Cost-utility comparison of escitalopram and sertraline in the treatment of major depressive disorder

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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 study examined two selective serotonin re-uptake inhibitors (SSRIs), escitalopram and sertraline, for the treatment of major depressive disorder (MDD). Escitalopram was initially given at 10 mg/day; the dose was assumed to increase to 20 mg/day if the patient did not respond to the initial dose. Sertraline was initially given at 50 mg/day; dose titration to 100, 150 and 200 mg/day was assumed for patients not responding to lower dosages.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients with MDD.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 2002 and 2007. Some resource use information was derived from a study published in 2007. The price year was not reported.

Source of effectiveness data
The clinical data used in the decision model were:

the probability of clinical response,

the probability of adverse events (nausea, diarrhoea, insomnia, headache, ejaculation disorder), and

the probabilities of dose titration, switching treatment and hospitalisation in the case of no treatment response.

Modelling
The authors reported extensive details of the decision tree. The time horizon of the model was 6 months according to treatment duration. The model took dose titration of both treatments, which might be a relevant aspect especially in the case of sertraline, into account. The structure of the main decision model and the sub-tree showing pathways for side effects were represented graphically. Changes in treatment due to non-response included the options of switching,
augmenting treatment with another agent, or discontinuation. Lack of efficacy could also lead to hospitalisation.

**Sources searched to identify primary studies**
Clinical data on treatment effectiveness, discontinuation and treatment change came from multiple sources, including a clinical trial of escitalopram 10 mg/day and sertraline 50 to 200 mg/day, and another clinical trial that employed an escitalopram 20-mg dose arm. Since clinical trials provided only 8-week data. Longer term estimates on side effects by drugs and by doses were derived by analysing a large managed-care database.

**Methods used to judge relevance and validity, and for extracting data**
The process used to identify the data was not reported. In addition, no inclusion criteria were specified for any of the parameters. However, the authors selected randomised clinical trials for short-term clinical data, while data not available from clinical trials were obtained from a large number of patients. Since each study provided a single estimate, there was no need to combine clinical data.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were estimated using a modelling approach. The utility weights used to calculate QALYs were derived from a study published in 2004, although no information on the approach used to elicit the utility estimates was given. Utility scores were presented as decrements due to adverse events. No discounting was performed, which was appropriate given the short-term time horizon.

**Direct costs**
The analysis of the costs was carried out from the perspective of the MCO. It included the costs of drugs, physician visits and the treatment of adverse events (ejaculation disorder, diarrhoea, nausea, insomnia and headache). The unit costs were reported but resource quantities were not given for all items. The estimates of drug dosages and frequency of side effects were derived from a clinical trial used in the analysis of effectiveness. The number of physician visits was based on the authors' opinions. The costs of medication were estimated using average wholesale prices minus 20% to reflect MCO discounts. Physician visits came from US Medicare fee schedules. The costs of side effects and treatment failures were derived from a study published in 2004. Discounting was not relevant as the 6-month costs were evaluated. The price year was not explicitly reported.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case, but 95% confidence intervals (CIs) around the total costs were reported.

**Indirect Costs**
Productivity costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
A univariate sensitivity analysis was performed to assess the impact of all model inputs on the results of the model. Tornado diagrams were presented. With the exception of drug costs, which were obtained from an Internet pharmacy, the sources of the alternative ranges of values were not stated. A probabilistic sensitivity analysis was also performed using a first-order Monte Carlo simulation. This generated 95% CIs around the QALYs, costs and cost-utility ratios. Thus, the analysis was replicated for 10,000 hypothetical patients, but no probabilistic distributions were assigned to
model parameters.

**Estimated benefits used in the economic analysis**
The expected QALYs over the 6-month period were 0.39268 with sertraline and 0.40269 with escitalopram.

The probabilistic sensitivity analysis showed that the expected QALYs were 0.39263 (95% CI: 0.29 to 0.424) with sertraline and 0.40237 (95% CI: 0.29 to 0.424) with escitalopram.

**Cost results**
The expected 6-month costs were $1,351 with sertraline and $919 with escitalopram.

The Monte Carlo simulation indicated that the expected 6-month costs were $1,315 (95% CI: 582 to 8,141) with sertraline and $929 (95% CI: 523 to 8,141) with escitalopram.

