Economic evaluation of donepezil treatment for Alzheimer's disease in Japan
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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.

Health technology
The use of donepezil (Aricept) for the treatment of mild and moderate Alzheimer's disease (AD). Patients were assumed to receive donepezil at 3 mg/day for 1 week after the start of treatment and at 5 mg/day thereafter. The comparator was standard therapy.

Type of intervention
Secondary prevention and palliative care.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients with mild to moderate AD.

Setting
The setting was secondary care. The economic study was carried out in Japan.

Dates to which data relate
The effectiveness data were derived from studies published in 1995 and 2000. The time period during which resource use was measured was unclear. The unit costs for the drugs were based on drug prices on 1 April 2000.

Source of effectiveness data
The effectiveness data for donepezil were derived from a single study, while the effectiveness data for standard therapy were derived from another single study. The estimates were supplemented with some assumptions.

Link between effectiveness and cost data
The costing was carried out retrospectively on a different sample of patients to that used in the effectiveness study for donepezil.

Modelling
A Markov Model was created to characterise the progression of patients between the AD states. The authors estimated two sets of transition probabilities, those with standard therapy and those with donepezil. The authors also estimated quality of life (QoL) data. This allowed them to estimate the difference, in terms of the quality-adjusted life-years (QALYs), between the two treatments.
Outcomes assessed in the review
The authors assessed the transition probabilities between pathologic states of AD for patients treated with standard therapy and those treated with donepezil.

Study designs and other criteria for inclusion in the review
The effects of donepezil were estimated from a placebo-controlled trial. The transition probabilities were derived using data from a US database.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
The authors appear to have chosen sources that provided the data necessary for their study.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Two primary studies were included in the review.

Methods of combining primary studies
The authors used a single source for each effectiveness estimate. Therefore, they did not combine the results of the primary studies.

Investigation of differences between primary studies
Not reported.

Results of the review
The 4-week transition probability from mild to moderate AD was 0.597-fold that of the placebo group (95% confidence interval, CI: 0.23 - 1.554).

The 4-week transition probability from moderate to mild AD was 6.899-fold that of the placebo group (95% CI: 0.791 - 60.207).

These factors were multiplied with the relevant standard therapy transition probabilities specified below. However, this only appears to account for two of the probabilities.

The transition probabilities of standard therapy were:

for mild to mild, 0.614;
for mild to moderate, 0.322;
for mild to severe, 0.042;
for mild to dead, 0.021;
for moderate to mild, 0.043;
for moderate to moderate, 0.565; 
for moderate to severe, 0.339; 
for moderate to dead, 0.053; 
for severe to severe, 0.847; and 
for severe to dead, 0.153.

Methods used to derive estimates of effectiveness
The authors supplemented their estimates with an assumption.

Estimates of effectiveness and key assumptions
The authors assumed that compliance was 100%, and that treatment was discontinued when severe AD was confirmed.

Measure of benefits used in the economic analysis
The summary measure of benefit was the QALYs. QoL scores were taken from a study that elicited patient preferences using the Health Utilities Index Mark III (HUI-3) questionnaire. This study elicited health related utilities in eight health dimensions (vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain) for the Canadian population. The benefits were discounted at a rate of 3% per annum.

Direct costs
The costing was carried out from the perspective of the third-party payer over a time horizon of 2 years. Both the direct costs to the hospital and the cost of drugs were included. The costs were discounted at a rate of 3% per annum. The authors estimated the costs from the two social insurance systems (medical care and long-term care). For long-term care, the costs were based on the maximum eligibility criteria, which were reported separately from the quantities. The drug costs were derived from the drug prices on 1 April 2000, and were reported separately. Resource use was not reported separately. Although not explicitly stated, the costing may have been based on claims data since the authors adopted the perspective of the third-party payer. A co-payment paid by "clients for both insurance systems" was included in the cost analysis.

Statistical analysis of costs
No statistical analysis of the costs was presented.

Indirect Costs
The authors did not include time lost from work due to AD, or gained in work as a result of treatment. Since AD may have a significant impact on QoL, this may have been a relevant factor.

Currency
Japanese yen (¥).

