Cost-effectiveness of disease-modifying therapy for multiple sclerosis: a population-based study

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 evaluate the cost-effectiveness of disease-modifying therapies, compared with basic supportive therapy, without disease-modifying therapy, for patients with relapsing multiple sclerosis. The authors concluded that it was very unlikely that disease-modifying therapies might be considered cost-effective, in the USA. The methods were adequate and, if the randomised controlled trial data were representative of the main evidence, the authors' conclusions seem appropriate.

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

Study objective
The objective was to evaluate the cost-effectiveness of disease-modifying therapies, compared with basic supportive therapy, without disease-modifying therapy, for patients with relapsing multiple sclerosis.

Interventions
The interventions were basic supportive treatment, without disease-modifying therapy; intramuscular interferon beta-1a; interferon beta-1b; glatiramer acetate; and subcutaneous interferon beta-1a.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A Markov model of the annual disease progression of patients with multiple sclerosis was developed. The patient characteristics that affected disease progression were based on participants in one clinical study. The time horizon was 10 years. The perspective was not explicitly reported.

Effectiveness data:
The disease progression probabilities, depending on patient characteristics, were mainly from the 2000 to 2005 Sonya Slifka Longitudinal Multiple Sclerosis study. This study was a mail survey of a nationally representative panel of over 2,000 people with multiple sclerosis, who were followed-up annually. For effectiveness, 844 of the 1,271 survey participants provided sufficient data. Disease progression was the main parameter for the model. Relative risks from randomised controlled trials were used to adjust the disease progression and relapse probabilities.

Monetary benefit and utility valuations:
The utility estimates were from 1,212 patients in the Sonya Slifka study. These patients completed the Short Form (SF)-36 questionnaire and their responses were converted into preference scores using the SF-6D.

Measure of benefit:
The measures of benefit were relapse-free years and quality-adjusted life-years (QALYs) gained. Future benefits were discounted at an annual rate of 3%.

Cost data:
The direct medical costs included: hospital admissions, emergency room visits, hospital day treatment, therapy visits, mental health visits, physician office visits, home health, blood tests, medications, and magnetic resonance imaging. The resource use was valued using estimates from the Medical Expenditure Panel Survey and average Medicare reimbursement rates. The indirect costs included unemployment periods, part-time labour, interruptions to schooling, and short-term absences from either work or school. These absences were valued using age- and gender-specific wages published by the Bureau of Labor Statistics. The resource use was from 910 participants in the Sonya Slifka study. As allocation to treatment was not randomised, regression analysis was used to control for variations in patient characteristics. Future costs were discounted at an annual rate of 3% and all costs were reported in US $.

Analysis of uncertainty:
Sensitivity analyses were conducted, using bootstrapping and Monte Carlo simulation, to examine how robust the model results were to variations in medication prices and the discount rate. One-way sensitivity analyses were conducted.

**Results**
The average undiscounted costs per patient were $267,710 for basic supportive care, $467,712 for intramuscular interferon, $492,310 for interferon beta-1b, $476,228 for glatiramer acetate, and $485,832 for subcutaneous interferon. The average discounted QALYs gained per patient were 6.500 for basic supportive care, 6.692 for intramuscular interferon, 6.673 for interferon beta-1b, 6.582 for glatiramer acetate, and 6.626 for subcutaneous interferon.

Compared with basic supportive care, the incremental cost-utility ratios were $901,319 per QALY gained (95% CI 807,884 to 1,157,624) for intramuscular interferon, $1,123,162 per QALY gained (95% CI 944,463 to 1,422,342) for interferon beta-1b, $2,178,555 per QALY gained (95% CI 1,591,107 to 2,876,617) for glatiramer acetate, and $1,487,306 per QALY gained (95% CI 1,209,560 to 1,914,390) for subcutaneous interferon.

In no scenario in the sensitivity analyses, was the cost-utility ratio of disease-modifying therapies, compared with basic supportive care, below $500,000 per QALY gained.

**Authors' conclusions**
The authors concluded that it was very unlikely that disease-modifying therapies might be considered cost-effective, in the USA.

**CRD commentary**
**Interventions:**
The interventions were described and a range of treatments was considered.

**Effectiveness/benefits:**
The authors stated that randomised controlled trial (RCT) data were used to adjust the treatment effects, but the identification, inclusion criteria, synthesis, and quality of these trials were not reported and no references were given. The clinical data were mainly from the Sonya Slifka study, which was described including the patient sample and follow-up methods. Many patients were excluded due to missing data and it's not clear how this affected the applicability of the results to the target population. The authors stated that healthier patients might be more likely to enrol in a registry, such as that used for the Sonya Slifka study. Details of how the utility estimates were derived were reported.

**Costs:**
The perspective was not explicitly reported, but the inclusion of indirect costs indicates that a societal perspective was adopted. All the major cost categories and costs relevant to this perspective appear to have been analysed. The sources for the unit costs and resource use were reported. It is not clear how exclusions for missing data might have affected the applicability of the results to the target population. The price year was not reported, which will hamper future inflationary exercises. The time horizon and discount rate used were reported.

**Analysis and results:**
The outcome and cost information were synthesised in a Markov model. The model structure was described and a diagram was provided. The methods used in the sensitivity analysis were briefly explained, but it was unclear how
thorough these analyses were. As the main limitation to the analysis, the authors reported that there was potential for sample selection bias.

Concluding remarks:
The methods were adequate and, if the RCT data were representative of the main evidence, the authors' conclusions seem appropriate.

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