MSBEST

MULTIPLE SCLEROSIS BEST EVIDENCE-BASED STRATEGIES
AND TREATMENT/THERAPIES FOR REHABILITATION

Team-Based Rehabilitation: Functional and Quality of Life Outcomes

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Key Points

- Team-based rehabilitation may result in improved self-care as measured by the Functional Independence Measure in progressive MS. However, the evidence is conflicting regarding whether or not team-based rehabilitation improves self-care for persons with relapsing remitting MS as studies involve both relapsing and progressive disease courses. The evidence is also conflicting for the acute MS relapse population.

- Team-based rehabilitation may result in improved participation outcomes in persons with MS; however, the evidence is conflicting. More standardized approaches for including and measuring participation outcomes are needed.

- It is unclear whether or not team-based rehabilitation is effective in improving quality of life in persons with MS as assessed by various outcome measures.

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Abbreviations

2MW	2-Minute Walk Test
6MW	6-Minute Walk Test
9HPT	9 Hole Peg Test
ADLs	Activities of Daily Living
AMCA	Amended Motor Club Assessment
ANSNAP	Australian National Subacute and Non-Acute Patient
AROC	Australian Rehabilitation Outcomes Centre
AUA QoL	American Urological Association Symptom Index & Quality of Life Questionnaire
B&B	Box and Blocks Test
BBS	Berg Balance Scale
BDI	Beck Depression Inventory
BI	Barthel Index
CDQ	Clinical Depression Questionnaire
CG	Control Group
CGI	Clinical Global Impression
CIS-20R	Checklist Individual Strength
COPM	Canadian Occupational Performance Measure
COVS	Clinical Outcome Variables
CPMS	Chronic Progressive Multiple Sclerosis
DIP	Disability and Impact Profile
EDSS	Expanded Disability Status Scale
ESS	Environmental Status Scale
FAMS	Functional Assessment in Multiple Sclerosis
FIM	Functional Independence Measure
FIS	Fatigue Impact Scale
FMS	Fatigued Multiple Sclerosis
FSS	Fatigue Severity Scale
GAS	Goal Attainment Scaling
GCIS	Global Clinical Impression Scale
GHQ-28	General Health Questionnaire
GNDS	Guy's Neurological Disability Scale
HADS	Hospital Anxiety and Depression Scale
HAP	Human Activity Profile
HAS	Handicap Assessment Scale
HVLT	Hopkins Verbal Learning Test
ICP	Integrated Care Pathway
IG	Intervention Group
IIQ7	Incontinence Impact Questionnaire
IMD	Integrated Multidisciplinary
IP	Individualized patient
IPA	Impact of Participation and Autonomy
ISS	Incapacity Status Scale
IVMP	Intravenous Methylprednisolone
LASQ	Life Appreciation and Satisfaction Questionnaire
LHS	London Handicap Scale

LORS-II	Revised Level of Rehabilitation Scale
LOS	Length of Stay
MDR	Multidisciplinary Rehabilitation
MFIS	Modified Fatigue Impact Scale
MHI	Mental Health Inventory
MMSE	Mini-Mental State Examination
MS	Multiple Sclerosis
MSFC	Multiple Sclerosis Functional Composite
MSIS	Multiple Sclerosis Impairment Scale
MSIS-29	Multiple Sclerosis Impact Scale-29
MSQoL-54	Multiple Sclerosis Quality of Life-54
MSSE	Multiple Sclerosis Self-Efficacy Scale
NC	Nurse consultation
NFMS	Non-Fatigued Multiple Sclerosis
NIS	Neurological Impairment Scale
NPTDA	Northwick Park Therapy Dependency Assessment
OP	Outpatient
OT	Occupational Therapy
PASAT	Paced Auditory Serial Addition Test
PCT	Prospective Controlled Trial
PDQ	Perceived Deficits Questionnaire
PEDro	Physiotherapy Evidence Database
PPMS	Primary Progressive Multiple Sclerosis
PRMS	Progressive Relapsing Multiple Sclerosis
PT	Physiotherapy/Physical Therapy
PwMS	Persons with Multiple Sclerosis
QoL	Quality of Life
QRS	Questionnaire on Resource and Stress
RCS	Rehabilitation Complexity Scale
RCT	Randomized Controlled Trial
RIC-FAS	Rehabilitation Institute of Chicago Functional Assessment Scale
RMI	Rivermead Mobility Index
RRMS	Relapsing-Remitting Multiple Sclerosis
SD	Standard Deviation
SET	Social Experience Tempelaar Checklist
SF-36	36-Item Short Form Health Survey
SIP	Sickness Impact Profile
SPMS	Secondary Progressive Multiple Sclerosis
STAI	State Trait Anxiety Inventory
STAXI	State Trait Anger Expression Inventory
T25FW	Timed 25ft Walk Test
T50MW	Timed 50m Walk
TT	Tinetti Test
TW10	10 Metre Walk Test
UDI6	Urogenital Distress Inventory
VAS	Visual Analog Scale

