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*Title* **The Clinical and Cost Effectiveness of Donepezil, Rivastigmine, Galantamine, and Memantine for Alzheimer's Disease**

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www.hta.ac.uk/execsumm/summ1001.htm

## Aim

To review the best quality evidence on the clinical and cost effectiveness of donepezil, rivastigmine, and galantamine for mild to moderately severe Alzheimer's disease (AD) and of memantine for moderately severe to severe AD.

## Conclusions and results

For mild to moderately severe AD, the study suggested that all 3 treatments were beneficial when assessed using cognitive outcome measures. Global outcome measures were positive for donepezil and rivastigmine, but mixed for galantamine. Results for measures of function were mixed for donepezil and rivastigmine, but positive for galantamine. Behavior and mood measures were mixed for donepezil and galantamine, but showed no benefit for rivastigmine. Two published RCTs of memantine were included, suggesting it is beneficial based on functional and global measurements. The effect of memantine on cognitive and behavior and mood outcomes is less clear. Literature on the cost effectiveness of donepezil, rivastigmine, and galantamine was dominated by industry-sponsored studies that varied in methods and results.

Of the 3 UK studies, 2 report donepezil as not cost effective. Cost-effectiveness analysis undertaken in this review suggests that the cost per quality-adjusted life-year (QALY) exceeds 80 000 British pounds (GBP) for donepezil. Treatment reduces the mean time spent in full-time care by 1.42 to 1.59 months (over a 5-year period). From 4 published cost-effectiveness studies, 2 UK studies report additional costs with rivastigmine treatment. Cost-effectiveness analysis undertaken in this review suggests that the cost per QALY exceeds GBP 57 000 for rivastigmine. Treatment reduces the mean time spent in full-time care by 1.43 to 1.63 months (over a 5-year period). From 5 published cost-effectiveness studies, 1 UK study reports a cost per QALY of GBP 8693 for 16 mg galantamine treatment and GBP 10 051 for 24 mg galantamine treatment. Cost-effectiveness analysis undertaken in this review suggests that the cost per QALY exceeds GBP 68 000 for galantamine. Treatment reduces the time spent in full-time care by 1.42 to 1.73 months (over a 5-year period). From 2 published cost-effectiveness studies, 1 reports on an analysis for the UK, finding that memantine treatment saves cost and delays disease progression. Our review did not model the cost effectiveness of memantine separately. However, where alternative parameter inputs on the cost structure and utility values were used in a reanalysis (industry model), the cost effectiveness ranged between GBP 37 000 and GBP 52 000 per QALY.

## Recommendations

For donepezil, rivastigmine, and galantamine, the costs saved by reducing the mean time spent in full-time care do not adequately offset the costs of treatment to bring estimated cost effectiveness to levels generally accepted by NHS policy makers. It is difficult to draw conclusions on the cost effectiveness of memantine; it is suggested that further amendments to the potentially optimistic industry model (measure of effect) would offer higher cost per QALY estimates.

## Methods

A systematic review of the literature and an economic evaluation were undertaken.

## Further research/reviews required

Future research should address the quality of outcome measures, quality-of-life instruments for patients and carers, effects of interventions lasting beyond 12 months, comparisons of benefits between interventions, and predictions of disease progression.

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