PAPER

Home based management in multiple sclerosis: results of a randomised controlled trial

C Pozzilli, M Brunetti, A M V Amicosante, C Gasperini, G Ristori, L Palmisano, M Battaglia

J Neurol Neurosurg Psychiatry 2002;**73**:250–255

See end of article for authors' affiliations

Correspondence to: Dr C Pozzilli, Dipartimento di Scienze Neurologiche, Università "La Sapienza", Viale dell'Università 30, 00185 Rome, Italy; carlo.pozzilli@uniroma1.it

Received 15 January 2002
In revised form 16 May 2002
Accepted 20 May 2002

Background: Home based medical care is a popular alternative to standard hospital care but there is uncertainty about its cost-effectiveness.
Objectives: To compare the effectiveness and the costs of multidisciplinary home based care in multiple sclerosis with hospital care in a prospective randomised controlled trial with a one year follow up.
Methods: 201 patients with clinically definite multiple sclerosis were studied. They were randomised in a ratio 2:1 to an intervention group (133) or a control group (68). They were assessed at baseline and one year after randomisation with validated measures of physical and psychological impairment and quality of life (SF-36 health survey). The costs to the National Health Service over the one year follow up were calculated by a cost minimisation analysis.
Results: There were no differences in functional status between the home based care group and the hospital group. There was a significant difference between the two groups favouring home based management in four SF-36 health dimensions—general health, bodily pain, role-emotional, and social functioning (all $p \leqslant 0.001$). The cost of home based care was slightly less (822 euros/patient/year) than hospital care, mainly as a result of a reduction in hospital admissions.
Conclusions: Comprehensive planning of home based intervention implemented by an interdisciplinary team and designed specifically for people with multiple sclerosis may provide a cost-effective approach to management and improve the quality of life.

Multiple sclerosis is a chronic disabling disease that strikes early in life, with a median age at onset of 30 years. It has a female preponderance. The initial course of the disease is usually relapsing-remitting (RR) followed by a secondary progressive (SP) course. A minority of patients suffer from primary progressive (PP) multiple sclerosis, a clinical variant in which the disease is progressive from the onset, without a history of clear cut relapses or remissions.[1] The mean time until aids for ambulation are required is approximately 15 years.[2]

Apart from the personal suffering, the financial consequences for the patients with multiple sclerosis and their family are enormous, as is the economic burden for society. Cost areas consist of expensive medical treatments, lost earnings for both patients and caregivers, and the provision of social security and social services.[3 4]

Patients with multiple sclerosis often have complex needs that require an input from a wide range of community services. Despite a shift of emphasis from hospital to community care in recent years, many people with moderate or severe disease still fail to receive adequate assistance. It is common for the burden of care to fall on the family and unpaid carers.[5] Medical and therapeutic measures capable of promoting health and independence, relieving discomfort, and preventing medical complications are often not put into practice,[6–8] and the urgent need for a review of community services in multiple sclerosis has recently been highlighted.[9 10]

"Hospital at home" schemes, which provide the kinds of care in the patient's home that have traditionally been supplied in hospital, have grown in importance in health services in both Europe and North America. This is partly because of the growth of inpatient costs, which has increased the pressure on hospitals to reduce the length of stay. Recently, several randomised controlled trials comparing "hospital at home" care with hospital inpatient care have been undertaken in elderly medical patients,[11 12] in people with terminal illness,[13 14] and in those who need follow up care after a stroke or myocardial infarct.[15 16] These studies have provided important insights into our understanding of the potential for developing home based services.

Patients with multiple sclerosis may represent an appropriate population for the evaluation of home care delivery systems as an alternative to traditional hospital based health care approaches. Home based services can offer support, nursing care, rehabilitation, and the administration of drugs, thus decreasing the need for hospital admission.

Our objective in this randomised controlled trial was to compare health outcomes and cost-effectiveness between home based care and traditional hospital care delivered in a multiple sclerosis centre. The hypothesis to be tested was that home based care would improve patient health outcomes without increasing health care costs.