Team-Based Rehabilitation: Functional and Quality of Life Outcomes

1.0 Introduction

Team-based rehabilitation for individuals with multiple sclerosis (MS) may encompass a variety of team compositions, structures and settings. The National Institute for Health and Care Excellence and others recommend a coordinated, multidisciplinary approach to care, involving professionals with expertise in MS who can best meet the needs of persons with MS (PwMS) (National Institute for Health and Care Excellence, 2014; Rieckmann et al., 2013). PwMS may survive well into their 8th decade and live a large proportion of their adult life with disability (Bronnum-Hansen, Koch-Henriksen, & Stenager, 2004; Kingwell et al., 2012). They may experience seemingly stable periods, unpredictable relapses and symptoms, and disability progression.

Authors of a Cochrane review of multidisciplinary rehabilitation for adults with MS concluded that although multidisciplinary rehabilitation does not appear to influence impairment, it may improve activity and participation (Khan, Turner-Stokes, Ng, & Kilpatrick, 2007). The review also highlighted existing knowledge gaps regarding intensity and frequency of rehabilitation, as well as the need to assess cost and long-term effectiveness. A subsequent systematic review of rehabilitation treatments by Haselkorn et al. (2015) and an overview of reviews by Khan and Amatya (2017) also included single-discipline rehabilitation interventions. These later reviews concluded that higher quality evidence was needed to guide evidence-based recommendations. The authors emphasized the need for a focus on outcome measures specific to goals of the intervention which are meaningful and sensitive. Therefore, this module addresses separately team-based rehabilitation approaches where the goals of treatment include an impact on three main outcomes: i. basic self-care, ii. participation, or iii. quality of life (QoL). Only studies which evaluated team-based rehabilitation care are included in this module. For the purpose of this review, a team must consist of at least two or more health care providers. Single-discipline interventions and other outcomes of importance to PwMS (i.e., MS symptoms, gait function, etc.) will be discussed in subsequent modules.

2.0 Outcomes in Team-Based Rehabilitation Care

2.1 Self-Care Activities

Sidney Katz was a pioneer in developing the concept of activities of daily living (ADLs) within the twentieth century (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963). Basic ADLs include, among other things, bathing, dressing, eating, transferring, toileting, and continence, and this concept remains a focus within physiatry today. This module defines self-care activities in terms of basic ADLs. Outcome measures commonly used to assess independence with one or more of the basic ADLs within studies examining team-based rehabilitation for MS include the following:

- The Functional Independence Measure [FIM; (Keith, Granger, Hamilton, & Sherwin, 1987)] is a widely-used assessment tool in rehabilitation and consists of 18 tasks scored on an ordinal scale from 1 (total assistance) to 7 (complete independence). Thirteen tasks compose the motor sub-score including: eating, grooming, bathing, dressing upper body, dressing lower body, toileting, transfers (bed/chair/wheelchair, toilet), bath/shower, walking and/or wheeling, and stairs). Three tasks assess cognition and two assess communication resulting in total FIM scores ranging from 18 (total assist) to 126 (independence). The FIM has been shown to be sensitive to change in rehabilitation settings (Ottenbacher, Hsu, Granger, & Fiedler, 1996).

