The cost-effectiveness of continuous subcutaneous insulin infusion compared with multiple daily injections for the management of diabetes

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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 use of continuous subcutaneous insulin infusion (CSII) was compared with multiple daily injections (MDI) for the treatment of diabetes.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised 10,000 simulated patients with insulin-dependent diabetes mellitus (IIDM) who were using an insulin pump.

Setting
The setting was unclear, but it was likely to have been primary care. The economic analysis was conducted in the UK.

Dates to which data relate
The effectiveness data were gathered from two key papers published in 2001 and 2002. The authors also referred to studies analysed in these papers, which were published between 1996 and 2002. The dates to which the cost data related were not reported. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from completed studies.

Modelling
A Markov model was constructed using Data Pro, to estimate the costs and effectiveness for two hypothetical cohorts of patients with IIDM, one treated with CSII and the other with MDI. The model consisted of two health states (well and dead), with transition states including hypoglycaemic events (requiring hospital treatment or requiring non-inpatient treatment) and ketoacidosis. Monthly cycles over a time horizon of 8 years were used. Monte Carlo simulations were undertaken to identify the distribution of the costs, effectiveness and cost-effectiveness.

Outcomes assessed in the review
The outcomes assessed in the review and used as model inputs were the incident rates of:
hypoglycaemic events;

admission to a hospital;

non-inpatients who attended the accident and emergency department, paramedic treatment, or who were assisted by family or colleagues;

ketoacidosis events;

insulin use; and

death from hypoglycaemia and from ketoacidosis.

Study designs and other criteria for inclusion in the review
There were two key papers. One was a systematic review (Lenhard et al., see Other Publications of Related Interest) and the other a meta-analysis (Pickup et al., see Other Publications of Related Interest). These papers were used as the basis for the model and for identifying randomised controlled trials to supplement any weak evidence and/or parameter values.

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
The effectiveness data were estimated from 9 studies.

Methods of combining primary studies
The authors referred first to a meta-analysis. To supplement any weak evidence and/or parameter values, the authors referred directly to randomised controlled trials.

Investigation of differences between primary studies
Not reported.

Results of the review
With MDI:

the incidence of hypoglycaemic events per person per year was 0.404 (standard deviation, SD=0.661);

the incidence of admission to a hospital was 0.242 (SD=0.099);

the proportion of non-inpatients who attended the accident and emergency department was 0.390 (SD=0.133), the proportion of those who received paramedic treatment was 0.670 (SD=0.228), and the proportion of those who were assisted by family or colleagues was 0.090 (SD=0.031);
the incidence of death from hypoglycaemia was 0.0005 (SD=0.0002);

the incidence of ketoacidosis events per person per year was 0.027 (SD=0.165); and

the incidence of death from ketoacidosis was 0.100 (SD based on authors’ assumption 0.034).

The effectiveness data for CSII compared with MDI (risk reduction) were as follows.

The incidence of hypoglycaemic events per person per year was 0.432 (SD=0.177).

The incidence of ketoacidosis events per person per year was 0.025 (SD=0.010).

The rate of insulin use was 0.142 (SD=0.057).

**Methods used to derive estimates of effectiveness**
The authors assumed the risk reduction in the incidence of admission to a hospital for CSII relative to MDI.

**Estimates of effectiveness and key assumptions**
The risk reduction in the incidence of admission to a hospital for CSII compared with MDI was assumed to be 0.050 (SD=0.020).

**Measure of benefits used in the economic analysis**
The authors used the quality-adjusted life-years (QALYs) as the summary benefit measure. To derive the utility weights, the authors resorted to a global quality of life score from a study of young adults (Boland et al., see Other Publications of Related Interest). The additional utility for CSII compared with MDI was 0.053. The monthly disutility weight associated with hypoglycaemic and ketoacidosis events, as estimated from the authors’ assumption, was 0.067. The health outcomes were discounted at 1.5%.

**Direct costs**
The perspective adopted was that of the UK NHS health care system. Only the direct costs were included in the analysis. These were for hypoglycaemic and ketoacidosis events, hospitalisation and non-inpatient treatment, a CSII pump, CSII and MDI consumables, and insulin. The baseline cost used for the CSII pump was the cost of a MiniMed pump marketed in the UK (Medtronics), which was similar to other CSII pumps. The costs and the quantities were not reported separately. The costs were estimated from NHS reference costs, the Personal Social Services Research Unit, the British National Formulary, and Drug Tariffs from the NHS for England and Wales. The costs were discounted at 6.0% due to the long time horizon of the model. All the costs were reported in year 2001 UK pounds.

**Statistical analysis of costs**
Each cost item was assigned a probabilistic distribution, which was used in the Monte Carlo simulation. A triangular distribution was assigned to the cost of the pump with a minimum and a maximum cost. The distribution of the remaining costs was represented through gamma distributions.

