Department of Veterans Affairs

Journal of Rehabilitation Research and Development Vol. 37 No. 4, July/August 2000
Pages 455–461

The effectiveness of neurological rehabilitation in multiple sclerosis

Alan J. Thompson, MD, FRCP, FRCPI
Institute of Neurology, Queen Square, London

Abstract—The difficulties inherent in demonstrating the effectiveness of an intervention that is as all-inclusive and poorly defined as neurorehabilitation, especially in a condition as unpredictable and variable as Multiple Sclerosis (MS), are not to be underestimated. They require strict adherence to rigorous methodology and, in particular, the consistent use of a range of clinically appropriate and scientifically sound measures of outcome. Incorporating this approach, it is possible to evaluate rehabilitation at four different levels, including (1) the broadest concept of service delivery; (2) packages of comprehensive care; (3) individual components of the package; and finally, (4) the intrinsic elements of the rehabilitation process. Most recent studies have focused on in-patient rehabilitation and have demonstrated benefits across disability, handicap, and quality of life in patients with mild to severe disability. Such benefits persist following discharge into the community. Studies evaluating service delivery and components of the rehabilitation package are in progress, but few investigators have taken on the intrinsic elements or 'black box' of rehabilitation. These recent studies underline the fact that the evaluation of rehabilitation is feasible. Such studies are important, not simply to justify funding but to ensure continuing improvement of the way in which MS is managed.

Address all correspondence and requests for reprints to: Alan J. Thompson, Professor of Clinical Neurology and Neurorehabilitation, Institute of Neurology Queen Square, London WC1N 3BG;email: A.Thompson@ion.ucl.ac.uk.

Key words: *effectiveness, multiple sclerosis, neurorehabilitation, outcome measures.*

INTRODUCTION

There is increasing pressure in these days of evidence-based practice to demonstrate the effectiveness of what we do and to show that our interventions are justified. At first glance, it may appear tempting to suggest that to demonstrate the effectiveness of a poorly defined and all-inclusive intervention such as neurorehabilitation, in a condition such as multiple sclerosis (MS) in which the mechanisms of disability are so poorly understood, utilizing measures which we acknowledge are inadequate, is an impossible task. In this paper, I would like to show that, although the task is extremely difficult, it is not impossible, and that recent studies are encouraging in demonstrating that such evaluation is feasible, provided adequate care is given to trial methodology and the choice of outcome measures.

Evidence supporting the effectiveness of rehabilitation in disability resulting from neurological disorders is best demonstrated in the evaluation of the role of Stroke Units in the management of stroke (1). In this instance, meta-analysis of a number of relatively small studies demonstrated clearly that Stroke Units reduced mortality

and morbidity and increased the likelihood of discharge home in patients with mild, moderate and severe stroke. However, such evidence has only recently become available and should serve to stimulate evaluation of our management/rehabilitation in MS. One major difference is, of course, that stroke is a single incident (albeit approximately 25 percent of patients are left with residual disability) whereas MS is a progressive neurological disorder, at least for the majority of patients. Skeptics have suggested that while there may be a case for rehabilitation in single incident events such as stroke and brain injury, it is difficult to justify its role in a condition that is inevitably going to worsen. This shows a profound lack of understanding of the philosophy of rehabilitation but does place an even greater pressure on us to demonstrate the appropriateness and effectiveness of rehabilitation in MS. Furthermore, MS is an excellent model of progressive neurological disease; if you can manage this condition effectively, you can manage most other disorders.

Evaluating Interventions in Multiple Sclerosis

Multiple Sclerosis

The difficulty in evaluating any intervention in MS has been well demonstrated by the discussion and controversy surrounding studies of immuno-modulatory agents in this disease (2). Many of the reasons for these difficulties are inherent in the disease itself. It is highly variable and unpredictable and, at least in the early stages, there is the potential for spontaneous recovery. This diversity of disease course is well illustrated by the range of diagnostic categories in MS which include relapsing/remitting, secondary progressive, progressive relapsing and primary progressive disease, and the differing mechanisms underlying this disability which include, from the clinical point of view, failure to recover from relapse and slow progression. Pathologically, these mechanisms are poorly understood, though, inevitably, severe demyelination and axonal loss are likely to be major contributors.

