Cost effectiveness of duloxetine compared with venlafaxine-XR in the treatment of 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.

Health technology
The study examined the use of duloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI), in the treatment of moderate to severe major depressive disorder (MDD).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The hypothetical study population comprised patients with moderate to severe MDD. MDD was defined according to American Psychiatric Association DSM-IV criteria or equivalent. Moderate to severe disease was defined as a score of at least 15 on the Hamilton Rating Scale for Depression (HAM-D), or a score of at least 18 on the Montgomery-Asberg Depression Rating Scale (MADRS). The inclusion criteria stipulated non-suicidal patients with no recent history of abuse or dependence. The patients were required to receive treatment for at least 8 weeks with a daily dose of 40 to 120 mg duloxetine or 75 to 225 mg venlafaxine-XR.

The exclusion criteria included diagnosis of any psychiatric condition other than MDD, any major co-morbidity, and use of other psychotropic drugs during the study (with the exception of occasional hypnotic agents or tranquilisers). A further exclusion criterion was evidence of therapy resistance (prior treatment with one of the study drugs, or failure of more than one antidepressant treatment).

Setting
The hypothetical setting was the community and secondary care. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data were derived from a review of the literature, including several meta-analyses. These studies related to 1999 to 2005. The primary clinical data were based on a meta-analysis conducted by the study authors (Vis et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details). The cost data referred to 1994 to 2005. The price year was 2005.

Source of effectiveness data
The effectiveness data were derived from a review of published studies.

Modelling
A decision-tree model was used to combine data from the studies identified from the review, and to estimate the costs and effects over a 6-month time horizon. The decision tree was based on a published model (Einarson et al. 1997, see 'Other Publications of Related Interest' below for bibliographic details). The decision tree included adverse drug reactions (ADRs), lack of efficacy (LOE), remission and secondary treatment for MDD. Secondary treatment was assumed to be treatment with a selective serotonin reuptake inhibitor (SSRI). Patients who achieved remission were assumed to continue treatment for the entire time horizon of the model. The patients accrued symptom-free days (SFDs) while in remission. The titration period was assumed to last 2 months. Relapse rates were assumed to be equal between the study drugs. The costs of managing ADRs were not considered as these were assumed to be equal between the study drugs.

Outcomes assessed in the review
The outcomes assessed in the review included the rates of remission, discontinuation due to ADRs, and LOE associated with SNRIs. The same outcomes were assessed for SSRIs. The authors sought to obtain the remission rate for SSRIs conditional on failure with SNRI treatment. The review also assessed the probabilities of titration and switching on SSRIs and SNRIs.

Study designs and other criteria for inclusion in the review
The authors did not report the methods used for review of the literature review. They did, however, report the inclusion criteria for the meta-analysis on which the remission, ADR and LOE rates of SNRIs were based. This review included only randomised placebo-controlled studies. The patient inclusion and exclusion criteria for this meta-analysis have been reported already (see 'Study Population' section). The primary clinical data for SNRIs were based on a meta-analysis conducted by the study authors (Vis et al. 2005).

Sources searched to identify primary studies
The authors did not specify the sources searched to identify the primary studies. It appears that the selection might have been based, in part, on publications by the study authors.

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
The review included at least 4 primary studies.

Methods of combining primary studies
Separate studies were used to inform separate model parameters, thus no synthesis was conducted. The results of the studies were combined in a decision tree model to estimate the effectiveness over a 6-month time horizon.

Investigation of differences between primary studies
The authors did not explore differences between the primary studies.

Results of the review
The remission rate was estimated to be 0.365 with duloxetine and 0.401 with venlafaxine-XR.
The drop-out rate due to ADRs was estimated to be 0.088 with duloxetine and 0.092 with venlafaxine-XR.

The drop-out rate due to LOE was estimated to be 0.046 with duloxetine and 0.050 with venlafaxine-XR.

**Measure of benefits used in the economic analysis**
The measures of health benefit used were the SFDs and number of treatment successes. Treatment success (remission) was defined as a decrease to a score of less than or equal to 7 on the HAM-D scale, or a score of less than or equal to 10 on the MADRS scale. Treatment success was measured 8 weeks after therapy initiation and was calculated using last-observation-carried-forward. The decision-tree model included a full probabilistic analysis in which all the uncertainty around the effectiveness parameters was characterised using a triangular distribution based on the reported 95% confidence intervals.

**Direct costs**
The study reported the unit costs but not the quantities of resource use. The analysis included the direct costs to a third-party payer. These consisted of the costs of drugs, medical care (e.g. general practitioner or psychiatrist visits) hospitalisations and laboratory tests. A decision-tree model was used to estimate the costs over a 6-month time horizon. The prices and unit costs were based on published lists and reimbursement rates, with the exception of the price of duloxetine. Since duloxetine was not available in the study setting, the price was estimated by prorating the cost of venlafaxine-XR according to the ratio of the prices of duloxetine and venlafaxine-XR in the USA. Discounting was not relevant given the short time horizon of the model. The study reported the average and incremental costs. The price data related to 2005 and, where needed, the costs were adjusted using the Consumer Price Index for medicines. The authors excluded the costs of treating ADRs as they assumed the types of ADR experienced would be the same for both study drugs.

