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 compared the cost-effectiveness of insulin aspart and human soluble insulin for the management of patients with type 2 diabetes. The authors concluded that insulin aspart with insulin detemir as a basal-bolus was more effective than human soluble insulin and resulted in cost savings in Sweden and Spain. It was also cost-effective in Italy, but not in Poland. Overall, the study was based on valid methodology and, despite some limitations, the authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to compare the long-term cost-effectiveness of two options for the management of patients with type 2 diabetes who were on basal-bolus therapy.

Interventions
The treatment options were insulin aspart (IAsp) and human soluble insulin (HI). Both were given as the bolus component of a basal-bolus insulin regimen, with insulin detemir (IDet) as the basal component.

Location/setting
Italy, Poland, Spain, and Sweden/secondary care.

Methods
Analytical approach:
The Center for Outcomes Research and Evaluation (CORE) Diabetes Model, a non-product-specific diabetes policy model, was used. Full details of this model were reported in a separate paper (Palmer, et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). The time horizon was 35 years. The authors reported that a third-party payer and a societal perspective were adopted, for Sweden, and the third-party payer perspective was adopted for Italy, Poland and Spain.

Effectiveness data:
The patient characteristics were mainly derived from a large multi-centre observational study; the Predictable Results and Experience in Diabetes through Intensification and Control to Target: An International Variability Evaluation (PREDICTIVE) study. This was augmented with published data from country-specific sources. The treatment efficacy data were obtained from the European subsample of the PREDICTIVE study. The primary clinical outcomes were the reductions in glycosylated haemoglobin (HbA1c) and body mass index (BMI).

Monetary benefit and utility valuations:
The diabetes-related health state utilities and event disutilities were derived from published studies, but the methods used to derive them were not reported.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary measure of benefit and were discounted at an annual rate of 3% for Italy and Sweden, 5% for Poland, and 6% for Spain.
Cost data:
The economic analysis included the costs of medication (including oral anti-diabetic drugs, excluding value added tax), administration devices, blood glucose monitoring, several screening tests, and the direct costs of diabetes-related complications, such as cardiovascular disease, renal complications, eye disease, neuropathy, amputation, ulcer, and gangrene. These costs were obtained from official national sources and augmented with data from the published literature. They were reported as macro-categories. Costs were in Swedish Kroner (SEK) for the year 2005, for Sweden, and in Euros (EUR) for the year 2006 for Italy, Poland, and Spain. They were discounted at an annual rate of 3% for Italy and Sweden, 5% for Poland, and 6% for Spain.

Analysis of uncertainty:
The mean values and standard deviations (SDs) were calculated using non-parametric bootstrap estimates, and cost-effectiveness acceptability curves were generated for each country. The uncertainty around patient characteristics and treatment effects was investigated using probabilistic sensitivity analysis. A series of one-way sensitivity analyses was also performed by varying the discount rate, the time horizon, the effect of IAsp on HbA1c reduction, and the rate of hypoglycaemic events in the two treatment groups.

Results
Compared with HI, the additional expected QALYs were 0.077 in Sweden, 0.080 in Spain, 0.120 in Italy, and 0.003 in Poland.

Over a patient's lifetime from the societal perspective, the total costs per patient in Sweden were SEK 521,538 in the IAsp group and SEK 532,256 in the HI group. From the third party payer perspective, the total costs per patient in Spain, were EUR 45,805 (SD 12,915) in the IAsp group and EUR 47,187 (SD 12,470) in the HI group, resulting in cost-savings. In Italy and Poland, IAsp resulted in additional direct total costs per patient when compared with HI (EUR 2,235 in Italy and EUR 743 in Poland).

In Sweden and Spain IAsp was the dominant treatment as it was more effective and less costly compared with HI.

The incremental cost per QALY gained for IAsp compared with HI was EUR 18,597 in Italy and EUR 290,486 in Poland.

The cost-effectiveness acceptability curve suggested that IAsp had a 63.7% probability of being cost-effective in Italy and 37.6% probability in Poland at a willingness-to-pay threshold of EUR 30,000 per QALY gained. One-way sensitivity analyses demonstrated that these results were sensitive to variation in the effect of IAsp on HbA1c reduction.

Authors' conclusions
The authors concluded that IAsp bolus, with IDet in a basal-bolus treatment, was clinically more effective than HI and resulted in cost savings in Sweden and Spain and it was a cost-effective option in Italy, but not in Poland.

CRD commentary
Interventions:
The interventions were chosen with reference to a large observational study. You should decide if these are valid comparators in your own setting.

Effectiveness/benefits:
The clinical evidence was mainly from a large observational study, supplemented by published sources. No information on the method and conduct of the literature review was provided. Apart from the main observational study, no details on the sources were provided, making an objective assessment of the validity of the data difficult. No information was reported on the methods used to derive the utilities. QALYs are an appropriate measure of benefit and allow comparisons to be made with the benefits of other health care interventions.

Costs:
It appears that the categories of costs were appropriately selected for the third party payer perspective. For the societal perspective in Sweden, however, it was unclear which indirect costs were included and their sources were not reported.
The costs were presented as macro-categories and unit costs and resource quantities were not presented separately, which limits the transparency of the economic analysis. The exchange rate used for Poland was not reported, but the price year and discounting were well reported.

Analysis and results:
The synthesis of costs and benefits was appropriately performed. The issue of uncertainty was investigated extensively using non-parametric bootstrap techniques, in probabilistic sensitivity analysis and cost-effectiveness acceptability curves, and using one-way sensitivity analyses for specific parameters. The results of the sensitivity analyses were reported briefly, and the authors stated that detailed results would be provided at the reader's request. They discussed some potential limitations of their analysis, mainly relating to short-term clinical evidence.

Concluding remarks:
Overall, the study was based on valid methodology and the results of the base-case analysis were well reported. Although the results of the sensitivity analysis were not reported in detail, the methods appear to have been appropriate. The authors' conclusions are appropriate.

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Other publications of related interest


Indexing Status
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MeSH
Aged; Cohort Studies; Computer Simulation; Cost Savings; Cost of Illness; Cost-Benefit Analysis; Diabetes Mellitus, Type 2 /diagnosis /drug therapy /economics; Europe; Female; Humans; Hypoglycemic Agents /economics /therapeutic use; Insulin /analogs & derivatives /economics /therapeutic use; Insulin Aspart; Male; Middle Aged; Multicenter Studies as Topic; Predictive Value of Tests; Quality of Life; Quality-Adjusted Life Years; Risk Assessment; Sensitivity and Specificity; Severity of Illness Index; Treatment Outcome

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