Because of these factors, MS results in diffuse and diverse deficits that interact to produce a complex pattern of disability, which in the majority of patients is progressive. It has a huge impact on the patient, family and society, affecting mood, relationships, employment and social interaction. Not surprisingly, this results in a huge cost to society, much of which relates to indirect effects of the disease, including loss of employment for both patient and caretaker (3). In terms of the evaluation of any intervention, these factors mandate randomized, double blind, placebo-controlled trials and incorporation of the patient's perspective.

Evaluating Rehabilitation

The philosophy of rehabilitation, which addresses the needs of the whole patient and emphasizes patient education and self-management, is ideally suited to the needs of patients with such a complex and progressive neurological disorder. It aims to improve independence and coping in order to minimize disability and handicap and maximize quality of life. However, the very nature of rehabilitation, which must, by definition, be shaped to match the specific needs of an individual patient and which attempts to address such a broad range of issues, poses further difficulties for the process of evaluation. The majority of the studies which have been carried out have had difficulty overcoming these problems, which include:

- lack of description and standardization of input;
- variation in location and duration of rehabilitation input;
- reluctance to use a control group;
- inadequacy or absence of blinding;
- lack of independent assessors; and,
- absence of agreement and inconsistent use of limited, and often inappropriate, outcome measures.

Selection of Outcome Measures for Rehabilitation

The selection of outcome measures is crucial in any evaluation. Although we can glibly say that measures must be scientifically sound (i.e., reliable, valid and responsive) and clinically useful (i.e., short, simple, etcetera), they must also be appropriate for the sample under study, the intervention being evaluated, and the expected change resulting from that intervention. In the evaluation of an intervention as comprehensive as rehabilitation in a progressive disorder, with little effect on longevity, such as MS, this is particularly challenging. While we are encouraged in stroke to use simple outcomes, such as mortality, they are clearly inappropriate in MS. Other measures, such as relapse rate or magnetic resonance imaging (MRI) activity are equally inappropriate to rehabilitation. Wheelchair use is also problematic in a condition with such variability and tendency to sponta-

neous recovery. In broad terms, this question can be addressed in two different ways. One could look at the "success" of the patient during the rehabilitation program, as measured by goal achievement, and secondly, one could evaluate the effect of the rehabilitation process on the patient, using a range of outcome measures. In relation to goal achievement, it is acknowledged that this is a very difficult area to evaluate but one possible approach is the use of integrated care pathways which are a simple but effective way of both monitoring the process of rehabilitation and evaluating goal achievement (4).

In relation to outcome measures, most studies in MS have relied on Kurtzke's Expanded Disability Status Scale (EDSS). The use of this scale in clinical trials of therapeutic agents has proven problematic, mainly as a result of its limited scientific evaluation and particularly its poor responsiveness (5,6). The EDSS measures a mixture of impairment and disability (depending on the severity of the disease); therefore, it is even less appropriate for the evaluation of rehabilitation. Furthermore, outcome measures must attempt to capture the entire impact of the rehabilitation process, looking not just at disability and handicap but incorporating quality of life, coping skills and self-efficacy. Consequently, many previous studies have used generic measures of disability (Bartel Index, Functional Independence Measure - FIM), handicap (London Handicap Scale, LHS, et cetera) and quality of life (Short Form 36 Health Survey Questionnaire, SF36)(7). As these scales are not disease-specific, there is an inherent concern that they will not be sensitive to the changes that are peculiar to the disease under study. Equally, it is essential to ensure that they are appropriate to the sample under study. For example, it has recently been shown that the SF36 has serious floor effects (i.e., even if patients improve, their score does not go above zero) in the MS patient population undergoing rehabilitation (8). A number of new scales have been developed in the last five years, though none has yet been fully evaluated. These include the Guy's Hospital Disability Scale (6), and a number of scales in quality of life (9,10,11).

