Cost-effectiveness analysis of escitalopram compared with paroxetine in treatment of generalized anxiety disorder in the United Kingdom
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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 compared escitalopram (10 to 20 mg/day) and paroxetine (20 to 50 mg/day) as the first-line treatment for generalised anxiety disorder (GAD).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with moderate-to-severe GAD as defined by the American Psychiatric Association's DSM criteria (DSM-IV) with a baseline Hamilton Anxiety Rating Scale (HAM-A) score of at least 18.

Setting
The setting was primary care in the UK.

Dates to which data relate
The effectiveness data were derived from studies published between 1993 and 2005. Some resource use data were estimated from studies published in 2004 and 2005. The price year for the costs was 2005.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' assumptions.

Modelling
A decision tree model with a 36-week time horizon was used with sensitivity analyses and Monte Carlo simulation to evaluate the effect of uncertainty. General practitioner (GP) visits took place at weeks 2, 4, 6 and 12 after the start of the therapy. At the end of the next 12-week period, efficacy was evaluated and decisions about whether patients should be switched from escitalopram to paroxetine, or vice versa, were made. If the therapy lacked effectiveness at the end of the third 12-week, patients were referred to a specialist.

Outcomes assessed in the review
The outcomes estimated from the literature were:
the drug-specific rate of discontinuation due to adverse events, short-term response and relapse; and
the non drug-specific rate of discontinuation due to adverse events, short-term response, and relapse at 12-week continuation period and 18-week continuation period.

**Study designs and other criteria for inclusion in the review**
Some of the effectiveness outcomes were derived from a double-blind comparative trial and a relapse prevention study of 375 patients.

**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**
Five primary studies provided the clinical data.

**Methods of combining primary studies**
Not reported.

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

**Results of the review**
**Drug-specific outcomes.**

The rates of discontinuation due to adverse events for escitalopram versus paroxetine were 0.066 (95% confidence interval, CI: 0.018 to 0.139) versus 0.226 (95% CI: 0.132 to 0.337).

The short-term response rates for escitalopram versus paroxetine were 0.65 (95% CI: 0.526 to 0.764) versus 0.557 (95% CI: 0.432 to 0.679).

The relapse rates for escitalopram were 0.183 (95% CI: 0.131 to 0.241) for the active treatment arm and 0.524 (95% CI: 0.405 to 0.547) for the placebo arm. Those for paroxetine were -0.29 (95% CI: -0.357 to -0.221) for difference versus placebo and 0.235 for active treatment.

**Non-drug-specific outcomes.**

For both escitalopram and paroxetine, the rate of discontinuation due to adverse events was 0.146 (95% CI: 0.090 to 0.214), and the short-term response rate was 0.603 (95% CI: 0.515 to 0.688).

The relapse rates for escitalopram were 0.126 for the 12-week continuation period and 0.155 for the 18-week continuation period.

**Methods used to derive estimates of effectiveness**
The authors made an assumption to derive the non drug-specific clinical estimates.

**Estimates of effectiveness and key assumptions**
The authors assumed equal success and tolerability rates after switch for both groups. These rates were derived from pooled data from a published head-to-head trial.

**Measure of benefits used in the economic analysis**
The main benefit measure used was the success rate of first-line treatment. This was defined as an initial response to treatment after 12 weeks and without relapse during the following 24-week period. This was estimated using the decision model. Other model outcomes (i.e. the maintained response to SSRI treatment 36 weeks after initiation, and the referral rate to the secondary care) were also reported.

**Direct costs**
The perspective of UK society was adopted in the cost analysis. The health services in the economic evaluation were drugs, GP visits and specialist visits. The unit costs were presented separately from the quantities of resources used. Resource use was estimated from published data. The costs came from the UK National Health Service drug tariffs, the UK Unit Cost of Health and Social Care, and published studies. The total costs were calculated using a modelling approach. Discounting was not relevant given the short timeframe of the model. The price year was 2005.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

**Indirect Costs**
Productivity losses were included in the cost analysis. The indirect costs were calculated using the human capital approach. The sick leave days were estimated on the basis of expert opinion. The cost of absence from work was derived from typical UK sources. The unit costs were presented separately from the quantities of resources used. Discounting was not relevant and was not performed. The price year was 2005.

