An economic evaluation of pediatric small bowel transplantation in the United Kingdom

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 paediatric small bowel transplantation (SBTx) for the treatment of chronic intestinal failure in children.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children with chronic intestinal failure who were assessed for their suitability for SBTx. The study divided the patient population into three groups:

- those in need of SBTx because of life threatening complications and who were placed on the transplant waiting list;
- those not in need of SBTx because complications were not life threatening; and
- those terminally ill from long-term complications and so unable to survive a transplantation operation.

Setting
The setting was secondary care in Birmingham Children's Hospital, UK. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data related to 1997 to 2001. The price year was 1998/99.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The resource use data were collected prospectively from the same patient sample used in the effectiveness analysis.

Study sample
No power calculations were performed. This was justified given the rarity of the disease and the fact that a randomised controlled trial was not ethically feasible. All patients considered for SBTx suitability at Birmingham Children's Hospital were included in the study. The authors asserted that the study recruited approximately one third of the UK patient population receiving parenteral nutrition. Fifty-three patients were recruited to the study. Of these, 23 were identified as requiring transplantation, 24 were identified as stable and not requiring transplantation, and 6 were
identified as terminally ill.

**Study design**
This was a single-centred, prospective, cohort study. The length of follow-up was 30 months.

**Analysis of effectiveness**
The analysis of effectiveness was conducted in three ways. The first merely calculated the costs and survival of each of the three categories of patient. The second analysis used a prognostic model to compare and predict the costs and survival for patients who received transplantation had they not received transplantation. The third analysis compared patients awaiting transplant with those who received a transplant. The primary health outcome was survival.

**Effectiveness results**
The mean survival over 30 months for patients who fulfilled the criteria for transplantation was 1.77 years (95% confidence interval, CI: 1.94 to 2.43) (these figures match those reported in the trial, which appear to be in error as the mean estimate lies outside the confidence limits).

The mean survival over 30 months among patients not requiring transplant was 2.33 years (95% CI: 1.33 to 2.14) (again, these figures match those reported in the study).

All patients who were categorised as terminally ill died before the 30-month follow-up. Mean survival was 0.31 years (95% CI: 0.13 to 0.48).

The prognostic model was applied to the 14 patients who received a transplant. It estimated that transplantation increased survival by 0.12 years (95% CI: -0.52 to 0.74).

The “intent-to-treat” model was applied to the 23 patients who fulfilled the criteria for transplantation (including the 14 that went on to receive transplant). It estimated that transplantation reduced survival by 0.24 years (95% CI: -0.93 to 0.45).

**Clinical conclusions**
The authors concluded that the prognostic model was likely to be less biased than the intent-to-treat analysis, as allocation of transplant organs to recipients was not randomised. They concluded that the analysis suggested that SBTx was life-extending, but the small size of the study meant that it should only be provided in the context of further assessment of the technology.

**Modelling**
A prognostic model was used to estimate what the survival and costs for patients who received transplants would have been had they not undergone transplantation. This model was used to calculate cost-effectiveness in the “prognostic model” analysis. The prognostic model included patient age and prothrombin times, and it was assumed that patient costs in the absence of transplantation would be the same as their pre-transplantation costs. An “intent-to-treat” model estimated cost-effectiveness by comparing the costs and outcomes of patients who received transplantation with the costs and outcomes of patients awaiting transplantation.

**Measure of benefits used in the economic analysis**
The measure of benefits used was the life-years gained.

**Direct costs**
The study included the direct costs to the health service. These were length of inpatient stay, number of outpatient,
physician and dietician attendances, laboratory tests, medication, treatments and blood products received, details of parenteral and enteral nutrition, and length of transplant operation. The costs and the quantities were not reported separately. Local unit costs were obtained from Birmingham Children's Hospital and the price year was reported as 1998/99. A discount rate of 3.5% per annum was applied to the costs, which was in line with UK guidelines. The study reported the average costs. Medical staff time costs were not included beyond those already incorporated in the unit costs of inpatient stay, outpatient stay and transplant operation.

