A cost-effectiveness analysis of rhDNase in children with cystic fibrosis

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 daily recombinant human deoxyribonuclease (rhDNase) for the treatment of respiratory-tract infections in children with cystic fibrosis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of children with cystic fibrosis.

Setting
The setting was a hospital or community services. The economic analysis was carried out in the UK.

Dates to which data relate
The dates to which the effectiveness data related were not reported. The resources used were estimated from a variety of sources, but the dates to which the resources related were not reported. All the unit costs were adjusted to 1999 - 2000 prices using the hospital and community health services price index.

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

Link between effectiveness and cost data
The costing was undertaken prospectively on the same group as that used in the effectiveness study.

Study sample
The methodology of the study has been detailed elsewhere (Suri et al., see Other Publications of Related Interest). The inclusion criteria were not stated. A total of 47 patients were recruited to the study. Seven patients withdrew from one or all of the treatment periods and were excluded from the analysis. The remaining 40 children had consecutively received 12 weeks of daily rhDNase, alternate-day rhDNase and HS, with a 2-week washout period between treatments. No evidence was given that the initial study sample was appropriate for the clinical study question. Power calculations were not used to determine the sample size.
Study design
The methodology of the study has been detailed elsewhere (Suri et al., see Other Publications of Related Interest). The study was based on a randomised controlled trial with a crossover design, and was carried out in a single centre. The duration of follow-up was 12 weeks of treatment. No further details were reported within this paper.

Analysis of effectiveness
The analysis of the clinical study conducted on the basis of treatment completers only. The primary health outcome was the patients’ lung function, as measured by the forced expiratory volume in 1 second (FEV1). The incremental effectiveness was calculated on a log scale and the results were interpreted in percentage differences in FEV1. For each treatment period, the change in effectiveness was calculated by assessing the difference in the natural log of FEV1 between the end and beginning of treatment, and then the difference was compared between treatments.

Effectiveness results
In the HS group, no change in effectiveness was observed. In the daily rhDNase group, a 14% change in FEV1 was observed.

In the alternate-day rhDNase group, a 12% change in FEV1 was observed.

Compared with HS, there was a 14% improvement in FEV1 for daily rhDNase (95% confidence interval, CI: 5 - 13) and a 12% improvement (95% CI: 2 - 22) for alternate-day rhDNase.

There was no significant advantage for daily compared with alternate-day rhDNase (2% improvement in FEV1, 95% CI: -6 - 12).

Clinical conclusions
The administration of rhDNase on an alternate or daily basis was more effective than HS. Daily rhDNase did not improve the patient's lung function in comparison with alternate-day rhDNase.

Measure of benefits used in the economic analysis
The authors did not develop a summary benefit measure. The primary health outcome, gain in FEV1, was expressed as benefits.

Direct costs
The resources included hospital contacts (inpatient, outpatient, and day case), radiological investigations, blood tests, drugs and the use of community services. Community services included the community nurse, physiotherapist and general practitioner. The resource data were recorded from the patients’ hospital notes, discharge letters, and by contacting the supervising physicians. The unit costs of the health services were collected at two postgraduate hospitals where the patients were recruited, and from a local district general hospital. The drug costs were taken from the British National Formulary, while the community care costs from Netten et al. (see Other Publications of Related Interest). All the costs were adjusted to 1999 - 2000 prices using the hospital and community health services price index. The resource quantities were reported, but not the unit costs. Discounting was not carried out since the costs were incurred over less than 2 years.

Statistical analysis of costs
The costs were treated statistically. The mean incremental cost was reported with 95% CIs, and calculated using the non-parametric bootstrap method.

Indirect Costs
No indirect costs were reported.

**Currency**
UK pounds sterling ( ).

**Sensitivity analysis**
Sensitivity analyses were carried out on the British National Formulary prices (varied by 10 - 30%) and on the costs per hospital day.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
The total cost was 4,285 in the HS group, 5,694 in the daily rhDNase group and 5,230 in the alternate-day rhDNase group.

The main reason for the difference in the total cost was that the unit cost of rhDNase (20.39 per day) was higher than that for HS (0.38 per day).

