Cost-utility of somatropin (rDNA origin) in the treatment of growth hormone deficiency in children

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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 somatropin (recombinant DNA origin) for the treatment of growth hormone deficiency (GHD) in children and adolescents.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The hypothetical study population comprised children and adolescents aged 5 to 16 years and 3 to 18 years with GHD.

Setting
The setting was not specified. The economic analysis was conducted in the USA.

Dates to which data relate
The effectiveness data appear to have been derived from authors' assumptions. The cost data were derived from two publications published in 2005. Resource use was derived from estimates of adolescent weights published in 1994. The price year was 2005.

Source of effectiveness data
The effectiveness data were derived from authors' assumptions.

Modelling
A decision-analytic model of the epidemiology and treatment of GHD was developed to estimate the costs and benefits of treatment. The time horizon considered was the life span of the population. This was assumed to be approximately 78 years in males and 80 years in females. No graphical representation or narrative description of the model pathways was provided.

Outcomes assessed in the review
It was unclear from the paper which, if any, of the model input parameters were obtained from a review of the literature.
Study designs and other criteria for inclusion in the review
Not reported.

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
Not reported.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
Not reported.

Methods used to derive estimates of effectiveness
The authors made assumptions to derive some of the estimates of effectiveness.

Estimates of effectiveness and key assumptions
The authors made the following assumptions:

gender made no difference to treatment outcome;

discontinuation after 12 months was equal to 20%;

the probability of success for treatment starting at 3 years and continuing up to 18 years was 90%; and

the probability of success for treatment starting at 5 years and continuing up to 16 years was 75%.

Measure of benefits used in the economic analysis
The NHYs gained was the measure of benefit used in the cost-effectiveness study, while the QALYs gained was the measure of benefit in the cost-utility assessment. The Index of Health Related Quality of Life (IHQL) was the quality of life measure used in the study. The IHQL utility values used in the study were one level lower than the rating reported in the literature in order to reflect more accurately real world situations in which patients would not achieve full utility gains.
Direct costs
The direct costs included were those incurred once a diagnosis of GHD had been confirmed. Resource use was assumed, whilst costs were derived from Medicare and published sources. The cost of the drugs was based on dose needed for weight, based on the weight for age derived from National Centre for Health Statistics. The resource quantities and the unit costs were reported separately. Discounting was carried out at a rate of 3%, which was appropriate since the costs were incurred during more than one year. The price year was 2005.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
Inline with the perspective adopted, the indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Both univariate and multivariate sensitivity analyses were used to test the robustness of the model to variations in the key assumptions and input parameters. The analyses considered:

- two alternate daily dosing assumptions (0.024 and 0.34 mg/kg per day);
- variation in the 1-year discontinuation rate from 0 to 50%;
- discount rates of 3% and 6% for the costs and 0% for the benefits;
- variation in the probabilities of attaining normal height from 50 to 110% of the base-case;
- increasing the number of primary care physician (PCP) visits to 4 per patient per year;
- using a pre-treatment utility score of 0.884;
- using weights of 0.5 and 0.8 for gain in partial success QALYs compared with successful treatment QALYs; and
- reducing the time periods over which post-treatment QALYs were applied to 20 and 40 years.

The authors used combinations of the above in different multivariate analyses.

Estimated benefits used in the economic analysis
Non-discounted NHYs gained through treatment with somatropin were estimated to range from 51.4 years (treatment from ages 3 to 18 years) to 41.6 years (treatment from ages 5 to 16 years). The corresponding values for discounted NHYs gained were 21.1 and 17.4 years.

Non-discounted QALYs were estimated to range from 12.6 years (treatment from ages 3 to 18 years) to 10.2 years (treatment from 5 to 16 years). The corresponding values of discounted QALYs gained were 4.6 and 4.2 years.

Cost results
Compared with no treatment, the incremental cost of somatropin therapy was $184,428 undiscounted ($155,005 discounted) for the cohort aged 5 to 16 years and $252,030 undiscounted ($195,758 discounted) for the cohort aged 3 to 18 years.
Synthesis of costs and benefits
The cost of treatment between 5 and 16 years was $8,909 per NHY gained and $36,995 per QALY gained.

The cost of treatment between 3 and 18 years was $9,277 per NHY gained and $42,556 per QALY gained.

The outcomes of the model were found to be relatively insensitive to variation in the sensitivity analysis.

Authors’ conclusions
The treatment of growth hormone deficiency (GHD) in children with somatropin appears likely to be cost-effective according to generally accepted standards.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. It represented standard practice in the authors’ setting. You should decide if it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was heavily reliant on the authors’ assumptions. It was not clear if the assumptions were well informed and constructed from the literature, or if they were assumed based on conjecture. There does not appear to have been a review of the literature as the authors did not report any findings. The high number of assumptions represents a threat to the validity of the measure of effectiveness. The sensitivity analysis helps, but poor reporting of the initial model inputs makes it difficult to ascertain the validity of the outcomes.

Validity of estimate of measure of benefit
The measure of benefit used in the incremental cost-effectiveness analysis was the NHYs gained. This is disease specific and so cannot be directly compared in terms of value with the results for other diseases. The measure of benefit in the cost-utility analysis was the QALYs gained using the IHQL, which is a widely used method and permits comparison with other interventions. Both outcomes were obtained through modelling. However, only limited details of the model were presented. A more thorough description of pathways and structure would have enhanced the paper.

Validity of estimate of costs
The direct costs were reported. These appear to have included all those relevant to the perspective adopted. The unit costs and resource use were presented separately, which will aid generalisability. However, resource use was based on assumptions and it is not immediately clear how appropriate the assumptions were. Discounting was performed, which was appropriate since the costs were incurred during more than one year. The discount rate was subjected to extensive sensitivity analysis, although other cost and resource parameters were not.

Other issues
The authors acknowledged the limitation to their study imposed by their need to use assumptions to populate their model. However, they also pointed out that the sensitivity analysis suggests that the conclusions were robust even after varying the model parameters. The reliance on assumptions is likely to reflect the situation regarding evidence in the literature. However, to enhance the quality of the study, a more thorough presentation on the methods used to attempt to populate the model from the literature and the methods used to obtain the assumed estimate is required.

Implications of the study
Future research on patient quality of life and associated utilities appears warranted and it would improve understanding of the impact of treatment from a patient perspective.
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Other publications of related interest
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Child; Child, Preschool; Costs and Cost Analysis; DNA, Recombinant; Dwarfism, Pituitary /drug therapy /economics; Female; Great Britain; Human Growth Hormone /administration & dosage /economics /genetics /therapeutic use; Humans; Male; Quality-Adjusted Life Years

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