METHODS

Study sample

The study was conducted in Rome and was approved by the ethics committee of La Sapienza University. Patients were recruited from the multiple sclerosis centre of the neurological department of La Sapienza University, or from other institutional centres for multiple sclerosis in Rome. To be eligible, all patients screened for study participation had to be affected by clinically definite multiple sclerosis[17] and live in the

Abbreviations: CDQ, clinical depression questionnaire; EDSS, expanded disability status score; FIM, functional independence measure; FSS, fatigue severity scale; MCS, mental component score; MMSE, mini-mental state examination; PCS, physical component score; SF-36, 36 item short form health survey questionnaire; STAI, state trait anxiety inventory; STAXI, state trait anger expression inventory

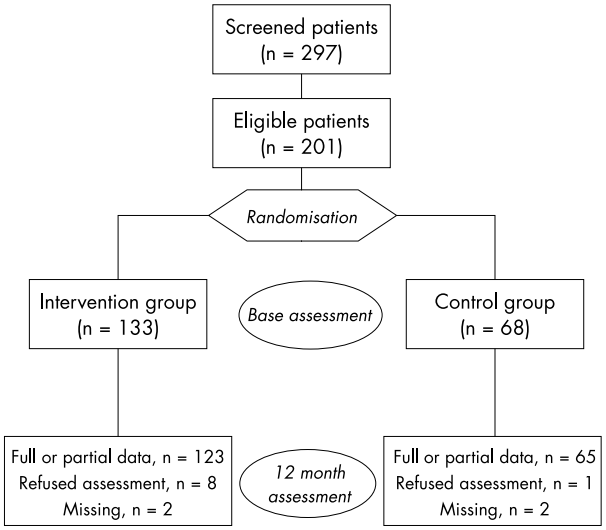

Figure 1 Trial profile.

Rome service area. Eligible patients were assessed for suitability by the coordinator of the home based care team (LP). Written informed consent was obtained for entry into the trial from the patients and, when appropriate, from their carers.

Randomisation

Of the 297 consecutive patients screened, 201 were willing to participate in the study. Ninety six patients declined to participate. The majority of refusers (n = 62) were young, fully ambulant, and employed. They were uncertain that home based management could be adopted in their situations. A minority of refusers (n = 34) did not consent to take part to the study because they were referred to the multiple sclerosis centres only for a second opinion but were regularly followed by their own neurologists.

The patients were randomised to home (intervention) or hospital care (control) in a ratio of 2:1, in order to ensure that the home care population was sufficiently represented. Randomisation (in blocks of six) was stratified by age and expanded disability status score (EDSS),[18] because both health outcomes and costs differ according to disease disability and age[5 19] and a valid conclusion can be drawn only by comparing similar patients. Randomisation was done using a computer generated algorithm.

Baseline interview

Baseline data for both groups (that is, demographic information, neurological and psychological assessment, cognitive and functional abilities, and health related quality of life measures) were collected after randomisation, using standardised instruments. Neurological impairment and cognitive abilities were evaluated by the EDSS and the mini-mental state examination (MMSE).[20] Disability and fatigue were measured using the functional independence measure (FIM)[21] and the fatigue severity scale (FSS).[22] Mood measures included the state trait anger expression inventory (STAXI),[23] the state trait anxiety inventory (STAI),[24] and the clinical depression questionnaire (CDQ).[25] Quality of life was measured by means of the 36 item short form health survey questionnaire (SF-36).[26 27]

Treatment schedules

Based on individual needs, patients randomised to home based care were followed through home visits and telephone follow up. A dedicated phone number was available five days a week from 9 am to 5 pm, where an operator addressed questions or concerns from patients and caregivers and contacted the different specialists according to the specific requirement. After 5 pm and during the weekend an answering machine was on, and recorded messages were regularly listened to by the operator. The home based care multidisciplinary team included two neurologists, a urologist, a rehabilitation physician, a psychologist, a physical therapist, a nurse, a social worker, and a coordinator. These were provided with cell phones and could easily be reached for advice (telephone intervention) or direct face to face intervention when required.

The multidisciplinary team collaborated with the patient, physician, and caregiver in designing individualised clinical care and in coordinating home services as appropriate for the individual patient. The type of care was more than is normally available in the community through National Health Service care. It consisted of observation, administration of intravenous drugs, nursing care, rehabilitation of the patients in their home, patient and caregiver education, psychological support, and the services of the social secretariat.

Patients randomised to routine hospital care were followed as usual in their multiple sclerosis referral centres. A brief monitoring phone call once a month was used to obtain information about the patient's medical visits and hospital admissions in the previous month.