One of the most encouraging developments in outcome measurement is the increasing awareness of the science of measurement (psychometrics), combined with the fact that these scientific techniques may be utilized to address the important issue of the patient's perception of disease impact (12). The development of a new scale, although a daunting prospect, is feasible provided that these scientific rules are strictly adhered to and that any new measure is based on a sound concept. Item generation must be based not just on clinical expertise (usually inadequate) (13) and literature review, but also patient and physician perspectives. The resulting items must be evaluated in a pilot study so that those which are redundant or inappropriate may be removed (item reduction), and the resulting scale must be subjected to a thorough and comprehensive evaluation that addresses not just reliability, validity and responsiveness but also the inherent scaling assumptions. Currently, a Disease Impact Scale is being developed at the Institute of Neurology at Queen Square, London, along strict psychometric guidelines (14).

The Evaluation of Rehabilitation in MS: from Broad to Specific

The evaluation of rehabilitation may be addressed at four different levels, moving from broad to specific:

1. the broadest concept of service delivery (perhaps the most appropriate in a progressive condition such as MS);

2. packages of comprehensive care, be they inpatient, outpatient or community based;

3. individual components of these packages, such as physiotherapy, occupational therapy, etcetera; and,

4. the intrinsic elements of the rehabilitation process, such as expert assessment, selection, goal setting, etcetera.

This fourth level, sometimes called the "black box" of rehabilitation, is without doubt the most difficult to tackle and, as there are no studies to date, will not be discussed further. Conversely, over the last three years there have been a number of randomized control trials (RCT) which have attempted to evaluate the other three levels, and I would now propose to discuss these in reverse order.

Components of Rehabilitation

The first of the recent studies in this area has been that of Petajan et al. (15) which looked at the role of aerobic exercise in patients with relatively mild MS. Despite looking at a rather small group of patients (n=46) who were randomly assigned to an exercise (n=21) or non-exercise (n=25) group over a 15-wk period, this study demonstrated a significant benefit in aerobic capacity, isometric strength and the Sickness Impact Profile. No

effect on either the EDSS or fatigue was seen. A randomized control trial (RCT) of inpatient physiotherapy (6.5 h over 2 wk) involving 45 patients did not show any benefit in mobility or activities of daily living but did show reduction in mobility-related distress (16). More recently, Lord et al. has compared two types of physiotherapy in a small group of patients (n=23) (17). Ten patients received what was described as a "facilitation approach", which is impairment-based (e.g., the Bobath approach) while ten others had a more task-orientated approach which was disability based (e.g., the Carr and Shepherd approach). Patients received at least 15 sessions over 5–7 wk from the same therapist. A range of outcome measures was used including the 10-m timed walk, the Rivermead Mobility Index, Stride length, and the Rivermead Visual Gait assessment. The study showed no difference between the groups, which was not surprising given the small numbers, though both groups improved in measures of impairment and disability ($p<0.05$). The authors concluded that such comparative trials are feasible and acknowledged that much larger numbers would be required to evaluate different physiotherapy techniques.

Rehabilitation Package

Of the three potential locations for rehabilitation - inpatient, outpatient and community - the vast majority of studies have been carried out in inpatient units. The key questions that arise are: (1) is comprehensive inpatient rehabilitation effective in reducing disability and/or handicap, and (2) do these benefits carry over in the longer term? In relation to the first of these questions, a number of studies have been carried out prior to 1996 (see **Table 1**), beginning with Feigenson in 1981 (18,19,20,21). However, although these studies were single-group design and have focussed almost exclusively on impairment and disability, all suggested that rehabilitation was helpful in MS. In relation to carry over of effect, two single group studies suggested that carry over does occur, though one of these was retrospective (22,23).

