Cost-effectiveness evaluation in Sweden of escitalopram compared with venlafaxine extended-release as first-line treatment in 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.

CRD summary
This study investigated the cost-effectiveness of escitalopram compared with venlafaxine extended release, as first-line treatment for adults with major depressive disorder. The authors concluded that escitalopram was more effective and less costly than venlafaxine. The methods, analyses and results were mostly clear and comprehensive, but the conclusions reached by the authors are uncertain, due to the alternative interpretation of their results.

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

Study objective
The aim was to examine the costs and health benefits of escitalopram versus venlafaxine extended release, for the first-line treatment of patients, aged 18 to 65 years, who were diagnosed with moderate-to-severe major depressive disorder.

Interventions
Escitalopram was initially given for two months, at 10mg per day, with an adjustment to 20mg per day allowed in the second month. This was compared with generic venlafaxine extended release, given for two months at 75mg per day, with a possible increase, in the second month, to 150mg per day.

Location/setting
Sweden/primary care.

Methods
Analytical approach:
A published decision model was used to synthesise the evidence from published studies or observational data. The time horizon was six months and the authors stated that a Swedish societal perspective was taken.

Effectiveness data:
The key clinical outcome was the probability of sustained remission, defined as remission that was achieved during the first eight weeks of treatment and maintained up to six months. Remission was defined as a score of 12 or less on the Montgomery and Asberg Depression Rating Scale (MADRS). The probabilities of remission at eight weeks were from a pooled analysis of two double-blinded randomised controlled trials. The probabilities of sustained remission, switching or stopping treatment, and relapse were mainly based on data from a longitudinal Swedish real-life survey; the Health Economics of Depression In Sweden (HEADIS) study.

Monetary benefit and utility valuations:
The utility estimates for remission, treatment cessation, and switching treatment were measured, using the European Quality of life (EQ-5D) questionnaire, given to participants in the HEADIS study. Decrements in the utility scores for adverse events were from a published economic model in depression.

Measure of benefit:
The measures of benefit were the probability of sustained remission and quality-adjusted life-years (QALYs).

Cost data:
The direct medical costs included drugs; contacts with the general practitioner, specialist, nurse, psychologist, and emergency services; hospital stay; laboratory tests; clinical examinations; and the treatment of adverse events. The resource quantities were from the HEADIS study, for health service use, and average patient-level data from IMS Heath, for antidepressant medications and adverse-event treatment. The unit costs were from the Dental and Pharmaceutical Benefits Agency, and the Southern Sweden Health Care Region price list. Productivity losses were based on the reported sick days in the HEADIS study. Items were valued in Swedish kronor, inflated to 2009 prices, and converted to Euros (EUR), at a rate of one kronor equalled EUR 0.096.

Analysis of uncertainty:
Ten thousand Monte Carlo simulations were run to produce means and 95% confidence intervals, using gamma and normal distributions for the model inputs. One-way sensitivity analyses were performed on the key parameters. A conservative scenario assumed that generic venlafaxine cost 5% of its branded price. The sensitivity analysis results were illustrated in a scatter plot and cost-effectiveness acceptability curves.

Results
The average total costs were EUR 7,378 (95% CI 1,518 to 21,630) for escitalopram, compared with EUR 7,547 (95% CI 1,571 to 21,371) for venlafaxine extended release; a difference of -EUR 169 (95% CI -1,632 to 1,070) per patient with escitalopram (cost saving).

The mean QALYs were 0.3151 (95% CI 0.2993 to 0.3302) for escitalopram and 0.3065 (95% CI 0.2903 to 0.3217) for venlafaxine; a gain of 0.009 QALYs (95% CI -0.002 to 0.020) with escitalopram.

The conservative scenario and the one-way sensitivity analyses showed that the findings were most sensitive to changes in the remission probability, and relatively insensitive to changes in the sick leave days, general practitioner visits, and incidence of nausea.

There was a 78.4% chance that escitalopram was cost-effective at a willingness-to-pay of EUR 22,080 per QALY gained (equivalent to £20,000 per QALY gained), compared with venlafaxine, and a 62.2% chance that escitalopram was dominant, being more effective and less costly.

Authors' conclusions
The authors concluded that escitalopram was more effective and less costly than venlafaxine, for patients with major depressive disorder, partly due to its better tolerability.

CRD commentary
Interventions:
The interventions were well described and the two drugs may be available and have similar prices in other settings.

Effectiveness/benefits:
The estimates of clinical effectiveness came from two randomised controlled trials, which were not described. This design is recommended for comparing interventions, but it was unclear if the data were appropriated combined, as the participant baseline profiles might not have been similar. The original trials should be consulted to assess their validity. The utility values were measured directly from the intended patient group, using a validated instrument.

Costs:
The cost categories included productivity losses and community-based health care, which was appropriate for the stated societal perspective. The resource quantities and unit costs were clearly presented. The resources appear to have been comprehensive and relevant. The unit costs were from national Swedish sources. Other aspects of the cost assessment, such as the price year and inflation adjustments, were reported.

Analysis and results:
The authors interpreted their results by stating that escitalopram was less expensive and more effective than venlafaxine, but the differences were small and both confidence intervals spanned zero. A more reasonable conclusion might be that the costs and QALYs of escitalopram and venlafaxine were equivalent. The authors discussed their findings in relation to a Cochrane review of escitalopram and venlafaxine, which came to similar conclusions for
Efficacy and tolerability. Limitations were acknowledged, such as the combination of data sources and some assumptions that could have introduced bias. It was unclear whether the model included drug compliance in its estimates.

Concluding remarks:
The methods, analyses and results were mostly clear and comprehensive. The conclusions reached by the authors are uncertain, due to the alternative interpretation of their results.

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