Population based cost utility study of interferon beta-1b in secondary progressive 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

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population consisted of patients with secondary progressive multiple sclerosis.

Setting
The study setting was a hospital (specialist outpatient clinic). The economic analysis was conducted in the Tayside region of Scotland.

Dates to which data relate
1993-1995 effectiveness data were used along with 1995 prices.

Source of effectiveness data
Effectiveness data were derived from case records.

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

Study sample
The study sample was 132 patients diagnosed with secondary progressive disease on 1 January 1993. In order to have a representative cohort of residents from the Tayside region (population 395,600), patients with multiple sclerosis were identified from four sources: neurology department records, visual evoked response requests, Scottish morbidity records and a survey of the region's general practitioners. Capture-recapture methods indicated that the point estimate of prevalence on the 1 September 1996 was 94% complete and people with secondary progressive disease were identified from recent information in case records through cross reference to accepted definitions. A neurology subset of the study sample consisting of 17 patients was also identified. This subset was used to explore the effect of limiting prescriptions to ambulatory patients with more active disease. Patients eligible for the neurology subset were either admitted to the neurology unit or referred to neurology outpatient clinics at Tayside hospitals between January 1993 and
June 1993. The entire cohort was followed up until 31 December 1995.

**Study design**
Case records were assessed. Major outcomes were the rate of relapse and the proportion of patients who became wheelchair dependent over three years.

**Analysis of effectiveness**
The analysis appears to have been conducted on an intention to treat basis. The rate of relapse requiring hospital admission and the rate of community-treated relapse were calculated, and confidence intervals were estimated using a method for proportions. Episodes of oral corticosteroid prescription were identified from the University of Dundee's Medicines Monitoring Unit prescribing database using a record linkage method. It was assumed that each corticosteroid prescription represented a community-treated relapse. Prescriptions associated with bronchodilators were assumed to be for asthma and therefore were excluded. A previous study of relapse frequency in secondary progressive multiple sclerosis showed a reduction in relapse from the first year after onset to the second year. These data were not used in the model since the study cohort contained people who had had the disease for more than two years and were likely to have a lower relapse rate. A recent survey of British neurologists showed that 47% of neurologists treated at least half of the multiple sclerosis relapses with corticosteroids. Therefore it was assumed that, for every relapse treated (hospital or community), there was a further untreated relapse. Clinical outcomes were relapse rate and the percentage of patients who became wheelchair dependent.

**Effectiveness results**
24 (18%) of the cohort became wheelchair dependent within 36 months of follow-up.

The number needed to treat (NNT) for 30 months to postpone wheelchair dependence in one person by nine months was estimated to be 18 (95% CI: 5 - 26).

4 (24%) of the neurology subset became wheelchair dependent.

The number needed to treat to postpone wheelchair dependence by nine months in the neurology subset was 14.

32 admissions were identified for treatment of relapse in the 36 month follow-up period, generating a rate of 0.08 (95% CI: 0.06 - 0.11) per patient-year.

56 discrete corticosteroid episodes were identified in 21 people, but 3 people had concomitant bronchodilators prescribed and were excluded, and one oral steroid prescription preceded an admission to hospital for relapse by 15 days.

The rate of community treated relapses was 0.15 (95% CI: 0.11 - 0.18) per patient-year.

The neurology subset experienced 7 hospital admissions for relapse and 4 community corticosteroid prescriptions in the 30 months to the end of December 1995. This suggested an estimated 11 untreated relapses.

**Clinical conclusions**
Although interferon beta shows benefits in the treatment of multiple sclerosis, these benefits are modest.

**Modelling**
A population based cost-utility model was used. Effectiveness was modelled using data on relative risk reductions from a randomized trial of interferon beta-1b.

**Measure of benefits used in the economic analysis**
Three years after the end of follow-up (Spring 1998), a postal survey of people with multiple sclerosis in Tayside was conducted to create a baseline from which to estimate the effect of interferon beta. The EuroQOL and a postal ambulation scale (based on the scale of McAlpine and Compston) were administered. The number of quality-adjusted life years (QALYs) gained by postponing wheelchair dependence by 9 months was equal to the change in EQ-5D value associated with a change in postal ambulation scale score from 4 to 5 multiplied by 0.75 years. The number of QALYs gained by preventing a one-month hospital relapse was equal to the change in EQ-5D value associated with a change in postal ambulation scale score from 4 to 5 multiplied by 0.083 years. For each community-treated relapse and untreated relapse, postal ambulation scale scores changed from 3 to 4 for one month. It was assumed that 40% of QALYs were gained in years 1 and 2 and 20% were gained in the final six months of the 30-month programme. A discount rate of 6% was applied to QALYs gained in years 2 and 3.