More recently, Freeman et al. (24) designed a randomized control trial that attempted to address some of the methodological issues discussed. The study involved 66 patients with progressive MS, and in order to overcome potential problems with the control group, a wait list control was used with all control patients receiving rehabilitation when the study was over. In order to ensure homogenous groups, patients were stratified according to their EDSS. One group was randomized to a short period of rehabilitation (20 d) and was reassessed at 6 wk, while the second group was put on a waiting list for 6 wk and was, therefore, assessed without any therapy intervention. The groups were well matched in relation to age, sex, disease pattern and duration, and level of disability (see **Table 1**), and the results of the study showed a significant benefit in the FIM ($p<0.001$) and the LHS ($p<0.01$). The difference between the groups was partly due to the fact that the control group deteriorated during the period of study, which is consistent with the fact that they were referred because they had very active disease.

A more recent randomized, single blind, control trial of 50 ambulatory patients compared 3-wk inpatient rehabilitation with a home exercise program (25). Evaluation was again with EDSS, FIM and the SF36. Patients were evaluated at base line and at 3, 6, 9 and 15 wk. A significant benefit was seen in disability at 3 ($p=0.004$) and 9 wk ($p=0.001$), though not at 15 wk. Significant benefit was seen in the mental component of the SF36 at 3 and 9 wk.

The suggestion from earlier studies that there may be some carry over following inpatient rehabilitation was further supported by a recent, single group, longitudinal study of 50 patients (26). This study used a wider range of outcome measures, including not just disease severity (EDSS), disability (FIM), and handicap (LHS), but also health-related quality of life (SF36) and emotional wellbeing (general health questionnaire). Patients were evaluated on admission and discharge from an inpatient rehabilitation unit and were then followed up at 3-mo intervals for the subsequent 12 mo. Twelve month data were collected from 92 percent of patients. Not surprisingly, the EDSS deteriorated over the 12 mos, from a median of 6.8 on admission to 8.0 twelve months following discharge, though this varied greatly from patient to patient—a feature of all the outcome measures. Disability was at its lowest on discharge but benefits gradually reduced during follow-up. Handicap continued to improve following discharge but, again, benefit reduced subsequently. A similar pattern was seen in the quality of life and emotional wellbeing scales, though the benefits persisted for longer. Summary measures were used to calculate the time taken to return to baseline and indicated that improvements were maintained in disability and handicap for approximately 6 mo, emotional well-being for 7 mo, and health-related quality of life (physical component) for 10 mo, despite the worsening neurological state. It was concluded that no single measure adequately reflected the outcome of rehabilitation and suggested that a range of measures is required, covering all relevant dimensions. The results underlined the need for adequate follow up

Table 1.
Summary of outcome studies of comprehensive inpatient rehabilitation in people with MS.