At the end of a one year follow up period, all patients underwent the same comprehensive interview as at baseline.

Table 1 Baseline characteristics by treatment allocated

Characteristic	Intervention group (n=133)	Control group (n=68)
Age (years)	47 (10.3)	46.7 (13.3)
Women (n (%))	86 (65)	47 (69)
Married (n (%))	77 (58)	36 (53)
Working (n (%))	31 (23)	19 (28)
Disease duration (years)	18.4 (9.5)	18.6 (11)
Disease type		
RR (n (%))	26 (19.6)	14 (20.6)
PP (n (%))	27 (20.5)	14 (20.6)
SP (n (%))	80 (59.9)	40 (58.8)
EDSS	6.0 (2.0)	5.8 (2.2)
FIM	87.3 (27.7)	87.4 (28.6)
MMSE	27.8 (3.1)	27 (4.5)

Values are mean (SD) unless stated otherwise.
EDSS, expanded disability status scale; FIM: functional independence measure; MMSE: mini mental state examination; PP, primary progressive; RR, relapsing-remitting; SP, secondary progressive.

Statistical analysis

Sample size considerations

With a two tailed 5% significance level, a total sample size of 201 (with a 2:1 randomisation ratio and taking into account a drop out rate of 10%) would yield about 90% power to detect a standardised difference of 0.5 standard deviations on the SF-36 general health perception domain. The figure was obtained assuming a standard deviation of 10 for the pre-post differences in SF-36 general health perception domain and a five point difference between the two groups, which is the smallest change in score considered clinically relevant.[27]

Statistical calculations

Baseline data for intervention and control groups were compared using a χ^2 test for categorical variables, a *t* test for normally distributed continuous variables, and the Wilcoxon rank-sum test for abnormally distributed variables.

For each scale of the SF-36 and separately for the case and control group, we adopted a regression model in which score changes at the end of the follow up period were adjusted for the baseline values. Changes in scores were approximated by a

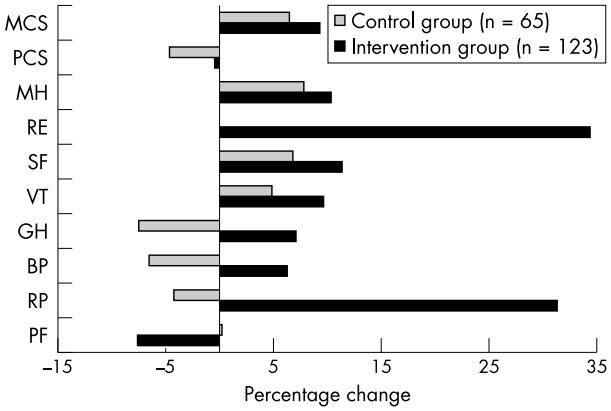

Figure 2 Percentage change in SF-36 scales after one year of follow up. BP, bodily pain; GH, general health; MCS, mental component score; MH, mental health; PCS, physical component score; PF, physical functioning; RE, role, emotional; RP, role physical; SF, social functioning; VT, vitality.

normal distribution and so the primary analysis after adjustment for baseline assessment was by two sample *t* test.

Economic evaluation

We adopted a cost minimisation analysis to test the hypothesis that home based care and traditional hospital care delivered in a multiple sclerosis centre are associated with an equivalent consumption of resources. The economic analysis was conducted from a third party payer perspective; accordingly, only direct health care costs were considered.[28] Indirect costs (lack of productivity for the patient and for caregivers) and non-medical costs were not included. The resources considered were the cost of inpatient, outpatient, and home care services, as well as the cost of the home based coordination programme. We did not included costs of pharmaceuticals and aids for daily life activities.

The costs of inpatient care (ordinary, rehabilitation, day hospital, and diagnostic tests) were estimated using Italian third party payer reimbursement for diagnosis related groups (DRGs) as a proxy for the real cost. Outpatients and community resources were calculated through the outpatient prices developed by the National Health Service.[29] An additional fee for service reimbursement established by a national contract was used to cost domiciliary visits. Telephone intervention was estimated directly in the trial as half of the resources of an outpatient visit; this estimate was tested in the sensitivity analysis.

