The health economic impact of antidepressant usage from a payer's perspective: a multinational study
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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 use of extended release venlafaxine XR, a serotonin norepinephrine reuptake inhibitor, as an antidepressant for the treatment of patients suffering from major depressive disorders (MDDs).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients suffering from acute MDD. These were diagnosed with a score of either greater than 15 on the Hamilton depression scale, or greater than 18 on the Montgomery-Asberg depression rating scale. In addition, these patients were not suffering from bipolar depression, psychotic, metabolic or endocrine disorders.

Setting
The study setting was the community. The economic study was carried out in ten European and American countries.

Dates to which data relate
The dates during which the data on effectiveness and resource use were gathered were not reported. The price year was not stated.

Source of effectiveness data
The effectiveness evidence was derived from a review of published studies and from the opinions of experts.

Modelling
A decision analytic model (decision tree) was used to examine the costs and outcomes associated with the three antidepressants over a period of 6 months, for each country. The model was constructed using assumptions derived from the experts’ panel (decision nodes). After construction, the model was populated with the data obtained from the review of the relevant literature (chance nodes).

Outcomes assessed in the review
The outcomes assessed in the review were the inpatient and outpatient efficacy rates, and the drop-out rates due to lack of efficacy or adverse drug reactions of the three drugs under examination. The efficacy rates were defined as a 50%
reduction in depression scores on the Hamilton depression scale or the Montgomery-Asberg depression rating scale.

**Study designs and other criteria for inclusion in the review**
All the primary studies were based on randomised controlled clinical trials.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
Not reported.

**Methods of combining primary studies**
The authors conducted a meta-analysis to combine the estimations obtained from the different primary studies. However, the meta-analysis was published separately (see Other Publications of Related Interest).

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The inpatient success rate was 73.7% (confidence interval, CI: 68.9 - 78.4) for venlafaxine XR, 61.4% (CI: 55.7 - 67.0) for SSRIs, and 59.3% (CI: 50.1 - 68.6) for TCAs.

The outpatient success rate was 62.3% (CI: 49.7 - 74.9) for venlafaxine XR, 58.6% (CI: 48.2 - 69.0) for SSRIs, and 58.2% (CI: 43.0 - 73.5%) for TCAs.

The drop-out due to lack of efficacy was 4.8% (CI: 1.8 - 7.8) for venlafaxine, 8.4% (CI: 4.6 - 12.3) for SSRIs, and 6.8% (CI: 4.6 - 9.0) for TCAs.

The drop-out rate due to adverse drug reactions was 10.9% (CI: 7.9 - 13.9) for venlafaxine, 17.4% (CI: 17.4 - 21.3) for SSRIs, and 23.1% (CI: 16.2 - 30.0) for TCAs.

**Methods used to derive estimates of effectiveness**
A Delphi panel of 42 clinical experts was consulted to support assumptions relating to the decision tree. Also, to determine the most appropriate representation of MDD patient treatment in each country.

**Estimates of effectiveness and key assumptions**
The decision tree was shown and the outcomes were extrapolated to 6 months.
Measure of benefits used in the economic analysis
Two benefit measures were assessed in the economic analysis:

- the expected success rate, as defined from the effectiveness analysis and obtained from the decision model; and
- the expected number of symptom-free days (SFDs), defined as 6 months minus the time elapsed before clinical determination of success and then used as a proxy for patient utility.

Direct costs
Discounting was not carried out due to the short time horizon of the study (6 months). The resource quantities and the unit costs were not reported separately. The unit costs were given only per service. The resource/boundary adopted was consistent with the perspective adopted in the analysis. The costs included the drugs, physician visits, laboratory tests, and hospitalisation. The costs and the resources were estimated from actual data, validated by local economists in each country, and from published studies. The dates during which the resources used were collected were not reported. The price year was not reported.

Statistical analysis of costs
No statistical analysis of costs was reported.

Indirect Costs
No indirect costs were included.

Currency
US dollars ($). Costs were expressed in the currency of the country then converted into US dollars for comparison.

Sensitivity analysis
Several sensitivity analyses were conducted to test the assumptions and variables used in the model. Univariate break-even analyses (rank order stability analyses) were performed on variables stated to have included success rates and drug prices. A multivariate (Monte Carlo simulation) analysis was conducted by varying the inputs for success rates and drop-out rates within the 95% CIs. In addition, the cost variables were varied within +/-20% of the estimated costs.

Estimated benefits used in the economic analysis
The expected success rates for the drugs in each country were as follows.