Study	Design	Size	Out/Ins	Time	Results
Feigenson et al (18)	Prospective, single group, pre- and post-study design	20	Impairment, disability and handicap: MS functional profile (a modified version of BUSTOP). Costs of intervention	Admission and discharge; costs were also measured at 12 mo (Tele)	Significant benefit in disability and handicap, no change in impairment
Greenspun et al. (19)	Retrospective, single group, pre- and post-study design	28	Disability: CRDS	Admission, discharge, and 30-mo review; (Tele if necessary)	Benefits across a range of disabilities which were maintained at 3 mo
Reding et al (30)	Retrospective study, using case-matched analysis	20 pairs	Disability: ISS; Hospital re-admission rate; Cost of intervention; Need for home assistance	Review at 16 mo (Tele)	No difference between groups
Carey et al (20)	Retrospective, multi-center study assessing a range of conditions; single group, pre- and post-study design	6194 (196 with MS)	Disability: LORS-II	Admission and discharge	Improvements in ADL and mobility
Francabandera et al (31)	Prospective, stratified randomized study	84	Disability: ISS; need for home assistance (hours)	Admission and at 3-mo - intervals for 2 yrs (3-mo results reported in this article)	Preliminary results suggest marginal benefit in inpatient group
Kidd et al (21)	Prospective, single group, pre- and post-study design	79	Impairment, DSS; Disability: Bathel Index; Handicap: ESS	Admission and discharge	Statistically significant improvement in disability and handicap
Aisen et al (22)	Retrospective, single group, pre- and post-study design	37	Impairment: FS and EDSS; Disability: FIM	Admission, discharge and Tele follow-up (between 6 and 36 mo post discharge)	Significant improvement in both FIM and EDSS
Kidd, Thompson (23)	Prospective, single group, pre- and post-study design	47	Impairment: EDSS; Disability: FIM; Handicap: ESS	Admission, discharge and 3-mo follow-up	Gains in disability maintained at 3 months, handicap improved over study period
Freeman et al (24)	Stratified, randomized, wait list controlled study design	66*	Impairment, FS and EDSS; disability: FIM; Handicap: LHS	Baseline and 6 wks	Significant benefit in disability and handicap
Freeman et al. (26)	Prospective, single group, longitudinal study design	50*	Impairment: FS and EDSS; Disability: FIM; Handicap: LHS; QoL: SF-36; Emotional well-being: GHQ-28	Admission, discharge and at 3-mo intervals for 1 yr	Benefits in disability, handicap, QoL and emotional well being persist for 6-9 mo
Solari et al (25)	Randomized single group study comparing inpatient and home exercise programs	50@	Impairment: EDSS; Disability: FIM; QoL: SF-36	Baseline, 3, 9, and 15 wks	Benefits in disability and some aspects of QoL

Design=study design; Size=sample size; Out/Ins=main outcomes and instruments; Time=time of assessments; Tele=by telephone; BUSTOP=Burke Stoke Time-oriented Profile; CRDS=Computerized Rehabilitation and Data System; DSS: Disability Status Scale; EDSS: Expanded Disability Status Scale, ESS: Environmental Status Scale; FIM: Functional Independence Measure; LORS-II: Revised Level of Rehabilitation Scale; FS: Functional Systems; ISS=Incapacity Status Scale; LHS=London Handicap Scale; SF-36=Short Form 36 Health Survey Questionnaire; GHQ-28=28 item General Health Questionnaire, *=all in the progressive stage; QoL=Quality of Life; @=ambulatory.

arrangements and community support following discharge from an inpatient unit.

Few studies have attempted to evaluate outpatient rehabilitation, though a recent study by Fabio et al. (27) randomly assigned 46 patients with progressive MS to an active treatment group (20 patients receiving 5 h/wk for 1 y) and wait list controls (26 patients). A range of outcomes was used, including the MS- related symptoms checklist composite score, fatigue frequency, and items from the Rehabilitation Institute of Chicago-Functional Assessment Scale (RIC-FAS). Reductions in both fatigue and in MS-related symptoms were observed in this study.

Service Delivery

However difficult it might be to evaluate aspects of service such as inpatient rehabilitation, it is even more difficult to evaluate the service in its entirety and to compare different models in a way that is both realistic and scientific. Part of the problem is that in many countries no clearly defined system of care is as yet available, though the development of standards of care (28) and attempts to define the key components of the service (29) may go some way toward addressing this deficit. In the past, inpatient rehabilitation has been compared with hospital care (30). The numbers involved were very small and no difference between the two groups was seen in relation to disability. Similarly, a comparison of inpatients and outpatients (31) failed to show any difference between the two methods of delivery. Acknowledging the desire for rehabilitation to be carried out in the community, but the need for appropriate expertise to be available, an Italian study has attempted to compare what has been described as "hospital" home care versus routine care. The patients in the treatment group remained in the community but had immediate access to relevant members of the multidisciplinary team, as and when it was required. This was a randomized control trial where 133 patients received active treatment and 68 were in the control group. The range of outcome measures included EDSS, FIM, SF36 and measures of anxiety and mood, and these were carried out at baseline and 12 mo later. Though no difference in disability was detected between the two groups, a significant benefit in depression and in aspects of general health was seen in the treated group. Initial analysis of cost suggested that there may be a 25 percent saving in the proposed hospital-supported home care (Pozzilli et al.[1]). Another study is planned in the United Kingdom that proposes comparing multidisciplinary MS clinics with general neurology outpatients and community-based general practice in 150 patients with MS (50 in each group). In this single blind, randomized control trial, patients will be evaluated at baseline and at 3,6,9 and 12 mo, with a range of measures from impairment to self-efficacy (32).

