen is potentially cost-effective in preventing breast cancer in women at high risk. However, its cost-effectiveness as a preventive therapy is highly sensitive to whether these cancers are permanently prevented or their clinical presentation is only delayed.

CRD COMMENTARY - Selection of comparators
The authors based their analysis on published RCTs. Therefore, the technology used as the comparator was placebo, as in those RCTs. The use of placebo as the comparator allowed the active value of the treatment to be evaluated.

Validity of estimate of measure of effectiveness
This study incorporated data from RCTs and meta-analyses of randomised trials, which appear to have high internal validity. However, the authors used the data from these studies selectively. Moreover, they did not consider the impact of differences between the primary studies when estimating the effectiveness. Finally, it was not stated that a systematic review of the literature had been undertaken. All these factors undermine the external validity of the study.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. A general measure of benefit (QALY) was used. The authors chose a utility weight value to reflect the average utility in women with a diagnosis of breast cancer over their remaining years of life. This point estimate was varied in the sensitivity analysis. The ranges were chosen from clinician-based standard gamble method and patient-based healthy-years equivalent, time trade-off-based method studies. This was appropriate for allowing for uncertainty within the benefit estimation.

Validity of estimate of costs
All the categories of costs relevant to the perspective (health care system) adopted seem to have been included in the analysis. The authors modelled their costs relying on data from published studies and Australian National Diagnostic-related Groups, but it was unclear whether all the relevant costs were included in the analysis. However, as these costs were included in both arms, it is unlikely that any possible omissions could have affected the authors’ conclusions. The fact that the costs and the quantities were not reported separately could possible undermine the generalisability to other settings. Finally, appropriate cost conversions were developed (to express the costs in the same year) and discounting was appropriately undertaken.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. However, they did not address the issue of generalisability of their findings to other settings. The results were not presented selectively. The
authors’ conclusions were an accurate reflection of the results presented in the study. No limitations of the study were presented.

**Implications of the study**
Preventive care with tamoxifen or other drugs should be restricted to large-scale RCTs. Long-term follow-up in a RCT is crucial in informing health policy.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
14705265

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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