Assessing the cost-effectiveness of the rivastigmine transdermal patch for Alzheimer's disease in the UK using MMSE- and ADL-based models

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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 rivastigmine patches or capsules for patients with mild-to-moderate Alzheimer's disease, compared with best supportive care. The authors concluded that rivastigmine patches and capsules were cost-effective alternatives to best supportive care. They stated that incorporating activities of daily living evidence made a marginal, but important difference to the estimates. The methods and reporting of the study were satisfactory and the authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study evaluated the cost-effectiveness of rivastigmine patches or capsules for patients with mild-to-moderate Alzheimer's disease, compared with best supportive care.

Interventions
The interventions were rivastigmine patches (9.5mg per day) and rivastigmine capsules (12mg per day). These were compared with best supportive care.

Location/setting
UK/primary care.

Methods
Analytical approach:
Two analytic models were used to synthesise the effectiveness and cost data. One model was based on Mini-Mental State Examination (MMSE) scores. The second model also included activities of daily living (ADL) measured by the Alzheimer's Disease Cooperative Study scale and converted to Townsend Disability Scale scores. The time horizon was five years. The authors stated that a health and social care perspective was used.

Effectiveness data:
The clinical evidence was from a double-blind randomised controlled trial (RCT), the Investigation of transDermal Exelon in Alzheimer's disease (IDEAL) trial. This trial compared the efficacy and safety of rivastigmine patches (250 patients) with rivastigmine capsules (256 patients) and placebo (281 patients). Patients were followed-up for 24 weeks, and after a further 28-week open-label extension. The main outcome was the MMSE score. Published equations were used to predict the natural decline of patients' MMSE scores and the probability of institutionalisation after the IDEAL trial period and extension. Long-term ADL scores were derived using linear regression and data from the clinical trial. The disease progression models were validated using MMSE and ADL data from a two-year RCT comparing rivastigmine and donepezil in patients with Alzheimer's disease.

Monetary benefit and utility valuations:
The utility values were estimated using regression to convert the MMSE scores to utility values, based on published mapping functions for the Health Utilities Index version III.

Measure of benefit:
The measures of benefit were quality-adjusted life-years (QALYs) and the MMSE scores. Both of these were discounted at an annual rate of 3.5%.

Cost data:
The cost categories included institutionalisation, standard community care, and drug acquisition. Clinical monitoring costs for a further three months were included for patients who discontinued treatment. The drug cost was based on UK NHS prices and other costs were from published UK sources, such as the Personal Social Services Unit. All costs were in UK pounds sterling (£), the price year was 2008, and discounting was applied at an annual rate of 3.5%.

Analysis of uncertainty:
A one-way sensitivity analysis was performed to assess the impact of varying the key model inputs, such as the probability of institutionalisation, the inclusion of informal care costs, and the type of regression used to predict the ADL scores. A probabilistic sensitivity analysis, using Monte Carlo simulation, was performed to assess the uncertainty in all the parameters of the model. The results were presented in a cost-effectiveness acceptability curve and cost-effectiveness scatter plots.

Results
MMSE model: Compared with best supportive care, the incremental costs were £1,174 for rivastigmine patches, and £1,336 for rivastigmine capsules. The QALYs gained were 0.1109 for rivastigmine patches, and 0.0882 for rivastigmine capsules.

The incremental cost-effectiveness ratio (ICER) was £10,579 per QALY gained or £158 per MMSE score gained with rivastigmine patches, and £15,154 per QALY gained or £226 per MMSE score gained with capsules. Compared with the capsules, the patches were associated with marginally more QALYs (0.0228) and slightly lower costs (a difference of −£162 over five years).

MMSE-ADL model: Compared with best supportive care, the incremental costs were £1,011 with rivastigmine patches and £1,213 with rivastigmine capsules. The QALYs gained were identical to those in the MMSE model.

The ICERs were £9,114 per QALY gained or £136 per MMSE score gained with rivastigmine patches, and £13,758 per QALY gained or £205 per MMSE score gained with capsules. Compared with capsules, the patches were associated with more QALYs and MMSE score gained, and slightly lower costs (a difference of −£202 over five years).

The main difference between the two models was more institutionalised days avoided with rivastigmine versus best supportive care in the MMSE-ADL model than in the MMSE model. The probabilistic sensitivity analysis showed that compared with best supportive care, the patches were cost-effective at a willingness-to-pay threshold of £20,000 per QALY in 100% of simulations and the capsules were in 89.7% of simulations (MMSE model).

Authors’ conclusions
The authors concluded that both their models suggested that rivastigmine patches and capsules were cost-effective alternatives to best supportive care. They stated that incorporating ADL evidence made a marginal, but important difference to the estimates.

CRD commentary
Interventions:
The comparators were selected to include the available treatments for patients with mild-to-moderate Alzheimer's disease, including the usual care.

Effectiveness/benefits:
The treatment effect data were from an appropriately selected RCT. The key information on this trial, such as its design, sample size, and follow-up periods, was given. Its design should have produced internally valid data and generalisable findings. Only one trial was used and the authors did not report whether a systematic review was performed to identify it, making it impossible to determine if all the relevant evidence was considered. QALYs were an appropriate measure of benefit, given the impact of Alzheimer's disease on quality of life. The utility derivation was...
well reported and it considered the health status of the Alzheimer's disease patients in the clinical trial.

Costs:
The costs were consistent with the perspective and all the relevant costs appear to have been considered. Only the category totals for the costs were presented and the unit costs were not given separately from the resource quantities, which limits the ability to replicate the study. The costs were from published studies. The price year was reported and discounting was appropriately applied.

Analysis and results:
The results were clearly reported and an incremental synthesis of the costs and benefits was well conducted. The overall uncertainty in the model parameters was investigated in both deterministic and probabilistic sensitivity analyses. The results were generally robust to the variations investigated. The model was validated using data from another published trial. The use of two models provided an interesting comparison of the inclusion or exclusion of cognitive measures of executive and global function, such as ADL, to predict disease progression and the probability of institutionalisation. The authors provided a discussion of the limitations of their study, such as the use of regression analyses (relating ADL to MMSE) that were based on relatively short-term data.

Concluding remarks:
The methods and reporting of the study were satisfactory and the authors’ conclusions appear to be appropriate.

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