- The Incapacity Status Scale (ISS) is a 16-item ordinal scale where the first nine items assess the level of assistance for activities of daily function relevant to self-care. It was incorporated into the 1985 version of the Minimal Record of Disability for Multiple Sclerosis (Haber & LaRocca, 1985) and was based on work by Granger (Granger, 1981) and Kurtzke (Kurtzke, 1981).
- The Barthel Index [BI; (Mahoney & Barthel, 1965)] provides a record of disability or dependence among ten ADLs. It uses an ordinal scale and is typically completed by a healthcare provider in collaboration with the patient and caregiver(s).
- The Rivermead Mobility Index [RMI; (Collen, Wade, Robb, & Bradshaw, 1991)] assesses functional mobility (e.g., transfers, standing, stairs, walking, running, etc.) with 14 self-report items and one observer-rated item. All items are scored as either 1 (can complete) or 0 (cannot complete). Its use with PwMS has been supported (Vaney, Blaurock, Gattlen, & Meisels, 1996).
- The Handicap Assessment Scale [HAS (Nicholas, Playford, & Thompson, 2000)] was developed at the National Hospital for Neurology and Neurosurgery in the UK. Information on this scale is scant, but according to authors of a study of Guillain-Barre syndrome, it includes items concerning productivity, financial status, personal residence, transportation, social activity, and autonomy. Each is scored 0-5, with lower scores indicating less handicap.
- The Guy's Neurological Disability Scale [GNDS; (Sharrack & Hughes, 1999)] assesses twelve domains of disability, each on a 0-5 scale (ranging from normal to total loss of function), based upon a guided clinical interview. It was designed for use with PwMS.
- The Amended Motor Club Assessment [AMCA; (De Souza & Ashburn, 1996)] represents a modification of the stroke-focused MCA. The AMCA was intended for physiotherapists to assess motor and functional deficits in PwMS. It includes 53 items assessing lower limb movement, upper limb movement, and functional activities, and is intended to be completed in a single visit of less than an hour.
- The Revised Levels of Rehabilitation Scale [LORS-II; (R. Carey & Posavac, 1982)] is intended to measure three areas of functional independence – ADLs, mobility, and communication (verbal, gestural, and written). In its standard form, ratings are provided by nurses and/or appropriate therapists on a five-point scale (0 - does not perform function; 4 - patient performs the function reliably and independently).
- The Rehabilitation Institute of Chicago Functional Assessment Scale [RIC-FAS V.2; (Cichowski & Simantel, 1989)] is a measure of function, disability, and status. Function items are measured on a 7-point scale from total assistance (1) to complete independence (7).

Table 1. Studies Examining Team-Based Rehabilitation on Self-Care Activity Outcomes in Multiple Sclerosis

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
Nedeljkovic et al. 2016	**Population:** *Intervention Group (IG; n=17):* Mean age=41.3yr; Gender: males=6, females=11; Disease course: RRMS; Mean	1. On the FIM motor, there was a significant improvement between baseline and 1mo that was sustained up to 3mo in both

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Self-Care Activity Results**
Multidisciplinary rehabilitation and steroids in the management of multiple sclerosis relapses: a randomized controlled trial Serbia RCT PEDro=5 $N_{Initial}$=49, N_{Final}=37	EDSS=4.5; Mean disease duration=104.5mo. *Control Group (CG; n=20):* Mean age=39.4yr; Gender: males=5, females=15; Disease course=RRMS; Mean EDSS=4.0; Mean disease duration=80.6mo. **Intervention:** Subjects were randomized to a multidisciplinary inpatient rehabilitation program (IG) or standard care (CG) after receiving intravenous methylprednisolone (1g/d, 5d). Rehabilitation was comprised of physiotherapy (1h/d, 5d/wk) and occupational therapy (30min/d, 3d/wk) for a total of 3wks. Outcomes were assessed at baseline, 1mo, and 3mo. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Functional Independence Measure (FIM). **Other Outcome Measures:** EDSS; Beck Depression Inventory (BDI); Multiple Sclerosis Quality of Life-54 (MSQoL-54).	groups (p<0.001). There was no significant difference between groups at baseline (p=0.288), 1mo (p=0.102), or 3mo (p=0.217). 2. On the FIM cognition, there was no significant difference found between baseline and 1mo or 3mo in either group. There was no significant difference between groups at baseline (p=0.228), 1mo (p=0.284), or 3mo (p=0.657).
Pappalardo et al. 2016 *Inpatient versus outpatient rehabilitation for multiple sclerosis patients: Effects on disability and quality of life* Italy RCT PEDro=6 $N_{Initial}$=146, N_{Final}=146	**Population:** *Group A outpatient (n=49):* Mean age=48.0yr; Gender: males=18, females=31; Disease course: PPMS=18, SPMS=31; Mean EDSS=6.5; Disease duration: unspecified. *Group B inpatient (n=49):* Mean age=46.0yr; Gender: males=17, females=32; Disease course: PPMS=17, SPMS=32; Mean EDSS=6.5; Disease duration: unspecified. *Group C control (n=48):* Mean age=45.0yr; Gender: males=18, females=30; Disease course: PPMS=18, SPMS=30; Mean EDSS=6.4; Disease duration: unspecified. **Intervention:** MS patients were randomized to three groups: the outpatient treatment group (Group A), the inpatient treatment group (Group B), and the control waiting list (Group C). Assessments were performed at baseline (T0) and at 6mo follow-up (T1). **Primary Outcome Measures:** Functional Independence Measure (FIM). **Self-Care Outcome Measures:** FIM. **Other Outcome Measures:** 36-Health Survey Questionnaire (SF-36).	1. Total FIM score improved by a minimum of 20% in 22.6% of patients in the outpatient group A and 14.6% in inpatient B (p=0.5). 2. Motor FIM sub-items improved by a minimum of 20% in 32 % of patients in the outpatient group A and 21.4% in the inpatient group B (p=0.4) while cognitive FIM sub-items showed no improvement in the outpatient group A and an improvement in 3.5% of the inpatient group B. 3. A significant difference was found in terms of total FIM score between T0 and T1 in Group A (p=0.03), in Group B (p=0.008) and Motor FIM sub-items score in Group A (p=0.02). 4. In Group C, no significant variation was found between T0 and T1 in total FIM scores and its sub-items. 5. A significant difference in total FIM scores between the three groups was found (p=0.0003). Pairwise comparisons showed a significant difference between Group A and Group C (p=0.003) and Group B vs. Group C (p=0.001). 6. Motor FIM sub-item scores were significantly different between groups (p=0.0001). Pairwise comparisons showed a significant difference between