- Germany (outpatient): venlafaxine XR, 79.7%; SSRIs, 70.7%; and TCAs 70.2%.
- Germany (inpatient): venlafaxine XR, 73.3%; SSRIs, 69.3%; and TCAs 69.0%.
- Italy (outpatient): venlafaxine XR, 83.1%; SSRIs, 74.4%; and TCAs, 73.2%.
- Italy (inpatient): venlafaxine XR, 78.0%; SSRIs, 74.2%; and TCAs, 72.9%.
- The Netherlands (outpatient): venlafaxine XR, 80.9%; SSRIs, 70.5%; and TCAs, 70.1%.
- The Netherlands (inpatient): venlafaxine XR, 74.0%; SSRIs, 68.9%; and TCAs, 68.6%.
- Poland (outpatient): venlafaxine XR, 80.0%; SSRIs, 70.9%; and TCAs, 70.5%.
- Poland (inpatient): venlafaxine XR, 74.6%; SSRIs, 70.7%; and TCAs, 70.1%.
Spain (outpatient): venlafaxine XR, 82.9%; SSRIs, 74.1%; and TCAs, 73.0%.
Spain (inpatient): venlafaxine XR, 76.7%; SSRIs, 72.8%; and TCAs, 71.7%.
Sweden (outpatient): venlafaxine XR, 82.2%; SSRIs, 73.2%; and TCAs, 72.2%.
Sweden (inpatient): venlafaxine XR, 75.8%; SSRIs, 71.8%; and TCAs, 70.9%.
Switzerland (outpatient): venlafaxine XR, 84.1%; SSRIs, 80.8%; and TCAs, 79.1%.
Switzerland (inpatient): venlafaxine XR, 77.2%; SSRIs, 75.7%; and TCAs, 74.2%.
UK (outpatient): venlafaxine XR, 80.8%; SSRIs, 79.4%; and TCAs, 71.2%.
UK (inpatient): venlafaxine XR, 74.5%; SSRIs, 74.2%; and TCAs, 70.0%.
USA (outpatient): venlafaxine XR, 82.8%; SSRIs, 73.0%; and TCAs, 72.2%.
USA (inpatient): venlafaxine XR, 75.6%; SSRIs, 70.7%; and TCAs, 70.1%.
Venezuela (outpatient): venlafaxine XR, 81.4%; SSRIs, 79.2%; and TCAs, 70.8%.
Venezuela (inpatient): venlafaxine XR, 74.9%; SSRIs, 73.8%; and TCAs, 69.5%.

Thus, venlafaxine XR was the most successful treatment both in an outpatient and inpatient setting. The analysis showed similar results in terms of the expected SFDs in all countries.

Cost results
The expected costs of the drugs in each country were as follows.

Germany (outpatient): venlafaxine XR, $2,323; SSRIs, $3,046; and TCAs, $3,077.
Germany (inpatient): venlafaxine XR, $11,909; SSRIs, $12,747; and TCAs, $12,907.
Italy (outpatient): venlafaxine XR, $924; SSRIs, $979; and TCAs, $935.
Italy (inpatient): venlafaxine XR, $9,036; SSRIs, $9,399; and TCAs $9,567.
The Netherlands (outpatient): venlafaxine XR, $1,182; SSRIs, $1,510; and TCAs, $1,544.
The Netherlands (inpatient): venlafaxine XR, $12,853; SSRIs, $14,143; and TCAs, $14,307.
Poland (outpatient): venlafaxine XR, $491; SSRIs, $339; and TCAs, $331.
Poland (inpatient): venlafaxine XR, $1,433; SSRIs, $1,314; and TCAs, $1,314.
Spain (outpatient): venlafaxine XR, $1,307; SSRIs, $1,552; and TCAs, $1,539.
Spain (inpatient): venlafaxine XR, $7,686; SSRIs, $7,955; and TCAs, $8,053.
Sweden (outpatient): venlafaxine XR, $2,081; SSRIs, $2,449; and TCAs, $2,424.
Sweden (inpatient): venlafaxine XR, $8,299; SSRIs, $8,664; and TCAs, $8,801.
Switzerland (outpatient): venlafaxine XR, $2,304; SSRIs, $2,576; and TCAs, $2,563.
Switzerland (inpatient): venlafaxine XR, $11,883; SSRIs, $12,411; and TCAs, $12,610.

UK (outpatient): venlafaxine XR, $1,714; SSRIs, $1,987; and TCAs, $2,104.

UK (inpatient): venlafaxine XR, $7,948; SSRIs, $8,288; and TCAs, $8,505.

USA (outpatient): venlafaxine XR, $3,089; SSRIs, $4,300; and TCAs, $4,317.

USA (inpatient): venlafaxine XR, $16,235; SSRIs, $17,843; and TCAs, $18,135.

Venezuela (outpatient): venlafaxine XR, $2,202; SSRIs, $2,346; and TCAs, $2,828.

Venezuela (inpatient): venlafaxine XR, $25,391; SSRIs, $26,489; and TCAs, $27,449.