The mean incremental cost of daily rhDNase compared with HS was 1,409 (95% CI: 354 - 2,277). This cost was 945 (95% CI: -509 - 2,301) for alternate-day rhDNase compared with HS, and 464 (95% CI: -647 - 1,510) for daily compared with alternate-day rhDNase.

**Synthesis of costs and benefits**
Alternative measures of cost-effectiveness, including cost-effectiveness-acceptability curve and net benefit statistic, have been developed. The non-parametric bootstrapping approach was used to plot the incremental costs and effects on the cost-effectiveness plane using 2,000 samples. Net benefits on the cost scale were defined on the basis of the ceiling ratio, costs and effects (equation provided). The ceiling ratio, defined as the healthcare decision makers’ willingness to pay, was varied from 0 to 400 per 1% improvement in FEV1.

The incremental cost-effectiveness ratio (ICER) of daily rhDNase compared with HS was 110. The ICER of alternate-day rhDNase compared with HS was 89. The ICER of daily compared with alternate-day rhDNase was 214. If the decision-maker had a ceiling ratio of 200 for a 1% gain in lung function (i.e. forced expiratory volume in 1 second) over a 12-week period then, on average, either rhDNase strategy has positive net benefits compared with HS and should be adopted. In addition, the provision of alternate-day rhDNase may be the more cost-effective alternative.

**Authors’ conclusions**
Recombinant human deoxyribonuclease (rhDNase) improves outcomes at an increased cost. If the decision-makers are prepared to pay 200 for a 1% gain in lung function (i.e. forced expiratory volume in 1 second) over a 12-week period then, on average, either rhDNase strategy has positive net benefits compared with HS and should be adopted. In addition, the provision of alternate-day rhDNase may be the more cost-effective alternative.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the comparator used. The comparator (HS) was chosen because it represented a treatment alternative for cystic fibrosis in the authors' setting. You should consider whether this is a widely used health
technology in your own setting.

**Validity of estimate of measure of effectiveness**
The estimate of effectiveness is likely to be internally valid given that a randomised controlled trial was used. However, this should not be assumed without reference to the original paper where the details of the randomised controlled trial have been published. The authors justified the choice of the effectiveness measure in preference to a measure health-related quality of life, which would have been unlikely to have been sensitive to a change in treatment regimen over 12 weeks. Although a randomised controlled trial was conducted, the outcomes were analysed for treatment completers only.

**Validity of estimate of measure of benefit**
The authors did not derive a measure of health benefit. The authors acknowledged the narrowness of the outcome measure used, which limits comparisons of ICER with other studies, and that quality-adjusted life-years would have been more appropriate. However, the authors justified their final choice (see above).

**Validity of estimate of costs**
The perspective adopted for the economic analysis was not specifically stated, but it is likely to have been that of the UK National Health Service. The authors did not include the indirect costs in the analysis. The exclusion of these is unlikely to have affected the authors' conclusions, because these costs should be common to the treatment alternatives. The resource quantities and total cost were reported. A statistical analysis of the quantities was performed. Also, a sensitivity analysis of the prices was conducted. Since all the costs were incurred over less than one year, discounting was unnecessary.

**Other issues**
The authors noted that the possibility of comparing their results to other competing interventions was limited due to the outcome measure used. The authors conducted a sensitivity analysis on the prices to assist with the generalisability of the results, but the generalisability of the results to other settings or countries was not specifically discussed. The authors did not present their results selectively. The study enrolled children with cystic fibrosis and this was not clearly reflected in the authors' conclusions. The extension of the study period over at least one year would have been more appropriate and would have allowed comparisons with other studies. The methods used in the study to assess the uncertainty around the cost-effectiveness measures were particularly relevant and useful for the decision-maker's understanding.

**Implications of the study**
A larger study would be required to establish that alternate-day rhDNase is more cost-effective than daily rhDNase. Further studies are also needed to assess the cost-effectiveness of new high-cost interventions for cystic fibrosis. Further work should examine the extent to which incorporating statistical measures of uncertainty in unit costs may change the estimation of the magnitude of uncertainty surrounding the cost-effectiveness results.

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Other publications of related interest


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