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
		Group A and Group C ($p<0.001$) and Group B vs. Group C ($p<0.001$). 7. No significant differences in cognitive FIM sub-item scores were observed between the three groups.
Rietberg et al. 2014 *Effects of multidisciplinary rehabilitation on chronic fatigue in multiple sclerosis: a randomized controlled trial* The Netherlands RCT PEDro=7 $N_{Initial}=48$, $N_{Final}=44$	**Population:** *Multidisciplinary outpatient rehabilitation (MDR) group (n=23):* Mean age=45yr; Gender: males=9, females=14; Disease course: RRMS=16, PPMS=2, SPMS=5; Median EDSS=3; Mean disease duration=7yr. *Nurse consultation (NC) group (n=25):* Mean age=47yr; Gender: males=8, females=17; Disease course: RRMS=12, PPMS=6, SPMS=7; Median EDSS=4; Mean disease duration=8yr. **Intervention:** MS patients with chronic fatigue were randomized to MDR or to MS-NC groups. Assessments were performed at baseline and after intervention. **Primary Outcome Measures:** Checklist Individual Strength (CIS-20R). **Self-Care Outcome Measures:** Functional Independence Measure (FIM). **Other Outcome Measures:** MS Impact Scale (MSIS-29); Impact on Participation and Autonomy (IPA); Modified Fatigue Impact Scale (MFIS); Fatigue Severity Scale (FSS); Disability and Impact Profile (DIP).	1. No significant between-group differences were found for the FIM from baseline to 12wks ($p=0.13$) or from 12wks to 24wks ($p=0.34$). 2. No significant within-group effects were found for multidisciplinary rehabilitation or nurse consultation with respect to the primary and secondary outcome measures from baseline to 12 or 24wks.
Salhofer-Polanyi et al. 2013 *Benefits of inpatient multidisciplinary rehabilitation in multiple sclerosis* Austria RCT PEDro=5 $N_{Initial}=21$, $N_{Final}=19$	**Population:** *Intervention Group (n=10):* Mean age=53.8yr; Gender: males=5, females=5; Disease course: RRMS=2, PPMS=2, SPMS=6; Median EDSS=6; Mean disease duration=17.6yr. *Control Group (n=9):* Mean age=52.9yr; Gender: males=3, females=6; Disease course: RRMS=2, SPMS=7; Median EDSS=5.5; Mean disease duration=15.9yr. **Intervention:** Subjects were randomized to a multidisciplinary inpatient rehabilitation program (intervention) or a waiting list (control). Rehabilitation was provided 5d/wk with 4-5 sessions/d, for a total of 3wks. Outcomes were assessed at baseline and after 15wks. **Primary Outcome Measures:** Timed 50m Walk (T50MW); 2-min Walk Test (2MW); 6-min Walk Test (6MW); Walking Speed. **Self-Care Outcome Measures:** Rivermead Mobility Index (RMI). **Other Outcome Measures:** Functional Assessment in Multiple Sclerosis (FAMS); EDSS; Berg Balance Scale (BBS); Tinetti Test (TT); MS Functional Composite: 9 Hole Peg	1. There was no significant difference between the intervention group and the control group in mean change on the RMI ($p=0.350$) after treatment. 2. RMI showed some improvement in the intervention group, although without reaching statistical significance.

