Economic impact of using mirtazapine compared to amitriptyline and fluoxetine in the treatment of moderate and severe depression in the UK

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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
Mirtazapine compared to amitriptyline and fluoxetine in the treatment of moderate and severe depression in the UK.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients in the UK, with moderate and severe depression, and within the age range 18 to 93 years.

Setting
Primary care and hospital. The economic study was set in the UK.

Dates to which data relate
Effectiveness data were collected from studies published between 1998 and 1999. Resource use data were taken from a panel of 10 GPs and 3 psychiatrists. Cost data were collected from studies published between 1997 and 1999. The price year was 1997-1998.

Source of effectiveness data
Effectiveness data were derived from a literature review and from estimates made by the authors.

Modelling
Decision analytic models were used to determine the cost-effectiveness of antidepressant drugs.

Outcomes assessed in the review
The review assessed the number of consultations with a GP and psychiatrist, and the percentage of hospital admissions.

Study designs and other criteria for inclusion in the review
Data on mirtazapine and amitriptyline were taken from a meta-analysis of four randomised, double blind trials conducted in the USA. Data on mirtazapine and fluoxetine were based on a six-week, randomised, double blind trial performed in the UK, Belgium, and The Netherlands.
Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
At least two studies were included.

Methods of combining primary studies
The narrative method was used.

Investigation of differences between primary studies
Not stated.

Results of the review
Of those who entered the long-term trials significantly more mirtazapine-treated than amitriptyline-treated patients were classified as cured (17-HAM-D score of 7 or less) 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 trials, (p=0.040) and long-term trials, (p=0.001). Sixty-seven percent of mirtazapine-treated patients and 46% of fluoxetine-treated patients showed at least a 50% reduction in 17-HAM-D score at the end of six weeks’ treatment.

Methods used to derive estimates of effectiveness
Estimates of effectiveness were also derived from a panel of general practitioners and psychiatrists.

Estimates of effectiveness and key assumptions
Of the patients who contacted their GP, 88.7% were managed by the GP, 10.4% were managed by a psychiatrist, and 0.9% were treated as psychiatric inpatients. Patients managed by a GP and who did not respond to their initial treatment had the frequency of their visits increased to 0.81 consultations per week. 21.4% of patients managed by a GP and who did not respond to their initial treatment, were managed by a psychiatrist and had a mean of 0.39 visits per week. 1% of patients managed by a GP and who did not respond to their initial treatment were hospitalised for a mean of 16.4 days. Patients managed by a psychiatrist and who did not respond adequately to their initial treatment had a mean of 0.48 consultations per week. In 11.1% of cases, they would be treated as psychiatric inpatients for 18 days. Once patients managed by a GP or a psychiatrist no longer suffered from depressive symptoms, the frequency of visits was reduced to 0.18 (GP-managed) and 0.06 (psychiatrist-managed) consultations per week. Once patients no longer felt depressed, antidepressant treatment continued for 21.2 weeks, although the daily dose was reduced by 22%. 47.8% of patients of working age were not in work before they commenced a depressive episode.

Measure of benefits used in the economic analysis
The proportion of successfully treated patients was used as the measure of benefits. This was determined by the 17-HAM-D score (7 or less) or if patients were doing well (according to the criteria specified in source trials).
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 included costs of hospitalisation, GP visits, visits to psychiatrists, antidepressant and concomitant medication, community psychiatric nurse visits, community mental health team visits, and attendance at day wards. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. Costs and quantities were collected from a panel of 10 GPs and 3 psychiatrists, and from the literature. The price year was 1997/1998.

Statistical analysis of costs
No statistical analysis was 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 included costs of lost productivity. The quantity/cost boundary adopted was that of society. The estimation of quantities and costs was based on actual data. Costs and quantities were collected from published sources. The price year was 1997/1998.

Currency
UK pounds sterling (¥).

Sensitivity analysis
Sensitivity analyses were conducted on the cost of treating adverse events, the cost of managing a patient who discontinued antidepressant treatment, the number of psychiatric consultations with GPs, the number of consultations with psychiatrists, the percentage of hospital admissions, and the effectiveness of mirtazapine.

Estimated benefits used in the economic analysis
Seven months' treatment with mirtazapine compared to amitriptyline increased the proportion of successfully treated patients from 19.2% to 23.2%. Six months' treatment with mirtazapine, compared to fluoxetine, increased the proportion of successfully treated patients from 15.6% to 19.1%.

Cost results
The direct NHS cost of managing a patient who discontinued antidepressant treatment ranged from 50 to 504 over five months. The direct NHS cost of managing a patient with moderate and severe depression with mirtazapine was 413 per patient over seven months, compared with 448 for amitriptyline. The indirect societal cost of managing a patient with moderate and severe depression with mirtazapine was 1,513 per patient over seven months, compared with 1,519 for amitriptyline. The direct NHS cost of managing a patient with moderate and severe depression with mirtazapine was 420 per patient over six months, compared with 394 for fluoxetine. The indirect societal cost of managing a patient with moderate and severe depression with mirtazapine or fluoxetine was 1,360 per patient over six months.

Synthesis of costs and benefits
Mirtazapine was dominant compared to amitriptyline. Six months' treatment with mirtazapine compared to fluoxetine increased the proportion of successfully treated patients by 22% at a net additional cost to the NHS of 27 per patient. Mirtazapine's cost-effectiveness relative to amitriptyline was sensitive to the cost of managing adverse events. Mirtazapine's cost-effectiveness relative to fluoxetine was sensitive to the cost of managing patients who discontinue antidepressant treatment, the number of psychiatric consultations with GPs and the percentage of patients who completed six weeks' treatment with mirtazapine and achieved a 50% reduction in the 17-HAM-D score.
Authors' conclusions
Mirtazapine is a cost-effective antidepressant compared to amitriptyline and fluoxetine in the management of moderate and severe depression in the UK. Mirtazapine's relative cost-effectiveness is robust to changes in patient management strategies and national healthcare systems.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used namely a currently employed strategy. You, as a user of the database, should decide if these health technologies are relevant to your setting.

Validity of estimate of measure of benefit
The authors did not state that a systematic review of the literature had been undertaken, although the principal effectiveness estimates were derived from a meta-analysis. More information about the design of the review could have been reported. The estimation of benefits was obtained directly from the effectiveness analysis.

Validity of estimate of costs
Positive features of the cost analysis were that all relevant direct and indirect cost categories were included, sensitivity analyses were conducted on costs and quantities, quantities and costs were reported separately, the price year was reported and no charges were used to proxy prices.

Other issues
The authors made appropriate comparisons of their findings with those from other studies and addressed the issue of generalisability to other settings. The authors did not present their results selectively. The study considered patients with moderate and severe depression and this was reflected in the authors’ conclusions. The authors stated that the direct NHS costs were likely to be an under-estimate, because the cost of managing those adverse events that were not significantly different between treatment groups had been excluded from the analysis. The authors had to extrapolate six-week data to six months using assumptions derived from the literature.

Implications of the study
Mirtazapine is a cost-effective antidepressant compared to amitriptyline and fluoxetine in the management of moderate and severe depression in the UK. Mirtazapine's relative cost-effectiveness is robust to changes in patient management strategies and national healthcare systems.

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