The cost effectiveness of rapid-acting insulin aspart compared with human insulin in type 2 diabetes patients: an analysis from the Japanese third-party payer perspective

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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 evaluated the cost-effectiveness of insulin aspart (man-made insulin analogue) versus normal human insulin in Japanese patients with type 2 diabetes. The authors concluded that insulin aspart resulted in increased quality of life and decreased costs when compared with human insulin. The study methodology was adequate, but it is not clear if the authors’ conclusions are appropriate as the uncertainty around the clinical outcomes was not reported.

Type of economic evaluation
Cost-utility analysis

Study objective
The study evaluated the cost-effectiveness of insulin aspart versus normal human insulin in Japanese patients with type 2 diabetes.

Interventions
The study investigated the use of short-acting insulin aspart (man-made/analogue) compared with normal human insulin.

Location/setting
Japan/primary care.

Methods
Analytical approach:
A discrete-time cohort-level model was used to assess the costs and outcomes associated with the two interventions under study. The time horizons of the study were five years and 10 years. The authors reported that the perspective adopted was that of the Japanese third-party payer.

Effectiveness data:
Clinical and effectiveness data came from previous studies. Five-year effectiveness data was from the Nippon Ultra-Rapid Insulin and Diabetic Complication Evaluation-Study (NICE Study: NCT00575172). The study was a five-year, open-label, randomised controlled trial (RCT) in which 162 patients were treated with human insulin and 163 patients were treated with insulin aspart. The main measures of effectiveness from the trial were the rates of myocardial infarction, angina pectoris, cerebral infarct, coronary artery bypass graft and percutaneous coronary intervention. Results from the trial were extrapolated using long-term effectiveness data from the United Kingdom Prospective Diabetes Study (UKPDS, Stevens, et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details).

Monetary benefit and utility valuations:
Baseline utility estimates came from the UKPDS trial, which assessed patients’ quality of life using the EQ-5D. Utility estimates for other health states, such as myocardial or cerebral infarction, came from previously published studies.

Measure of benefit:
Quality-adjusted life-years (QALYs) gained. As benefits could be generated over a five-year and 10-year period, future benefits were discounted using an annual rate of 3%.
Cost data:
The direct costs were those for insulin treatments, and treatment of diabetes complications (including myocardial infarction, cerebral infarction, coronary artery bypass graft, percutaneous coronary intervention and severe hypoglycaemia). Adverse events costs came from the Japanese Medical Data Centre. Costs of hypoglycaemia were from a Spanish study. Insulin costs came from the manufacturers. The price year was 2008. As costs could be incurred over five-year and 10-year periods (depending on the time horizon), future costs were discounted using an annual rate of 3%. All costs were reported in Japanese Yen (JPY).

Analysis of uncertainty:
The authors reported that one-way, two-way and multi-way sensitivity analyses were performed to assess the impact of model outcomes to changes in the input parameters.

Results
For a five-year time horizon, the average QALYs gained per patient were 3.80 with insulin aspart and the average cost per patient was JPY 481,586; for human insulin, the QALYS gained were 3.776 per patient and the average cost per patient was JPY 594,717.

For a 10-year time horizon, the average QALYs gained per patient were 6.942 with insulin aspart and the average cost per patient was JPY 926,472; for human insulin, the QALYS gained were 6.879 per patient and the average cost per patient was JPY 1,179,395.

For both the five-year and 10-year time horizon, insulin aspart was found to be dominant over human insulin (it was more effective and less costly).

Given a willingness to pay threshold of JPY 5,000,000 per QALY gained, results of the sensitivity analysis showed that insulin aspart remained cost-effective even if the effectiveness of insulin aspart as measured in the trial was down to 18%.

Authors' conclusions
The authors concluded that insulin aspart resulted in increased quality of life and decreased costs when compared with human insulin.

CRD commentary
Interventions:
Brief details of the interventions under study were provided.

Effectiveness/benefits:
Clinical and effectiveness data were primarily from an RCT undertaken in Japan. Adequate details of the trial were provided, including sample size, follow-up, and primary and secondary outcomes. The authors acknowledged that the sample size was relatively small, so they recommended caution when interpreting the results given the uncertainty surrounding mean estimates. Effectiveness data was then extrapolated to 10 years using the results of an RCT conducted in the UK (UKPDS trial).

Costs:
The perspective adopted in the economic analysis was explicitly reported to be that of Japanese third-party payer. For this perspective, all relevant cost categories were included. However, some important costs associated with diabetes, including costs of amputations and diabetic retinopathy were not included in the analysis. The sources from which cost information came were adequately reported. The price year, time horizon, discount rate used and currency details were all provided.

Analysis and results:
Outcome and cost data were synthesised using a discrete-event simulation model. Although adequate details of the model structure were provided, a diagram was not provided. One-way, two-way and multi-way sensitivity analyses were undertaken. Although these type of analyses go some way in exploring the impact of uncertainty, the use of probabilistic sensitivity analyses would have been a better method to assess overall model uncertainty, especially when
some input parameters (such as effectiveness) may have had high uncertainty given the small sample sizes. No measure of uncertainty was reported for clinical outcomes. The authors acknowledged that one of the main limitations to their study was that data from outside Japan was used to obtain quality of life estimates and extrapolate results from the Japanese trial.

Concluding remarks:
The study methodology was adequate, but it is not clear if the authors’ conclusions are appropriate as no uncertainty around the clinical outcomes were reported.

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