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Self-Care Activity Results**
	Test (9HPT), Timed 25ft Walk (T25FW), Paced Auditory Serial Addition Test (PASAT); MS Self-Efficacy Scale (MSSE); Global Clinical Impression Scale (GCIS).	
Khan et al. 2010 *A randomised controlled trial: outcomes of bladder rehabilitation in persons with multiple sclerosis* Australia RCT PEDro=9 $N_{Initial}$=74, N_{Final}=58	**Population:** *Treatment group (n=24):* Mean age=49.9yr; Gender: males=9, females=15; Disease course: RRMS=6; PPMS=4; SPMS=14; EDSS: 0-3=5, 3.5-6.0=9, 6.5 or greater=10; Mean disease duration=12.2yr. *Control group (n=34):* Mean age=51.1yr; Gender: males=5, females=29; Disease course: RRMS=14, PPMS=4, SPMS=16; EDSS: 0-3=9, 3.5-6.0=21, 6.5 or greater=4; Mean disease duration=10.0yr. **Intervention:** Patients were randomized to either the intervention group where they received a multifaceted, individualized, bladder rehabilitation programme, or to the control group (no intervention). Ten participants randomized to control group required some treatment during the study. **Primary Outcome Measures:** Urogenital distress inventory (UDI6); Incontinence impact questionnaire (IIQ7). **Self-Care Outcome Measures:** Guy's Neurological Disability Scale (GNDS – bladder subscale only). **Other Outcome Measures:** AUA Symptom Index.	1. There was a statistically significant difference in change scores between the treatment and control groups with respect to the GNDS (p<0.001). The effect size was large (0.58), as per Cohen's criteria.
Khan et al. 2008 *Effectiveness of rehabilitation intervention in persons with multiple sclerosis: a randomised controlled trial* Australia RCT PEDro=8 $N_{Initial}$=101, N_{Final}=98	**Population:** *Treatment Group (n=49)*: Mean age=49.5yr; Gender: males=18, females=31; Disease course: RRMS=13, PPMS=7, SPMS=29; EDSS: 0-3=7, 3.5-6.0=27, 6.5+=15; Mean disease duration=10.69yr. *Control Group (n=52)*: Mean age=51.1yr; Gender: males=11, females=41; Disease course: RRMS=18, PPMS=7, SPMS=27; EDSS: 0-3=12, 3.5-6.0=32, 6.5+=8; Mean disease duration=9.73yr. **Intervention:** The treatment group underwent multidisciplinary rehabilitation and received either individualized patient (IP) or outpatient (OP) rehabilitation. IP rehabilitation: 3-6wks, 3 or more times/wk, 3h therapy/d, 2 blocks of 45min physiotherapy and occupational therapy with other blocks comprised of speech pathology, neuropsychology and social work. OP rehabilitation: Up to 6wks, 2-3times/wk, 30min sessions for physiotherapy, occupational therapy, social work and speech	1. There were significant differences post treatment between the treatment and control groups for FIM motor total scores (p<0.001) and FIM cognitive subscale scores (p<0.016). 2. The treatment group showed significantly greater improvement in FIM motor scores (p<.001; effect size= 1.13). 3. More patients in the treatment group had improved FIM scores throughout the study (70.8% vs. 13%) and more patients in the control group had FIM scores suggesting deterioration compared to the treatment group (58.7% vs. 16.7%). The difference in these proportions was significantly different (p<0.001).

