Cost-effectiveness of somatropin for the treatment of short children born small for gestational age

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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
The objective was to determine whether somatropin was a cost-effective treatment for children born small for gestational age, who remained of short stature. The authors concluded that somatropin was cost-effective for these children, from the perspective of the UK NHS. The methods were satisfactory, and they and the results were sufficiently reported, except for the effectiveness data. The authors' conclusions appear to be appropriate.

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

Study objective
The aim was to determine whether somatropin was a cost-effective treatment for children born small for gestational age (SGA) and of short stature.

Interventions
A daily injection of somatropin (0.033mg per kg) was compared with no pharmacologic intervention.

Location/setting
UK/secondary care.

Methods
Analytical approach:
A Markov model was constructed to combine the data from a clinical trial and published sources. The time horizon was the lifetime of the children. The authors stated that the perspective was that of the UK NHS.

Effectiveness data:
The effectiveness data were from an unpublished somatropin trial (data on file at Novo Nordisk Ltd. study reference GHRETARD/BPD/14-20-21/NL, 2007). This was a multicentre, double-blinded, trial, with 79 children, more than two standard deviations below the mean height, randomised to receive low-dose (0.033mg per kg) or high-dose (0.067mg per kg) daily somatropin. An intention-to-treat analysis of patients in the low-dose arm (0.033mg) who met defined criteria was performed and this included 19 children. The somatropin trial had an initial two-year study period, with subsequent follow-ups to assess growth to adult height. Growth hormone treatment was continued for 13 years after the initial two-year period (a total of 15 years). UK mortality was applied for each year of the model. The main clinical effectiveness estimate was the patient's height.

Monetary benefit and utility valuations:
The utility data were from a UK study of the general population and were elicited using the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
The primary measure of benefit was quality-adjusted life-years (QALYs). A secondary measure was centimetres of height gained. The long-term benefits were discounted at a rate of 3.5%.

Cost data:
The cost categories were drugs, endocrinologist's time, specialist and community nurse visits, blood tests, and radiography of the hands. These costs were from published sources including the British National Formulary. The unit cost of somatropin was from the monthly index of medical specialities and the resource use was based on a health technology assessment. All costs were presented in 2007 to 2008 UK pounds sterling (£) and discounted at a rate of 3.5% per annum.

Analysis of uncertainty:
One-way, two-way, and probabilistic sensitivity analyses were undertaken. The one-way analysis varied each model parameter within its 95% confidence interval. The results were displayed in a tornado diagram. The two-way analysis assessed the impact of the discount rate on the costs and outcomes. The probabilistic analysis used 10,000 simulations. These results were presented in a cost-effectiveness acceptability curve.

Results
Over a patient's lifetime, somatropin was associated with an additional height gain of 16.12cm and a cost per cm of height gained of £4,359, compared with no treatment.

The total incremental cost of somatropin was £70,263, with a QALY gain of 2.95, compared with no treatment. This resulted in an incremental cost per QALY of £23,807, which was below the widely accepted cost-effectiveness threshold in the UK of £30,000.

The one-way sensitivity analysis showed that the results were sensitive to changes in the discount rate for outcomes, the starting height, and the utility values. The probabilistic analysis found that somatropin was cost-effective, in 68.74% of simulations, at a willingness-to-pay threshold of £30,000 per QALY.

Authors' conclusions
The authors concluded that somatropin was cost-effective for short children born SGA, from the perspective of the UK NHS.

CRD commentary
Interventions:
The interventions were well reported and appear to have been appropriate comparators.

Effectiveness/benefits:
The effectiveness data were from one clinical study. This study was described as a multicentre, double-blinded, randomised clinical trial, which should ensure that it was of good quality, but without consulting the unpublished manufacturer's report it is not possible to fully assess its quality. The authors noted that the small sample of the clinical trial was a limitation of their study. The intervention group was well described, but little information was given on the no treatment group. It is unclear how similar these groups were, and no confounding analysis was discussed to control for differences between the groups. The benefit measure appears to have been appropriate, as it incorporated both the morbidity and mortality of the patients. The methods used to derive this estimate were described and it was appropriately discounted.

Costs:
The perspective was clearly reported and the costs appear to have been relevant. The costs of adverse events were not included, but were relevant; these events were rare and so were not included. The unit costs and resource use data were sufficiently reported. The costs were appropriately discounted and adjusted for inflation.

Analysis and results:
The decision model was described and a diagram was included. The model appears to have appropriately synthesised the data and the results were reported adequately. Several methods were used to assess the uncertainty of the model; these were described and the results were well reported. The authors discussed some of the limitations to their study.

Concluding remarks:
The methods were satisfactory, and they and the results were sufficiently reported, except for the effectiveness data.
The authors' conclusions appear to be appropriate.

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