For the intervention group, we estimated the costs to cover the local management and administration of the home based management scheme (for the operator, coordinator, telephone, and overheads). The costs used in the analysis were calculated on the basis of 1999 Italian prices converted to euros. The one year time horizon did not require discounting in the analysis.[28]

Sensitivity analysis was used to test the robustness of the economic results. We employed a multivariate sensitivity analysis, altering each variable simultaneously to take the most optimistic/pessimistic value in order to generate a best/worst case scenario.

RESULTS

Between January 1997 and January 1998, 201 consecutive patients were randomised (133 to the intervention group and 68 to the control group). Data on the follow up assessment at 12 months were available in 188 patients (123 in the intervention group and 65 in the control group) (fig 1).

Baseline characteristics

Table 1 summarises the baseline sociodemographic and clinical characteristic of the patients. Many of those in the study were unemployed or retired people and were in the progressive phase of the disease.

The two groups were similar in all baseline variables measured, including functional and cognitive abilities. However, baseline differences between the two groups emerged in four of the eight SF-36 domains (role, physical: $p = 0.01$; bodily pain: $p = 0.01$; general health: $p = 0.05$; role, emotional: $p = 0.03$), with the intervention group reporting a lower quality of life than the control group. To correct for these observed differences, all analyses of SF-36 were adjusted for the relevant baseline assessment.

Functional outcomes

Functional outcomes were calculated as the mean change of scores from baseline to the final follow up at 12 months. No significant differences between intervention and control groups were detected for outcome measures, including EDSS, FIM, MMSE, CDQ, FSS, STAI, and STAXI. There was a trend in favour of the intervention group for changes in depression as measured by the CDQ score. A decrease in CDQ score was seen in the intervention group (–7.8%) while it was slightly increased (+0.7%) in the control group ($p = 0.11$).

Figure 2 shows the percentage changes in the SF-36 scores at one year. In the intervention group we observed an improvement in eight SF-36 scales. In the control group, an increase in the score of four SF-36 scales was detected; however, the improvement was less consistent than in the intervention group. Table 2 shows the changes in SF-36 scales at one year, with the positive differences being in favour of the intervention group. The intervention group had a significant

Table 2 Difference between mean changes in SF-36 scores of patients who were allocated to intervention or control group, after adjustment for baseline assessment*

SF-36	Difference	95% CI†	p Value‡
Physical functioning (PF)	0.27	(–0.53 to 1.06)	0.55
Role, physical(RP)	3.67	(–1.19 to 8.53)	0.09
Bodily pain (BP)	3.46	(2.38 to 4.54)	0.0001
General health (GH)	5.01	(4.50 to 5.51)	0.0001
Vitality (VT)	0.28	(–0.38 to 0.94)	0.41
Social functioning (SF)	1.09	(0.51 to 1.67)	0.001
Role, emotional (RE)	12.39	(9.85 to 14.93)	0.0001
Mental health (MH)	–0.10	(–0.25 to 0.05)	0.19
Physical component score (PCS)	1.19	(1.04 to 1.34)	0.0001
Mental component score (MCS)	0.75	(0.58 to 0.91)	0.0001

*From (separate) regression model.
†Scores from intervention group minus those for control group.
‡By unpaired *t* test.
CI, confidence interval.

Table 3 Resource and cost per patient (in euros) in each arm of the trial

	Number of events per patient				Cost per patient (euros)		
	Intervention (n=133)	Control (n=68)	Difference (95% CI)	p Value	Intervention (n=133)	Control (n=68)	Difference
Inpatient care*	0.34	1.01	– 0.67 (–1.15 to – 0.19)	0.0001	1173	2193	–1020
Outpatient and home care							
Medical†	4.49	2.59	1.90 (0.90 to 2.91)	0.0002	103	64	39
Non-medical‡	6.00	0.50	5.50 (3.97 to 7.03)	0.0067	22	9	13
Home care programme§					146		
Total cost					1443	2265	–822

*Includes ordinary, rehabilitation, and day hospital.
†Includes outpatients, home care, and telephone service provided by neurologist, urologist, and rehabilitation physician.
‡Includes outpatients, home care, and telephone service provided by psychologist, social walker, physical therapist, and nurses.
§Includes personnel and overheads.
CI, confidence interval.

improvement in bodily pain ($p = 0.0001$), general health ($p = 0.0001$), social functioning ($p = 0.001$), and role, emotional ($p = 0.0001$) when compared with the control group. In addition, scores on the eight SF-36 dimensions were reduced to two summary scores—a physical component (PCS) and a mental component (MCS)—by means of component analyses.[27] There was a significant difference between the two arms of the trial in favour of the intervention group for both PCS ($p = 0.0001$) and MCS ($p = 0.0001$).