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
	pathology in addition to doing stretching home exercises. The control group received no intervention, only an 8 weekly monitoring phone call for information about medical hospital visits in the previous month and received no other information. **Primary Outcome Measures:** Functional Independence Measure (FIM) motor subscale. **Self-Care Outcome Measures:** FIM motor and cognitive subscales. **Other Outcome Measures:** Multiple Sclerosis Impact Scale (MSIS-29); General Health Questionnaire (GHQ-28).	
Storr et al. 2006 *The efficacy of multidisciplinary rehabilitation in stable multiple sclerosis patients* Denmark RCT PEDro=8 $N_{Initial}$=106, N_{Final}=90	**Population:** *Control group (n=52)*: Mean age=50.1yr; Gender: males=16, females=36; Disease course: RRMS=12 (23%), PPMS=11 (21%), SPMS=29 (56%); Median EDSS=6.5; Median disease duration=9.0yr. *Intervention group (n=38)*: Mean age=53.0yr; Gender: males=16, females=22, Disease course: RRMS=5 (13%), PPMS=9 (24%), SPMS=24 (63%); Median EDSS=6.5; Median disease duration=9.0yr. **Intervention:** Individuals were randomized either to the control group and received no rehabilitation treatment, or to the intervention group and received rehabilitation treatment from the MS rehabilitation hospital in Haslev Denmark. **Primary Outcome Measures:** Functional Assessment in Multiple Sclerosis (FAMS). **Self-Care Outcome Measures:** Guy's Neurological Disability Scale (GNDS). **Other Outcome Measures:** Multiple Sclerosis Impairment Scale (MSIS); EDSS; Visual Analog Scale for symptoms (VAS); 10 meter walk test (TW10); Nine-Hole Peg Test (9HPT); Life Appreciation and Satisfaction Questionnaire (LASQ).	1. No significant difference was found between the control and the intervention groups on any of the outcome measures.
Craig et al. 2003 *A randomised controlled trial comparing rehabilitation against standard therapy in multiple sclerosis patients receiving intravenous steroid treatment*	**Population:** *Control group (n=20)*: Mean age=42yr; Gender: males=4, females=16; Disease course: active relapsing; Mean EDSS=5.1; Mean disease duration=5.69yr. *Intervention group (n=20)*: Mean age=38yr; Gender: males=9, females=11, Disease course: active relapsing; Mean EDSS=5.4; Mean disease duration=7.42yr. **Intervention:** All MS participants were randomized to either the control group and received standard ward routine care and 3d of intravenous methylprednisolone (IVMP), or	1. The difference in the mean scores from baseline to 3mo between treatment and control groups was significant for GNDS (p=0.030), AMCA (p=0.035), and BI (p=0.018).

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
UK RCT PEDro=5 $N_{Initial}$=41, N_{Final}=40	to the intervention group and received planned coordinated multidisciplinary team treatment and 3d of IVMP. Participants were assessed at baseline upon receiving IVMP treatment, at 1mo and at 3mo after the first day of IVMP. **Primary Outcome Measures:** Guy's Neurological Disability Scale (GNDS); Amended Motor Club Assessment (AMCA). **Self-Care Outcome Measures:** GNDS; AMCA; Barthel Index (BI). **Other Outcome Measures:** Human Activity Profile (HAP); 36-Item Short Form Health Survey (SF-36).	
Patti et al. 2003 *Effects of a short outpatient rehabilitation treatment on disability of multiple sclerosis patients - a randomised controlled trial* Italy RCT PEDro=8 $N_{Initial}$=111, N_{Final}=111	**Population:** *Outpatient rehabilitation (n=58)*: Mean age=45.2yr; Gender: males=24, females=34; Disease course: PPMS=12, SPMS=46; Mean EDSS=6.2; Mean disease duration=17.2yr. *Home exercise (n=53)*: Mean age=46.1yr; Gender: males=23, females=30; Disease course: PPMS=11, SPMS=42; Mean EDSS=6.1; Mean disease duration=17.2yr. **Intervention:** Patients were randomized to a comprehensive rehabilitation program and a home exercise group. The patients in the comprehensive rehabilitation group received an individualized, goal-oriented program involving an interdisciplinary team, addressing a wide range of areas for 6wks (6x/wk) and a home exercise program for a further 6wks. The home exercise group received the home exercise program for 12wks. Both groups were assessed at baseline and at 12wks. **Primary Outcome Measures:** Functional Independence Measure (FIM). **Self-Care Outcome Measures:** FIM. **Other Outcome Measures:** EDSS; Functional System Scale; Social Experience Tempelaar Checklist (SET).	1. There were significantly greater improvements for the rehabilitation program group compared to the home exercise group on FIM scores ($p<0.0001$); particularly in locomotion, self-care and transfers ($p<0.001$).
Pozzilli et al. 2002 *Home based management in multiple sclerosis: results of a randomised controlled trial* Italy RCT	**Population:** *Intervention group (n=133):* Mean age=47yr; Gender: males=47, females=86; Disease course: RRMS=26, PPMS=27, SPMS=80; Mean EDSS=6.0; Mean disease duration=18.4yr. *Control group (n=68):* Mean age=46.7yr; Gender: males=21, females=47; Disease course: RRMS=14, PPMS=14, SPMS=40; Mean EDSS=6.0; Mean disease duration=18.6yr. **Intervention:** MS patients were randomized to receive either individually tailored	1. No significant differences between intervention and control groups were detected for the FIM.