**Statistical analysis of costs**
Sampled data were not available for the costs.

**Indirect Costs**
The study included the costs of the patients' lost productivity using the human capital approach. The average hourly wage rate was based on published statistics, and patients were assumed to remain off work until they experienced remission. The inclusion of productivity costs was necessary for the analysis conducted from a societal perspective. Discounting was not relevant given the short time horizon of the model. The quantities and the costs were not analysed separately.

**Currency**
Canadian dollars (Can$). The conversion rate was Can$1.00 = US$0.80 for January 2005.

**Sensitivity analysis**
Several one-way sensitivity analyses and a full probabilistic analysis were performed. A 15% standard deviation was applied to costs to account for fluctuations, and a triangular distribution was assumed for the probabilistic analysis.

**Estimated benefits used in the economic analysis**
The overall success rate was estimated to be 53% for duloxetine and 57% for venlafaxine-XR over a 6-month period. Over the same time horizon, the number of SFDs was estimated to be 52.72 for duloxetine and 57.03 for venlafaxine-XR.

**Cost results**
The total direct medical costs per patient were estimated to be Can$7,081 for duloxetine and Can$6,551 for venlafaxine-XR over a time horizon of 6 months. Over the same time horizon, the total indirect costs per patient were estimated to be Can$13,906 for duloxetine and Can$13,446 for venlafaxine-XR.

Synthesis of costs and benefits
The costs and benefits were combined to calculate the cost per success and cost per SFD, and an incremental analysis was performed. In a deterministic analysis, venlafaxine-XR was found to be the dominant strategy (i.e. it was more effective and less costly than duloxetine). In the probabilistic analysis, venlafaxine-XR was found to have a 78.8% probability of being the dominant treatment strategy from a Ministry of Health perspective, and a 78.3% probability of being dominant from a societal perspective.

Authors’ conclusions
Venlafaxine-XR was the most cost-effective treatment strategy for major depressive disorder.

CRD COMMENTARY - Selection of comparators
The comparator, venlafaxine-XR, was explicitly chosen to represent current practice in the study setting. This was compared with a new drug from the same class that had not yet been introduced in the study setting. You must consider whether these comparators are relevant in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were based on a meta-analysis conducted by the study authors (Vis et al. 2005). The authors acknowledged that the calculation of remission rates using last-observation-carried-forward was inferior to an intention to treat analysis, as drop-outs might be counted as successes. The authors acknowledged that the meta-analysis showed little difference in effectiveness between the two study drugs, so the conclusion that venlafaxine-XR was the more effective of the two should be viewed with caution.

Validity of estimate of measure of benefit
The estimation of benefits was modelled using a published decision tree (Einarson et al. 1997). This model was appropriate for the study question.

Validity of estimate of costs
The study employed two cost perspectives. All the categories of cost relevant to those perspectives were included in the analysis. The authors omitted the costs of ADRs as they assumed that the type of ADR would be the same regardless of treatment. However, the model included different rates of ADRs when on duloxetine and venlafaxine-XR, thus although the type of ADR experienced might be the same, the total costs would not be. This assumption was therefore not justified. The costs were reported, but the quantities estimated to be consumed in the economic model were not. This may affect the generalisability of the study results. The majority of the price data were based on the study setting. A statistical analysis of the prices was not undertaken. The price of duloxetine was estimated for the study setting as a published price was not available, but the authors demonstrated that the study results were robust to variations in this price. Since the time horizon of the model was 6 months, discounting was not relevant.

Other issues
The authors compared their findings with the results of studies in different patient populations. The issue of generalisability to settings outside of Canada was not addressed. The authors do not appear to have presented their results selectively and their conclusions accurately reflected the scope of the analysis.

Implications of the study
The authors called for further head-to-head studies of the two drugs to confirm their findings.

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None stated.

**Bibliographic details**

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adolescent; Adult; Cost of Illness; Cost-Benefit Analysis; Cyclohexanols /economics /therapeutic use; Decision Trees; Depressive Disorder, Major /drug therapy /economics; Duloxetine Hydrochloride; Economics, Pharmaceutical; Health Care Costs; Humans; Middle Aged; Models, Econometric; Norepinephrine /antagonists & inhibitors; Ontario; Outpatients; Serotonin Uptake Inhibitors /economics /therapeutic use; Thiophenes /economics /therapeutic use; Treatment Outcome; Venlafaxine Hydrochloride

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