Resource use and costs

Table 3 shows the resource consumption and costs in each arm of the trial. Patients included in the home based care scheme had less inpatient stay than the control group ($p = 0.001$). The needs of patients receiving home based care increased substantially for problems requiring both medical care and nursing, social, and psychological support ($p = 0.0002$ and 0.0067, respectively). Nevertheless, home based care presented a saving of 822 euros per patient compared with the controls.

In the best case scenario (an increase of 10% in reimbursement for admissions, a decrease of 10% for home based management costs, and the upper limit of the 95% confidence interval (CI)), each home based care patient presented a saving of 2086 euros. In the worst case scenario (a decrease of 10% in reimbursement for admissions, an increase of 10% for home based management costs, and the lower limit of the 95% CI), there was an incremental cost of 234 euros per patient.

DISCUSSION

Home based medical care is a popular alternative to standard hospital care, but there is uncertainty about its cost-effectiveness. There are two basic assumptions implicit in establishing home based health care—that is preferred by patients, and that is economically advantageous.[30] However, comparisons of the two modes of care, both in terms of patient outcomes and in terms of the cost to the health service, often produce conflicting results.[31] The types of patient admitted to home based care may influence its cost-effectiveness significantly: patients suffering from chronic conditions such as multiple sclerosis are likely to require long term provision of care, with fewer occurrences of "emergencies" and more requests for social support and help for caregivers.

This study showed that a comprehensive home based follow up intervention implemented by an interdisciplinary team and designed specifically for patients with multiple sclerosis improved some aspects of their quality of life without increasing the cost of care. Thus the intervention suggested great economic potential, with improved outcomes being achieved at similar cost mainly by reducing hospital admissions and length of stay.

The results of the trial depend on local service provision, which may have influenced recruitment to the study, as well as on the characteristics of patients recruited. In the first place, the multidisciplinary team was well trained in order to ensure that the members had adequate case management skills. Secondly, patients with a strong preference for a hospital centre may have declined to enter the study, and patients could be admitted to the scheme only if they agreed to be randomised. Although it was randomised, our study could not be performed within the rigid criteria of a clinical trial. Because of the nature of the intervention all the professionals concerned were aware of the assignment of patients to either group. Also, as a result of the need for informed consent, patients and physicians were aware of the ongoing project. By chance, there was an imbalance between the groups in some of the quality of life dimensions at baseline, but this was reflected in the fact that randomisation to intervention occurred before the baseline interview. Thus it was not possible to fully blind patients or interviewers to the intervention during the baseline interview. To minimise the absence of blinding in the follow up interview, the assessors had no access to initial scores.

The quality of standard care in the control group must be also considered in the interpretation of the results. It could be argued that the study compared a rapid, responsive, and flexible type of care (home based management) with less responsive standard hospital care, which involving prebooked clinic visits and hospital access only in cases of significant medical deterioration. However, our control group was regularly followed in multiple sclerosis centres, where no more than one or two weeks are generally required to obtain an outpatient appointment, and hospital admissions are rapid in cases of need. The difference between conventional and home based care seems more related to the characteristics of home based intervention, implemented by a multidisciplinary team, than to the speed and flexibility of the service.

The results of our study indicated that home based management did not influence the most common measures of neurological impairment/disability (EDSS, FIM) but led to an improvement of SF-36 dimensions related to daily living and basic social routines. On the other hand, changes in the quality of life measures that are highly correlated with EDSS (that is, physical functioning and physical role limitation)[19] were also similar in the intervention group and the control group. Physical disability may not be the main determinant of overall health related quality of life in multiple sclerosis. While physicians are usually more concerned than patients about the physical manifestations of disease, the patients identified role limitations caused by emotional problems as the most important determinant of their overall quality of life.[32 33] It is worth noting that the greatest difference between patients receiving home based care and the control group was observed within this dimension.

