The cost-utility of maintenance treatment with venlafaxine in patients with recurrent major depressive disorder

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
The objective was to assess the cost-effectiveness of a two-year maintenance treatment with venlafaxine for the treatment of adult patients with recurrent major depressive disorders. Venlafaxine was a cost-effective alternative to no treatment in this patient population from the perspective of Swedish society. The study relied on a validated methodology, which enhances the robustness of the analysis. The authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of a two-year maintenance treatment with venlafaxine for the treatment of adult patients with recurrent major depressive disorders.

Interventions
A two-year maintenance treatment with venlafaxine extended-release (XR) was compared with placebo. The average dosage was 217mg in the first year and 200mg in the second year.

Location/setting
Sweden/primary and secondary care.

Methods
Analytical approach:
This economic evaluation was based on the modified version of a published Markov model which depicted the natural course of depression and the impact of the treatment strategies. The time horizon of the analysis was two years. The authors stated that the perspectives of the health-care payer and society were adopted.

Effectiveness data:
The clinical data were mainly derived from a double-blind, multi-centre, randomised controlled trial (RCT) assessing the efficacy and tolerability of venlafaxine, namely the Prevention of Recurrent Episodes of Depression with venlafaxine XR for Two Years study. This study was used to estimate the probabilities of changing health states (risk of a depressive episode and probability of remission). A meta-analysis was used in the sensitivity analysis to estimate risk of relapse and recurrence. The death rates were taken from Swedish life tables.

Monetary benefit and utility valuations:
The utility data were derived from a Swedish naturalistic observational study, namely the Health Economic Aspects of Depression In Sweden (HEADIS) study using the EuroQol-5D health status questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure and the annual discount rate was 3%.

Cost data:
The economic analysis included the costs of drugs, hospitalisations, outpatient visits, and productivity losses. The data on costs and quantities of resources were derived from the HEADIS study. The cost of venlafaxine was based on the
drug price listed in the National Pharmaceutical Drug Price list. The costs were in US dollars ($) and the price year was 2005. All costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken in order to address the issue of uncertainty in the model inputs. This was conducted using a bootstrapping technique that generated confidence intervals around mean cost and benefits and allowed the construction of an acceptability curve. A deterministic one-way sensitivity analysis investigated the robustness of the model outcomes to variations in key model inputs. The costs of adverse events, which were not statistically different between groups, were included in the sensitivity analysis. Similarly, the sensitivity analysis also considered a scenario in which patients could recover from a relapse in the maintenance treatment phase. Assumptions on re-relapses and recovery were made using data from a meta-analysis of RCTs. Finally, a long-term analysis was also carried out based on an extended model.

Results
Over two years, maintenance treatment with venlafaxine led to a gain of 0.055 QALYs over placebo.

The additional cost associated with venlafaxine was $1,978 from the perspective of the health care payer and $1,020 from the perspective of society.

The incremental cost per QALY gained with venlafaxine was $35,968 from the perspective of the health care payer and $18,548 from the perspective of society.

The probabilistic sensitivity analysis indicated that venlafaxine had an 80% probability of being cost-effective at a willingness to pay of $40,000 per QALY gained. At a threshold of $67,000 this probability rose to 90%.

The deterministic sensitivity analysis showed that, under unfavourable assumptions (i.e. with a time horizon of only 6 months), the worst incremental cost per QALY was $86,100. Otherwise, cost-utility figures did not vary dramatically, except for changes in venlafaxine drug cost which had a substantial impact on final cost-effectiveness ratios. Longer time horizons suggested further improvements in QALYs and cost-utility ratios to $31,314 (at four years) from the health care perspective and around $17,600 from the societal perspective.

Authors' conclusions
The authors concluded that a two-year maintenance treatment with venlafaxine was a cost-effective strategy in patients with recurrent major depressive disorders from the perspective of Swedish society. The results of the analysis depended on the maintenance treatment period and the economic viewpoint.

CRD commentary
Interventions:
The authors stated that the selection of placebo as the comparator for venlafaxine was necessary because the optimal duration of maintenance treatment had not yet been defined. Thus, patients may receive no maintenance treatment in a real-world setting. However, comparisons with other antidepressants would be interesting once data from head-to-head trials are available.

Effectiveness/benefits:
The clinical data were derived from a selection of known, relevant studies and the bulk of the evidence came from a single RCT, the key characteristics of which such as inclusion criteria and patients' characteristics were reported. This may help in transferring the study findings to other patient populations with similar features. A strong point of the analysis was the extensive use of sensitivity analysis, in which alternative assumptions on clinical data were considered. Utility weights were obtained from a Swedish population which was very similar to the patients enrolled in the trial. Furthermore, the use of QALYs enhances the validity of the analysis not only because QALYs allow cross-disease comparisons of treatment benefits, but also because they capture the impact of treatment on patients' health in terms both of survival and of quality of life.

Costs:
The two perspectives adopted in the study were appropriate in terms of making the economic findings relevant for different payers. The costs were presented as disease categories and were not broken down into individual items, which may limit the possibility of replicating the economic analysis in other settings. The economic data were derived from a longitudinal study, in which the patients' characteristics were similar to those of patients enrolled in the RCT. Thus, the use of resources was applicable to the cohort of patients used to derive the clinical data. The price year and the use of discounting were reported and statistical distributions were assigned to costs in the sensitivity analysis.

Analysis and results:
The synthesis of costs and benefits was appropriately performed and presented. The issue of uncertainty was satisfactorily addressed in the sensitivity analysis, which considered multiple scenarios and used validated instruments to deal with uncertain assumptions. The authors discussed the results from other studies and some limitations of the analysis were also pointed out, such as the fairly short follow-up period and the potential underestimation of treatment costs.

Concluding remarks:
The study relied on a validated methodology, which enhances the robustness of the analysis. The authors' conclusions appear to be valid.

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MeSH
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AccessionNumber