[1]Pozzilli C, Pisani A, Palmisano L, Battaglia MA, Fieschi C, and the Roman Home Care Multiple Sclerosis Group. Service location in multiple sclerosis: home or hospital. In Fredrikson S and Link H, eds. Advances in Multiple Sclerosis: Clinical Research and Therapy. Martin Dunitz, London 1999.

CONCLUSIONS

In an editorial in Neurology, the recent papers by Freeman and Solari were described as "a few steps forward in justifying neurorehabilitation" and the author rightly stated that further, more detailed and more comprehensive studies were required, with better study design and outcome measures (33). It has, however, become clear that such studies are now feasible and need to be carried out. These studies need to be done not simply to justify funding for our activities but to encourage us to evaluate further what we do, to ensure it is on a sound evidence base and to stimulate further improvements in the services available to the MS population.

REFERENCES

1. Langhorne P, Dennis M, editors. Stroke units: an evidence based approach. BMJ Books 1998. London: BMA House; 1998.
2. Hughes R. Modulating the immune response in demyelinating diseases. J Neurol Neurosurg Psychiatry 1998;64(2):148
3. Carton H, Loos R, Pacolet J, Versieck K, Vlietinck R. Utilisation and cost of the professional care and assistance according to disability of patients with multiple sclerosis in Flanders (Belgium). J Neurol Neurosurg Psychiatry 1998; 64:444–50.
4. Rossiter DA, Edmundson A, Al Shahi R, Thompson AJ. Integrated care pathways in multiple sclerosis rehabilitation: completing the audit cycle. Multiple Sclerosis 1998;4:85–9.
5. Hobart J, Freeman J, Thompson A. Kurtzke scales revisited: the application of psychometric methods to clinical intuition. Brain 2000; 123: 1027–1040.
6. Sharrack B, Hughes RAC, Soudain S, Dunn G. The psychometric properties of clinical rating scales used in multiple sclerosis. Brain 1999;122:141–59.
7. Van der Putten JJMF, Hobart JC, Freeman JA, Thompson AJ. Measuring change in disability after inpatient rehabilitation: comparison of the responsiveness of the Barthel Index and the Functional Independence Measure. J Neurol Neurosurg Psychiatry 1999;66:0–4.
8. Freeman JA, Hobart JC, Langdon DW, Thompson AJ. Improving measurement scales: is adding items the answer? (Abstract)Ann Neurol 1999;46:507.

