A health economic analysis of clinical islet transplantation
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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 islet cell transplantation, compared with standard insulin therapy, for adults with type one diabetes mellitus and hypoglycaemic unawareness. The authors concluded that islet cell transplantation was more effective than insulin therapy and became cost saving after nine or 10 years. The cost-effectiveness framework was conventional, but the data sources were not extensively reported. The authors’ conclusions appear to be robust, but further studies are needed.

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

Study objective
This study examined the cost-effectiveness of islet cell transplantation, compared with standard insulin therapy, for adults with type one diabetes mellitus and hypoglycaemic unawareness.

Interventions
The two strategies were islet cell transplantation and standard insulin therapy in patients with type one diabetes mellitus.

Location/setting
USA/tertiary and primary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a 20-year time horizon and a hypothetical cohort of 20-year-old patients with type one diabetes. The authors did not explicitly state the perspective.

Effectiveness data:
Most of the clinical inputs, for disease progression in patients receiving standard insulin therapy, were from the Diabetes Control and Complications Trial, which was carried out in the USA between 1990 and 1993. The proportions of patients with full graft function and graft failure were key inputs for the model and the short-term data were from a clinical trial of 30 patients receiving transplantation. The long-term data were based on logarithmic regressions. It was assumed that there were no differences in mortality between the two strategies.

Monetary benefit and utility valuations:
The utility values were from published studies.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years were the summary benefit measures. The QALYs associated with each health state in the model were from published studies.

Cost data:
The economic analysis included the costs of the insulin therapy, islet cell transplantation (donor organ, islet manufacturing, screening, and various medical procedures), immunosuppressive therapy, various diabetes-related complications, post-transplant complications, and death. The costs of labour, medication, tests, materials, and procedures were considered within complication costs. The cost data were from published studies. The cost of islet cell transplantation was from the manufacturer and the cost of immunosuppression was based on the highest priced...
combination of drugs. All costs were in US $, the price year was 2007, and a 3% annual discount rate was applied.

Analysis of uncertainty:
A probabilistic sensitivity analysis was carried out, using Monte Carlo simulation. Normal distributions were assumed for each parameter, with a standard deviation of 25%. One-way sensitivity analyses were carried out considering alternative assumptions for graft survival, diabetes complications, hypoglycaemic unawareness in the insulin arm, two donors per recipient, and the inclusion of trial costs.

Results
The expected 20-year costs were $663,000 with insulin, and $519,000 with islet transplantation. The QALYs were 9.3 with insulin and 10.9 with transplantation. The life-years were 15.0 with insulin and 15.0 with transplantation.

The average cost per QALY was $71,000 with insulin and $47,800 with islet cell transplantation. Transplantation was dominant as it was more effective and less expensive than insulin. When life-years were considered, transplantation was cost saving and equally effective.

The costs of transplantation were higher at the start of the model, given its high initial cost, but the breakeven level was reached after nine years. The QALYs were higher with transplantation than with insulin throughout the simulation.

The results of the probabilistic analysis confirmed these findings. At 10 years, the average cost-utility ratios were $40,000 with islet cell transplantation and $44,800 with insulin. At five years, they were $48,900 with transplantation and $27,700 with insulin, due to the initial costs of transplantation.

The model was not sensitive to variations in the parameters considered in the one-way sensitivity analyses. Transplantation remained dominant up to an initial procedure cost of $240,000.

Authors' conclusions
The authors concluded that islet cell transplantation was more effective than insulin therapy and became cost saving after nine or 10 years.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the proposed intervention was compared with the usual therapy for these patients.

Effectiveness/benefits:
The data on disease progression and the treatment effect were from clinical trials, but the estimates for insulin were from trials conducted almost 20 years before this study, and the estimates for islet cell transplantation were from a trial with a very small sample and short follow-up. Important assumptions were made for the long-term impact of islet cell transplantation and that mortality was the same for each option. These assumptions were tested in the sensitivity analysis and the base-case results were robust, but only based on average cost-effectiveness ratios. QALYs and life-years were appropriate benefit measures, as they capture the impact of the interventions on patients’ health. The QALYs were from various publications that estimated quality of life in diabetic patients. These sources were not described. No discounting of benefits was reported and it would have been relevant given the length of the analysis (20 years).

Costs:
The economic viewpoint was not explicitly stated, but those costs borne by the health care provider were included. The reporting of the economic details was poor; the costs were presented as category totals and not for individual items. The unit costs and quantities of resources were not reported and the data sources were not described. It is likely that US sources were used for all the economic estimates. The costs were varied in the sensitivity analysis and they were appropriately discounted. The price year was reported, allowing reflation exercises.

Analysis and results:
The results were extensively presented. Average cost-utility ratios were calculated to combine the costs and benefits of
the strategies. An incremental analysis was not performed as islet cell transplantation was dominant. Appropriate sensitivity analyses were carried out to assess uncertainty. The results of all simulations were clearly presented and confirmed the base-case findings, but these analyses focused on changes in average cost-effectiveness ratios, rather than assessing changes in the incremental cost-effectiveness ratio for the two options. The distributions assigned to the model parameters were not justified. This analysis appears to be specific to the US context and might be difficult to transfer to other settings given the low external validity of the data.

Concluding remarks:
The cost-effectiveness framework was conventional, but the data sources were not extensively reported. The authors’ conclusions appear to be robust, but further studies are needed.

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