Long term treatment of multiple sclerosis with interferon-beta may be cost effective

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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 interferon (IFN)-beta for the treatment of multiple sclerosis (MS). Due to the lack of a cure for MS, IFN-beta is intended to slow the disease process.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients with MS.

Setting
The setting was not stated. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data were derived from studies published in 1996 and 1998. The price year was 1995.

Source of effectiveness data
The effectiveness evidence was derived from a review of published studies, supported by the authors’ assumptions.

Modelling
A model of MS progression was derived from a published study. The model assumed that relapses, clinical progression and brain atrophy were all reduced with continued IFN-beta treatment. Consequently, the benefits of the treatment will continue to accrue and will be retained over the lifetime of the patient. The data on disease progression, which were derived from a primary study, were then extrapolated to obtain data referring to a 20-year time horizon.

Outcomes assessed in the review
The outcomes assessed from the published studies were progression of disability of patients with MS on the expanded disability status scale (EDSS) and utility values associated with different health states. The EDSS ranged from 0 (full health) to 10 (death from MS). A score of 4 represented moderate disability, while a score higher than 7 equated to severe disability. The utility values were derived using the EuroQol (EQ-5D).
Study designs and other criteria for inclusion in the review
The primary studies were a clinical trial for the assessment of disease progression, and a cost-utility analysis for the utility values.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Two primary studies were used in the effectiveness analysis.

Methods of combining primary studies
The data derived from the primary studies were not combined.

Results of the review
In the short-term analysis, the progression of disability to an EDSS score of at least 4 was 5% for patients treated with INF-beta and 14% for placebo recipients. The progression of disability to an EDSS score of at least 6 was 1% for patients treated with INF-beta and 7% for placebo recipients.

The values of the utility scores associated with each level of disability were 0.71 for an EDSS score of 3, 0.66 for an EDSS score of 4, 0.52 for an EDSS score of 5, 0.49 for an EDSS score of 6, and 0.35 for an EDSS score of 7.

The utility transition values from each EDSS score to the next were 0.05 from EDSS score 3 to 4, 0.14 from EDSS score 4 to 5, 0.03 from EDSS score 5 to 6, and 0.14 from EDSS score 6 to 7.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
The authors assumed that treatment started in patients with an average EDSS score of 2.5. Also, if the treatment with INF-beta was halted, then disability progression would proceed at the same rate as it would have progressed if no treatment had been used.

Measure of benefits used in the economic analysis
The benefit measure used in the economic analysis was the number of quality-adjusted life-years (QALYs) gained with the interventions. A 6% discount rate was used for future benefits. The results obtained from extrapolating the EDSS scores over a 20-year period, as carried out in the disease progression model, were also reported.
Direct costs
A 6% discount rate was used in the economic analysis since the time horizon of the analysis was 20 years. The unit costs and the quantities of resources used were not reported. The items included in the economic analysis were medical costs and nonmedical costs. The medical costs included hospitalisation, medical and paramedical consultations, laboratory tests and procedures, drugs and medical supplies. The nonmedical costs included community assistance and patient transportation. The cost/resource boundary for the direct costs was that of the health service. The costs were estimated from a study published in 1998, based on the extracontractual referral tariffs and market prices for drugs. The total costs were derived using modelling. The price year was 1995.

Statistical analysis of costs
No statistical analysis of the costs was carried out.

Indirect Costs
A 6% discount rate was used for the indirect costs, which were incurred over 20 years. The unit costs and the quantities of resources used were not reported. The analysis of the indirect costs included home modifications, transport, community assistance, work days lost, and time lost by the patients and caregivers. The cost/resource boundary adopted was that of society. The source of the cost data was market prices and average daily wages. The price year was 1995.

Currency
UK pounds sterling (\). 

Sensitivity analysis
Sensitivity analyses were not performed.

Estimated benefits used in the economic analysis
The EDSS scores were extrapolated over a 20-year period. The results suggested that placebo recipients progressed to an EDSS score of 4 by approximately 4 years after the start of the study, while patients receiving IFN-beta progressed to the same EDSS score by 11 years. Placebo recipients progressed to an EDSS score of 6 by 9 years, compared with over 20 years for patients receiving IFN-beta. The estimated QALYs for IFN-beta were 0.49 after 2 years, 1.09 after 5 years, 1.74 after 10 years, and 2.18 after 20 years.

Cost results
From the perspective of the health care system, the estimated incremental costs of IFN-beta over no intervention were 13,375 after 2 years, 30,539 after 5 years, 52,663 after 10 years, and 82,527 after 20 years.

From the perspective of society, the estimated cost-savings of IFN-beta over no intervention were 5,541 after 2 years, 13,160 after 5 years, 24,949 after 10 years, and 32,953 after 20 years.

Synthesis of costs and benefits
An incremental cost-utility analysis was carried out to combine the costs and benefits of the interventions. From the perspective of the health care system, the incremental cost per QALY of IFN-beta over no intervention was 27,036 after 2 years, 28,097 after 5 years, 30,183 after 10 years, and 37,845 after 20 years. From the perspective of society, the incremental cost per QALY gained was negative, meaning that the intervention led to cost-savings for the society.

Authors' conclusions
Long-term analysis of the use of interferon (IFN)-beta for the treatment of multiple sclerosis (MS) resulted in an
acceptable cost per quality-adjusted life-year (QALY) from the perspective of the health care system. It also resulted in cost-savings for society as a whole.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. No treatment was selected, as the aim of the study was to assess the long-term active value of the study treatment. In the two related studies, placebo was used as the comparator. You should assess whether a treatment for MS is currently implemented in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness used data derived from two published studies, but a formal review of the literature was not undertaken. The study results depended on the assumptions made by the authors, which reversed the results of prior analyses. However, the robustness of the assumptions was not tested and sensitivity analyses were not carried out. An extrapolation process was carried out in the disease progression model, as the primary data referred to a short time horizon. The effectiveness results, therefore, should be treated with caution. They could only be confirmed through long-term studies of MS patients receiving the intervention.

**Validity of estimate of measure of benefit**
QALYs were used as the benefit measure in the economic analysis. They were appropriately discounted and were derived using a model of disease progression. The use of QALYs ensured the comparability of the study results with those from other interventions carried out in the health care system.

**Validity of estimate of costs**
The analysis of the costs was carried out from two different perspectives. It would appear that all the relevant categories of costs have been included. The source of the cost data was a published study, and the validity of the estimates used in the economic analyses was not assessed in sensitivity analyses. The unit costs and the quantities of resources were not reported. The price year was given and a breakdown of the costs was provided. Discounting was relevant since the time horizon of the analysis was 20 years, and was carried out.

**Other issues**
The authors made limited comparisons of their findings with those from other studies, although it seems likely that none were actually available. The issue of the generalisability of the study results to other settings was not addressed, and sensitivity analyses were not carried out. Thus, the external validity of the analysis was limited. The analysis referred to a population of patients with MS and this was reflected in the conclusions of the study.

**Implications of the study**
The findings, particularly from a societal perspective (relevant to the UK), support the use of INF-beta for MS patients over long-term timeframes. The authors suggested that "the use of INF-beta would have to be recommended and actively promoted by all health services".

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