Cost-effectiveness analyses for mirtazapine and sertraline in dementia: randomised controlled trial

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
The objective was to assess the cost-effectiveness of sertraline and mirtazapine, for the treatment of depression, in patients with dementia. The authors concluded that neither intervention was cost-effective in reducing depression scores, but if unpaid carer costs and quality of life were analysed, mirtazapine appeared to be cost-effective. The study methods and reporting were good, and the authors' conclusions appear to be appropriate.

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

Study objective
This study evaluated the cost-effectiveness of sertraline and mirtazapine, for the treatment of depression, in patients with suspected dementia, who were referred to old age psychiatric services.

Interventions
Two interventions were assessed within a clinical trial: sertraline and mirtazapine. The comparator was placebo. All participants received normal care. The target doses were 150mg sertraline or 45mg mirtazapine daily, with titration over eight weeks; according to the clinician's adjustments.

Location/setting
UK/hospital and community.

Methods
Analytical approach:
An economic analysis was conducted alongside a pragmatic, multicentre, randomised placebo-controlled trial of 339 patients. Cost-effectiveness and cost-utility were analysed over 13 weeks, and 39 weeks. Bootstrapping was used for each analysis. The authors stated that two perspectives were adopted: that of the health and social care agencies; and that of the health and social care agencies and unpaid carers.

Effectiveness data:
The primary effectiveness outcome was the reduction in depression, measured on the Cornell Scale for Depression in Dementia (CSDD). Patients were diagnosed with dementia of the Alzheimer's type according to the National Institute of Neurological and Communicative Disorders and Stroke, and the Disease and Related Disorders criteria. Patients initially had a score of more than seven on the CSDD; higher scores were associated with a worse outcome. The CSDD score was measured at 13 weeks and at 39 weeks. Analyses were conducted using intention to treat. A clinical trials unit independently allocated patients to treatment.

Monetary benefit and utility valuations:
The utility values were derived using EQ-5D scores, from the trial participants, which were valued using UK population data.

Measure of benefit:
The measures of benefit were quality-adjusted life-years (QALYs), and improvement (reduction) in CSDD score.
Cost data:
The health and social care perspective included the costs for drugs and service use. Service use included hospital care, community care (nurse, chiropodist, dentist, etc.), day services and lunch, and social club visits. Unpaid carer costs included informal care (volunteer support, befriending and telephone support, and care from friends and relatives). The resource use was collected retrospectively for the six months before randomisation, at 13 weeks, for the previous three months, and at 39 weeks, for the previous six months. Drug use was from the trial medication log. Other resource use was from questionnaires adapted from the Client Service Receipt Inventory. Participants estimated the hours of unpaid care and support received in an average week, and opportunity costs were calculated. Other sources included the NHS Schedule of Reference Costs, and the British National Formulary 59. All unit costs were at 2009 to 2010 prices, in UK £.

Analysis of uncertainty:
Non-parametric bootstrapping was used to estimate 95% confidence intervals for the mean costs and outcomes. The impact on the costs of uncertainty in the estimates for informal care (carer perspective) was assessed in one-way deterministic sensitivity analysis. Uncertainty was explored in cost-effectiveness acceptability curves, covering a range of willingness-to-pay values, for a unit improvement in CSDD score, and for an additional QALY.

Results
Excluding informal care, over 39 weeks, the incremental cost for a unit improvement in CSDD score, compared with placebo, was £13,860 for sertraline, and £505 for mirtazapine; and it was £321 for mirtazapine, compared with sertraline. The incremental cost per QALY gained, over the same period, compared with placebo, was £23,100 for sertraline, and £8,080 for mirtazapine. Mirtazapine dominated sertraline, as it was more effective and less costly.

Including informal care, the incremental cost for a unit improvement in CSDD score, compared with placebo, was £14,100 for sertraline, and £1,382 for mirtazapine; and it was £2,012 for mirtazapine compared with sertraline. The incremental cost per QALY gained, compared with placebo, was £23,500 for sertraline, and £22,120 for mirtazapine. Mirtazapine dominated sertraline.

The cost-effectiveness acceptability curve for mirtazapine, compared with placebo, showed that, at a willingness-to-pay of zero for a unit improvement in CSDD score, the mirtazapine was cost-effective in around 30% of simulations; at a threshold of £5,000 this rose to 80% and stayed at this level up to £30,000.

At a threshold of zero for an additional QALY, excluding unpaid care costs, mirtazapine was cost-effective in around 14% of simulations, rising to around 20% at a £30,000 threshold. Including unpaid care costs, it was cost-effective in 89% of simulations, rising to around 100% at a £30,000 threshold.

Altering the carer costs in the sensitivity analysis did not alter the findings.

Authors’ conclusions
The authors concluded that neither intervention was cost-effective in reducing depression scores, but if unpaid carer costs and quality of life were analysed, mirtazapine appeared to be cost-effective.

CRD commentary
Interventions:
The interventions appear to have been appropriate. Dosages for the two interventions were clearly reported. The authors justified their choice of interventions, stating that they were two of the most commonly used classes of anti-depressants. They did not discuss other relevant alternatives.

Effectiveness/benefits:
The effectiveness evidence was from a randomised controlled trial, which potentially had good validity. Independent randomisation was conducted, but it was not clear if allocation concealment was maintained. The method used to measure the CSDD scores was not reported. The methods used to measure and value the QALYs were clear, for those measures obtained from the patients, but not clear for those measures obtained from society. The results for the effectiveness and benefit outcomes were clearly reported. The benefits were not discounted, which was reasonable given the short time horizon (39 weeks).
Costs:
The resource use and costs were clearly reported. The methods and sources used for the resource use and costs were clearly reported. The costs were appropriate for the two perspectives. The list of service use items was comprehensive. The costs were specific to the UK. No discounting was applied, which was reasonable given the short time horizon.

Analysis and results:
Limited trial methods and patient characteristics were reported. The number of bootstrap re-samples for the cost-effectiveness acceptability curves was not reported; this affects their reliability. A full incremental analysis was completed, for both perspectives, and the results were clearly reported. Appropriate methods were used to assess uncertainty, and the results were clearly reported. A key limitation was the short time horizon: if the costs or benefits differed after 39 weeks, the results may not be accurate. The authors noted that there were some missing data from the Client Service Receipt Inventories; appropriate imputation was used. Also, the analysis relied on self-reported hours spent supporting trial participants, which means that the costs may be inaccurate. They stated that their sample included patients with probable and possible dementia, making it representative of clinical practice, but for patients with Alzheimer's disease and mixed dementia only, rather than subtypes, such as vascular dementia. They recommended further research on mirtazapine, for behavioural and psychological symptoms, in dementia patients.

Concluding remarks:
The study methods and reporting were good, and the authors' conclusions appear to be appropriate.

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