Cost-effectiveness of mirtazapine compared to amitriptyline and fluoxetine in the treatment of moderate and severe depression in Austria

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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 mirtazapine, amitriptyline, and fluoxetine in the treatment of moderate and severe depression in Austria.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Austrian people with moderate and severe depression.

Setting
Community and primary care.

Dates to which data relate
Effectiveness data were collected from two studies published in 1998. The date to which resource use data relate was not reported. Cost data were collected from studies published between 1995 and 1997. The price year was 1996.

Source of effectiveness data
Effectiveness data were derived from a literature review and expert opinion.

Modelling
Two decision trees were used to model the management of moderate and severe depression in Austria with mirtazapine and amitriptyline for 28 weeks and with mirtazapine and fluoxetine for 6 months. A five-month decision tree was used to model the management of patients who discontinue antidepressant treatment.

Outcomes assessed in the review
The review assessed the following outcomes: response to treatment, and treatment dropout.

Study designs and other criteria for inclusion in the review
The comparison between mirtazapine and amitriptyline was based on a meta-analysis of four randomised, double-blind, placebo-controlled trials in the USA. The comparison between mirtazapine and fluoxetine was based on a randomised, double-blind trial in the UK, Belgium and the Netherlands.
Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Randomisation and blind assessment.

Methods used to judge relevance and validity, and for extracting data
Summary statistics from each study.

Number of primary studies included
Two studies were included.

Methods of combining primary studies
Not relevant.

Investigation of differences between primary studies
Not relevant.

Results of the review
Outpatients, aged between 18 and 93 years, were treated with either mirtazapine (mean dose: 18.9 mg/d) or with amitriptyline (mean dose: 115.9 mg/d). 36% of mirtazapine-treated and 43% of amitriptyline-treated patients who completed six week trials were entered into 22 week long-term trials on their initial antidepressant. Of those who entered the long-term trials, significantly more mirtazapine-treated than amitriptyline-treated patients were classified as cured (17-HAM-D score < 7), or withdrew from the trials because they were doing well (64 versus 46%, \(p=0.022\)). The incidence of adverse events was significantly higher among the amitriptyline-treated patients in both the short-term \(p=0.04\) and the long-term \(p=0.001\). Patients, aged between 18 and 75 years, were treated with mirtazapine (mean dose: 38.2 mg/d) or fluoxetine (mean dose: 23.8 mg/d). 67% of mirtazapine-treated and 46% of fluoxetine-treated patients showed at least 50% reduction in the 17-HAM-D score at the end of six weeks' treatment. Of the 63.4% of patients who were assumed to continue taking their antidepressant for a minimum of six months, 58.3% were assumed to be successfully treated.

Methods used to derive estimates of effectiveness
An Austrian Delphi panel comprising psychiatrists and GPs was used to determine treatment paths and health care resource use attributable to patients who discontinue antidepressant treatment.

Estimates of effectiveness and key assumptions
94% of patients contact their GP and 6% contact a psychiatrist. 32.6% of patients who initially contact their GP are then referred to a psychiatrist. A patient managed by a psychiatrist and by a GP has a mean of 0.9 and 1.6 consultations per week, respectively. 6.1% of patients are initially treated as psychiatric inpatients for a mean of 21 days. 12.6% of patients who do not respond to their initial therapy are treated as psychiatric inpatients for a mean 29.9 days. Once patients no longer feel depressed, antidepressant treatment continues for a mean of 21.4 weeks and the daily dose is reduced by 23.8%. Patients who complete six weeks’ treatment, but do not respond adequately to treatment are switched to another antidepressant. 52% of patients who discontinue treatment spontaneously enter remission. Otherwise, patients remain moderately or severely depressed for the 28 weeks. Once patients switch from their original antidepressant, 69.7% remain on this treatment and 30.3% discontinue. Resource use attributable to managing patients who discontinue antidepressant treatment was documented in the paper.
Measure of benefits used in the economic analysis
The primary measure of benefits used was the proportion of patients successfully treated.

Direct costs
Direct costs were not discounted given the short time frame of the study (less than 1 year). Quantities and costs were reported separately. Direct costs reflected the expected cost to Austrian Sick Funds of managing a patient with moderate or severe depression and included costs related to antidepressants, inpatient stay, outpatient visits, and specialist outpatients visits. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. Costs estimates were derived from previously published studies. The price year was 1996.

