Evaluation of the cost-effectiveness of insulin glargine versus NPH insulin for the treatment of Type 1 diabetes in the UK

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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 study examined the use of insulin glargine compared with NPH insulin for patients with Type 1 diabetes. Five comparison scenarios were investigated.

Scenario 1: 25% risk reduction in severe hypoglycaemic events, 22% rate reduction in nocturnal hypoglycaemia, no improvement in glycaemic control (indicated by glycosylated haemoglobin, HbA1c).

Scenario 2: 26% risk reduction in severe hypoglycaemic events, 17% rate reduction in nocturnal hypoglycaemia, no improvement in HbA1c.

Scenario 3: 28% risk reduction in severe hypoglycaemic events, 22% rate reduction in nocturnal hypoglycaemia, no improvement in HbA1c.

Scenario 4: no change in risk or rate of hypoglycaemic events, 0.19% improvement in HbA1c.

Scenario 5: no change in risk or rate of hypoglycaemic events, 0.45% improvement in HbA1c.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis

Study population
The study population comprised a hypothetical cohort of 10,000 persons aged 27 years old with Type 1 diabetes, weighing 72 kg and being 1.75 m in height, with a high-density lipoprotein cholesterol of 1.33 mmol/L.

Setting
The setting was secondary care. The study was conducted in the UK.

Dates to which data relate
Background data on hypoglycaemia related to published studies dating from 1993 to 2006. The effectiveness data related to a systematic review and meta-analyses of insulin glargine and NPH insulin and Types 1 and 2 diabetes (Medical Research Matters Limited 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). The costs for resource outlays were derived from various current UK sources and were indexed to 2005.

Modelling
A discrete event simulation model with a maximum 40-year time horizon was constructed. Full details of the health events (or complications), cycle length and model structure were presented in the paper. All data sources were referenced.

Study designs and other criteria for inclusion in the review
The clinical data used as an effectiveness measure comprised glycaemic control measured as HbA1c.
events. The event complications included ischaemic heart disease, myocardial infarction, congestive heart failure, stroke, retinopathy, renal disease, peripheral vascular disease and ketoacidosis.

Sources searched to identify primary studies
The clinical effectiveness data were derived from two meta-analyses (Medical Research Matters Limited 2006). Relative risk reductions of severe, nocturnal and symptomatic hypoglycaemia were used in the model.

Methods used to derive estimates of effectiveness
Specific details of the methods used to source the literature and other publications used in the study were not stated. The authors stated that they used the most up-to-date sources available.

Measure of benefits used in the economic analysis
The summary measure of benefit used was the quality-adjusted life-years (QALYs). The type of utility measurement was not stated but the sources were clearly referenced. Regression models were generated to associate frequency and severity of hypoglycaemia with fear of hypoglycaemia, in order to determine changes to utility rates.

Direct costs
Direct costs relevant to the NHS perspective were included. These covered maintenance and therapy costs for hypoglycaemia, insulin, fatal or nonfatal macrovascular conditions, retinopathy, blindness, nephropathy, peripheral vascular disease and ketoacidosis. The secondary data on resources were obtained from UK sources found in the literature and the Department of Health Prescription Cost Analysis data. The costs were discounted at a rate of 3.5% and indexed to the year 2005 using UK Treasury rates. Weighted average costs were generated for hypoglycaemia and renal dialysis. Upper and lower cost estimates were provided with base values.

Statistical analysis of costs
The data were deterministic.

Indirect Costs
Productivity costs were not included.

Currency
UK pounds sterling (£).

Sensitivity analysis
One-way sensitivity analyses were undertaken on model parameters that were expected to change the base results, e.g. different ages, cost and likelihood of hypoglycaemic events, cost of insulin glargine, utility score of hypoglycaemia and individual weight. These different scenarios were described and illustrated in a tornado diagram. Sensitivity analyses were conducted to test the impact of variability in data parameters on differences between treatments and hypoglycaemia reductions.