9. Fischer JS, LaRocca NG, Miller DM, Ritvo PG, Andrews H, Paty D. Recent developments in the assessment of quality of life in multiple sclerosis (MS). Multiple Sclerosis 1999; 5:251–259.
10. Cella DF, Dineen K, Arnason B, Reder A, Webster KA, Karabatsos G, Chang C, Lloyd S, Steward J, Stefoski D. Validation of the functional assessment of multiple sclerosis quality of life instrument. Neurology 1996; 47(1):129–39.
11. Ford HL, Tennant A, Johnson MH. The Leeds MS QoL scale: a disease specific measure of quality of life in multiple sclerosis. (Abstract) J Neurol Neurosurg Psychiatry 1997; 62:210.
12. Hobart J. The multipe sclerosis impact scale (MSIS-29) is a new, patient based, and rigorous measure of the health impact of MS. Abstract. Annals of Neurology (in press).
13. Rothwell PM, McDowell Z, Wong CK, Dorman PJ. Doctors and patients don't agree: cross sectional study of patients' and doctors' perceptions and assessments of disability in multiple sclerosis. BMJ 1997; 314(31 May):1580–3.
14. Thompson AJ, Hobart JC. Multiple sclerosis: assessment of disability and disability scales. J. Neurol. 1998; 245(4):189–96.
15. Petajan JH, Gappmaier E, White AT, Spencer MK, Mino L, Hicks RW. Impact of aerobic training on fitness and quality of life in multiple sclerosis. Ann Neurol 1996;39(4):432–41.
16. Fuller KJ, Dawson K, Wiles CM. Physiotherapy in chronic multiple sclerosis: a controlled trial. Clin Rehabil 1996;10:195–204.
17. Lord SE, Wade DT, Halligan PW. A comparison of two physiotherapy treatment approaches to improve walking in multiple sclerosis: a pilot randomized controlled study. Clin Rehabil 1998;12:477–86.
18. Feigenson JS, Scheinberg L, Catalano M. The cost-effectiveness of multiple sclerosis rehabilitation: a model. Neurology 1981;31:1316–22.
19. Greenspun B, Stineman M, Agri R. Multiple sclerosis and rehabilitation outcome. Arch Phys Med Rehabil 1987;68:434–7.
20. Carey RG, Seibert JH. Who makes the most progress in inpatient rehabilitation? An analysis of functional gain. Arch Phys Med Rehabil 1988;69:337–43.
21. Kidd D, Howard RS, Losseff NA, Thompson AJ. The benefit of inpatient neurorehabilitation in multiple sclerosis. Clin Rehabil 1995;9:198–203.
22. Aisen ML, Sevilla D, Fox N. Inpatient rehabilitation for multiple sclerosis. J Neurologic Rehabil 1996;10:43–6.
23. Kidd D, Thompson AJ. A prospective study of neurorehabilitation in multiple sclerosis (letter). J Neurol Neurosurg Psychiatry 1997;62:423–4.
24. Freeman JA, Langdon DW, Hobart JC, Thompson AJ. The impact of inpatient rehabilitation on progressive multiple sclerosis. Ann Neurol 1997;42(2):236–44.
25. Solari A, Filippini G, Gasco P, Colla L, Salmaggi A, La Mantia L, Farinotti M, Eoli M, Mendozzi L. Physical rehabilitation has a positive effect on disability in multiple sclerosis patients. Neurology 1999;52(1):57–62.
26. Freeman JA, Langdon DW, Hobart JC, Thompson AJ. Inpatient rehabilitation in multiple sclerosis: Do the benefits carry over into the community? Neurology 1999;52:50–6.
27. Di Fabio RP, Soderberg J, Choi T, Hansen CR, Schapiro RT. Extended outpatient rehabilitation: its influence on symptom frequency, fatigue and functional status for persons with progressive multiple sclerosis. Arch Phys Med Rehabil 1998; 79(2):141–6.
28. Hatch, J., Johnson, J., and Thompson, A.J. Standards of health care for people with MS. MS Management 1999;5(1):16–25.
29. Thompson AJ, Johnston S, Harrison J, Sheil R, Burnard S. Service delivery in multiple sclerosis: the need for co-ordinated community care. MS Management 1997;4(1):11–8.
30. Reding MJ, La Rocca NG, Madonna M. Acute hospital care versus rehabilitation hospitalisation for management of nonemergent complications in multiple sclerosis. J Neurologic Rehabil 1987;1:13–7.
31. Francabandera FL, Holland NJ, Wiesel-Levison P, Scheinberg LC. Multiple sclerosis rehabilitation: inpatient versus outpatient. Rehabil Nurs 1988;13:251–3.
32. Young CA, Boggild M, Lloyd M, Craig J, Shakespeare D. A prospective study comparing different models of outpatient care for people with multiple sclerosis. Multiple Sclerosis (abstract in press).
33. Aisen ML. Justifying neurorehabilitation: a few steps forward. Neurology 1999;52/1:8–10.

Submitted for publication August 5, 1999. Accepted in revised form January 6, 2000.