Economic evaluation of treating clinically isolated syndrome and subsequent multiple sclerosis with interferon beta-1b

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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.

CRD summary
This study evaluated the cost-effectiveness of early treatment with 250μg interferon beta-1b in patients with clinically isolated syndrome compared with treatment when the patient's condition converted from clinically isolated syndrome to clinically definite multiple sclerosis. Early treatment with interferon was highly cost-effective for the Italian National Health Service and dominant from the societal viewpoint. There were a few limitations in the reporting, but the authors' conclusions appeared appropriate given the robustness of the results in the sensitivity analyses.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to determine the cost-effectiveness of starting early treatment with 250μg interferon beta-1b in patients with a diagnosis of clinically isolated syndrome (CIS), versus treatment at the point where the patient's condition converted from CIS to clinically definite multiple sclerosis (MS).

Interventions
The intervention was 250μg interferon β-1b administered subcutaneously every other day in two patient populations, which were those with a diagnosis of CIS and those at clinically definite MS conversion.

Location/setting
Italy/secondary care.

Methods
Analytical approach:
An epidemiological model was constructed to determine the clinical and economic impact of the two treatment regimens, using published evidence. A 25-year time horizon was adopted and 2,000 patients entered the model in each year. So 2,000 patients were followed-up for 25 years, 4,000 were followed-up for 24 years, and those entering the model at year 25 were followed-up for one year. The authors stated that the costs were calculated from both an Italian National Health Service (NHS) and a societal viewpoint.

Effectiveness data:
Annual conversion rates from CIS to clinically definite MS were derived from a clinical trial (the Betaferon/Betaseron in newly emerging multiple sclerosis for initial treatment, BENEFIT, trial). Assumptions were made for the annual patient drop-out rate and the proportion of patients who converted to secondary progressive MS. The authors assumed that MS had no effect on mortality and supported this with references. They also assumed that those patients who converted to clinically definite MS entered the relapsing-remitting phase of MS and that after 19 years from conversion approximately half these patients converted to secondary progressive MS.

Monetary benefit and utility valuations:
To determine the utility values for different CIS and MS health states, the patients’ disability was estimated using the Expanded Disability Status Scale (EDSS) and these scores were then converted into utilities.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained. These were discounted at an annual rate of 3%.

Cost data:
Resource use was estimated from one key report, which was a cost-of-illness study performed in Italy (Amato, et al. 2002, see ‘Other Publications of Related Interest’ below for bibliographic details). This also provided the quarterly costs, which were converted into annual costs for two categories health care sector resources, and patients’ and family resources. Patients’ and family resources included non-walking disability aids, transport, working days lost by patients and caregivers, and informal care. For the Italian NHS perspective, only the health care sector resources were included; both were included for the societal perspective. Tariffs were used for the Italian NHS perspective, whereas costs were used for the societal perspective. As interferon was dispensed directly by the Italian local health units and hospital trusts, the cost of interferon was conservatively valued at the ex-factory price, which was approximately 40% less than the consumer price. The price year was 2006 and all prices were in Euros (EUR). Costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
A series of one-way sensitivity analyses were performed on the annual consumption of and average annual compliance rate for interferon, the use of interferon β-1a instead of interferon β-1b, the absence of a relationship between increasing the non-drug costs for clinically definite MS and clinically definite MS duration, the utility estimates, and the discount rates. Multi-way sensitivity analysis was performed on the annual conversion rates for clinically definite MS. Re-sampling methods were also used to assess the uncertainty around the incremental cost-effectiveness ratio (ICER).

Results
From an Italian NHS perspective the annual cost per patient for early treatment (from CIS diagnosis) was EUR 170,133 and the total QALYs were 7.84. The annual cost for late treatment (from clinically definite MS diagnosis) was EUR 169,239 and the total QALYs were 7.49.

From a societal perspective the annual cost per patient for early treatment was EUR 220,416 and the annual cost for late treatment was EUR 226,022.

From an Italian NHS perspective early treatment with interferon resulted in an incremental cost per QALY of EUR 2,574.94 and from a societal perspective it was dominant, which means it was more effective and less costly. The sensitivity analyses did not significantly affect the results.

Authors’ conclusions
The authors reported that early treatment with interferon was highly cost-effective for the Italian NHS and dominant from the societal viewpoint. Early treatment with interferon delayed conversion to clinically definite MS in CIS patients and was good value for money.

CRD commentary
Interventions:
The intervention and dosage for early treatment were clearly defined. It was assumed that the same dosage was used for later treatment. The authors did not refer to current practice so it is not clear if it was included in the analysis.

Effectiveness/benefits:
The economic evaluation was based on the BENEFIT trial. The authors did not explain why this trial was used as the basis of the model, nor give any indication as to whether or not other relevant RCT evidence exists. Sensitivity analysis was performed to evaluate the effect of different effectiveness estimates. The sources for all the clinical evidence were clearly reported. The methods for the identification of evidence to inform other clinical data were not reported. The sources for all assumptions were reported, but, as no literature review was described, it is not possible to ascertain if the best available evidence was used. Details of the sources used to derive the utility estimates were given.

Costs:
The two perspectives were clearly defined and all the relevant costs seem to have been included. The cost estimates
were from appropriate sources, but an assumption was needed for the cost of interferon. The costs were reasonably well reported and referenced. The price year, sources of data, and details of discounting were all provided.

Analysis and results:
The three state model could have been more neatly summarised. The incremental analysis was appropriate for determining the cost-effectiveness of the treatment regimens. The issue of uncertainty was appropriately addressed in both one-way and multi-way sensitivity analyses. The results of the base case and the sensitivity analysis, from both perspectives, were well reported, which enhances the generalisability of these results to other settings. The authors highlighted the strengths and limitations of their study.

Concluding remarks:
There were a few limitations in the reporting, but the authors’ conclusions appeared appropriate given the robustness of the results in the sensitivity analyses.

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