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
PEDro=5 $N_{Initial}$=201, N_{Final}=188	multidisciplinary home-based medical care with regular phone support available 5d/wk (intervention group) or routine care involving multidisciplinary care coordinated through a hospital-based MS centre (control group). Assessments were performed at baseline and at 12mo. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Functional Independence Measure (FIM). **Other Outcome Measures:** 36 item short form health survey questionnaire (SF-36); EDSS; Mini-Mental State Examination (MMSE); Fatigue Severity Scale (FSS); State Trait Anger Expression Inventory (STAXI); State Trait Anxiety Inventory (STAI); Clinical Depression Questionnaire (CDQ); cost resource assessment.	
Guagenti-Tax et al. 2000 *Impact of a comprehensive long-term care program on caregivers and persons with multiple sclerosis* US RCT PEDro=5 $N_{Initial}$=73, N_{Final}=59 (patient-caregiver units)	**Population:** *Patients (n=59)*: *Experimental*: Mean age=44.0yr; Gender: males=8 (13.3%), females=51 (86.7%); Disease course: CPMS=39 (66.7%); Mean EDSS=7.06; Mean disease duration=8.9yr. *Control*: Mean age=49.0yr; Gender: males=18 (31.0%), females=41 (69.0%); Disease course: CPMS=51 (86.2%); Mean EDSS=7.24; Mean disease duration=14.2yr. *Caregivers (n=59)*: *Experimental*: Mean age=44.9yr; Gender: males=43.3%, females=56.7%. *Control*: Mean age=51.8yr; Gender: males=48.3%, females=51.7%. **Intervention:** Patient-caregiver units were randomized to a comprehensive rehabilitation program or a standard care group. The comprehensive rehabilitation program consisted of 4 coordinated components: 1) twice-monthly medical day-care program, 2) a series of semi-annual workshops for persons with MS and family caregivers, 3) monthly home visits by social workers, nurses, and volunteers, 4) case management and liaison services. Patients and caregivers were assessed at baseline, 12 and 24mo. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Incapacity Status Scale (ISS). **Other Outcome Measures:** EDSS; Number of acute hospital admissions; Perceived deficits	1. There was significant decline in ISS scores (p=0.000) for all patients. 2. No interaction effects (only main effects) were reported for the above findings. 3. All patients reported an increase in satisfaction with the help they received from their caregivers for their daily routines (p=0.005) and within a reasonable time frame (p=0.039). 4. On the QRS, caregivers reported an increase in martyrdom (p=0.000). 5. Control patients reported significantly greater satisfaction with getting help with their daily routine compared to the rehabilitation patients (p=0.004).