Estimated benefits used in the economic analysis
The incremental gain in discounted QALYs ranged from 0.12 to 0.34 for insulin glargine over NPH insulin across the five scenarios.

The highest incremental gain in QALYs (0.34) was found for scenario 5 'no change in risk or rate of hypoglycaemic event of any severity and 0.45% improvement in HbA1c'.

Cost results
Across the five scenarios, the total discounted costs ranged from £9,746 to £10,084 for insulin glargine and from £8,703 to £8,825 for NPH insulin, producing an additional cost of £1,043 to £1,371 for insulin glargine.

Synthesis of costs and benefits
The incremental cost-utility ratio ranged from £3,189 to £9,767 per QALY gained for the five scenarios. Scenario 5
had the lowest ratio while scenario 4 had the highest. Scenarios 1 to 3 had similar results, ranging from £7,391 to £8,807 per QALY gained.

The results of the one-way sensitivity analyses showed that all mean incremental cost-utility ratios were within £20,000 per QALY gained. The ratios were most sensitive to the price of insulin glargine, the utility decrement associated with hypoglycaemia, and the mean weight of the cohort. Duration of HbA\(_1c\) treatment effect also had a substantial impact on the base results, with the costs per QALY increasing from £3,189 for 10-year treatment effects up to £47,445 for 2-year treatment effects.

Authors' conclusions
The authors stated that the use of insulin glargine to treat Type 1 diabetes was highly cost-effective compared with insulin NPH in the UK. The results were found to be stable whether the effectiveness was due to either a reduction in hypoglycaemia or an improvement in glycaemic control as the primary benefit. The authors considered their findings as conservative, owing to the effectiveness of glargine being higher in research designs than in clinical trials.

CRD COMMENTARY - Selection of comparators
Two common insulin drugs for the treatment of Type 1 diabetes were compared. The authors provided an adequate justification for their choice of insulin drugs. You should decide if these treatment options are widely used in your own setting.

Validity of estimate of measure of effectiveness
The clinical effectiveness data on glycaemic control and reductions in hypoglycaemic events were derived from two meta-analyses. Potentially, this represents the highest quality of evidence for use in modelling analyses. However, the reader would need to separately assess the methods and quality of this pivotal study (Medical Research Matters Limited 2006) since the authors did not provide any information about the pooled studies or statistical methods. In addition, this report does not appear to have been peer-reviewed.

Validity of estimate of measure of benefit
The authors have chosen a longer-term health benefit and commonly used generic outcome measure (i.e. QALYs) to fully capture health-related quality of life and survival benefits. Although the authors did not discuss their results in relation to other studies, using this outcome measure will facilitate comparisons of their results with other studies of insulin drugs over similar time horizons. It is unclear what type of method was used to derive the utility values associated with the different health events since the reader was merely referred to the literature. In addition, for hypoglycaemic events, there was little detail of the utility functions used to predict changes in utility values.

Validity of estimate of costs
All costs relevant to the perspective of the UK NHS appear to have been included in the analysis. Discounting was necessary given the longer timeframe of the analysis, and was applied to both the costs and consequences. The sources of the resource quantities and unit costs, which were reported, appear to have been appropriate for the study setting and population. The costs and the quantities of health events were reported separately and clearly in the report.

Other issues
A clear conclusion was reached regarding which option was the most efficient choice and the likelihood on the reliability of the model. The authors did not discuss issues of generalisability to other settings or different population groups. They did, however, discuss the limitations and strengths of their study, indicating that the model is only as good as the data it is populated by, but stating that the data used were the best available in the UK at the time of the study.

Implications of the study
The model presented in this study confirms that patients treated with insulin glargine have superior clinical outcomes, and that this treatment is cost-effective to the UK NHS. Further research is required on the real effectiveness of insulin treatments in more naturalistic settings as opposed to clinical trials.

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Other publications of related interest
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Subject indexing assigned by NLM

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