Cost effectiveness of venlafaxine compared with generic fluoxetine or generic amitriptyline in major depressive disorder in the UK

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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 cost-effectiveness of venlafaxine versus either generic fluoxetine or generic amitriptyline for the first-line treatment of patients with major depressive disorder. The authors concluded that, despite its relatively high acquisition price, venlafaxine was a cost-effective alternative to either fluoxetine or amitriptyline. The analysis appears to have been based on valid methodology, but some assumptions were needed. In general, the authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of venlafaxine, versus either generic fluoxetine or generic amitriptyline, for the first-line treatment of patients with major depressive disorder.

Interventions
The three treatments were venlafaxine, generic fluoxetine, and generic amitriptyline, and all were given for eight weeks. An alternative scenario was also considered with 24 weeks of treatment and possible switching between the three options.

Location/setting
UK/primary care.

Methods
Analytical approach:
This economic evaluation was based on a decision tree model with a six-month time horizon. The authors did not explicitly state the perspective adopted.

Effectiveness data:
The clinical data came from a review of the literature in the MEDLINE database and in the authors' database. Only head-to-head randomised controlled trials (RCTs) were selected and there were 13 of these; other inclusion and exclusion criteria were reported. The data from each trial were pooled to provide mean estimates. The key clinical outcome was the remission and response rate. Remission was defined as a score of less than seven on the 17-point Hamilton Depression Scale (HAM-D17) and response was defined as a 50% decrease in the HAM-D17 score.

Monetary benefit and utility valuations:
The estimation of the utility values was based on the number of depression-free days (DFDs), which were converted into utility values using a published approach. The numbers of DFDs were derived from published evidence and authors’ opinions.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The economic analysis included the costs of drugs, laboratory tests, diagnostic tests, visits to health care professionals, and hospital stay. Some of the resource use data were based on assumptions made by a Delphi panel. The unit costs of drugs were derived from the British National Formulary and other costs came from official UK National Health Service (NHS) sources. The price year was 2006 and all costs were in UK pounds sterling (£).

Analysis of uncertainty:
The sensitivity analysis considered alternative assumptions, such as utility valuations based on DFD data from a different source. In an alternative scenario, the remission rate was the summary benefit measure. The overall uncertainty was investigated in a rank order stability assessment.

Results
Assuming an eight-week treatment duration, the expected total costs per patient were £199.22 with venlafaxine, £154.98 with fluoxetine, and £156.48 with amitriptyline. The QALYs gained were 0.0169 with venlafaxine, 0.0147 with fluoxetine, and 0.0137 with amitriptyline.

The incremental analysis showed that amitriptyline was dominated by fluoxetine and the incremental cost per QALY gained with venlafaxine over fluoxetine was £20,597.

Assuming 24-week treatment duration and possible switching, the strategies starting with venlafaxine were the most cost-effective. Switching to fluoxetine on failure with venlafaxine, had an incremental cost per QALY gained of £7,215 over switching to amitriptyline on failure with venlafaxine. All the other sequences of treatments were dominated.

The findings were similar when the remission rate was the summary benefit measure.

The sensitivity analysis did not substantially alter the base-case findings. When reducing the cost of both amitriptyline and fluoxetine to zero, strategies starting with venlafaxine remained the most cost-effective.

Authors’ conclusions
The authors concluded that, despite its relatively high acquisition price, venlafaxine was a cost-effective alternative to either fluoxetine or amitriptyline.

CRD commentary
Interventions:
The authors justified their selection of the comparators. Fluoxetine was the most commonly prescribed selective serotonin re-uptake inhibitor in the UK, venlafaxine was a typical selective serotonin and noradrenaline re-uptake inhibitor, and amitriptyline was a typical tricyclic antidepressant. The selection of the comparators appears to have been appropriate.

Effectiveness/benefits:
The use of a literature review to identify the sources of data was appropriate and aimed to include all relevant studies. Some key details were given on the inclusion and exclusion criteria used to select these studies. The selection of head-to-head RCTs improves the internal validity of the clinical estimates. Where data were not available, experts’ opinions were used. Extensive information on the derivation of the QALYs was provided, especially for the assessment of utility values and a disease-specific benefit measure was also considered in the sensitivity analysis.

Costs:
The perspective of the NHS appears to have been adopted although this was not explicitly stated. This viewpoint was indicated by the categories of costs and their sources. Details on the unit costs and quantities of resources used were reported, for most items, and the price year was reported. In general, the economic analysis was presented transparently. As in the clinical analysis, some assumptions were required and made by a Delphi panel of experts for the data on resource consumption.

Analysis and results:
The costs and benefits were appropriately combined using an incremental approach, and the results were clearly
presented and discussed. The issue of uncertainty was extensively investigated, although the methodology was not clearly described. The current study was an update of a previous model and some aspects of the analysis were described elsewhere. The authors acknowledged some limitations of their analysis, such as the need for assumptions and the fact that only one RCT comparing venlafaxine with amitriptyline was found.

Concluding remarks:
The analysis appears to have been based on valid methodology, but some assumptions were needed. In general, the authors’ conclusions appear to be valid.

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