Statistical analysis of costs
Not reported.

Indirect Costs
Indirect costs were not discounted given the short time frame of the study (less than 1 year). Quantities and costs were reported separately. Indirect costs reflected the cost per patient to Austrian society due to lost productivity. The estimation of quantities and costs was based on actual data. The cost estimate was derived by dividing the Austrian Gross Domestic Product by the Austrian population eligible to work by the 52 weeks in the year. The price year was 1996.

Currency
Austrian Schilling (ATS).

Sensitivity analysis
One-way sensitivity analyses were performed on those parameters which, either strongly influenced the results, or were based on uncertain estimates of resource use. With respect to patients who discontinue antidepressant treatment, one-way sensitivity analyses were performed on the probabilities used in the model.

Estimated benefits used in the economic analysis
28 weeks' treatment with mirtazapine compared to amitriptyline increases the proportion of successfully treated patients by 21% (from 19.2 to 23.2%). Six months' treatment with mirtazapine compared to fluoxetine increases the proportion of successfully treated patients by 22% (from 15.6 to 19.1%).

Cost results
The direct cost associated with mirtazapine is ATS 30,299 per patient over 28 weeks, compared to ATS 31,411 for managing a patient with amitriptyline. The indirect cost associated with mirtazapine is ATS 58,787 per patient, compared to ATS 61,851 for a patient treated with amitriptyline. The cost difference between a mirtazapine- and amitriptyline-treated patient was sensitive to changes in the proportion of patients absent from work. The direct cost associated with mirtazapine is ATS 29,613 per patient over 28 weeks, compared to ATS 29,205 for managing a patient with fluoxetine. The indirect cost is ATS 58,787 per patient for treatment with either mirtazapine or fluoxetine. The cost difference between a mirtazapine- and fluoxetine-treated patient was sensitive to changes in the proportion of hospital admissions and, to a lesser extent, to changes in the proportion of patients absent from work and the unit cost of consultations with psychiatrists.

Synthesis of costs and benefits
Mirtazapine is a dominant treatment compared to amitriptyline. Six months' treatment with mirtazapine compared to fluoxetine increases the proportion of successfully treated patients by 22% at a net additional cost of ATS 408 per patient. The cost-effectiveness of mirtazapine relative to fluoxetine was sensitive to changes in the proportion of patients who complete six weeks' treatment with mirtazapine and achieve a 50% reduction in 17-HAM-D score from the baseline value of 52% to 42 and 62%.

**Authors' conclusions**
Mirtazapine is a cost-effective antidepressant compared to amitriptyline and fluoxetine, supporting the adoption of this treatment in the management of moderate and severe depression in Austria.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was not clear. You, as a user of this database, should verify whether these health technologies are relevant to your own settings.

**Validity of estimate of measure of benefit**
Effectiveness estimates were derived from two randomised, double-blind trials. The authors did not consider quality of life measures. Since long-term comparative data on mirtazapine and fluoxetine were not available, six week data had to be extrapolated to six months using the published literature for fluoxetine and assumed similar effectiveness for both drugs over the extrapolated period. The proportion of patients remaining in remission has been shown to be significantly higher among mirtazapine-treated patients than those treated with amitriptyline. However, the amitriptyline model assumed that the relapse prevention rate is the same for both antidepressants. Treatment paths and resource use for patients who discontinue antidepressant treatment were derived using a Delphi panel approach.

**Validity of estimate of costs**
An advantage of this study is that both direct and indirect costs were considered, although indirect costs incurred by family and friends of patients were not included. Cost estimates were derived from various published sources and, hence, it is difficult to assess the generalisability of the cost results.

**Other issues**
Given that two different studies were used for deriving the effectiveness estimates, the costs and outcomes associated with mirtazapine treatment were different in the mirtazapine-amitriptyline model and the mirtazapine-fluoxetine model. The authors did not justify the choice of these three particular antidepressants. Adequate comparisons with other relevant studies were not made.

**Implications of the study**
The use of mirtazapine in the treatment of moderate and severe depression in Austria is recommended.

**Source of funding**
Support from Organon GesmbH.

**Bibliographic details**

**PubMedID**
10572352
Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
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