Mortality and treatment costs have a great impact on the cost-effectiveness of disease modifying treatment in Alzheimer's disease – a simulation study

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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 cost-effectiveness of a hypothetical disease-modifying treatment for Alzheimer's disease. The authors concluded that it was reasonable to think that the treatment was cost neutral, from a Swedish willingness-to-pay perspective. The analysis and results were clearly presented, but the model assessed a hypothetical treatment with insufficient evaluation of uncertainty. It is unclear if these results could be useful for decision-makers, and they should be treated with caution.

Type of economic evaluation
Cost-utility analysis

Study objective
This study evaluated the cost-effectiveness of a hypothetical disease-modifying treatment for Alzheimer's disease.

Interventions
The hypothetical treatment was compared with standard care. Disease-modifying treatment consisted of immunotherapy or other potential treatment. Standard care consisted of cholinesterase inhibitors and memantine.

Location/setting
Sweden/social care.

Methods
Analytical approach:
The economic evaluation used a 20-year Markov model to simulate the costs and benefits of disease progression and survival, for a cohort of Swedish patients with cognitive impairment or dementia. The model had five states: minor cognitive impairment; mild, moderate, and severe Alzheimer's disease; and death. The authors stated that a societal perspective was taken.

Effectiveness data:
Patient characteristics were from Swedish prevalence statistics. The conversion rate was the primary measure of effectiveness. This was the rate at which patients with minor cognitive impairment developed mild Alzheimer's disease. There were no effectiveness data for the treatment. It was assumed that it halted the conversion from minor cognitive impairment, for half the patients, and that overall survival was improved. Patients who started the model in the minor cognitive impairment state had a probability of transition to mild Alzheimer's disease that was based on a systematic review of minor cognitive impairment. The probability of death in the minor cognitive impairment state was based on Swedish epidemiological data. The transition probabilities between other states were from the Kungsholmen Project. The states and progression were defined using the Mini Mental State Examination.

Monetary benefit and utility valuations:
Utility scores were from a Swedish study of utility for patients with minor cognitive impairment and dementia. These scores were assigned to each model state.

Measure of benefit:
The primary measure of benefit was quality-adjusted life-years (QALYs). The benefits were discounted at 3% annually.
Cost data:
The costs of disease-modifying treatment were assumed. The resource use data, for each model state, were from the Nordanstig-Kungsholmen Project. The unit costs were from a Swedish National Board of Health and Welfare report. State-specific costs included long-term institutional care, hospital care, hospital clinic visits, day care, home services, and informal care. Informal care assumed a mix of employed and retired informal carers. The costs were in 2005 Swedish kronor (SEK). They were discounted at 3% annually.

Analysis of uncertainty:
One-way and probabilistic sensitivity analyses were conducted. The discount rates were varied between zero and 5%; the conversion risk was increased from 10% to 25%; the treatment drug costs were assumed to be similar to those of standard care (SEK 10,000) or much greater (SEK 300,000); the costs of informal care were raised to reflect professional care; and no survival benefit with treatment was assumed. The probabilistic sensitivity analysis varied mortality and the rate of conversion from minor cognitive impairment to Alzheimer’s disease, for 1,000 simulations.

Results
The total cost per case was SEK 1,129,695 for disease-modifying treatment and SEK 890,634 for standard care; an incremental cost of SEK 239,061 with the treatment.

Survival with treatment was 8.7 years, and with standard care was 7.8 years. Disease-modifying treatment produced 5.33 QALYs per case, while standard care produced 4.52 QALYs; an incremental QALY gain of 0.82 with the treatment.

The incremental cost-effectiveness ratio (ICER) with treatment, was SEK 293,002 per QALY gained, which was under the estimated willingness-to-pay threshold for Sweden of SEK 600,000 per QALY gained.

The authors stated that all sensitivity analyses, except increasing the treatment drug cost to SEK 300,000, produced ICERs below SEK 600,000 per QALY gained. Increasing the drug cost produced an ICER of SEK 2.1 million per QALY gained. The probabilistic analysis found that disease-modifying treatment was cost-effective in 99% of simulations.

Authors’ conclusions
The authors concluded that it was reasonable to think that disease-modifying treatment was cost neutral, from a Swedish willingness-to-pay perspective.

CRD commentary
Interventions:
There was little explanation of the dosages or protocols for the cholinesterase inhibitors in standard care. The disease-modifying treatment was not based on any real intervention. It was not possible to ascertain if standard care represented the care given in practice.

Effectiveness/benefits:
The effectiveness data for standard care appear to have been from appropriate sources. The authors stated that the effectiveness of the hypothetical treatment was assumed for conversion to Alzheimer’s disease, and for survival in the model states. It was unclear whether the conversion assumption was reasonable, and the mechanism for determining its effects on survival in other states was not reported. It was unclear whether treatment was assumed to have any effect on progression beyond conversion from minor cognitive impairment to mild Alzheimer’s disease, but this was analysed in the sensitivity analyses. These analyses assessed a higher risk of conversion, but not a lower risk. As the treatment was hypothetical, it is not possible to assess how a real treatment would perform.

Costs:
The study perspective was clearly stated and the costs appear to have been appropriately derived. The costs for disease-modifying treatment were assumed to be roughly five times more than those of standard care. Only a brief justification for this assumption was provided; this cost could have been varied more in the sensitivity analyses.

Analysis and results:
The model was adequately described and the results were clearly presented. Given the number of assumptions, additional sensitivity analyses should have been performed, particularly on the cost of treatment, and it is not clear if the results could be of practical use to decision-makers.

Concluding remarks:
The analysis and results were clearly presented, but the model assessed a hypothetical treatment with insufficient evaluation of uncertainty. It is unclear if these results could be useful for decision-makers, and they should be treated with caution.

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