Cost-effectiveness of newer antidepressants compared with tricyclic antidepressants in managed care settings

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
Newer antidepressant drugs (nefazadone, fluoxetine) compared with tricyclic antidepressants.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
Hypothetical 30-year-old women who had one previous episode of major depression. This group was chosen because of its relatively high prevalence of diagnosed depression and to simplify the estimation of survival, which was based on standard life tables.

Setting
Managed Care Organisations (MCOs) in the USA.

Dates to which data relate
Effectiveness data were derived from studies conducted between 1989 and 1995. 1994 cost data were used.

Source of effectiveness data
Effectiveness data were based on a review or synthesis of previously completed studies and on estimates by a panel of clinicians.

Modelling
A clinical decision model derived from published medical literature and a modified Delphi technique. The model simulated the clinical management pathways and pattern of recurrences of major depression to estimate the lifetime health outcomes and medical cost of different antidepressants. A Markov state transition model was constructed.

Outcomes assessed in the review
The outcome measures assessed were percentages of patient response to treatment and compliance rates.

Study designs and other criteria for inclusion in the review
Not stated.
Sources searched to identify primary studies
Unspecified journals were searched.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
30 studies were included in the review.

Methods of combining primary studies
Studies were not combined.

Investigation of differences between primary studies
Differences between studies were not investigated.

Results of the review
60% to 80% of patients treated with an antidepressant respond to treatment. 60% of those who do not respond initially, respond to a second or third antidepressant resulting in an overall response rate of 88%. The remaining 12% were considered treatment resistant. Patients could either drop out of treatment altogether, or be fully, partially, or minimally compliant with their antidepressant therapy. This was dependent on the side effects of the drugs and the number of times the drug was administered.

Methods used to derive estimates of effectiveness
A panel of physicians were provided with a description of the decision model and summaries of the medical literature and were asked to complete a questionnaire on depression treatment.

Estimates of effectiveness and key assumptions
Ideal clinical practice was reflected, that is to say, it was assumed that treatment for each episode continued for 9 months regardless of treatment arm. Full compliance was estimated to be taking 80% or more prescribed drugs, partial compliance was assumed to be 50-79% and minimal compliance was less than 50%. It was estimated that, for imipraminetreated patients, 30% would drop out after 6 weeks and, of the remainder, 40% would be fully compliant, 30% would partially compliant while 30% would be minimally compliant. Compliance rates for nefazodone and fluoxetine were higher: 20% would discontinue after 6 weeks and, of the remainder 50% would be fully compliant, 30% partially compliant and 20% minimally compliant. These estimates formed the input probabilities to the model.

Measure of benefits used in the economic analysis
The outcome measure was quality adjusted life years, (QALY). A Markov state transition model was constructed to track QALYs and medical costs. The valuation tool for depression related health states was standard gamble involving 70 patients who had completed at least 8 weeks of antidepressant therapy.

Direct costs
The resources used for acute treatment were estimated by the panel of physicians. A discount rate of 5% was used. Items measured included the annual number and type of physician visits, the number hospitalised and length of hospital stay, the proportion receiving ECT and the number of sessions, laboratory costs, and the number of days receiving pharmacotherapy.

**Statistical analysis of costs**
Not carried out.

**Indirect Costs**
Indirect costs were not indicated as the study looked at the costs from the MCOs' perspective.

**Currency**
US dollars ($).

**Sensitivity analysis**
In order to test for variability in the data, sensitivity analyses were carried out on discount rate (0% and 10%), variation of compliance rates and maintenance of treatment. The impact on overall cost and QALYs (cost-utility ratio) was determined. Sensitivity analyses were also carried out on model duration (5, 10, 15 and 20 years).

**Estimated benefits used in the economic analysis**
QALYs were greatest for treatment with nefazodone (14.64), compared with 14.32 for imipramine, 14.40 for the step approach, and 14.5 for fluoxetine.

**Cost results**
The lowest estimated lifetime costs (discounted at 5%) were for imipramine treatment ($15,348). Costs for treatment with nefazodone were estimated at $16,669 against $16,998 for fluoxetine.

**Synthesis of costs and benefits**
Cost per QALY was estimated. All costs and benefits were discounted to present value using a 5% rate. Incremental cost analysis was carried out as nefazodone treated patients cost $1,321 more than imipramine treated patients and resulted in 0.32 more QALYs. The cost effectiveness ratio comparing nefazodone with imipramine was $4,065 per QALY gained. The cost effectiveness ratio comparing nefazodone with the step approach was $2,555 per QALY gained. There were only minor differences in costs and QALYs between nefazodone and fluoxetine. The cost effectiveness ratio comparing fluoxetine and imipramine was $6,346 per QALY gained. The ratio comparing fluoxetine with the step approach was $5,206 per QALY gained. Using base case analysis a series of analyses were performed, in which the duration was varied from 5 to 20 years. The authors noted that cost effectiveness ratios were lower for shorter duration models. The model was most sensitive to assumptions concerning compliance rates.

**Authors' conclusions**
Nefazodone and fluoxetine treatments were found to be cost-effective compared with both imipramine alone and a step approach, where access to newer antidepressant therapies was restricted. The price of the drug was not the only factor to be considered in decisions on the antidepressants' clinical efficacy and safety and all relevant health care costs should also be taken into consideration. The two drugs had clinical efficacy comparable to, and better side effects profiles than, TCAs. Based on the model, patients may benefit from the two treatments and there may also be saving in health care costs associated with nefazodone compared with fluoxetine treatment of major depression.
CRD COMMENTARY - Selection of comparators
A justification was given for the selection of comparators. Two new antidepressant drugs were compared with TCAs and the new drugs were also compared with each other and there was a combination of new and old.

Validity of estimate of measure of benefit
The estimate of benefit was the QALY as produced by the model and based on the standard gamble results of a high number of patients (70). Although the search criteria were not given, the authors utilised a wide range of studies which were used to provide source data to the panel of clinicians in estimating input probabilities for the model. The solutions were also tested by comprehensive sensitivity analyses. As such, the benefit measure is likely to be valid.

Validity of estimate of costs
No statistical analysis was carried out but the authors indicated that the medical costs were comparable with those reported in other studies or within the range of existing studies. Sensitivity analysis, however, was applied to discount rate.

Other issues
The methods adopted were extremely detailed and a comprehensive range of results were provided both in terms of the baseline solution and in the sensitivity analyses conducted. Due to the limitations of the abstracting process it has not been possible to present all the details reported. The study also addressed generalisability issues in relation to Canada.

Implications of the study
More research is needed as indicated by the authors. The studies carried out in the USA do not take into account the fact that depression can be a chronic lifetime disorder, therefore the long term cost and effects should also be considered.

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