A Markov model of the cost effectiveness of olanzapine treatment for agitation and psychosis in Alzheimer's 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
The study examined the cost-effectiveness of olanzapine, a new atypical antipsychotic treatment, for patients with Alzheimer's disease (AD) in comparison with no treatment, in order to identify the optimal strategy to reduce agitation and psychosis. The authors concluded that olanzapine represents a cost-effective treatment for AD patients with agitation and psychosis from the perspective of the US health care system. The quality of the study methodology was good in terms of both the sources used to derive the data and the transparent reporting of the methods and results.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective of the study was to examine the cost-effectiveness of olanzapine, a new atypical antipsychotic treatment, for patients with Alzheimer's disease (AD) in comparison with no treatment. The authors aimed to identify the optimal strategy to reduce agitation and psychosis, whilst also considering the side-effects of olanzapine and its cost. The typical patient was older than 65 years of age and was suffering from AD with psychosis and/or agitation.

Interventions
The study examined the use of olanzapine for the treatment of agitation and/or psychosis in patients with AD. The comparator was no treatment.

Location/setting
USA/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a Markov model that simulated patient progression and treatment in different scenarios. A patient's lifetime horizon (i.e. 13 years) was considered. The authors stated that the perspective of the US health system was adopted.

Effectiveness data:
The clinical estimates were derived from multiple sources, which might have been identified selectively. Data on treatment effectiveness for olanzapine were retrieved from a pivotal clinical trial, the Clinical Antipsychotics Trial of Intervention Effectiveness - Alzheimer's Disease (CATIE-AD), which enrolled 421 participants who were followed for up to 36 weeks. Transition probabilities among health states used for the decision model were obtained from the Consortium to Establish a Registry for Alzheimer's disease (CERAD) cohort, which is a longitudinal database enrolling over 1,100 US patients with long-term follow-up. Other estimates used in the model were derived from published studies, key features of which were reported.

Monetary benefit and utility valuations:
The utility values for specific health conditions were derived from the literature, on the basis of patients with schizophrenia. Other details of these studies were not given.

Measure of benefit:
The summary benefit measure was the quality-adjusted life-years (QALYs). These were estimated using the decision model. QALYs were discounted at an annual rate of 3%.

Cost data:
The cost items included in the analysis were grouped into direct and indirect costs. The direct costs were for physician visits, inpatient and outpatient hospital care, long-term care and medications. The indirect costs included the value of unpaid caregiving time. The unit costs and resource quantities for patients with AD were derived mainly from a cross-sectional study conducted in the USA. For medications, dosages were taken from the CATIE-AD trial and unit costs from the Red Book. The approach used to calculate all costs was described clearly. The costs were in US dollars ($) and the price year was 2006. Given the long timeframe of the analysis, an annual rate of 3% was applied to future costs.

Analysis of uncertainty:
A deterministic sensitivity analysis was undertaken to assess the impact of variations in transition probabilities, treatment effectiveness and costs on cost-utility ratios. Model inputs were varied in one-, two- and three-way sensitivity analyses.

Results
The total (13-year) cost per patient was $39,781 with olanzapine and $35,899 without olanzapine, but olanzapine resulted in an increase of 0.15 QALYs over a patient’s lifetime.

When only direct costs were considered, the incremental cost per QALY gained with olanzapine over no intervention was $37,331.

When the value of unpaid caregiving time was considered, the incremental cost per QALY gained with olanzapine over no intervention was $13,230.

The sensitivity analysis showed that, when only direct costs were considered, the model results were robust to variations in clinical and economic inputs. When the total costs were calculated (including the value of unpaid caregiving time), the incremental cost per QALY varied substantially. Nevertheless, except for two extreme scenarios, the incremental cost per QALY remained below the commonly cited threshold of $50,000 per QALY gained with olanzapine.

Authors’ conclusions
The authors concluded that olanzapine represents a cost-effective treatment for AD patients with agitation and psychosis from the perspective of the US health care system. Future studies should be carried out to corroborate these findings when atypical antipsychotics become generic and as more information on health utilities in AD becomes available.

CRD commentary
Interventions:
The authors justified the choice of the comparators, i.e. olanzapine, which was more effective than other atypical antipsychotics in the CATIE-AD trial, and no treatment, which reflected the current approach in their own setting given the heavy side-effects of treatment with conventional antipsychotics.

Effectiveness/benefits:
The authors stated that the clinical data were derived from a selection of known, relevant studies in order to include the best evidence available. Each source used in the analysis was extensively described and the use of the pivotal trial appears to have been appropriate to the estimation of the treatment effect. A large prospective study was used for transition probabilities. It was noted that some estimates were not available from AD studies and were retrieved from populations of patients with similar symptoms, such as schizophrenia. In general, the authors justified the selection of the clinical estimates and, overall, the quality of the evidence appears to have been good. Information on the derivation of utility weights used in the calculation of QALYs was less clear. For example, the method used to elicit preferences for health states was not described. QALYs are an appropriate benefit measure and can be compared with the benefits of other health care interventions. Furthermore, quality of life is a key aspect of health for patients with AD and their caregivers.
Costs:
The analysis of the costs was consistent with the perspective of the analysis. A breakdown of the cost items was presented and unit costs were given for most items. However, some costs were presented as macro-categories. The information on resource use and costs was derived from a published study, the main characteristics of which were reported. The methodology used to calculate the costs was described in detail. Other aspects of the analysis, such as the price year and use of discounting, were reported. Overall, the cost analysis was carried out satisfactorily.

Analysis and results:
The synthesis of the costs and benefits was appropriate given that incremental ratios were calculated. The results of both the base-case and sensitivity analyses were generally presented clearly. The exception was the expected QALYs, which were reported only as incremental values. The issue of uncertainty was addressed in the sensitivity analysis, in which key model inputs were varied simultaneously and alternative scenarios were considered.

Concluding remarks:
The quality of the study methodology was good. The sources used were described clearly and the results were presented in detail. The authors' conclusions appear valid.

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Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Alzheimer Disease /complications /psychology; Antipsychotic Agents /economics /therapeutic use; Benzodiazepines /economics /therapeutic use; Cohort Studies; Cost-Benefit Analysis; Drug Costs; Ethnic Groups; Humans; Markov Chains; Mortality; Proportional Hazards Models; Psychomotor Agitation /drug therapy /etiology; Psychotic Disorders /drug therapy /etiology; Quality-Adjusted Life Years; Treatment Outcome; United States /epidemiology

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