Home versus outpatient administration of intravenous steroids for multiple-sclerosis relapses: a randomised controlled trial

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 study examined home versus outpatient administration of intravenous (iv) steroids for the treatment of relapses in patients with multiple sclerosis (MS). Hospital patients received 1 g of methylprednisolone over 1 hour, daily, for 3 days, in a dedicated infusion suite. Each day the patient was given a specific time to attend the suite to avoid any delay in steroid administration. Treatment was provided by the specialist MS nursing team at the hospital. Home patients left the hospital with a 3-day supply of iv methylprednisolone and a delivery team visited the patient during the next 3 days. The delivery team comprised generally trained nurses who were experienced in at-home chemotherapy treatment and who had received an educational programme on MS. In both groups, the cannula remained in place and appropriate care information was given.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who were older than 18 years, had clinically definite MS, and had sustained a definite relapse of more than 24 hours but less than 4 weeks in duration. Patients were excluded if their relapse was minor, such that the clinician would not prescribe steroids, or if their relapse was severe enough to need hospitalisation. They were also excluded if there was evidence of intercurrent infection, or if they had a history of adverse side effects after previous steroid use.

Setting
The settings were the home and a hospital. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness and resource use data were gathered between September 2003 and April 2005. The price year was not explicitly stated, but it might have been 2004.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

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

Power calculations were based on a preliminary study that suggested that, with 65 patients per group, the study would have 90% power at the 5% significance level (two-sided) to determine an improvement to 85% satisfaction in the treated group. All eligible patients admitted to the authors' institution were contacted. A sample of 285 patients was seen in the relapse clinic between September 2003 and April 2005, but 136 were initially excluded for the following reasons:

- 48 had minor relapses or were significantly improving;
- 25 had relapses of greater than 4 weeks' duration;
- 24 had participated in the trial then had a subsequent relapse;
- 9 had an intercurrent infection;
- 6 declined iv steroids;
- 14 had previous side effects, were aged younger than 18 years, needed urgent inpatient admission, or were not relapsing; and
- 10 had not used iv steroids before.

A further 11 patients declined to participate. The final study sample therefore contained 138 patients, 69 in each group. The median age was 40.3 years (interquartile range, IQR: 34.3 to 47.2) in the outpatient group and 36.8 years (IQR: 32.1 to 45.5) in the home group. The proportion of women was 78% in the outpatient group and 74% in the home group.

Study design

This was a prospective, randomised clinical trial that was carried out at a single centre, the National Hospital for Neurology and Neurosurgery in London. Randomisation was generated centrally, using block sizes of twelve, by a pharmacist who had no involvement in the rest of the trial. The length of follow-up was 6 weeks. The proportion of patients evaluable at the end of follow-up was 96% in the outpatient and 98% in the home group with respect to the primary end point, and 87 to 95% (outpatient group) and 90 to 96% (home group), respectively, with respect to the secondary outcomes. Some of the clinical end points were evaluated by clinicians blinded to the treatment allocation.

Analysis of effectiveness

The analysis of the clinical study was conducted on an intention to treat basis. The primary clinical end point was a measure of the patients' experience of relapse management, the MS relapse management scale (MSRMS). The MSRMS comprises four item groups (access to care, coordination of care, information and interpersonal care). It was administered to patients one week after their treatment had finished. Other clinical outcomes consisted of one disease-specific clinician-reported disability scale (Kurtzke's expanded disability status scale), two disease-specific patient-reported scales measuring walking ability and physical and psychological health (the MS walking scale and the MS impact scale). There was also one generic patient-reported health-status measure (medical outcome study 36-item health survey). Questionnaires were given at baseline and after 6 weeks of follow-up. The incidence of side effects was finally observed. The study groups were comparable at baseline in terms of their clinical and demographic characteristics, and were representative of a typical sample of patients with MS.

Effectiveness results

Of the four dimensions of the MSRMS, only coordination of care was significantly different between groups. The median score (high scores imply worse perceptions of care) was 12.1 (IQR: 3.0 to 18.6) in the outpatient group and 4.5 (IQR: 3.0 to 11.4) in the home group. The difference was 3.8 (IQR: 0.5 to 7.1; p=0.024).

None of the differences in the secondary clinical end points reached statistical significance. Almost all measures
improved over the 6-week treatment period. The only domains that did not improve significantly from baseline to the
6-week follow-up were SF-36 role emotional, (p=0.158), and SF-36 general health perceptions, (p=0.066).