We assessed quality of life by means of SF-36, which is generally considered to be the gold standard generic measure of health status and has been validated cross culturally in multiple sclerosis.[34] New scales have recently been developed for quality of life in multiple sclerosis by adding specific items to SF-36.[35 36] However, modifying existing measures by simply adding clinically chosen items may not be as useful as anticipated in improving the measurements properties of an instrument.[37]

SF-36, reflecting the patients' perspective, provides a broad measure of the disease impact in multiple sclerosis because all eight quality of life dimensions are reduced compared with the general population.[19] Problems in measuring quality of life in multiple sclerosis, however, may occur in longitudinal studies and are related to the poor responsiveness of SF-36 and to the "response shift." Response shift refers to the fact that the physical disability of the patients can change over time, thus influencing assessment of the quality of life.[38] We stress, however, that in the present study no significant differences between intervention and control groups occurred for scales measuring neurological impairment or physical disability such as EDSS and FIM.

The poor responsiveness of the SF-36 is particularly marked when patient selection is limited to those with moderate to severe disability, and it is related to the large floor effect in some of the SF-36 dimensions.[39] We investigated a wide range of patients with multiple sclerosis including those with RR disease. Thus our sample is representative of the entire multiple sclerosis population and it is not restricted to moderately or severely disabled patients. Two of the four health dimensions (emotional role limitation and bodily pain) which were significantly improved by home based management are influenced by floor and ceiling effects.[39] These effects, however, did not occur in the other two SF-36 dimensions (general health and social functioning) or in MCS and PCS, which were also favourably influenced by home based care.

Our economic analysis suggests that care in multiple sclerosis can be provided in patients' homes using a model of home based management at the same or lower cost than an equivalent admission to hospital. At 12 months, the intervention generated a mean saving of 822 euros per patient. The higher costs in the control group were entirely related to the greater proportion of patients being admitted to hospital. A significant increase in both medical and non-medical resources was observed in the intervention group. This is likely to reflect the nature of our scheme based on a multidisciplinary approach and a comprehensive model of care.

Our study suggests a lower annual direct cost of multiple sclerosis (2265 euros in the control group) compared with other studies performed in European countries.[5 40] Our lower figures may reflect a different approach to multiple sclerosis in Italy, but also the exclusion of drugs and disability aids from the analysis. Further limits of the economic analysis could be the use of reimbursement values to approximate costs[24] and the use of third party payer perspective, not including the indirect costs. Nevertheless, despite the important role of the indirect costs in the multiple sclerosis burden,[3 4 40] there is still considerable variability in the measurements depending on the methods used to collect resource.[41]

Conclusions

This is the first controlled study investigating the effectiveness of home based management in patients with multiple sclerosis. Our results show that the scheme is effective at improving the quality of life in people with multiple sclerosis and may provide a viable alternative to a hospital centre. One of the best features of the home based care is that it allows family members to receive instruction and help from formal caregivers. Moreover, the family can remain involved and assist in the care of their loved ones.

Home based care is an appropriate model of care for severely disabled patients who are still living at home but usually spend long periods in hospital. Given the current attention to new models of patient care in multiple sclerosis, we consider the study findings especially important for decision makers in the definition of priorities for multiple sclerosis patients. Home based care could also be run as a complement to hospital care, and play a role in managing the demand for hospital admission. More research is required to define the exact size of home based schemes in multiple sclerosis and its relation to hospital and community services.

ACKNOWLEDGEMENTS

We thank A Mancini, T Koudriavtseva, E Frascaro, D Di Diego, S Gagliarducci, M Ricci, S Leoncini, P Di Giuseppe, T Corlianò, F Cipriani, and A Bracci of the home based care multidisciplinary team for their cooperation with the study; S Cifani and P Pasqualetti for their statistical suggestions; Prof C Fieschi for his continuous support; and Prof A Thompson for comments on the manuscript. Support for the study was provided by the Fondazione Italiana Sclerosi Multipla, the Istituto Superiore di Sanità, and Dompé Biotec.

Portions of this article were presented at the International Meeting held in Bari, Italy, in April 1999: "Toward the standardisation of a home based care delivery system in multiple sclerosis: report of a Round Table." In: *MS Management* 2000;**7**:26–32.

