Cost-utility model of rasagiline in the treatment of advanced Parkinson's disease in Finland

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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 rasagiline and entacapone as adjunctive therapies to levodopa in Parkinson's disease (PD) with motor fluctuations. Defined daily doses (DDD) from the World Health Organization were used.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study used modelling techniques. The costs and benefits were studied in a hypothetical cohort of patients with PD who were experiencing motor fluctuations.

Setting
The setting was unclear, but it was likely to have been the community. The economic analysis was conducted in Finland.

Dates to which data relate
The effectiveness and resource use data in the model were derived from papers published between 1998 and 2005. The costs were adjusted to 2004. The drug costs were calculated using prices from 2005.

Source of effectiveness data
The effectiveness data were derived from a review of the literature.

Modelling
A literature-based Markov model was developed to simulate patient progression through three health states. The health states studied were defined by the time spent in the "off" state per waking day (>25% off time per day, <25% off time per day). The third health state was "dead". The time horizon for the model was 2 years and the cycle length was 4 months. The software used was Data version 4.

Outcomes assessed in the review
The initial distribution of patients in the different health states, the drug-specific probabilities of improvement and deterioration, the time spent in the off-state and the mortality probability were derived from the review. Utilities per health state were also assessed from the literature.
Study designs and other criteria for inclusion in the review
The study design and criteria for inclusion in the review were not specified.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

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

Number of primary studies included
Approximately 3 studies were included in the review.

Methods of combining primary studies
The primary studies were not combined.

Investigation of differences between primary studies
Not reported.

Results of the review
The outcomes are too numerous to report in this abstract.

The transition probability for improvement from >25% to ≤ 25% off time in the first cycle was 56.3 (95% confidence interval, CI: 46.5 to 65.5) with rasagiline, 50.6 (95% CI: 41.2 to 59.7) with entacapone and 32.6 (95% CI: 24.0 to 42.6) with standard care.

The probability for deterioration from ≤ 25% to >25% off time in the first cycle was 11.8 (95% CI: 6.8 to 17.9) with rasagiline, 9.9 (95% CI: 5.2 to 15.8) with entacapone and 15.9 (95% CI: 6.6 to 17) with standard care.

The mean utility was 0.68 (standard deviation, SD=0.195) for patients experiencing 25% or less off time per day and 0.39 (SD=0.195) for patients experiencing greater than 25% off time per day.

Measure of benefits used in the economic analysis
The primary effectiveness measure was the quality-adjusted life-years (QALYs) gained. The secondary effectiveness measure was the number of months with 25% or less off time per day. These were derived from the literature (US study). Discounting was applied at a rate of 5%.

Direct costs
The health service costs were included in the analysis. The estimates of resource use and costs were derived from the literature and from authors' assumptions. The quantities and the costs were not reported separately. The drug costs were calculated from retail prices of best-selling products obtained through the Finnish University Pharmacy. The costs were adjusted to 2004 values using the Finnish Consumer Price Index. Discounting was carried out at a rate of 5% for economic outcomes, which was appropriate for the 2-year time horizon chosen.
Statistical analysis of costs
The average costs and their SDs were calculated using a stochastic approach (Monte Carlo simulations with 10,000 iterations), with a priori distributions to take variability in each parameter into account.

Indirect Costs
The indirect costs were included in the primary analysis. The estimates of resource use and costs were derived from the literature, specifically from a paper published in 2003. The quantities and the costs were not reported separately. Discounting (5%) was carried out and this was appropriate for the 2-year time horizon chosen. The costs were adjusted to 2004 values using the Finnish Consumer Price Index.

Currency
Euros (EUR).

Sensitivity analysis
A probabilistic multivariate approach was used to take uncertainty surrounding all variables into account. Best- and worst-case scenarios were also used to test the efficacy assumptions in the standard care group. A sensitivity analysis, in which the price of rasagiline was varied relative to that of entacapone, was also performed.

Estimated benefits used in the economic analysis
The benefits after 2 years were 0.13 (95% CI: 0.08 to 0.17) additional QALYs and 5.2 (95% CI: 3.6 to 6.7) additional months for rasagiline and 0.12 (95% CI: 0.08 to 0.17) additional QALYs and 5.1 (95% CI: 3.5 to 6.6) additional months for entacapone, both in adjunct to levodopa, compared with levodopa alone.

Cost results
At 2 years, from the societal perspective, rasagiline cost EUR 930 less per treated patient compared with standard care and was associated with an increased direct cost of EUR 2,130.

At 2 years, from the societal perspective, entacapone cost EUR 830 less per treated patient compared with standard care and was associated with an increased direct cost of EUR 2,170.

Synthesis of costs and benefits
From the third-party-payer perspective, the incremental cost-effectiveness ratios (ICERs) with rasagiline were EUR 17,800 per additional QALY gained and EUR 430 per additional month spent with 25% or less time off per day. Rasagiline dominated standard care from the societal perspective, resulting in a total cost-saving of EUR 930 per patient treated.

From the third-party perspective, the ICERs with entacapone were EUR 18,600 per additional QALY gained and EUR 450 per additional month spent with over 25% or less time off per day. Entacapone dominated standard care from the societal perspective, resulting in a total cost-saving of EUR 830 per patient treated.

In the sensitivity analysis, in the worst-case scenario, neither drug dominated standard care since they were both more effective but more costly. In the best-case scenario, both drugs were dominant compared with standard care from the societal perspective. When assuming similar costs in both health states, neither drug dominated standard care. The results were robust to a 10% increase and a 20% decrease in the price of rasagiline compared with the price of entacapone.

Authors' conclusions
The economic model supported the use of rasagiline and entacapone as cost-effective treatment alternatives in PD.
patients with motor fluctuations. Rasagiline treatment was cost-effective and cost-saving in comparison with standard care with levodopa alone from a societal perspective.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparators was clear. They represented current practice in the authors’ setting. You should decide if the comparators represent current practice in your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not report their search strategy. They provided only limited information about the method used to assess the quality of the retrieved studies, thus making it difficult to comment on the quality of the effectiveness estimates. The principal estimates for the model were derived from a randomised controlled trial with high validity. Uncertainty around the effectiveness estimates was appropriately assessed through a sensitivity analysis.

**Validity of estimate of measure of benefit**
The authors used QALYs as their benefit measure. These facilitate the comparison of their results with those of other health care programmes. The utilities used were derived from a published model. This is a well established and valid approach.

**Validity of estimate of costs**
All the categories of cost relevant to the perspectives adopted appear to have been included in the analysis. From the societal perspective, the costs included early retirement due to PD and the cost of informal home care. The method used to estimate opportunity costs was not reported clearly. The unit costs and the resource quantities were not reported separately. The price year was stated and discounting was performed appropriately, given that the time horizon considered at analysis was more than one year. The cost estimates are likely to be specific to the Finnish setting.

**Other issues**
This was a well-conducted and transparently reported modelling study that contains important findings for health care decision-makers. The authors addressed generalisability issues and how the sensitivity analyses they performed enhanced the external validity of their results. The authors also discussed the drawbacks of their study. In particular, the fact that it used utilities from a US population in a Finnish setting. The authors compared their data with those from other studies and found them similar in terms of the clinical effects.

**Implications of the study**
The authors commented that the results of this study support the use of rasagiline and entacapone as adjunctive cost-effective alternatives to levodopa alone in PD patients with motor fluctuations in Finland. They suggested avenues for further research looking at the quality of time spent in the off-state with rasagiline over entacapone.

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