**Direct costs**
Costs saved by delaying the time to wheelchair dependence by nine months were estimated from a cost analysis based on information from 672 members of the Multiple Sclerosis Society of Great Britain and Northern Ireland. Resource utilisation data were valued using data from local NHS trust finance directories (personal communication). Fixed and non-fixed costs were differentiated when costing relapses, but this was not possible for wheelchair dependence as the study lacked information. It was assumed that each community-treated relapse required 20 minutes consultation with a general practitioner (GP) and that untreated relapses did not incur health service costs (although GP costs may have been incurred). Corticosteroid costs were taken from the 1995 British National Formulary. All costs were adjusted to 1995 using the Department of Health hospital and community health services price index. Treatment costs were discounted at 6% in the second and third years.

**Statistical analysis of costs**
Not stated.

**Indirect Costs**
Indirect costs were not included.

**Currency**
UK pounds Sterling (GBP).  

**Sensitivity analysis**
A series of one-way sensitivity analyses was performed to explore the effects of:

- increasing the cost of each additional nine months of wheelchair dependence (taking account of the societal perspective),
- changes in the unit cost of interferon beta-1b,
- changes in the number of, and discount rates applied to, QALYs gained, and
- assuming that the relative risk reduction in hospital admission and corticosteroid use was 31% (not 12% or 21%).

Also a threshold analysis was performed to determine the changes required in model variables to breach the thresholds of 10,000, 20,000, 30,000 and 50,000 per QALY gained.

**Estimated benefits used in the economic analysis**
Treatment of 18 members of the population cohort and 14 members of the neurology subset for 30 months would result in a gain of 0.397 and 0.357 QALYs respectively.
Cost results
The cost of an additional 9 months of wheelchair dependence was 2,840 to the health service (5,153 to society). Interferon beta-1b cost 800 per patient per month. Other costs associated with interferon beta treatment were not included as there were no reliable estimates from local practice.

Synthesis of costs and benefits
The cost per QALY gained was 1,024,666 (276,466 to 1,485,499). If treatment were restricted to patients attending neurology services, the number needed to treat was 14: cost per QALY gained 833,514 (161,358 to infinity).

In sensitivity analyses, the cost-utility ratio seemed to be robust to changes in the cost of care. Increasing the cost of each additional nine months of wheelchair dependence from 2,840 to 5,153 (which took into account the societal perspective) only reduced the cost per QALY gained by 0.2%. If the unit cost of interferon beta was halved to 4,800 per patient per year, the cost per QALY gained fell by 49.4% to 506,407. If it was assumed that 31% of hospital admissions and community-treated relapses were prevented (31% of all relapses were prevented in the trial, but only 12% of hospital admissions and 21% of steroid use was prevented), the cost per QALY gained was 832,3999 (221,831 -1,208,133) in the population cohort and 628,797 (122,079 to infinity) in the neurology subset. None of the proposed thresholds could be breached without extreme changes to the variables of the model.

Authors' conclusions
The authors concluded that, despite a recent trial showing benefit from interferon beta in secondary progressive multiple sclerosis and calls for the treatment to be made available immediately to all patients with that form of disease, this analysis showed that treatment with interferon beta-1b has a significant opportunity cost. The authors concluded that resources could probably be used better elsewhere.

CRD COMMENTARY - Selection of comparators
The authors chose best practice without interferon beta as this represented current practice in their setting and allowed the active value of the treatment to be evaluated.

Validity of estimate of measure of benefit
The authors mentioned that, ideally, they would have used effectiveness data from a meta-analysis of clinical trials, but only one completed trial existed with data in the public domain. Also they stated that ideally they would have calculated the proportion of the cohort that became wheelchair dependent within 30 months (as the follow-up in the trial by the European Study Group on Interferon beta-1b in Secondary Progressive Multiple Sclerosis, 1998) but the case-records lacked detail. Therefore, the number needed to treat to delay time to wheelchair dependence could be an underestimate. The validity of the methodology and the population used to calculate quality-adjusted life years was reliable.

Validity of estimate of costs
The cost methodology was presented adequately and no important cost items appear to have been omitted. The costs may not be generalisable to other settings or countries.

Other issues
In Tayside, people with secondary progressive multiple sclerosis are not routinely followed-up, but are referred to the outpatient clinic for specialist management of new problems such as relapses or other chronic symptoms. Also the disease course is different in secondary progressive multiple sclerosis, so evidence from trials in relapsing multiple sclerosis cannot be generalised to patients with secondary progressive disease. The results do not appear to have been presented selectively and the authors made appropriate comparisons of their findings with those from other studies for other healthcare interventions and relapsing-remitting multiple sclerosis.
Implications of the study
Interventions which improve the quality of life of people with multiple sclerosis more efficiently than interferon beta-1b need to be identified. Although it is probably appropriate to allocate more resources to people with secondary progressive multiple sclerosis, access to interferon beta-1b should be restricted. More benefit would be obtained by directing funds to improved supportive care.

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