Economic evaluation of the impact of memantine on time to nursing home admission in the treatment of Alzheimer disease
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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 assessed the cost-effectiveness of adding memantine to the usual cholinesterase inhibitor treatment for patients with Alzheimer's disease. The authors concluded that the addition of memantine was cost-effective, compared with a cholinesterase inhibitor alone. The methods were valid, but the clinical evidence was weak. Further studies are needed to support the authors’ findings.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of adding memantine to the usual cholinesterase inhibitor treatment for patients with Alzheimer's disease.

Interventions
A cholinesterase inhibitor, donepezil, rivastigmine, or galantamine, was compared against memantine plus a cholinesterase inhibitor.

Location/setting
Canada/community.

Methods
Analytical approach:
The analysis was based on a Markov model, with a seven-year time horizon. The authors stated that it was carried out from two perspectives, that of society and that of the Canadian health care system.

Effectiveness data:
Most of the clinical inputs were from an observational study of 289 patients who received a cholinesterase inhibitor alone and 140 patients who received memantine plus a cholinesterase inhibitor. This study had a follow-up of up to seven years and provided the transition probabilities between most of the health states in the model. The probability of death was from Canadian survival tables and was assumed to be the same for both interventions. The time to nursing home admission was a key input for the model.

Monetary benefit and utility valuations:
The utility values were from a published study that elicited preferences from patients with Alzheimer's disease.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 5%.

Cost data:
The economic analysis from the perspective of the health care system included the costs of medication, and care in the community or in nursing homes. For the societal perspective, the costs of the direct care and supervision provided by caregivers were added. The medication costs were based on the official reimbursement rates and the relative market
share for each cholinesterase inhibitor. The costs of care in the community and in nursing homes were from the Canadian Study of Health and Aging, which was a large-scale epidemiology study. The societal costs were from a published study. All costs were in Canadian dollars (CAD) and the price year was 2007. A 5% annual discount rate was applied.

Analysis of uncertainty:
In a scenario analysis, the patients' demographic characteristics were based entirely on the observational study and differed between groups. Deterministic sensitivity analyses were carried out, varying the costs and utilities within published or arbitrarily defined ranges of values. Best- and worst-case scenarios for the probability of institutionalisation were considered. A probabilistic sensitivity analysis was performed using conventional distributions and 10,000 Monte Carlo simulations.

Results
The expected QALYs were 2.82 with a cholinesterase inhibitor and 3.08 with the addition of memantine. The projected costs were CAD 122,888 with the cholinesterase inhibitor and CAD 101,497 with memantine, from the societal perspective, and CAD 68,666 with the cholinesterase inhibitor and CAD 38,154 with memantine, from the perspective of the health care system.

In the base case, memantine was dominant, as it was more effective and less expensive than a cholinesterase inhibitor, for both perspectives. The conclusion was similar in the scenario analyses and all the sensitivity analyses, even in the worst-case scenario. Memantine was dominant in 100% of the simulations from a health care system perspective and in 99.8% of simulations from the societal perspective.

Authors' conclusions
The authors concluded that memantine plus the usual cholinesterase inhibitor treatment was cost-effective, compared with a cholinesterase inhibitor alone.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as the proposed intervention was compared against the usual medications for Alzheimer's disease, which were considered as a group, on the basis of their market share. The dosages were not given.

Effectiveness/benefits:
The clinical inputs were mainly from an observational study conducted in the USA. The authors acknowledged some limitations of this study, such as the risk of selection bias (there were gender and age differences between the two groups), potential differences between the US and Canadian management of patients, and difficulty generalising the results to all patients with Alzheimer's disease. These were the main limitations of this analysis, but the results were generally stable to changes in the model parameters. The authors justified their use of QALYs as the summary benefit measure because of the substantial impact of Alzheimer's disease on patients’ quality of life. The derivation of the utility values was not fully described, but the authors stated that the weights were considered appropriate by the National Institute for Health and Clinical Excellence (NICE).

Costs:
The two perspectives were appropriate and the cost categories appear to have been appropriate. Most of the costs were presented as category totals and were not broken down into individual items. Most of the data were from a Canadian study, the methods of which were not reported, but the authors stated that this study was used as reference for Canadian patients with Alzheimer's disease. Reflation exercises will be possible as the price year was reported. Variations in the cost estimates were considered in the sensitivity analyses.

Analysis and results:
The results were clearly reported. The costs and benefits were combined using average cost-utility ratios, and an incremental analysis allowed the identification of the dominant strategy. Conventional discounting was applied to the model outcomes. Appropriate methods were used to assess the uncertainty and the results were clearly reported. The authors acknowledged the main limitations to their study, as mentioned earlier. They stated that some assumptions...
were conservative against memantine. The transferability of the results was not explicitly discussed, but the costs were varied over wide ranges, which might apply to other countries.

Concluding remarks:
The methods were valid, but the clinical evidence was weak. Further studies are needed to support the authors’ findings.

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