Venlafaxine XR was the cheapest treatment both in an outpatient and inpatient setting in 9 countries. Only in Poland did the use of venlafaxine XR cost more than the other drugs.

**Synthesis of costs and benefits**

Since two benefit measures were available, the costs and the benefits were combined by calculating the expected cost per successfully treated patient and the cost per SFD. In the countries considered (with the exclusion of Poland), venlafaxine XR was the dominant treatment (the least costly and most effective).

The expected cost per successfully treated outpatient was $2,913 in Germany, $1,112 in Italy, $1,460 in The Netherlands, $1,577 in Spain, $2,531 in Sweden, $2,741 in Switzerland, $2,121 in the UK, $3,732 in the USA, and $2,704 in Venezuela.

The expected cost per successfully treated inpatient was $16,257 in Germany, $11,590 in Italy, $17,367 in The Netherlands, $10,027 in Spain, $10,951 in Sweden, $15,398 in Switzerland, $10,672 in the UK, $21,474 in the USA, and $33,920 in Venezuela.

In Poland, the expected cost of venlafaxine XR per successfully treated outpatient was $614, compared with $478 for SSRIs and $470 for TCAs. The corresponding cost for an inpatient was $1,921, compared with $1,858 for SSRIs and $1,876 for TCAs.

The results in terms of the cost per SFD were similar. Both the univariate and multivariate sensitivity analyses were reported to show that the results were robust to variations in the above-mentioned variables. The rank order stability analyses indicated that the cost of venlafaxine treatment would have to increase by different amounts for different countries, except for Poland where it had to decrease, before the total costs were equivalent to the comparators. For example, in the UK, the daily treatment cost for venlafaxine XR would have to increase from 1.05 to 3.77 for an inpatient, in order for it to be equivalent to TCA.

The Monte Carlo simulation provided a "confidence" that venlafaxine would be cheaper than SSRI. This confidence ranged from 82 to 100%. The budgetary analysis showed that substantial savings were possible by introducing venlafaxine XR into the list of antidepressants used in the countries considered (excluding Poland), even when using a conservative treated prevalence rate (0.3%).

**Authors' conclusions**

Venlafaxine XR was a dominant strategy in almost all countries, excluding Poland. In other words, venlafaxine XR was the most successful treatment, and its costs were systematically lower than selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs). Venlafaxine XR was also well tolerated, with a high compliance rate. In addition, it produced the greatest number of symptom-free days (SFDs), reflecting a better quality of life.

**CRD COMMENTARY - Selection of comparators**

NHS Economic Evaluation Database (NHS EED)
Produced by the Centre for Reviews and Dissemination
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The selection of the comparators was based on the alternative drug therapies available in the primary studies selected. However, the authors did not justify their choice of the comparators. The reason why other available drug regimens were not considered as the comparators was not reported. You should assess whether the treatments represent routinely used therapies in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness measures were derived from a review of the literature and were then combined through a meta-analysis. However, few details of the conduct of either the review or the meta-analysis were reported, although the meta-analysis was published elsewhere (see Other Publications of Related Interest).

The authors acknowledged a possible limitation of the effectiveness analysis due to the use of secondary data and the adoption of a deterministic model design. A Delphi panel was consulted to build the decision tree. However, as noted by the authors, at the time of the study venlafaxine XR was not introduced in some countries. Therefore, the experience of some experts on the panel was based only on venlafaxine IR and other extended-release products.

Validity of estimate of measure of benefit
The benefit measures used in the economic analysis were modelled through the decision tree. Both measures, i.e. the success rate and SFDs, appear to have been appropriate to reflect the effectiveness of the disease. In particular, the number of SFDs was appropriate to assess indirectly the compliance rate and the "quality" of life of the patients.

Validity of estimate of costs
The resource quantities were not reported separately, but the average costs were indicated for each cost item used in the analysis. It appears that all categories of cost relevant to the perspective adopted were included in the analysis. Appropriate currency conversions were carried out, but neither the exchange rate nor the price years were reported. As reported by the authors, the inclusion of indirect and intangible costs (and the adoption of a wider perspective) would have improved the analysis, since these costs were estimated to represent 72 to 88% of the total cost of depression.

Other issues
Comprehensive sensitivity analyses were carried out on the crucial variables to enhance the generalisability of the study results to other settings. However, significant individual patient variations, and differences in practice patterns, may limit the external validity of the analysis. Also, the authors did not make comparisons of their results with those from other studies.

Implications of the study
The authors indicated that a significant implication of the study was that it is crucial to include all the resources involved in the treatment process in the analysis. In fact, they stated that prior studies and policies have focused mainly on drug prices, which do not reflect the true amount of resources consumed. Finally, venlafaxine XR should be increasingly used for the treatment of MDD to realise a favourable impact on most payer budgets.

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None stated.

Bibliographic details

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Other publications of related interest

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