Health-economic comparison of continuous subcutaneous insulin infusion with multiple daily injection for the treatment of Type 1 diabetes in the UK

Roze S, Valentine W J, Zakrzewska K E, Palmer A J

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
This study evaluated the use of continuous subcutaneous insulin infusion (CSII) versus multiple daily injections (MDI) for the treatment of patients with Type 1 diabetes.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 10,000 patients with Type I diabetes. The cohort had a mean age of 26 years and a mean duration of diabetes of 12 years. Fifty-four per cent were male and 90% were Caucasian.

Setting
The setting was unclear. The economic study was conducted in Switzerland.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1994 and 2003. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of studies and authors' assumptions.

Modelling
The CORE diabetes model was used within the study. The authors stated that this is a peer-reviewed and validated model which describes the long-term incidence and progression of diabetes-related complications through the use of standard Markov/Monte Carlo simulation. The authors pointed out that the model is described in full elsewhere (Palmer et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details of the two papers). Therefore, only limited details were provided in this paper.

Outcomes assessed in the review
The outcomes assessed in the review were glycated haemoglobin (HbA1c) events and complications.
Study designs and other criteria for inclusion in the review
The outcomes of haemoglobin events and complications were derived from the Diabetes Control and Complications Trial (DCCT) (Palmer et al. 2004) and a meta-analysis of insulin pump therapy (Weissberg-Benchell et al. 2003, see 'Other Publications of Related Interest' below for bibliographic details). The meta-analysis included 52 studies involving more than 1,500 patients. No further information was provided.

Sources searched to identify primary studies
None stated.

Criteria used to ensure the validity of primary studies
None stated.

Methods used to judge relevance and validity, and for extracting data
None stated.

Number of primary studies included
The effectiveness data were derived from seven primary studies.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
The reporting of the outcomes was very limited. Improvements in glycaemic control associated with CSII compared with MDI led to a lower incidence of diabetic complications over 60 years.

After 60 years:

- the cumulative incidence of end-stage renal disease was 28.8% lower in the CSII group than in the MDI group;
- the cumulative incidence of myocardial infarction was 10.1% lower with CSII than with MDI;
- the cumulative incidence of first amputation was 7.2% lower in the CSII group than in the MDI group; and
- the cumulative incidence of severe visual loss was 18.3% lower in the CSII group than in the MDI group.

Methods used to derive estimates of effectiveness
In order to fully populate the model, the authors made some assumptions based on the evidence available to them.

Estimates of effectiveness and key assumptions
The main assumption was that hypoglycaemic and ketoacidosis event rates were the same in both treatment groups.

Measure of benefits used in the economic analysis
The summary benefit measures used were life expectancy, quality-adjusted life expectancy and the quality-adjusted life-years (QALYs). The health state utilities and disutilities used in the analysis were taken from five other studies. No information on the methods used to elicit health utilities was reported. An annual discount rate of 3.0% was applied to expected benefits in the base-case analysis.

**Direct costs**
The perspective adopted was that of the UK NHS health care system. Thus, only the direct medical costs were considered. The health services included in the analysis were medications and the treatment of complications. The unit costs for CSII and MDI were reported, but aggregated costs per event were provided for complications. Medication costs and the costs of treating diabetes-related complications were derived from published sources. The annual costs of the CSII and MDI therapies were based on public prices, NHS Reference Costs 2002 and data from INPUT (a UK Diabetes Association). Discounting was relevant, as the costs were incurred over the patients' lifetime, and an annual rate of 3.0% was applied. The costs were inflated to 2003 values using NHS Guidelines.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not considered in the economic evaluation.

**Currency**
UK pounds sterling (£).

**Sensitivity analysis**
Univariate sensitivity analyses were carried out to examine the robustness of the base-case model results to variations in the discount rates, treatment effect on HbA1c, and variations in body mass index. Also investigated were variations in the hypoglycaemia event rate and ketoacidosis event rate for those receiving CSII. The alternative values tested in the sensitivity analysis, were based on published studies. A non-parametric bootstrapping approach was used, and 1,000 patients were run 1,000 times through the model in order to generate means (with standard deviations) and a cost-effectiveness acceptability curve.

**Estimated benefits used in the economic analysis**
Treatment of Type 1 diabetes with CSII was projected to increase life expectancy by 0.71 (+/- 0.28) years compared with MDI.

Mean discounted life expectancy was 17.44 (+/- 0.23) years with CSII compared with 16.73 (+/- 0.22) years with MDI.

Quality-adjusted life expectancy was 12.03 (+/- 0.15) years with CSII compared with 11.27 (+/- 0.14) years with MDI (difference of 0.76 +/- 0.19 years).

**Cost results**
The mean lifetime cost of CSII treatment was projected to be 80,511 (+/- 1,257) compared with 61,104 (+/- 1,249) for MDI (difference of 19,407 +/- 1,727).