**Synthesis of costs and benefits**
The average and incremental cost-utility ratios were calculated in order to combine the costs and benefits of the alternative strategies.

The average cost per QALY was $3,440 with sertraline and $2,280 with escitalopram.

In the probabilistic sensitivity analysis, the average cost per QALY was $3,944 (95% CI: 1,372 to 28,072) with sertraline and $2,699 (95% CI: 1,234 to 28,072) with escitalopram.

The incremental analysis revealed that escitalopram dominated sertraline, which was both less effective and more expensive.

The dominance of escitalopram held in the Monte Carlo simulation, where it was dominant in 88.5% of simulations.

The threshold analysis suggested that sertraline 50-mg tables would need to decrease to 2 cents each, or 100-mg tablets to 6 cents each, before sertraline became less costly than escitalopram.

The deterministic sensitivity analysis showed that the cost of treatment failure was a key determinant of the model. Nevertheless, escitalopram remained the dominant treatment under all scenarios.

**Authors’ conclusions**
From the perspective of a managed care organisation (MCO), escitalopram, used for the treatment of patients with major depressive disorder (MDD), was less costly and resulted in a slightly greater improvement in quality-adjusted life-years (QALYs) than sertraline. The cost-difference was mainly due to differences in the frequency of adverse events and dosage titration costs between products.

**CRD COMMENTARY - Selection of comparators**
The authors provided a justification for their choice of the comparators, which were chosen due to their high market share. Dosages were reported. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The clinical data were derived from the literature but no systematic search for data was reported. The majority of the clinical estimates were derived from a head-to-head clinical trial, which should ensure high internal validity. Other data for dose titration were derived from other clinical trials. Since no long-term estimates were available from these trials, a large database was used for drug side effects and discontinuation; this appears to have been an appropriate solution. Clinical estimates were varied in the sensitivity analysis.
Validity of estimate of measure of benefit
The use of QALYs ensures the comparability of the results with the benefits of other health care interventions. QALYs were mainly used to capture the impact of the interventions on quality of life, since the survival component of QALYs was not considered. The utility weights were obtained from a published paper, but no further details were given. The use of utility decrements for adverse events appears to have been appropriate.

Validity of estimate of costs
The cost analysis was consistent with the stated perspective of the study. All the relevant categories of costs appear to have been included. A detailed breakdown of cost items was given and the unit costs were presented. There was little information on resource consumption. The sources of the costs were presented for all items. The price year was not reported, which limits the possibility of replicating the analysis in other time periods. The cost estimates were varied in the sensitivity analysis, which represents a strength of the study.

Other issues
The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings, although their extensive sensitivity analysis should have enhanced the external validity of the study. However, since the analysis focused on US MCOs, caution will be required when extrapolating the results of the analysis to other health care systems. The authors noted two key limitations of the analysis. First, clinical data came from published studies, whereas the use of MCO-specific data would have been more appropriate. Second, the time horizon of the analysis was 6 months although most clinical studies had a more limited follow-up period (8 weeks).

Implications of the study
The study results appear to support the use of escitalopram for the treatment of MDD, owing to its lower costs and slightly better effectiveness in comparison with sertraline. The authors noted a further issue in favour of escitalopram: the use of a product without need for titration is a relevant end point for formulary decision-making, as it is simpler to administer and enhances patient compliance with therapy. This issue should therefore be considered, despite the similar effectiveness of the two treatments.

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MeSH
Adult; Antidepressive Agents /administration & dosage /adverse effects /economics /therapeutic use; Citalopram /administration & dosage /adverse effects /economics /therapeutic use; Cost-Benefit Analysis; Decision Support Techniques; Depressive Disorder /drug therapy /economics; Diarrhea /chemically induced /economics; Drug Costs; Erectile Dysfunction /chemically induced /economics; Female; Headache /chemically induced /economics; Humans; Male; Monte Carlo Method; Nausea /chemically induced /economics; Office Visits /economics; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic /statistics & numerical data; Serotonin Uptake Inhibitors /administration & dosage /adverse effects /economics /therapeutic use; Sertraline /administration & dosage /adverse effects /economics /therapeutic use; Sleep Initiation and Maintenance Disorders /chemically induced /economics

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