What impact would pancreatic beta-cell preservation have on life expectancy, quality-adjusted life expectancy and costs of complications in patients with Type 2 diabetes: a projection using the CORE diabetes model

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.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
A cohort of newly diagnosed patients with Type 2 diabetes similar to those of the UK Prospective Diabetes Study (UKPDS) (the authors referred to the UKPDS 33 and UKPDS 49, see 'Other Publications of Related Interest' below for bibliographic details)) were defined as study population. The baseline characteristics of the cohort included 61% male, 81% Caucasian, 8% Black and 1% Hispanic, and a mean age of 53 years. The patients were newly-diagnosed with diabetes. Other baseline characteristics included mean total cholesterol 206.6 mg/dL, mean high-density lipoprotein 40.94 mg/dL, mean low-density lipoprotein 133.9 mg/dL, mean triglyceride levels 207 mg/dL, and mean body mass index (BMI) 27.5 kg/m2.

Setting
The setting was primary care and secondary care. The economic analysis was carried out in the USA.

Dates to which data relate
The dates to which the data related were not reported in this article. The reader is referred to the parent study for detailed information (UKPDS). The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from the UKPDS. The authors also referred to another study (Palmer et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details).

Modelling
A simulation model was used to investigate the long-term clinical and economic outcomes of a hypothetical intervention that stabilised beta-cell function over time, compared with a cohort with diminishing beta-cell function and a typical increase in HbA1c over time. The type of model was not reported in the text. The lifetime horizon was defined as 50 years.

Two scenarios were performed to project the results. The first scenario assumed that the increase in HbA1c due to beta-cell failure over time was the same as that in the UKPDS (starting at approximately 7.0% HbA1c at baseline and progressing to approximately 9.25% after 15 years). The second scenario was performed assuming that HbA1c did not increase over time from diagnosis (HbA1c remained at 7.0%). This study is an application of the CORE Diabetes model.

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Model that is already validated and documented on the literature. A detailed explanation of this model can be found in Palmer et al. 2004.

Outcomes assessed in the review
The outcomes assessed were the transition probabilities and cumulative incidence of major diabetes-related complications.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
It appears that 3 studies have been included in the analysis to assess the outcomes.

Methods of combining primary studies
Some effectiveness parameters derived from the primary studies were combined using a narrative method.

Investigation of differences between primary studies
Not reported.

Results of the review
Not reported.

The original paper presented the cumulative incidences of major diabetes-related complications in graphical format; they were not reported in detail in the text. The authors reported that a hypothetical stabilisation of beta-cell function led to reductions in the cumulative incidence of major diabetes-related complications, including eye disease, renal disease, foot ulcers or amputation, cardiovascular disease and neuropathy.

Measure of benefits used in the economic analysis
The measures of benefits used were the life expectancy and quality-adjusted life expectancy. Both discounted (at 3% annually) and undiscounted life expectancy and quality-adjusted life expectancy were calculated.

Direct costs
The direct costs presented in the analysis were those of the US third-party payer. Only direct medical costs of complications were included in the analysis. The costs of everyday diabetes treatment were omitted. The costs were discounted at an annual rate of 3%. The final estimates for the costs of complications were derived from the 50-year NHS Economic Evaluation Database (NHS EED)
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time horizon used in the model. The price year was 2003. Detailed information on the sources of the unit costs and resource use were not presented on the paper. Further details on the costing exercise were given in Palmer et al. 2004.

**Statistical analysis of costs**

The costs were treated as point estimates (i.e. the model was deterministic).

**Indirect Costs**

The indirect costs were not included in the analysis.

**Currency**

US dollars ($).

**Sensitivity analysis**

A one-way sensitivity analysis was performed on the degree of stabilisation of beta-cell function. This assumed either 30% or 70% stabilisation of beta-cell function in comparison with the base-case scenario in which 100% stabilisation was assumed. A second sensitivity analysis was carried out on the rates of re-increase in HbA1c over time in the "typical increase in HbA1c" scenario, using either a 1% or 2% per year increment compared with the 1.5% per year used in the base-case analysis.

**Estimated benefits used in the economic analysis**

Assuming the increase in HbA1c that was seen in the UKPDS, the mean non-discounted life expectancy from baseline age of 53 years and quality-adjusted life expectancy were projected to be 17.48 (standard deviation, SD=0.28) years and 12.34 (SD=0.19) years, respectively.

Discounted life expectancy and quality-adjusted life expectancy were 12.82 (SD=0.17) years and 9.23 (SD=0.12) years, respectively.

