Evaluation of the long-term cost-effectiveness of insulin detemir compared with neutral protamine Hagedorn insulin in patients with type 1 diabetes using a basal-bolus regimen in Sweden

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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
This study examined the cost-effectiveness of insulin detemir, compared with neutral protamine Hagedorn (NPH) insulin, both combined with mealtime insulin aspart, for patients with type 1 diabetes. The authors concluded that insulin detemir was a cost-effective alternative to NPH insulin, for the health care payer, and was likely to be cost saving from a societal perspective. The methods were valid and the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of insulin detemir, compared with neutral protamine Hagedorn (NPH) insulin, both combined with mealtime insulin aspart, for patients with type 1 diabetes, using data from a recent clinical trial.

Interventions
Insulin detemir was compared against NPH insulin, both as part of a basal-bolus regimen, in patients with type 1 diabetes. The doses were titrated to a plasma glucose target of six millimoles per litre or less before breakfast and before dinner, with the option of adding a second basal insulin dose if required.

Location/setting
Sweden/primary care.

Methods
Analytical approach:
The analysis was based on a published and validated simulation model, namely the Center for Outcomes Research (CORE) Diabetes Model, that used Markov sub-models to project the costs and benefits to the long-term, for diabetes patients. A lifetime horizon was considered. The authors stated that the perspectives of the health care payer and society were adopted.

Effectiveness data:
The clinical data were from a selection of relevant studies. The efficacy of the two treatments was the key input for the model and these data were from a randomised controlled trial (RCT) carried out at 33 sites across 10 countries worldwide, with 497 patients randomly allocated to receive either once-daily detemir (331 patients) or NPH (166 patients) insulin. Other sources were the Swedish National Diabetes Register and a cross-sectional retrospective chart review of over 5,000 patients in Sweden. Basic data on the progression of disease were already incorporated in the simulation model and were based on Framingham equations. Some assumptions were required.

Monetary benefit and utility valuations:
The utility values were from the UK Prospective Diabetes Study, wherever possible. Otherwise, published sources were used.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years were the summary benefit measures and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the pharmacy costs (insulin, needles, and self-monitoring materials), costs of the treatment of diabetes-related complications, and the costs of productivity lost. The pharmacy costs were from a published source that included value added tax (VAT) and the pharmacy margin, with dosages based on the main clinical trial. The costs of complications were from the Swedish Association of Local Authorities and Regions and two published studies. The productivity losses were valued, using the human capital approach and official data from the Statistics Sweden website. All costs were in Swedish kronor (SEK). The price year was 2006 and a 3% annual discount rate was applied.

Analysis of uncertainty:
Monte Carlo simulation and non-parametric bootstrapping were used to examine the uncertainty in the model outputs. Cost-effectiveness acceptability curves were generated for various willingness-to-pay (WTP) thresholds. One-way sensitivity analyses were carried out on the key inputs (the time horizon, discount rate, efficacy of treatments, body mass index, hypoglycaemic event rates, and cohort characteristics). Alternative estimates were either from published sources or were assumed by the authors.

Results
The projected life-years were 15.02 with detemir and 14.88 with NPH insulin. The QALYs were 8.35 with detemir and 7.82 with NPH. The expected direct costs were SEK 995,025 with detemir and SEK 968,881 with NPH. The total (direct and indirect) costs were SEK 2,959,909 with detemir and SEK 3,040,022 with NPH insulin.

The incremental cost per life-year gained with detemir over NPH insulin was SEK 190,208 and per QALY gained it was SEK 49,757, from the perspective of the health care system. The likelihood of detemir being cost-effective was 86.1% at a WTP threshold of SEK 100,000 per QALY, 99.3% at a threshold of SEK 200,000, 99.9% at a threshold of SEK 300,000, and 100% at a threshold of SEK 400,000.

Detemir was the dominant treatment, from the perspective of society, as it was cheaper and more effective than NPH insulin. This conclusion held in the sensitivity analyses.

The main driver of the model was the efficacy of detemir and its impact on major hypoglycaemic events, but the model findings were generally robust, except when there were no incremental benefits for detemir over NPH insulin.

Authors' conclusions
The authors concluded that insulin detemir was a cost-effective alternative to NPH insulin for the health care payer and was likely to save money from a societal perspective.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. The two insulin treatments were the comparators in the RCT used as the main source of evidence.

Effectiveness/benefits:
No systematic review was conducted to identify the relevant sources of evidence, but the sources selected appear to have been appropriate and consistent with the objective of the study. The model was already populated with data on disease progression and the incidence of diabetes-related complications. The evidence for the efficacy of the two treatments was from a recent international head-to-head RCT, which was a valid source of evidence, given its methods. Further data were appropriately sourced from country-specific registries. More details on the derivation of the utility values would have been useful in assessing their validity. Life-years and QALYs were appropriate benefit measures that capture the impact of disease on both survival and quality of life. Both measures are also generalisable to other diseases.

Costs:
Two appropriate perspectives were selected and the cost categories were appropriate. The price year and discounting were reported. Appropriate statistical tests and sensitivity analyses were carried out on the economic inputs. There were limitations to the analysis; most of the costs were presented as category totals not individual items, and some data sources were not clearly described. These limitations reduce the transparency of the analysis. Other details, such as the price year and the discount rate, were reported.

Analysis and results:
The results were clearly presented. An incremental approach was used to combine the costs and benefits of the alternative insulins and to identify the preferred strategy. A validated simulation model was used to project the long-term economic and clinical impact of the two treatments. Valid approaches were used to investigate the uncertainty. The authors compared their results with those of other published economic evaluations, which had similar findings. The analysis should be generalisable to similar settings.

Concluding remarks:
The methods were valid and the authors’ conclusions appear to be robust.

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