Health economic effect of donepezil treatment for CDR 0.5 converters to Alzheimer's disease as shown by the Markov model
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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 compared donepezil therapy for patients with a clinical dementia rating (CDR) of 1.0; of 0.5; or of 0.5 who were identified as converters to 1.0. The authors concluded that the annual chance of decline had to be reduced from 15% to 12%, through the detection of CRD 0.5 converters, to produce an economic benefit. The reporting and discussion of the analysis was sufficient. The study was exploratory in nature and the conclusions should be considered in this light.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to assess the cost and health effects of donepezil for the treatment of patients with mild cognitive impairment, of whom about 15% progress to dementia each year. A hypothetical cohort of patients with mild cognitive impairment, defined by a clinical dementia rating (CDR) of 0.5, was evaluated.

Interventions
Three strategies were considered for donepezil treatment, at 3mg per day for two weeks then 5mg per day. The strategies were: donepezil therapy for all patients with a CDR of 1.0, assuming a 15% annual transition rate from CDR 0.5 to CDR 1.0; donepezil therapy for all patients with a CDR of 0.5, assuming an annual transition rate from CDR 0.5 to CDR 1.0 of 14%, 13%, 12%, 11%, or 10%; and donepezil therapy for a subgroup of patients with a CDR of 0.5 who were identified as converters to CDR 1.0, assuming an annual transition rate from CDR 0.5 to CDR 1.0 of 14%, 13%, 12%, 11%, or 10%.

Location/setting
Japan/out-patient care.

Methods
Analytical approach:
A Markov health transition model was constructed to investigate the impact of treatment on patient transitions through the CDR health states. The model synthesised published data from various sources including studies, epidemiological data, and national cost schedules. The authors stated that the study took a payer’s perspective and the analysis was covered a two-year period.

Effectiveness data:
The main clinical endpoints were the expected dementia progression rates and deaths. The annual progression rates from CDR 0.5 through the severity levels to CDR 3.0 and death, without donepezil treatment, were from previous studies (Petersen, et al. 1999, Morris, et al. 1989, and Neumann, et al. 1999, see ‘Other Publications of Related Interest’ below for bibliographic details). Author assumptions were made for a range of progression rates, with donepezil treatment.

Monetary benefit and utility valuations:
The health state values for CDRs 1.0 to 3.0 were those reported in previous studies that used the Health Utilities Index III (Feeny, et al. 2002, and Ikeda, et al. 2002, see ‘Other Publications of Related Interest’ below for bibliographic
The authors assumed two values, 0.34 and 1.0, for the CDR 0.5 health state and the results for both values were presented.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs), which were discounted at a rate of 3%.

Cost data:
The direct medical costs included medications, out-patient visits, and medical care for patients with Alzheimer’s disease. The values for medications and visits were estimated from published national sources. Assumptions for resource use were made and the costs were based on fees in hospitals with more than 200 beds, and pharmacies filling more than 4,000 prescriptions. The care costs were calculated based on data from the Long-term Care Insurance System. The costs were discounted at 3% and reported in Japanese yen (JPY).

Analysis of uncertainty:
Various scenarios were tested for the annual transition probabilities for the progression rates from CDR 0.5 to CDR 1.0, ranging from 10% to 14%; these scenarios formed a major part of the analysis.

Results
The total costs, over two years, for donepezil treatment for all patients with a CDR of 1.0 (15% transition rate) were JPY 341,412. The total costs for donepezil treatment for all patients with a CDR of 0.5 ranged from JPY 709,713 to JPY 639,487, with annual transition rates ranging from 14% to 10%. The total costs for donepezil treatment for converters, with a CDR of 0.5, ranged from JPY 375,090 to JPY 291,192, with annual transition rates from 14% to 10%.

Over two years, with a utility score for CDR 0.5 of 0.34, the estimated mean QALYs for treatment were 0.612 for all CDR 1.0 patients, and ranged from 0.613 to 0.620 for all CDR 0.5 patients and for converters only. With a utility score for CDR 0.5 of 1.0, the estimated mean QALYs for were 1.529 for all CDR 1.0 patients, and ranged from 1.550 to 1.635 for all CDR 0.5 patients and for converters.

With a utility of 0.34, the average cost per QALY ratio was JPY 558,236 for all CDR 1.0 patients, ranged from JPY 1,157,236 to 1,031,097 for all CDR 0.5 patients, and ranged from JPY 611,627 to JPY 469,513 with treatment for converters.

Authors’ conclusions
The authors concluded that it was necessary to reduce the annual transition probability from 15% to 12%, through the detection and treatment of CRD 0.5 converters, to produce an economic benefit. They suggested that the early detection of CDR converters was necessary and important for health policy planning.

CRD commentary
Interventions:
The authors provided brief descriptions of the treatment strategies. There was only one drug used in the three scenarios and this might have been the only treatment available, but this was not discussed. The evaluation focused on the appropriate strategy for treatment, rather than alternative treatments.

Effectiveness/benefits:
The authors made critical assumptions for the effectiveness of donepezil treatment in delaying the natural progression of cognitive impairment. This appears to have been the main focus of the paper, enabling them to ascertain the scenario in which donepezil treatment was economically viable. The utilities for the most important health state in the model (CDR 0.5) were also assumed by the authors. This means that the study should be regarded as exploratory until better quality evidence on the efficacy of donepezil and the utility scores becomes available; the authors reported this as an exploratory analysis.

Costs:
The direct medical costs were analysed and appear to have been appropriate for the perspective. Brief details on the
resource types and how they were valued were provided. There was no information on how these resources were measured and the unit costs were not stated. The price year was not provided and no cost adjustments were performed. The lack of these details might be due to the nature of the analysis.

Analysis and results:
The model structure was explicitly described and illustrated and all the inputs, data sources, and assumptions were provided. The costs and effects were combined into average cost-utility ratios. Incremental cost-utility ratios are often preferred in economic evaluations, as these indicate the additional cost for any additional QALYs between two options. Sensitivity analyses to test how robust the final results were to variations in the assumptions and data inputs were not undertaken, but changes in the rate of progression from CDR 0.5 to CDR 1.0 were thoroughly explored and the exploratory nature of this analysis means that this might have been sufficient. Further testing would not have allowed the authors to draw more robust conclusions.

Concluding remarks:
The reporting and discussion of the analysis undertaken was sufficient. The study was exploratory in nature and the conclusions should be considered in this light.

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