Cost-effectiveness of intermediate or long-acting insulin versus exenatide in type 2 diabetes mellitus patients not optimally controlled on dual oral diabetes medications

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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 three treatments for patients with Type 2 diabetes who did not attain adequate glycaemic control using two oral agents. The treatments compared were insulin glargine, neutral protamine hagedorn (NPH) insulin and exenatide. Specifically, exenatide was compared with the intermediate (NPH) and long-acting (glargine) insulin alternatives. Exenatide was given at a dose of 5 microg twice daily for 4 weeks then 10 microg twice daily thereafter, while both NPH and glargine were titrated to a target fasting plasma glucose level of less than 100 mg/dL.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals with Type 2 diabetes who were already receiving dual oral diabetes therapy with a sulfonylurea and metformin and who were not adequately controlled.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The clinical data and resource use information were derived from studies published in 2003 and 2005. The price year was 2005.

Source of effectiveness data
The clinical data used in the economic evaluation were the reductions in glycosylated haemoglobin A1c (HbA1C) and weight.

Sources searched to identify primary studies
The clinical data were derived from two randomised clinical trials (RCTs), the details of which (e.g. follow-up, sample size and baseline characteristics of the patients enrolled) were reported. One study compared exenatide against glargine insulin, whilst the other assessed the glycaemic efficacy of NPH insulin in addition to sulfonylurea-metformin therapy (placebo).

Methods used to judge relevance and validity, and for extracting data
A systematic review of MEDLINE was undertaken to identify relevant studies. The search criteria were reported. A clear justification for the selection of the two RCTs was provided. Specifically, one study was chosen on the basis of a head-to-head comparison between two of the drugs under analysis. The other trial was characterised by similar study duration, similar baseline glycaemic control, comparative population size and similar primary outcomes. A test of heterogeneity was conducted to compare the baseline characteristics of the patients in the two trials.

**Measure of benefits used in the economic analysis**
The two summary benefit measures used in the analysis were the reductions in HbA1C and weight. These were both derived directly from the literature.

**Direct costs**
The cost/resource boundary of the analysis was not explicitly stated. The analysis included only the costs of the drugs, which were based on average wholesale prices as at September 2005. The price year was also 2005. The unit costs were not presented separately from the resource quantities. Discounting was not relevant as the costs were incurred during a short time. Drug dosages were based on data from the two RCTs.

**Statistical analysis of costs**
No statistical analyses of the costs were performed.

**Indirect Costs**
Productivity costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
A one-way sensitivity analysis was carried out to assess the robustness of the cost-effectiveness ratios to variations in the two effectiveness measures (assumed to be 10% and 20% higher than the mean reported for exenatide) and the cost of exenatide (assumed to be 90% and 80% of the base-case values).

**Estimated benefits used in the economic analysis**
During the 24-week period, the reduction in HbA1C was 0.091% with exenatide, 0.655% with glargine and 0.201% with NPH.

Over the same period, exenatide was associated with a weight reduction of 0.19 kg, while both glargine and NPH led to a slight weight increase.

**Cost results**
The total costs of the drugs over the study period were not reported.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios (ICERs) were calculated in order to combine the costs and both benefit measures.

When considering the reduction in glycaemic control, the incremental analysis revealed that exenatide was dominated by both glargine and NPH, which were more effective and less expensive.
The results of the base-case analysis held when exenatide was compared with NPH. However, in the comparison with glargine, the ICERs (cost per 1% reduction in HbA1C) with exenatide were $6,552 and $3,120 when the effectiveness of exenatide was increased by 10% and 20%, respectively.

When considering the reduction in weight, the additional reduction of 1 kg in weight with exenatide was achieved at a cost of $235 in comparison with NPH and $128 in comparison with glargine.

The sensitivity analysis led to ICERs associated with exenatide that ranged from $81 to $223.

NPH dominated glargine for both HbA1C reduction and weight changes.

**Authors’ conclusions**

With respect to glycaemic control, exenatide was not a cost-effective alternative to intermediate (neutral protamine hagedorn, NPH) or long-acting insulin (glargine) in patients with Type 2 diabetes that was not optimally controlled by the use of two agents (a sulfonylurea and metformin).

**CRD COMMENTARY - Selection of comparators**

The authors justified the choice of the comparators, suggesting that bedtime insulin with either NPH or insulin glargine was a convenient once-daily insulin regimen in addition to oral therapy. Exenatide was considered an additional recent option. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

A systematic review of the literature was undertaken to identify the primary studies. The sources searched and inclusion criteria for the primary studies were reported. In general, the inclusion of RCTs should ensure the robustness of the clinical data. The authors reported baseline characteristics of the primary studies in order to show the baseline comparability of the patient populations. However, there were some differences in terms of age in the comparison between exenatide and glargine, and age, body mass index and baseline HbA1C in the comparison between exenatide and NPH. The authors acknowledged that despite a similar clinical and demographic profile of patient groups, these differences might represent a limitation of the analysis. This is especially so in the comparison between NPH and exenatide, which was based on an indirect comparison. No head-to-head RCT was found in the literature.

**Validity of estimate of measure of benefit**

The benefit measures were derived directly from the literature and were specific to the disease considered in the study. This precludes the possibility of comparing the benefits of the current treatments with those associated with other interventions. Reductions in HbA1C and weight represent two intermediate end points of treatments for Type 2 diabetic patients.

**Validity of estimate of costs**

The cost analysis was restricted to the drugs under examination in the study. Other costs related to prescription, monitoring and primary care visits were not included, although they might have been relevant. The sources of the data were reported, but the authors did not state which perspective was adopted in the study. The unit costs and quantities were not presented, which limits the possibility of replicating the analysis of in other settings. Further, the costs were treated deterministically and the total costs were not reported. Only the price year was given.

**Other issues**

The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Only a limited sensitivity analysis was performed and the results of the study should be considered country-specific. In general, the cost analysis was somewhat weak. The study referred to patients with Type 2 diabetes with poor glycaemic control while on oral therapy, and this was reflected in the authors' conclusions.

**Implications of the study**

The study results do not support the use of exenatide for the treatment of patients with Type 2 diabetes not optimally
controlled on both a sulfonylurea and metformin. The authors stated that future studies should directly assess the glycaemic effect and cost-effectiveness of other insulin therapies compared with exenatide.

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**Bibliographic details**

**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.


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Subject indexing assigned by CRD

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