A cost-utility analysis of interferon beta for multiple sclerosis

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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
Use of interferon beta (IFNB-1b) for people with relapse-remitting multiple sclerosis (MS).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
Ambulant patients with relapse-remitting multiple sclerosis.

Setting
The practice setting was the community. The clinical trial was conducted in the USA and Canada. Economic analyses were carried out in the UK.

Dates to which data relate
Effectiveness data were taken from a trial reported in 1993 and updated in 1995. QoL and resource data were collected during the study in 1996 and 1997. Price data referred to 1996 and 1997. The price year was not given.

Source of effectiveness data
The effectiveness data were derived from a single trial and a review of previous studies.

Study sample
In the clinical trial 372 ambulatory patients with clinically definite or laboratory-supported MS for more than 1 year were randomly allocated to placebo, low dose (1.6 MIU) IFNB-1b or high dose (8.0 MIU) IFNB-1b. 123 patients received placebo, 125 low dose treatment and 124 high dose treatment. Prior treatment with azathioprine or cyclophosphamide excluded patients from the trial.

Study design
The study was a randomised double-blind, placebo-controlled trial. The study was multicentred with 11 different medical centres in the US and Canada. The initial follow-up period was for 2 years, (later extended to 5 years for some patients). 65 patients discontinued treatment during the first 2 years (23 in the placebo, 16 low dose, 24 high dose).

Analysis of effectiveness

NHS Economic Evaluation Database (NHS EED)
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Analysis was based on intention to treat. The primary health outcomes were differences in exacerbation rates and the proportion of patients remaining exacerbation-free. The 3 groups were comparable in terms of baseline and demographic characteristics.

**Effectiveness results**
The annual exacerbation rate for placebo was 1.27, for low dose IFNB-1b it was 1.17 and for high dose it was 0.84, after 2 years. Exacerbation rates were significantly lower in both treatment groups compared to placebo (8 MIU versus placebo p=0.0001; 1.6 MIU versus placebo p=0.0101; 8 MIU versus 1.6 MIU p=0.0086)

**Clinical conclusions**
IFNB-1b is the only treatment that has substantially altered the natural history of MS in a properly controlled clinical trial.

**Modelling**
This study involved the construction of a cost-effectiveness model for IFNB-1b for relapse-remitting multiple sclerosis.

**Outcomes assessed in the review**
The outcomes assessed were the differences in QoL between groups of patients with MS and compared with the general population (MS-QoL & EQ-5D). Estimated changes in QoL arising from IFNB therapy.

**Study designs and other criteria for inclusion in the review**
There had only been one reported trial considering the effectiveness of IFNB-1b, which was a randomised, double-blind, placebo-controlled trial. This was included in the model. Other studies considering the natural history of the disease were included for their information about disease progression probabilities.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Only one trial of IFNB-1b has been carried out.

**Methods used to judge relevance and validity, and for extracting data**
Only one trial of IFNB-1b has been carried out.

**Number of primary studies included**
One study reporting the effectiveness of the drug in terms of relapse rates was used. Three other studies were used to inform disease progression probabilities.

**Methods of combining primary studies**
Not applicable as only one trial of IFNB-1b has been carried out.

**Investigation of differences between primary studies**
Not applicable as only one trial of IFNB-1b has been carried out.
Results of the review
The model combined data from the different sources. Over a five year period 1.52 fewer relapses were achieved in the IFNB-1b therapy group. This study also used figures showing a slightly slower worsening of the disease in those receiving IFNB-1b.

Measure of benefits used in the economic analysis
The measure of benefits was differences in cost between groups of patients with MS. Estimated changes in QoL and costs arising from IFNB therapy.

Direct costs
Costs were discounted at 6%. Quantities and costs were analysed separately. The resources measured were: inpatient stays, outpatient visits, procedures, appliances and diagnostic tests. The cost perspective was that of the health service (NHS). Quantities were based on actual data collected from patient notes in 1996 and 1997. Cost data were based on actual costs from local hospital sources, the CIPFA database and PSSRU community costs. Cost data referred to 1996 and 1997. No price year was given.

Statistical analysis of costs
The variability of cost data was not analysed. However, the relationship between cost and disability status was considered in a simple regression analysis.

Indirect Costs
Not considered.

Currency
UK Pounds Sterling ().