Assuming a stabilisation of HbA1c after diagnosis, non-discounted life expectancy and quality-adjusted life expectancy were projected to be 18.50 (SD=0.30) years and 13.30 (SD=0.22) years, respectively.

Discounted life expectancy and quality-adjusted life expectancy were 13.30 (SD=0.18) years and 9.72 (SD=0.13) years, respectively.

Undiscounted life expectancy was improved by 1.02 (SD=0.36) years and quality-adjusted life expectancy by 0.96 (SD=0.25) years.

Discounted life expectancy and quality-adjusted life expectancy were improved by 0.48 (SD=0.21) years and 0.50 (SD=0.16) years, respectively.

**Cost results**

The mean cost of complications per patient was projected to be $49,378 (SD=2,038) when assuming an increase in HbA1c that was seen in the UKPDS, and $43,002 (SD=1,908) when assuming stabilisation of HbA1c after diagnosis. Therefore, the costs of complications were reduced by $6,377 (SD=2,568) per patient.

**Synthesis of costs and benefits**

The costs and effects were not combined as the hypothetical drug was always the dominant strategy (i.e. the hypothetical drug was more effective and less costly). The sensitivity analysis showed that the results were robust under the assumptions defined above.
Authors’ conclusions
New treatments that stabilise pancreatic beta-cell function may lead to improvements in length and quality of life. They are also likely to reduce the incidence and the costs of complications in patients with Type 2 diabetes.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was relatively clear. The authors made use of a validated model to project the long-term clinical and economic outcomes of a hypothetical treatment to stabilise pancreatic beta-cell function in patients with Type 2 diabetes. The comparators used would be the available treatments which have been shown not to stabilise pancreatic beta-cell function. As the results presented here are based on the assumption that the hypothetical treatment would have the desirable effect, the reader must interpret the results presented here with caution.

Validity of estimate of measure of effectiveness
Detailed information on how effectiveness was derived was not reported in the text, as the model had already been published in another paper. Thus, it was unclear whether a systematic review was conducted or whether the authors based their assessment on the available literature. The authors referenced the main paper throughout the text to aid in the understanding of the model. The reader of this abstract is strongly advised to read the main publication (UKPDS).

Validity of estimate of measure of benefit
The authors used life expectancy and quality-adjusted life expectancy, which appear to be widely used outcomes in patients with diabetes.

Validity of estimate of costs
The perspective adopted was that of the US third-party payer. Only costs related to complications were included in the analysis. The day-to-day costs of diabetes care and indirect costs were not included. It is quite clear, and the authors recognised the issue in their discussion, that with these categories included in the costing exercise the results were likely to vary. Besides, the internal validity of the analysis would have benefited if more information on what resources were included in the costs of complications had been reported. It is likely that further details were given in the main paper (Palmer et al. 2004). There was no information on the unit costs, but again the authors referred to the main paper. To determine whether this analysis has the appropriate internal validity, it is crucial that the reader also reads the parallel publication about the description of the model.

Other issues
The investigators provided enough evidence to support the forthcoming existence of a new therapy to stabilise pancreatic beta-cell function. The authors made some comparisons on the basis of effectiveness, as well as comparisons with other health interventions. However, there were no comparisons with other available models in the field. It is likely that this is the only model simulating the event, but it was unclear from the text. This might have clarified whether the results may be generalised to other settings.

The authors reported some limitations of their study. First, the costs of the intervention (e.g. medication, monitoring) were not included. Second, the analysis did not consider any effects of beta-cell regeneration, which may lead to the effects of Type 2 diabetes being reversed, and hence improving long-term outcomes. Finally, compliance, drop-outs and potential side effects were not included in the analysis, although they may influence the effectiveness of the intervention and, therefore, affect the long-term outcomes and costs.

Implications of the study
New therapies that stabilise pancreatic beta-cell function are likely to improve life expectancy and quality of life. However, the results presented here must be compared with other diabetes-related models to have a better understanding of the results. The authors suggested that further research would be needed for future interventions.
Source of funding
Supported by an unrestricted research grant from Eli Lilly and Company Inc., Indianapolis (IN), USA.

Bibliographic details

PubMedID
15324517

DOI
10.1185/030079904X2024

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Computer Simulation; Decision Support Systems, Clinical; Diabetes Complications /economics /epidemiology /prevention & control; Diabetes Mellitus, Type 2 /complications /economics /physiopathology /therapy; Humans; Insulin Resistance /physiology; Islets of Langerhans /physiology; Life Expectancy; Models, Econometric; Preservation, Biological; Quality-Adjusted Life Years; Risk Reduction Behavior

AccessionNumber
22005008075

Date bibliographic record published
31/12/2005

Date abstract record published
31/12/2005