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 2 diabetes. The dose regimen was 0.40 IU/kg per day for both types of insulin.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis

Study population
The study population comprised a hypothetical cohort of 58 year-old persons with Type 2 diabetes, weighing 81 kg and being 1.75 m in height, with a high-density lipoprotein cholesterol of 1.04 mmol/L.

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

Dates to which data relate
The effectiveness data were related to studies in two reviews, the dates of which were not stated. The second review superseded the first and included an extra three studies, and was published in 2006 (Medical Research Matters Limited, see ‘Other Publications of Related Interest’ below for bibliographic details). Costs for resource outlays were derived from various current UK sources and indexed to 2005.

Modelling
A discrete event simulation model with a 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 fully referenced.

Study designs and other criteria for inclusion in the review
The clinical data related to glycaemic control measured as glycosylated haemoglobin (HbA1c) and annual expected 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 and Rosenstock et al. 2000, see ‘Other Publications of Related Interest’ below for bibliographic details). 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 public publications used in the study were not stated. The authors stated that they had 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...
used 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 from 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 resource use 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 2005 UK pounds sterling using UK Treasury rates. Weighted average costs were generated for hypoglycaemia and renal dialysis. The upper and lower cost estimates were provided with base values.

**Statistical analysis of costs**

The data were deterministic.

**Indirect Costs**

No productivity costs were included.

**Currency**

UK pounds sterling (£).

**Sensitivity analysis**

One-way sensitivity analyses were undertaken on all key model parameters using the upper and lower limits provided. Two-way sensitivity analyses were undertaken for hypoglycaemic background rates and risk reduction, costs and utilities. The upper and lower limits in resource values were derived from the literature. Sensitivity analyses were conducted to test for variability in data parameters relating to differences between treatments in hypoglycaemia and differences in HbA\(_1c\). Sensitivity analysis was also undertaken on discount rates and the model time horizon.

**Estimated benefits used in the economic analysis**

The incremental gain in discounted QALYs was 111 for insulin glargine over NPH insulin for hypoglycaemia only, and 111 for HbA\(_1c\) only.

**Cost results**

For the hypoglycaemia scenario, the total discounted costs were £6,021,676 for insulin glargine and £4,907,596 for NPH insulin, producing an additional cost of £1,114,080 for insulin glargine.

For the HbA\(_1c\) scenario, the total discounted costs were £6,433,160 for insulin glargine and £4,892,492 for NPH insulin, producing an additional cost of £1,540,668 for insulin glargine.

**Synthesis of costs and benefits**

The incremental cost-utility ratio was £10,027 per QALY gained for the hypoglycaemia scenario and £13,921 for the HbA\(_1c\) scenario.

The results of the one-way sensitivity analyses showed that all mean incremental cost-utility ratios were within £30,000 per QALY gained, and most 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. Reducing the treatment effect by 50% also had a substantial impact on the base results, with costs per QALY of £29,040 and £22,420 for the hypoglycaemia and HbA\(_1c\) scenarios, respectively.

**Authors' conclusions**

The authors stated that insulin glargine was cost-effective, compared with NPH insulin, when used to treat Type 2 diabetes in the UK, and reached cost-effectiveness ratios within the thresholds commonly accepted for treatments in the UK. The results were found to be stable when data parameters were altered over a range of plausible estimates.
CRD COMMENTARY - Selection of comparators
Two common insulin drugs for the treatment of Type 2 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 is the highest quality of evidence for use in modelling studies. However the reader would need to separately assess the methods and quality of the two studies (Rosenstock et al. 2000 and Medical Research Matters 2006) since the authors did not provide any information about the pooled studies or the statistical methods. In addition, the latter reference, although current, is a report that 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) in order 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 attached to the different health events since the reader is referred to the literature. In addition, for hypoglycaemic events, there is 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
The authors approached the analyses in a thorough manner, with careful attention to model validation and detailed sensitivity analyses to test how the results may change with movements in the cost or effectiveness estimates used. A clear conclusion was reached regarding which option was the most efficient choice, and the likelihood of 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 use to populate it, 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 for the UK NHS. Further research is required on the real effectiveness of insulin treatments in more naturalistic settings as opposed to clinical trials.

Source of funding
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Bibliographic details
McEwan P, Poole C D, Tetlow T, Holmes P, Currie C J. Evaluation of the cost-effectiveness of insulin glargine versus NPH insulin for the treatment of Type 2 diabetes in the UK. Current Medical Research and Opinion 2007; 23(Supplement 1): S21-S31

Other publications of related interest
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
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