**Indirect Costs**
The indirect costs were not included.

**Currency**
UK pounds sterling (£).
Sensitivity analysis
A sensitivity analysis was conducted to identify the parameters that had the greatest effect on the results. A multivariate analysis was conducted on all parameters, except for the discount rate. One-way sensitivity analyses were conducted on the life of a CSII pump and the variables that were statistically significant in the multivariate analysis. The one-way sensitivity analysis was conducted as a deterministic analysis by using the mean values of the parameter distributions. A regression analysis, in which the parameter values sampled from the Monte Carlo simulation were regressed against the incremental cost-effectiveness ratio (ICER), was conducted to test the relative effects and statistical significance. A two-way sensitivity analysis was conducted on two of the factors that were found to be dominant.

Estimated benefits used in the economic analysis
Patients on CSII could, on average, expect to have 7.32 (SD=0.39) QALYs, whereas MDI patients could have 6.85 (SD=0.48) QALYs. In other words, an additional 0.48 (SD=0.20) QALYs could be gained from CSII.

Cost results
CSII cost, on average, 9,514 (SD=1,337) per patient, whereas MDI cost 4,052 (SD=1,792). In other words, CSII cost an additional 5,462 (SD=897) per patient.

Synthesis of costs and benefits
An ICER was calculated to combine the costs and benefits of the two strategies under evaluation.

The mean additional cost per QALY for CSII was 11,461 (SD=3,656).

For the 2.5% of cases with the lowest ICER, the ICER was less than 3,000. For the 2.5% of cases with the greatest ICER, the ICER was greater than 24,000.

CSII was cost-saving in 0.2% of cases.

At a willingness to pay threshold of 12,500 per QALY, 70.1% of cases would be acceptable. At a threshold of 15,000 per QALY, 81.4% would be acceptable.

Those who benefited most from a CSII pump were those who had more than two severe hypoglycaemic events per year and required hospital inpatient treatment at least once every 8 months for hypoglycaemia. CSII reduced the number of hypoglycaemic events by 62.4% and the number of events requiring hospital treatment by 68.8%. Those who were least likely to benefit from CSII were those who had relatively few hypoglycaemic events.

The sensitivity analyses identified two dominant factors, the additional utility from CSII (standardised coefficient -0.654, p<0.0001) and the rate of hypoglycaemic events (standardised coefficient -0.463, p<0.001). At their lowest values, the two-way analysis resulted in an ICER of 33,000 per QALY. At their highest values, the ICER was 380 per QALY.

Authors’ conclusions
Continuous subcutaneous insulin injection (CSII) is a worthwhile investment when targeted at those who might benefit most, namely those who had more than two severe hypoglycaemic events per year and required hospital inpatient treatment at least once every 8 months for hypoglycaemia.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used i.e. MDI. The comparator was chosen because it represented the next best 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 principal input parameters for the model were derived from published studies. However, it was unclear whether
the review was conducted systematically to identify relevant research and minimise biases. The bulk of the evidence
came from a meta-analysis and a systematic review. The authors reported the method used to derive the estimates of
effectiveness. The estimates were investigated in a sensitivity analysis, using ranges that appear to have been
appropriate. Some assumptions were also made and tested in the sensitivity analysis. Each model parameter was
assigned a stochastic distribution that was then used in the Monte Carlo simulation.

Validity of estimate of measure of benefit
The authors derived utility weights for calculating QALYs using a global quality of life score from a published study
and assumptions. The authors acknowledged that the utility weights should have been derived directly from the
patients' preferences. This fact limits the validity of the benefit estimates. The use of QALYs enhances the
comparability with the benefits of other health care interventions.

Validity of estimate of costs
The costs and the quantities were not reported separately and no details were given of the cost quantities. Authors’
assumptions were used. The dates to which the cost data related were not reported, which hinders the reproducibility
of the results in other settings. The price year was reported, thus aiding reflation exercises. A statistical analysis of the
costs and a sensitivity analysis were performed. A different discount rate was used for the costs compared to the health
outcomes. This choice follows the National Institute for Clinical Excellence recommendations. In terms of the
potential inclusion of the indirect costs, the authors stated that better diabetes control and fewer hypoglycaemic events
could reduce time off work, thus the cost-effectiveness of CSII would become even more attractive. The source of the
cost data was reported. The costs were treated stochastically since each item was attributed a probabilistic distribution
that was then used in the Monte Carlo simulation, as for the effectiveness estimates.

Other issues
The generalisability of the results was not addressed and the findings were not compared with those from other studies.
However, extensive sensitivity analyses were performed, which enhanced the external validity of the analysis. The
authors highlighted the limitations of their study (see other commentary fields) and do not appear to have reported
their results selectively.

Implications of the study
Since MDI is more commonly instituted without structured training, the authors suggested that it might be more cost-
effective to implement a structured training programme using MDI and reserve CSII for those who continue to have
difficulties with hypoglycaemia.

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Bibliographic details
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Other publications of related interest
Lenhard MJ, Reeves GD. Continuous subcutaneous insulin infusion: a comprehensive review of insulin pump therapy.
Archives of Internal Medicine 2001;161:2293-300.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Cost-Benefit Analysis; Diabetes Mellitus, Type 1 /drug therapy; Humans; Hypoglycemic Agents /administration & dosage; Infusion Pumps; Injections, Subcutaneous /economics /methods; Insulin /administration & dosage /economics; Insulin Infusion Systems /economics; Multivariate Analysis; Patient Satisfaction; Quality of Life

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