Treatment costs were the greatest component of the total lifetime costs, and were 40,077 in the CSII group compared with 25,266 in the MDI group.

Complication costs were 2,191 less in the CSII group than in the MDI group (31,267 versus 33,458).
Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER) was calculated to combine the costs and benefits of the two strategies under evaluation.

The ICER was 25,648 per QALY gained with CSII versus MDI and 27,477 per life-year gained with CSII versus MDI.

The cost-effectiveness acceptability curve showed that CSII had a 74% probability that it would be cost-effective, if the willingness-to-pay threshold was 30,000.

The sensitivity analysis showed that the choice of the rates of hypoglycaemia and improvements in HbA1c had the greatest impact on the base-rate results. Altering the improvement in HbA1c levels associated with CSII compared with MDI from 1.2% to 0.51% increased the ICER to $61,564 per QALY. Reducing the hypoglycaemia rates in the CSII group by 50% improved the ICER to 20,104 per QALY gained for CSII compared with MDI. Reducing the hypoglycaemia rates by 75% further improved the ICER to 18,047 per QALY gained.

Varying the discount rates for costs and clinical outcomes from 0 to 6% led to ICERS for CSII versus MDI in the range of 12,377 to 29,863 per QALY.

Changes in body mass index and ketoacidosis event rates led to little change from the base-case.

Authors' conclusions
Compared with multiple daily injections (MDI), continuous subcutaneous insulin infusion (CSII) led to improved quality-adjusted life expectancy for patients with Type I diabetes because of the reduced incidence of diabetes-related complications. This resulted in a cost-effectiveness ratio within the range considered value for money in the UK.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used (i.e. MDI). The comparator was chosen because it represented a current treatment regimen in the authors' setting. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from the literature. However, the methods and conduct of the review were not reported and it was not apparent whether it was a systematic review. With no information on the search methods or the inclusion or exclusion criteria, the comprehensiveness is difficult to ascertain. Therefore, it is not possible to say whether the best available evidence has been used to populate the model. Where data were not available, some assumptions were made to derive clinical data with which to populate the model. The issue of parameter uncertainty was addressed in the probabilistic sensitivity analysis; this showed that the choice of the rates of improvements in HbA1c had a significant impact on the ICER. However, the use of probabilistic methods does not negate the need for a systematic review of the available evidence.

Validity of estimate of measure of benefit
QALYs were used as the summary benefit measure. The utility weights came from the literature, but only limited information on their values was provided. Discounting was applied, in accordance with recent UK guidelines, and the use of different discount rates was investigated in the sensitivity analysis. The use of QALYs as an outcome measure enhances the comparability with the benefits of other health care interventions.

Validity of estimate of costs
The costs included were consistent with the perspective adopted in the study, although they were restricted to direct medical costs. The authors acknowledged this and stated that they believed that, as CSII is associated with improved
glycaemic control and fewer complications, the inclusion of the indirect costs would improve the cost-effectiveness of CSII therapy compared with MDI. A detailed breakdown of the cost items was provided, with the unit costs for most items being reported. No statistical analysis of the costs was performed in the base-case, although non-parametric bootstrapping methods were used to evaluate uncertainty. The source of the costs was given with NHS reference case costs being used rather than diabetic-specific costs. The authors acknowledged that this might have led to an underestimation of the actual costs for diabetic patients. The price year was reported, which aids reflation exercises in other time periods.

**Other issues**
The authors compared their findings with those from other studies. However, they did not explicitly address the issue of the generalisability of the study results to other settings. Several sensitivity analyses were performed which enhance, in part, the external validity of the study. The authors acknowledged that the data used to generate the model were derived primarily from clinical studies, which meant that "real life factors" such as compliance and treatment drop-outs were not included. The use of a peer-reviewed and validated model should enhance the validity of the findings, although the use of a systematic review to identify key model parameters would have added more credence.

**Implications of the study**
The authors suggested that the use of CSII over MDI for patients with Type I diabetes represents good value for money by current standards in the UK.

**Source of funding**
Funded by an unrestricted grant from Medtronic AG.

**Bibliographic details**

**PubMedID**
16108855

**DOI**
10.1111/j.1464-5491.2005.01576.x

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Cohort Studies; Computer Simulation; Cost-Benefit Analysis; Diabetes Complications /epidemiology; Diabetes
Mellitus, Type 1 /drug therapy /economics /epidemiology; Drug Administration Schedule; Female; Great Britain; Health Care Costs; Humans; Hypoglycemic Agents /administration & dosage; Incidence; Injections; Insulin /administration & dosage; Insulin Infusion Systems; Life Expectancy; Male; Prognosis; Quality of Life

**AccessionNumber**
22005001484

**Date bibliographic record published**
30/09/2006

**Date abstract record published**
30/09/2006