Cost-utility analysis of intravenous immunoglobulin and prednisolone for chronic inflammatory demyelinating polyradiculoneuropathy


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
Two 6-week treatments for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) were examined. The treatments were prednisolone (PRE) and intravenous immunoglobulin (IVIg). The regimen for PRE was 60 mg/day during the first 2 weeks, 40 mg/day in week 3, 30 mg/day in week 4, 20 mg/day in week 5, and 10 mg/day in week 6. IVIg consisted of 2 g Sandoglobulin (Novartis) per kg of body weight (a standard weight of 75 kg was used for the analysis).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised adult patients fulfilling the following inclusion criteria:

- a clinical diagnosis of CIDP;
- progressive or relapsing motor and sensory dysfunction of more than one limb over more than 2 months caused by neuropathy;
- reduced or absent tendon reflexes;
- less than 10 white cells/microL in the cerebrospinal fluid;
- fulfilment of neurophysiological criteria for CIDP;
- significant physical disability in upper or lower limb function; and
- a stable or worsening clinical condition.

The exclusion criteria were:

- associated systematic diseases that could be associated with neuropathy;
- actual or planned pregnancy;
- concurrent medical conditions that could affect treatment;
- significant respiratory impairment;
treatment with IVIg, corticosteroids or plasma-exchange in the 6 weeks before treatment;
multifocal motor neuropathy; and
failure to respond to IVIg or corticosteroids.

Setting
The setting was secondary care and a hospital. The economic study was carried out in several European countries.

Dates to which data relate
The effectiveness and resource use data were gathered from July 1998 to November 1999. Costs were reported in 2000/2001 prices.

Source of effectiveness data
The effectiveness evidence was derived from a single study, the main results of which had been published elsewhere (Hughes et al., see Other Publications of Related Interest).

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
There was limited information on the study sample since most of the details had been published elsewhere. Thirty-two patients were identified in the initial study sample, but for the purpose of the current evaluation only 25 patients were included. There were 13 patients in the PRE group and 12 in the IVIg group. The patients in the PRE group had a mean age of 53.9 (+/- 17.3) years and 31% were female. The patients in the IVIg group had a mean age of 52 (+/- 13.6) years and 42% were female.

Study design
This was a prospective, double-blind, crossover, randomised clinical trial that was carried out in nine European centres (the UK, Belgium, Italy, Spain, the Netherlands, Greece and the Czech Republic). The method of randomisation was not described. The first treatment period lasted 6 weeks, followed by a 4-week washout period, after which the second 6-week treatment period with the other intervention began. However, only data from the baseline and first treatment periods were used. No patient was lost to the follow-up assessment.

Analysis of effectiveness
The analysis of the clinical study appears to have been restricted to treatment completers only. The primary outcome measures used were improvements in disability scores and quality of life. Disability scores were assessed using an 11-point scale. Quality of life was examined using the EuroQol EQ-5D instrument, which contains five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). The study groups were comparable at baseline.

Effectiveness results
There were no statistically significant differences in the disability score between the two groups, although the greatest improvement was observed in the PRE group.

Quality of life was relatively unchanged (0.64 to 0.63) for the PRE group, (p=0.956), whilst there was a relatively large improvement in the utility score (from 0.57 to 0.69) in the IVIg group, (p=0.072).
Clinical conclusions
The effectiveness results showed that none of the differences in the quality of life were statistically significant, but the trend favoured IVIg. The disability scores were comparable.

Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were obtained from the quality of life values obtained in the clinical trial. Discounting was not relevant as the QALYs were estimated over a 1-year time horizon.

Direct costs
Discounting was not relevant because the costs were incurred during a short timeframe. The unit costs were not presented separately from the quantities of resources used for all items. The health services included in the economic evaluation were inpatient stay (including intensive care, acute and rehabilitation wards), outpatient visits (neurology and others), attendance at day hospitals, drugs, other workers, and informal care (provided by family and friends). Contacts with physiotherapists, occupational therapists, general practitioners, nurses, social workers, surgical appliance officers, and chiropodists were also considered. The cost/resource boundary of the study was unclear. Resource use was estimated using patient-level data that were obtained from the sample of patients included in the effectiveness study. The Client Service Receipt Inventory (CSRI) was administered four times, covering the 6-month period prior to baseline, the first treatment period, the washout period, and the second treatment period. The costs were derived from a UK source (the Personal Social Service Research Unit). The cost of informal care was based on the unit cost of a home care worker. The costs were estimated in 2000/2001 prices.

Statistical analysis of costs
A multiple regression model was used to compare the treatment costs while adjusting for baseline estimates. Non-parametric bootstrapped confidence intervals (CIs) were also calculated, drawing 5,000 samples.

Indirect Costs
The indirect costs were not considered.