**Currency**
UK pounds sterling (£). The conversion rate to US dollars ($) was 1 = $1.818.

**Sensitivity analysis**
One-way sensitivity analyses were conducted to assess the robustness of the model to changes in model parameters. The parameters investigated were the tolerability rate and 12-week response rate (ranges based on the 95% CI), the number of sick leave days (range based on expert opinion), the use of only paroxetine 20 mg/day, and the use of a zero price for paroxetine. A Monte Carlo simulation was performed with 10,000 iterations to compute the model outcomes. All probabilities were assigned a beta-distribution, sick leave days were assigned a triangular distribution, and the remaining parameters were assigned normal distributions.

**Estimated benefits used in the economic analysis**
After 36 weeks, escitalopram had 49.6% first-line success and paroxetine 35.2%. There was 14.4% more patient response for escitalopram over paroxetine.

In considering the secondary outcomes after week 36, escitalopram showed 7.7% more responders for maintained response to SSRIs and 8.5% fewer responders referred to secondary care.
Cost results
The total costs over the 36 weeks were 8,434 for escitalopram and 9,843 for paroxetine. The saving was 1,408.

The direct costs per patient over the 36 weeks were 447 for escitalopram and 486 for paroxetine. The saving was 39.

Synthesis of costs and benefits
In comparison with paroxetine, the treatment with escitalopram yielded lower expected costs with greater effectiveness. Escitalopram dominated paroxetine.

The univariate sensitivity analyses showed that the base-case results were robust and not sensitive to changes in variations in either costs or probabilities in the comparison between paroxetine and escitalopram.

Authors' conclusions
Within the setting of primary care in the UK, escitalopram was a cost-effective treatment for generalised anxiety disorder (GAD) in comparison with paroxetine.

CRD COMMENTARY - Selection of comparators
The authors provided a justification for the choice of the comparators. Both escitalopram and paroxetine are the only SSRIs approved for the treatment of GAD in the UK. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were estimated from published studies, supplemented with authors' assumptions when published evidence was not available. It was unclear whether a systematic review of the literature was performed to identify the primary studies. Some of the evidence came from head-to-head clinical trials. Limited information on the other primary studies was reported. Sensitivity analyses were extensively performed on key estimates, in order to address the uncertainty around some clinical parameters.

Validity of estimate of measure of benefit
The main benefit measure was specific to the disease considered in the study. Whilst disease-specific measures are acceptable, you should consider if the benefit measures adequately cover the health outcomes of the intervention. In addition, you should note that it will not be possible to draw direct comparisons with the benefit of other health care interventions. The impact of the intervention on quality of life was not investigated, although this might have been an important dimension of health for GAD patients.

Validity of estimate of costs
The cost analysis was considered from two perspectives, namely those of UK society and the UK National Health Service. The source of the data was appropriate as typical sources were used to derive the costs. Resource consumption reflected UK treatment patterns. The unit costs and quantities of resources used were reported, which will facilitate replication of the analysis in other settings. No statistical analyses of the costs were carried out. The cost estimates were specific to the study setting but were varied in the sensitivity analysis. The price year was reported, which will assist with reflation exercises in other time periods. Discounting was not performed as the time horizon of the economic analysis was less than one year.

Other issues
The authors did not compare their findings with those from other studies. The issue of generalisability of the results does not appear to have been addressed. The authors did not present their results selectively and their results appear to have reflected the scope of the analysis. Extensive sensitivity analyses were carried out, which enhances the external
validity of the study. Some limitations to the study were acknowledged. For instance, the assumption that the number of secondary visits was the same as that in primary care is likely to lead to inaccurate estimates of costs of disease management. Also, the success rates in the model may be higher than those in clinical practice.

**Implications of the study**
The study results support the use of escitalopram for the treatment of GAD within the context of primary care in the UK.

**Source of funding**
None stated.

**Bibliographic details**

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**Other publications of related interest**
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**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Anxiety Disorders /drug therapy /economics /epidemiology; Citalopram /administration & dosage /economics; Cost-Benefit Analysis /economics; Decision Support Techniques; Great Britain /epidemiology; Humans; Paroxetine /administration & dosage /economics; Serotonin Uptake Inhibitors /administration & dosage /economics; Time Factors
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