Sensitivity analysis
A one-way sensitivity analysis was carried out to test the duration of the effects of donepezil. The authors explored whether the transition probabilities for patients treated with donepezil were equivalent to the probabilities for patients treated with conventional therapy after 24, 52 and 76 weeks. This analysis was carried out because the trial of the effectiveness of donepezil lasted only 24 weeks. Thus, there was some uncertainty in the effectiveness of donepezil.
over time.

**Estimated benefits used in the economic analysis**
For patients with mild AD, the expected number of QALYs was 0.51 for those treated with standard therapy and 0.58 for those treated with donepezil.

For patients with moderate AD, the expected number of QALYs was 0.23 for those treated with standard therapy and 0.31 for those treated with donepezil.

The estimates were for a 2-year period. The QALYs were discounted at a rate of 3% per annum.

The authors did not calculate the incremental benefits.

**Cost results**
For patients with mild AD treated with standard therapy, the expected cost per patient was Y2,600,000 for 2 years. The corresponding cost for those treated with donepezil was Y2,560,000.

For patients with moderate AD treated with standard therapy, the expected cost per patient was Y4,880,000 for 2 years. The corresponding cost for those treated with donepezil was Y4,590,000.

The authors did not calculate the incremental costs.

**Synthesis of costs and benefits**
For patients with mild AD, when the treatment effects of donepezil were equivalent to standard therapy after 1.5 or 2 years, the incremental cost-effectiveness ratio yielded a cost-saving per QALY gained. The exact value of the saving was not reported.

For patients with mild AD, when the treatment effects of donepezil were equivalent to standard therapy after 1 year, the incremental cost-effectiveness was Y1,462,658 per QALY gained.

For patients with mild AD, when the treatment effects of donepezil were equivalent to standard therapy after 6 months, the incremental cost-effectiveness was Y6,756,958 per QALY gained.

For patients with moderate AD, when the treatment effects of donepezil were equivalent to standard therapy after 1, 1.5 or 2 years, the incremental cost-effectiveness ratio yielded a cost-saving per QALY gained. The exact value of the saving was not reported.

For patients with moderate AD, when the treatment effects of donepezil were equivalent to standard therapy after 6 months, the incremental cost-effectiveness was Y305,476 per QALY gained.

**Authors' conclusions**
Donepezil was dominant over conventional therapy for patients with mild to moderate Alzheimer's disease (AD).

**CRD COMMENTARY - Selection of comparators**
The authors compared donepezil with 'standard therapy'. The exact drug(s) or treatment regime(s) that comprised standard therapy were not stated. Therefore, the reader cannot evaluate whether the comparator treatments represent standard therapy in their own setting.

**Validity of estimate of measure of effectiveness**
The study used two primary studies, of which few details were reported. However, it was reported that the effectiveness
data were derived from a placebo-controlled trial. Nevertheless, it is impossible to assess the validity of the data. There were no Japanese transition probabilities available so the authors had no other options. However, the USA transition probabilities may not be generalisable to Japan. The methods used to derive the estimates of effectiveness were clearly reported.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled using the Markov Model and utilities taken from published literature. This was appropriate for the objectives stated by the authors. The benefits were appropriately discounted.

**Validity of estimate of costs**
The authors stated that the costing was carried out from the perspective of the third-party payer, but they did not list the precise resources for which the costs were estimated. Therefore, it is not possible to comment on whether all of the costs relevant to this perspective were estimated. Since no confidence intervals were estimated for the difference in cost between the two treatment regimes, it was unclear whether the cost-saving achieved by donepezil was statistically different from zero. However, since the authors found that donepezil was a dominant treatment, the costs associated with this treatment would have to rise substantially to alter the principle results that donepezil was a more cost-effective drug. The unit costs of the drugs were reported separately and the price year was reported.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies, pointing out similarities as well as differences in research methodologies. However, the issue of generalisability to other settings was not addressed. The authors did not present their results selectively. The authors reported a number of limitations to their study. For example, problems with their use of insurance data, the short duration of the trial from which the donepezil effectiveness data were taken, and the use of Canadian values to ascertain utilities.

**Implications of the study**
The authors did not make any recommendations for policy or practice following their study. They did, however, suggest that the costs of informal care for AD patients should be analysed in future.

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None stated.

**Bibliographic details**

**PubMedID**
11731713

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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