Authors' affiliations

C Pozzilli, G Ristori, Dipartimento di Scienze Neurologiche, Università "La Sapienza", Rome, Italy
M Brunetti, A M V Amicosante, Istituto di Ricerche Farmacologiche "Mario Negri", Milan
C Gasperini, Dipartimento di Neurologia, Ospedale San Camillo-Forlanini, Rome
L Palmisano, M Battaglia, Fondazione Italiana Sclerosi Multipla, Rome

Competing interests: none declared.

REFERENCES

1 **Noseworthy JH**, Lucchinetti C, Rodriguez M, *et al*. Multiple sclerosis. *N Engl J Med* 2000;**343**:938–52.
2 **Weinshenker BG**, Bass B, Rice GPA, *et al*. The natural history of multiple sclerosis: a geographically based study. 1. Clinical course and disability. *Brain* 1989;**112**:133–46.
3 **Whetten-Goldstein FS**, Goldstein LB, Kulas ED. A comprehensive assessment of the cost of multiple sclerosis in the United States. *Multiple Sclerosis* 1998;**4**:419–25.
4 **Parkin D**, Jacoby A, McNamee P, *et al*. Treatment of multiple sclerosis with interferon beta: an appraisal of cost-effectiveness and quality of life. *J Neurol Neurosurg Psychiatry* 2000;**68**:144–9.
5 **Carton H**, Loos R, Pacolet J, *et al*. Utilization and cost of professional care and assistance according to disability of patients with multiple sclerosis in Flanders (Belgium). *J Neurol Neurosurg Psychiatry* 1998;**64**:444–50.
6 **Petajan JH**, Gappmaier E, White AT, *et al*. Impact of aerobic training on fitness and quality of life in multiple sclerosis. *Ann Neurol* 1996;**39**:432–41.
7 **Freeman JA**, Langdon DW, Hobart JC, *et al*. The impact of inpatient rehabilitation on progressive multiple sclerosis. *Ann Neurol* 1997;**42**:236–44.
8 **Solari A**, Filippini G, Gasco P, *et al*. Physical rehabilitation had a positive effect on disability in multiple sclerosis. *Neurology* 1999;**52**:57–62.
9 **Stolp-Smith KA**, Atkinson EJ, Campion ME, *et al*. Health care utilisation in multiple sclerosis. A population based study in Olmsted Country, MN. *Neurology* 1998;**50**:1594–600.
10 **Freeman JA**, Thompson AJ. Community services in multiple sclerosis: still a matter of chance. *J Neurol Neurosurg Psychiatry* 2000;**69**:728–32.
11 **Stuck AE**, Aronow HU, Steiner A, *et al*. A trial of in-home comprehensive discharge assessment for elderly people living in the community. *N Eng J Med* 1995;**333**:1184–9.
12 **Naylor MD**, Brooten D, Campbell R, *et al*. Comprehensive discharge planning and home follow-up of hospitalized elders. A randomized clinical trial. *JAMA* 1999;**281**:613–20.
13 **Cummings JE**, Hughes SL, Weaver F, *et al*. Cost-effectiveness of Veterans Administration hospital-based home care: a randomized clinical trial. *Arch Intern Med* 1990;**150**:1274–80.
14 **Bredin M**, Corner J, Krishnasamy M, *et al*. Multicentre randomised controlled trial of nursing intervention for breathlessness in patients with lung cancer. *BMJ* 1999;**318**:901–7.