Sensitivity analysis
Numerous sensitivity analyses were carried out. One-way analyses were carried out to test the robustness of the point estimate from the 5 year model. A range of variables was varied, the largest changes were associated with changes in the frequency and duration of relapses and their associated utility loss. Two types of sensitivity analysis were carried out on the 10 year model. First, a range of variables was changed to produce a 'best case' (optimistic views about the natural history of MS) and a 'worst case' scenario. Second, threshold analysis was carried out to show the values needed to achieve cost-effectiveness. The three parameters considered here were transition probabilities, speed of progression and severity of relapses.

Estimated benefits used in the economic analysis
Under the five year simple model a reduction in relapses of 1.52 was associated with the therapy: this translated to a gain of 0.054 discounted QALYs. In the five year complex model 0.13 QALYs were gained. In the ten year model 0.33 QALYs were gained.

Cost results
Under the five year simple model the total net costs of IFNB-1b were 43,600 per patient. In the five year complex model costs were 43,400. In the ten year model costs were 74,800.

Synthesis of costs and benefits
Cost per relapse avoided and cost per QALY gained were calculated. Costs and benefits were presented discounted and...
undiscounted. Under the five year simple model the cost-effectiveness ratio (costs discounted) was 28,700 per relapse avoided. This translates to a cost-utility ratio (costs & QALYs discounted) of 809,900 per QALY gained. The five year complex model (including progression) gave 328,000 per QALY gained. The ten year model gave 228,300 per QALY gained. Treatment side-effects were included in this study. Results were not very sensitive to changes in parameter values, the greatest impact on QALY gains was from improved transition probabilities.

(Note from CRD Research Fellow: The above results have now been updated by the authors following the findings of more recent research (see Health Technology Assessment 1998, Vol. 2: No 4 (Update 1999). Data from the prevention of Relapses and Disability by Interferon Beta-1a Subcutaneously in Multiple Sclerosis (PRISMS) Study Group, which considered interferon beta-1a for RRMS, produced estimates of 375,100 and 393,300 per QALY gained over 5 and 10 years, respectively. Higher figures were produced from the European Study group, which considered interferon beta-1b for secondary progressive disease, with cost per QALY gained estimates of 667,800 and 587,200 over 5 and 10 years, respectively.)

Authors’ conclusions
IFNB-1b produced important occasional short-term gains in QoL to people with relapse-remitting MS, but these translated into only small gains in QALYs overall. Even with optimistic estimates of longer-term gains the aggregate QALY gains are small. These benefits were achieved only with a large additional cost.

CRD COMMENTARY - Selection of comparators
The reasons for the choice of comparator was clear as INFB-1b is a recognised alternative to standard therapy for MS. However, other alternative treatments for MS were not considered in the analysis such as treatments used during relapses and in dedicated MS services. You, as a user of this database, should consider whether the technology used in this study is relevant to your own setting.

Validity of estimate of measure of benefit
The measure of benefit was quality of life (QoL) and relapses avoided as a result of the alternative treatments. The principal data were derived from a randomised double-blind, placebo-controlled trial and as such the findings are likely to be internally valid. However, the authors acknowledged that in translating the effectiveness data into an economic evaluation a number of assumptions were made although these were limited by the application of sensitivity analyses.

Validity of estimate of costs
The price year was not given. However, the authors applied good practice in analysing and reporting costs although they acknowledged that the lack of statistical analysis and power calculations may have introduced some limitations in the validity of costs. Some gaps in cost data were also experienced due to difficulties in collecting resource/cost data for patients, for example, with EDSS > 7.

Other issues
The results are only applicable to RRMS and there are therefore some limitations in terms of generalisability to other forms of MS and other settings.

Note by CRD Health Economist: The paper used to report this study is extensive in nature (57 pages in length as part of the Health Technology Assessment report series) and covers several other methodological issues concerned with economic evaluation before addressing the MS study itself. As such it is substantially larger, in terms of volume, than a standard ‘paper’ recorded on the NHS EED.

Implications of the study
Further research should apply itself to the study of QoL issues as an outcome measure in relation to alternative treatments for MS.
Source of funding
None stated.

Bibliographic details

Indexing Status
Subject indexing assigned by NLM

MeSH
Adjuvants, Immunologic /economics /therapeutic use; Adult; Aged; Cost-Benefit Analysis; Decision Support Techniques; Drug Costs; Female; Great Britain; Health Status; Humans; Interferon-beta /economics /therapeutic use; Male; Medical Records; Middle Aged; Models, Econometric; Multiple Sclerosis /drug therapy; Outcome Assessment (Health Care); Quality-Adjusted Life Years

AccessionNumber
21998008193

Date bibliographic record published
31/10/1998

Date abstract record published
31/10/1998