One severe side effect was observed in the home group, but it was unlikely to have been related to treatment. Other
side effects were of a minor nature.

Clinical conclusions
The clinical analysis showed that the two types of treatments were equally effective and safe.

Measure of benefits used in the economic analysis
A summary benefit measure was not used as the two treatments were considered equally effective.

Direct costs
The analysis of the costs was carried out from the perspective of the NHS. It included both direct medical and direct
non-medical costs. The latter (direct non-medical) costs were initially incurred by the patients, but the NHS later
refunds many of these expenses. The direct medical costs were for salaries, equipment, drugs, hospital overheads and
investigations. The direct non-medical costs were for transport (parking and congestion charge in London) and
childcare arising because of treatment. The costs arising from initial attendance at the MS relapse assessment clinic
were not included because these costs were incurred by all patients irrespective of the treatment received. The unit
costs were reported for most items, but details of the resource quantities were not. Resource use was derived from the
sample of patients included in the clinical trial using a specific questionnaire. The costs were derived from the
Personal Social Services Research Unit, University College London Hospital, Camden Council and Transport for
London. Discounting was not relevant as the time horizon of the study was short. The price year was not explicitly
stated, but it could have been 2004.

Statistical analysis of costs
The mean costs were calculated and bootstrap confidence intervals (CIs) were generated.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
UK pounds sterling (GBP).

Sensitivity analysis
A univariate sensitivity analysis was carried out to assess the robustness of cost estimates to variations of 25 to 50% in
individual cost items.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The mean direct medical costs were 345 in the home group and 499 (95% CI: 471 to 534) in the outpatient group.

The mean direct non-medical costs were 1 (95% CI: 0 to 2) in the home group and 61 (95% CI: 49 to 76) in the
outpatient group.
The mean total costs were 355 (95% CI: 354 to 356) in the home group and 560 (95% CI: 531 to 598) in the outpatient group.

The univariate sensitivity analysis corroborated the findings of the base-case analysis. In effect, outpatient treatment was cheaper than home delivery only in two cases: if the charge for health care at home was increased by 51% or more, or if NHS salaries were reduced by 50%.

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant as the two treatments were considered equally effective.

**Authors' conclusions**
Home delivery of intravenous (iv) methylprednisolone was a safe, effective and efficient alternative to outpatient treatment of relapses in patients with multiple sclerosis (MS) in the UK.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear and was consistent with the objective of the study. Dosages and modalities of administration were described. 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 clinical trial, which was appropriate for the study question. The method of randomisation was described and should have reduced the impact of selection bias. Extensive information on the approach used to select the sample of participating patients was reported, and the reasons for excluding patients were given. The study groups were well balanced at baseline, not only in their demographics but also in clinical aspects, and this enhanced the robustness of the comparison. The primary outcome was assessed by a clinician masked to treatment allocation, which represents a further strength of the analysis. The length of follow-up was appropriate for the objective of the analysis. The evidence came from a single centre, but the authors noted that the patients were representative of the typical MS population. Power calculations were performed to determine the appropriateness of the sample size, although the calculation of the number of patients required for each group was based on preliminary data. Statistical analyses were carried out to test the significance of differences between the groups. The use of intention to treat as the basis for the analysis of the clinical endpoints improved the internal validity of the study. The authors highlighted the development of a specific measure of relapse management that allowed several aspects relevant from the patients' perspective to be taken into account. These issues increase the internal validity of the study.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the analysis as the two treatments were considered to be equally effective. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
The analysis of the costs was consistent with the stated perspective. A detailed breakdown of the cost items was provided. While the unit costs were reported, there were few details on the quantities of resources used. This could limit the possibility of replicating the analysis in other settings. The authors extensively investigated the issue of variability in the cost estimates in the sensitivity analysis, and statistical analyses were conducted to deal with the non-normal distribution of the costs. The authors did not explicitly report the price year, which will make reflation exercises in other settings difficult. However, some costs referred to 2004 values. The sources of the costs were reported for each item.

**Other issues**
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings, although sensitivity analyses were performed on cost items. The study referred to patients with MS relapses and this was reflected in the authors' conclusions. However, it was pointed out that the results of the analysis are highly relevant in the UK setting given the Government's efforts to increase the amount of health and social care delivered in the community.

**Implications of the study**
The study results support the home administration of iv steroids for the treatment of MS relapses in the UK.

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**Other publications of related interest**


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