Analysis of health-related quality of life and costs based on a randomised clinical trial of escitalopram for relapse prevention in patients with generalised social anxiety 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.

CRD summary
This study examined the long-term clinical and economic impact of escitalopram in comparison with no treatment for patients with generalised social anxiety disorder. The authors concluded that escitalopram improved health-related quality of life without significantly increasing the cost of care. The additional drug costs were offset by savings in physician visits and in-patient care. Overall, the clinical and economic analyses were carried out transparently and credibly. The authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the long-term clinical and economic impact of escitalopram in comparison with no treatment, for patients with generalised social anxiety disorder (SAD), focusing on the differences in quality of life between responders and non-responders to treatment.

Interventions
The interventions were escitalopram (initial dose of 10mg per day, which could be increased to 20mg per day) and placebo.

Location/setting
UK/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a single study with a 36-week time horizon (split into three trimesters or 12-week periods). The authors stated that the perspectives of the National Health Service (NHS) and society were used.

Effectiveness data:
The clinical data came from a published multi-country, randomised controlled trial (RCT), which enrolled 571 patients with a primary diagnosis of generalised SAD. Of these patients, 371 responded to open-label treatment and were randomised to receive double-blind treatment with escitalopram (190 patients) or placebo (181 patients). The length of follow-up was 36 weeks. Statistical tests were carried out to take into account the differences in patients who responded to treatment and those who did not respond, and in patients who relapsed and those who did not. The primary clinical outcome was the probability of relapse.

Monetary benefit and utility valuations:
Health related quality of life (HR-QoL) was estimated from the sample of patients enrolled in the clinical trial using the Medical Outcome Study Short Form (SF)-36 which was administered at the initiation of the acute phase (baseline), the end of the acute phase, and at 12 and 24 weeks after randomisation. These values were then used to derive the SF-6D, a six-dimensional health state classification method.

Measure of benefit:
No summary benefit measure was used in the analysis since the HR-QoL estimates were not combined with costs.
Cost data:
The health services included in the economic evaluation were escitalopram, general practitioner visits, psychiatric consultations, psychologist consultation, nurse visit, social worker visit, and hospital stay (psychiatric ward or other wards). The cost of sick leave days related to SAD, and the costs of non-conventional medicines were also included for the societal perspective. The resource use data were derived from the RCT. The costs of health services were based on official NHS rates. The value of a lost work day was based on the mean gross UK daily earnings in 2006. All costs were in UK pounds sterling (£) and the price year was 2006. Statistical analyses of the costs were carried out.

Analysis of uncertainty:
The issue of uncertainty was not investigated. However, an alternative scenario, which assessed the total costs excluding the cost of hospitalisation, was considered.

Results
The probability of relapse was 2.8 times lower in patients receiving escitalopram (22%) compared with those who received placebo (50%, p<0.001).

At 12 weeks, the mean improvements in SF-6D score adjusted on baseline value were 0.049 (95% confidence interval, CI: 0.043 to 0.055, p<0.0001) for responders and 0.018 (95% CI: 0.006 to 0.029, p=0.0022) for non-responders. Similarly, the SF-6D score in non-relapsed patients exceeded the score in relapsed patients by 0.026 (p=0.0007).

Since fewer patients relapsed with escitalopram, their quality of life was better compared with placebo. Specifically, the HR-QoL scores in the escitalopram group did not vary substantially from randomisation to the last assessment point, suggesting that no significant changes were observed. In the placebo group, however, several mean domain scores decreased significantly from randomisation to the end of the continuation phase or to the last visit. The adjusted differences in SF-36 scores, at the last visit, between treatment groups, were statistically significant for some specific dimensions, in favour of escitalopram. Furthermore, the mean SF-6D score at the last assessment was higher by 0.018 in the escitalopram group (p=0.0087).

The total health care costs were significantly lower over the acute phase, than over the 12 weeks preceding the study, from the societal perspective (p=0.0410). This suggested that the acquisition cost of escitalopram was more than offset by savings in physician visits and in-patient care. However, from the NHS perspective, this difference was not statistically significant.

Authors' conclusions
The authors concluded that escitalopram improved HR-QoL without significantly increasing the cost of care in patients with SAD. The additional drug costs were offset by savings in physician visits and in-patient care.

CRD commentary
Interventions:
The selection of the comparators appears to have been appropriate, since they were those studied in the RCT.

Effectiveness/benefits:
The use of a RCT to derive the clinical data was appropriate given the strengths and robust nature of such a design. The RCT had been published elsewhere, but the authors provided extensive information on its methods. The randomised design, the use of a multi-centre framework, and the use of statistical tests to consider the baseline differences in HR-QoL scores, further enhanced the internal validity of the RCT. The use of quality of life as the main measure of benefit was appropriate, although it would have been interesting to combine this with costs.

Costs:
The cost analysis was carried out from two different perspectives, as well as excluding hospitalisation costs. Such an approach was appropriate given the dramatic impact of a hospital stay even for a relatively small number of patients. The derivation of costs was reported and their sources appear to have been appropriate. A breakdown of the cost items was presented, together with their respective unit costs. The resource use data were derived from the RCT using a specific questionnaire to determine the patterns of resource consumption in both the acute and maintenance phases of
the study. The price year was reported. The lack of discounting was justified given that costs were incurred over a period shorter than one year. Appropriate statistical analyses of the costs were carried out. The cost comparison was restricted to non-relapsed patients.

**Analysis and results:**
A synthesis of the costs and benefits was not required, as this was a cost-consequences analysis. The findings were extensively presented taking into account the differences between treatment responders and non-responders. The issue of uncertainty was not addressed, but extensive statistical tests were carried out to investigate the stability of the comparison between groups, with respect to both the clinical and economic data. The authors noted that a potential limitation of their analysis was the use of resource use data from several countries which might not reflect the treatment patterns in the UK.

**Concluding remarks:**
Overall, the clinical and economic analyses were carried out transparently and credibly. The authors’ conclusions appear to be valid.

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