Cost-effectiveness: cholinesterase inhibitors and memantine in vascular dementia

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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.

CRD summary
This study evaluated the incremental cost-effectiveness of cholinesterase inhibitors and memantine for mild-to-moderate vascular dementia. The authors concluded that, compared with standard care, cholinesterase inhibitors and memantine had small benefits in cognition and were all more costly. If an active treatment was approved, donepezil 10mg was the most cost-effective. There were a few limitations to the study and the authors’ conclusions should be considered with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to assess the cost-effectiveness of cholinesterase inhibitors and memantine, for mild-to-moderate vascular dementia.

Interventions
The interventions were: memantine, 10mg twice daily; rivastigmine, 6mg twice daily; galantamine, 8 to 12mg twice daily; donepezil, 10mg daily; and donepezil, 5mg daily. These were compared with standard care, which did not include cholinesterase inhibitors, nor memantine, in the authors’ setting.

Location/setting
Canada/primary and secondary care.

Methods
Analytical approach:
A decision tree, with a time horizon of 24 to 48 weeks, was used to synthesise the effect and cost data. The authors stated that a societal perspective in a Canadian health care setting was used.

Effectiveness data:
The clinical evidence was from a published systematic review of randomised, parallel-group, double-blinded, placebo-controlled trials (Kavirajan, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). An indirect comparison was conducted to derive the direct estimates of the benefits and harms for the individual drugs. The main outcome was the incremental effectiveness in units of the Alzheimer’s Disease Assessment Scale cognitive subscale (ADAS-cog). Minor adverse effects, such as nausea, vomiting, diarrhoea, anorexia, and insomnia, were also included.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
A unit decrease in the ADAS-cog was the summary measure of benefit.

Cost data:
The cost categories included drugs, treatment monitoring, and physician services for minor adverse events. The unit costs, reported in 2008 Canadian dollars (CAD), were from recognised British Columbian sources, plus some data from a large retail pharmacy.
Analysis of uncertainty:
Probabilistic sensitivity analysis, using second-order Monte Carlo simulation, was performed to generate confidence intervals for the costs and effects, and cost-effectiveness confidence ellipses. The parameter distributions were reported.

Results
All drug strategies had statistically significant benefits compared with standard care. The improvement was 1.14 units (95% CI 0.63 to 1.66) with donepezil 5mg; 2.16 units (95% CI 1.38 to 2.97) with donepezil 10mg; 1.6 units (95% CI 0.75 to 2.43) with galantamine; 1.06 units (95% CI 0.01 to 2.06) with rivastigmine; and 1.86 units (95% CI 1.03 to 2.77) with memantine.

The additional costs compared with standard care were: CAD 862 (95% CI 851 to 873) with donepezil 5mg; CAD 831 (95% CI 812 to 850) with donepezil 10mg; CAD 847 (95% CI 829 to 866) with galantamine; CAD 922 (95% CI 893 to 950) with rivastigmine; and CAD 872 (95% CI 854 to 890) with memantine.

Donepezil 10mg was the most cost-effective treatment, compared with standard care, with an expected incremental cost-effectiveness ratio of CAD 400.64 (95% CI 281 to 596) per unit decrease in the ADAS-cog. All other treatments, compared with standard care, were more costly and less effective than donepezil 10mg.

Authors’ conclusions
The authors concluded that, compared with standard care, cholinesterase inhibitors and memantine were all more costly, with only small benefits in cognition. If cholinesterase inhibitors were approved for mild-to-moderate vascular dementia, donepezil 10mg should be chosen by policymakers.

CRD commentary

Interventions:
The reporting of the interventions was sufficient and they appear to have represented all the relevant options.

Effectiveness/benefits:
The authors stated that the clinical estimates were from a systematic review, but no further details were provided and an assessment of the quality of this review was not possible. The authors acknowledged that there was a lack of data on utility and the time horizon was short. They also suggested that the clinical estimates, which were derived from separate trials, were open to confounding. There was also concern about the relevance of the ADAS-cog for vascular dementia, and that many of the patients in the trials probably had mixed dementia. All of these issues were highlighted and discussed and, whilst they impact on the results, the extent of this is unknown.

Costs:
The perspective was reported to have been that of society, but productivity costs were not included. This was probably due to the short time horizon and the minimal impact that these costs would have had in a 24-week period. The authors also excluded other major costs, such as community support services and long-term care, which are significant categories, but would have had little impact on the 24-week costs. The only costs considered, besides drug costs, were physician services and these were based on assumptions and not actual data. It is likely that the costs considered were sufficient, given the time horizon, but the omission of other resources and costs should be carefully considered in transferring the results to other settings.

Analysis and results:
The authors stated that they performed an incremental analysis, but all the interventions appear to have been compared with standard care. In an incremental analysis the treatments are ranked according to their costs or effects and each one is compared with the next best alternative. An indirect comparison was used for the effectiveness estimates, but the methods were not reported. These issues are unlikely to have had a huge impact on the results, but the reporting of these methods would have allowed a more informed assessment to be made. The impact of uncertainty was reasonably addressed and the confidence ellipses were clearly presented.

Concluding remarks:
There were a few limitations to the study and the authors’ conclusions should be considered with caution.

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