15 **Anderson C**, Rubenach S, Mhurchu CN, *et al*. Home or hospital for stroke rehabilitation? Results of a randomized controlled trial. I. Health outcomes at 6 months. *Stroke* 2000;**31**:1024–31.
16 **Jolly K**, Bradley F, Sharp S, *et al*. Randomised controlled trial of follow-up care in general practice of patients with myocardial infarction and angina: final results of the Southampton heart integrated care project (SHIP). *BMJ* 1999;**318**:706–11.
17 **Poser CM**, Paty DW, Scheinberg L, *et al*. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Ann Neurol* 1983;**13**:227–31.
18 **Kurtzke J**. Rating neurological impairment in multiple sclerosis: an Expanded Disability Status Scale (EDSS). *Neurology* 1983;**33**:1444–52.
19 **Nortvedt MW**, Riise T, Kjell-Morten M, *et al*. Quality of life in multiple sclerosis: measuring the disease effects more broadly. *Neurology* 1999;**53**:1098–103.
20 **Folstein M**, Folstein S, McHugh PR. Mini mental state: a practical method of grading the cognitive state of patients for the clinicians. *J Psychiatry Res* 1975;**12**:189–98.
21 **Kidd D**, Stewart G, Baldry J, *et al*. The Functional Independence Measure: a comparative validity and reliability study. *Disabil Rehabil* 1995;**17**:10–14.
22 **Krupp LB**, La Rocca NC, Muir-Nash J, *et al*. The Fatigue Severity Scale applied to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol* 1989;**46**:1121–3.
23 **Spielberger CD**. *Manual for the state-trait anger inventory*. Palo Alto: Consulting Psychologist Press, 1983.
24 **Spielberger CD**, Vagg PR, Barker LR. The factor structure of State–Trait Anxiety Inventory. In: Saranson IG, Spielberger CD, eds. *Stress and anxiety*, vol 7. New York: Hemisfere/Wiley, 1980.
25 **Krugg SE**, Scheier JH, Cattell RB. *Handbook for the IPAT anxiety scale*. Champaign Ill: IPAT, 1976.
26 **Ware JE**, Sherbourne CD. The MOS-36 item short-form healthy survey (SF-36): conceptual framework and item selection. *Med Care* 1992;**30**:473–83.
27 **Ware JE**, Kosinki M, Keller SD. SF-36 physical and mental health summary scales: a user's manual. Boston, MA: The Health Institute, New England Medical Center, December, 1994.
28 **Drummond MF**, O'Brien B, Stoddart GL, *et al*. *Methods for the economic evaluation of health care programmes*, 2nd ed. Oxford: Oxford Medical Publications, 1997.
29 **Nomenclatore Tariffario Ministero della Sanità**. *Prestazioni di assistenza specialistica ambulatoriale erogabili nell'ambito del SSN e relative tariffe*. Rome: Decreto Ministeriale 22 Luglio, 1996.
30 **Gundersen L**. There's no place like home: the home care alternative. *Ann Intern Med* 1999;**131**:639–40.
31 **Shepperd S**, Iliffe S. The effectiveness of hospital at home compared with in-patient hospital care: a systematic review. *J Public Health Med* 1998;**20**:344–50.
32 **Rothwell PM**, McDowell, Wong CK, *et al*. Doctors and patients don't agree: cross sectional study of patients and doctors perceptions and assessments of disability in multiple sclerosis. *BMJ* 1997;**314**:1580–3.
33 **O' Connor P**, Lee L, Tin Ng P, *et al*. Determinants of overall quality of life in secondary progressive MS: a longitudinal study. *Neurology* 2001;**57**:889–91.
34 **Pfennings L**, Cohen L, Miller D, *et al*. Using the short form-36 with multiple sclerosis patients in five countries: a cross-cultural comparison. *Psychol Rep* 1999;**85**:19–31.
35 **Vickrey BG**, Hayes RD, Harooni R, *et al*. A health-related quality of life measure for multiple sclerosis. *Qual Life Res* 1995;**4**:187–206.
36 **Vickrey BG**, Hayes RD, Genovese BJ, *et al*. Comparison of a generic to a disease-targeted health-related quality of life measure for multiple sclerosis. *J Clin Epidemiol* 1997;**50**:557–69.
37 **Freeman JA**, Hobart JC, Thompson AJ. Does adding MS-specific items to a generic measure (the SF-36) improve measurement? *Neurology* 2001;**57**:68–74.
38 **Pfennings L**, Cohen L, Van der Ploeg HM. Assessing the quality of the life of patients with multiple sclerosis. In: Thompson AJ, Polman CH, Hohlfeld R, eds. *Multiple sclerosis: clinical challenges and controversies*. London: Martin Dunitz, 1997.
39 **Freeman JA**, Hobart JC, Langdon DW, *et al*. Clinical appropriateness: a key factor in outcome measure selection: the 36 item short form health survey in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2000;**68**:150–6.
40 **Henriksson F**, Jonsson B. The economic cost of multiple sclerosis in Sweden in 1994. *Pharmacoeconomics* 1998;**13**:597–606.
41 **Henriksson F**, Fredrikson S, Jonsson B. Costs, quality of life and disease severity in multiple sclerosis – a population based cross-sectional study. *Eur J Neurol* 2001;**8**:27–35.