**Statistical analysis of costs**
Lin's method was used to adjust for censored cost data. A non-parametric bootstrapping method was used to generate confidence limits around mean estimates. This is appropriate when data are skewed, as is common with cost data. The bootstrapped estimates were also used to demonstrate the distribution of incremental cost-effectiveness ratios.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
Two alternative analyses were applied to calculate the cost-effectiveness of SBTx in the absence of randomised, controlled data: the "prognostic" model and the "intent-to-treat" model.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The mean cost over 30 months was 207,000 (95% CI: 168,000 to 253,000) for patients who fulfilled the criteria for transplantation, 159,000 (95% CI: 125,000 to 199,000) for patients not requiring transplantation, and 56,000 (95% CI: 12,000 to 171,000) for patients categorised as terminally ill. The cost per day was highest for patients categorised as terminally ill.

The results of the "prognostic" model indicated that transplantation reduced costs by 50,495 (95% CI: -49,448 to 38,301) over 30 months in comparison with parenteral nutrition. The results of the "intent-to-treat" model indicated that transplantation increased costs by 131,307 (95% CI: 51,450 to 211,517) in comparison with parenteral nutrition. A discount rate of 3.5% per annum was applied in these calculations.

**Synthesis of costs and benefits**
The costs and benefits were synthesised in order to calculate the cost per life-year gained.

The results of the "prognostic" model indicated that SBTx was dominant (i.e. more effective and less costly) than parenteral nutrition. On the cost-effectiveness plane 57% of ratios indicated that SBTx was dominant, while 29% indicated that it might be cost-saving but less effective than parenteral nutrition.

The results of the "intent-to-treat" model indicated that SBTx was dominated (i.e. more costly and less effective) by parenteral nutrition. On the cost-effectiveness plane 77% of ratios indicated that SBTx was dominated, while 23% indicated that SBTx may be cost-effective compared with parenteral nutrition, depending on the willingness-to-pay per life-year gained.
Authors' conclusions
The authors conclude that the "prognostic" model was least likely to be subject to bias. However, they stated that the conflicting results from the analyses meant that it was impossible to come to firm conclusions about the cost-effectiveness of small bowel transplantation (SBTx) relative to parenteral nutrition.

CRD COMMENTARY - Selection of comparators
The comparator was selected to represent current practice in the study setting. You must decide whether parenteral nutrition and SBTx procedures in the UK are representative of treatment for chronic intestinal failure in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single study. The authors stated that a randomised trial would not be possible in this area, so a cohort study design was used, alongside analyses that attempted to "impute" a control group. The study sample was representative of the study population. The authors applied two alternative analyses to calculate effectiveness and discussed the limitations of both. They stated that the prognostic model should ideally be validated in a larger study and that the intent-to-treat model was likely to be the more biased of the two.

Validity of estimate of measure of benefit
The measure of health benefit was proxied directly by effect on survival. The authors stated that it was not possible to assess the impact of SBTx on health-related quality of life in the present study.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. Although staff time costs were included in the unit costs for inpatient and outpatient visits and transplant operations, the staff time costs of dedicating a member of staff to monitoring the progress of patients were not included. The authors stated that this cost is likely to be higher in the parenteral nutrition group, as the costs of monitoring patients who receive a transplant may be expected to fall after 30 months. The unit costs were not reported separately from the resource quantities. The resource use quantities were collected prospectively from the same patient sample as that used in the effectiveness study. A non-parametric bootstrap method was applied to calculate confidence limits around the mean costs. Local unit costs were obtained from Birmingham Children's Hospital but were not reported in detail, which may limit the generalisability of the study results. The dates to which the prices related was reported.

Other issues
The authors compared their results with findings from similar evaluations conducted in adult populations. Patients were recruited from all over the UK, but the issue of generalisability to settings outside the UK was not addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors stated that, during the study, a new operation was devised which may increase the number of patients eligible for transplant.

Implications of the study
The authors recommended that further research be conducted to establish the cost-effectiveness of paediatric SBTx.

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