Currency
The costs were initially estimated in UK pounds sterling (£) then converted to euros (Euro). The conversion rate (applicable in October 2001) was Euro 1.58 = 1.

Sensitivity analysis
Sensitivity analyses were carried out to examine the uncertainty due to variability in the data. The price per gram of IVIg and the unit costs used in the cost calculations were varied. The price of IVIg was varied using lower and higher estimates. The unit costs were varied by multiplying all the unit costs by 0.47 (because the unit costs in Italy had unit costs 47% lower than the level in the UK).

Estimated benefits used in the economic analysis
The gain in QALYs associated with IVIg compared with PRE was 0.014.

Cost results
In the baseline period, the costs were Euro 2,000 (+/- 4,076) in the PRE group and Euro 1,500 (+/- 2,054) in the IVIg group.
During the treatment period, inpatient care was the most important category of cost (71% of total) in the PRE group, while the drug costs accounted for most of the costs (91% of total) in the IVIg group.

In the treatment phase of the study, the estimated costs were Euro 1,312 (+/- 3,035) in the PRE group and Euro (4,751 +/- 563) in the IVIg group. The cost-difference of Euro 3,439 favoured the PRE group.

After adjusting for baseline costs, the difference was Euro 3,754 (90% CI: 1,920 - 4,252; p<0.001).

**Synthesis of costs and benefits**

The costs and benefits were synthesised by calculating the net benefit (NB). The NB was defined as \( \lambda \) (lambda multiplied by the QALY gained) minus the net costs. Lambda was the value society placed on a one-unit gain in QALY. It ranged from Euro 0 to Euro 300,000.

The synthesis of the costs and benefits was presented using a cost-effectiveness acceptability curve (CEAC). The CEAC showed that the probability that IVIg was more cost-effective than PRE (i.e. it produced a NB greater than zero) only rose above 0.5 if society valued one QALY at more than Euro 250,000.

In the sensitivity analysis, implausible variations in the baseline factors were required for IVIg to be more likely to be more cost-effective than PRE. The costs of IVIg needed to be between Euro 1 and Euro 2 per gram (it was around Euro 26 in the base-case) for IVIg to be the dominant strategy (both more effective and less costly). The CEAC was only marginally affected by the use of alternative unit costs.

**Authors' conclusions**

Over a short timeframe, intravenous immunoglobulin (IVIg) was not a cost-effective alternative to prednisolone (PRE) in the treatment of patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). IVIg was substantially more expensive and did not lead to better disability scores in comparison with PRE, although some improvements in quality of life were observed.

**CRD COMMENTARY - Selection of comparators**

The authors stated that three main treatments were available for patients with CIPD, that is, IVIg, corticosteroids (PRE), and plasma exchange. However, only PRE and IVIg were examined. No justification was provided for excluding plasma exchange from the economic evaluation. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence came from a single study, which had a high internal validity due to the robustness of the design. The study was double-blinded and randomised. This reduced the potential impact of confounding factors and possible assessment or performance biases. Further, the use of a clinical trial was appropriate for the study question. The main drawback was the small sample size, which arose from the very low prevalence of disease. More complete information on the methods used in the trial can be found in the original publication (Hughes et al., see Other Publications of Related Interest). The evidence came from several centres across Europe, which makes the study sample quite representative of the patient population.

**Validity of estimate of measure of benefit**

The summary benefit measure was appropriate for capturing the impact of the treatments on quality of life and survival. The approach used to determine the utility weights was reported. No discounting was applied as the QALYs were estimated over a 1-year period. QALYs can be compared with the benefits of other health care interventions.

**Validity of estimate of costs**
Although the authors stated that a societal perspective was adopted, the indirect costs were not included in the analysis. The information on the unit costs and resource use was limited and a breakdown of the cost items was not reported. In fact, the costs were presented as macro-categories, which limits the possibility of replicating the study. The source of the data was specific to the UK and, to permit transferability to other countries, an alternative source of cost was used in the sensitivity analysis. However, the analysis revealed that variations in costs did not affect the conclusions of the analysis. The price year was reported, which simplifies reflation exercises in other settings. Statistical analyses were carried out to deal with the skewed distribution of the costs and to compare the costs estimated in the two patient groups. The authors stated that the study had sufficient power to detect statistically significant differences in the costs.

Other issues
The authors noted the difficulties in making comparisons with the findings from other studies, owing to differences in methodologies and epidemiological characteristics of the setting. The impact of side effects on the cost-effectiveness of IVIg was also discussed. The authors noted some limitations to the validity of their study. First, the small sample size. Second, the possibility that the EQ-5D was not the best tool for patients with CIDP. Finally, the timeframe of the analysis.

Implications of the study
The authors suggested that further and larger studies should be carried out to understand the long-term consequences of CIDP and the impact of side effects of treatment.

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Other publications of related interest


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