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Self-Care Activity Results**
	questionnaire (PDQ); Hopkins Verbal Learning Test (HVLT); Mental Health Inventory (MHI); Sickness Impact Profile (SIP); Revised UCLA Loneliness-Companionship Scale; Questionnaire on Resource and Stress (QRS); 36-Item Short Form Health Survey (SF-36); Satisfaction with care; Length of stay.	
Freeman et al. 1997 *The impact of inpatient rehabilitation on progressive multiple sclerosis* UK RCT PEDro=5 $N_{Initial}$=70, N_{Final}=66	**Population:** *Rehabilitation group (n=32)*: Mean age=43.2yr; Gender: males=11, females=21; Disease course: PPMS=2, SPMS=30; Median EDSS=6.5; Mean disease duration=9.6yr. *Waitlist group (n=34)*: Mean age=44.6yr; Gender: males=13, females=21; Disease course: PPMS=4, SPMS=30; Median EDSS=6.5; Mean disease duration=11.4yr. **Intervention:** Patients were randomized to either the rehabilitation or the waitlist groups. The rehabilitation program consisted of a multidisciplinary team approach, interventions tailored to meet the individual's needs and a patient centered functional goal setting approach. The waitlist group continued with their normal routine. Interventions were 6wks. Patients were tested at baseline and at 6wks. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Functional Independence Measure (FIM). **Other Outcome Measures:** EDSS; London Handicap Scale (LHS).	1. The rehabilitation group had significantly greater improvements compared to the waitlist group for overall FIM motor score (p<0.001) and on the subscales of: self-care (p<0.0001), transfers (p<0.001), and sphincter control (p<0.001).
Francabandera et al. 1988 *Multiple Sclerosis Rehabilitation: Inpatient vs. Outpatient* US RCT PEDro=4 $N_{Initial}$=84, N_{Final}=84	**Population:** *Inpatient group (n=42). Outpatient group (n=42).* Demographic data not reported. Inclusion criteria: severe disability (EDSS 6-9) and not institutionalized. **Intervention:** MS patients were randomized to either inpatient or outpatient rehabilitation. An individualized plan of care was instituted for each patient. An average of two 45min physical therapy sessions and one occupational therapy session per day was scheduled for each patient. Bladder management, speech therapy, and social services were provided as needed. Equipment needs were assessed, and appropriate devices were recommended and ordered. Assessments were performed at baseline and after 3, 6, 9, and 12mo. **Primary Outcome Measures:** Incapacity Status Scale (ISS). **Self-Care Outcome Measures:** ISS. **Other Outcome Measures:** None.	1. There was a statistically significant difference in ISS between the inpatient and outpatient groups at the 3mo follow-up (24.3 vs. 27.2, respectively; p<0.05). 2. Patients in the inpatient group on average improved slightly, while those in the outpatient group deteriorated slightly.

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
Liberatore et al. 2014 *Predictors of effectiveness of multidisciplinary rehabilitation treatment on motor dysfunction in multiple sclerosis* Italy Pre-Post $N_{Initial}$=266, N_{Final}=212	**Population:** Mean age=45.0yr; Gender: males=96, females=116; Disease course: RRMS=43, PPMS=38, SPMS=124, PRMS=7; Median EDSS=6.0; Mean disease duration=13.9yr. **Intervention:** MS patients underwent a short-term (3-7wks) intensive (2hr/d, 5d/wk), individualised, goal-oriented inpatient rehabilitation program. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Motor subscale of Functional Independence Measure (mFIM). **Other Outcome Measures:** EDSS; Functional Systems; Fatigue Severity Scale (FSS); Paced Auditory Serial Addition Test (PASAT).	1. Following rehabilitation treatment, at discharge, a significant improvement in the mFIM values (p<0.001) was observed. 2. 121 patients (57.1%) improved in activity limitation (mFIM responders), 113 patients (53.3%) in impairment (EDSS responders), 139 patients (75.1%) in either mFIM or EDSS or both (partial responders), and 75 (35.4%) in both outcomes (full responders). 3. Regarding the partial response, a baseline moderate-severe disability assessed by mFIM increased the probability to benefit from rehabilitation (p<0.001).
Judica et al. 2011 *Impact of fatigue on the efficacy of rehabilitation in multiple sclerosis* Italy PCT $N_{Initial}$=186, N_{Final}=86	**Population:** *Treated group (n=64):* Mean age=43.2yr; Gender: males=32, females=32; Disease course: RRMS=13, PPMS=12, SPMS=39; Mean EDSS=5.8; Mean disease duration=15.5yr. *Control group (n=22):* Mean age=46.3yr; Gender: males=12, females=10; Disease course: RRMS=6, PPMS=4, SPMS=12; Mean EDSS=5.4; Mean disease duration=16.9yr. **Intervention:** MS patients underwent an intensive, short-term inpatient rehabilitation program. Patients were classified into fatigued MS (FMS) in the case of a Fatigue Severity Scale (FSS) score of ≥36, and non-fatigued MS (NFMS) for FSS<36. An untreated control group was included for comparison. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Functional Independence Measure (FIM). **Other Outcome Measures:** EDSS; FSS; MS Functional Composite (MSFC).	1. 46 patients were defined as fatigued and 18 as non-fatigued in the rehab treated group. In the control group, 16 patients were fatigued and 6 were non-fatigued. 2. Comparing all (FMS and NFMS) patients before and after rehabilitation, there was an increase in FIM score (p<0.0001). 3. FIM significantly increased in FMS patients before and after the rehabilitation program (p<0.0001). 4. FIM significantly increased in NFMS patients before and after the rehabilitation program (p<0.0001).
Vidmar et al. 2011 *Time trends in ability level and functional outcome of stroke and multiple sclerosis patients undergoing comprehensive rehabilitation in Slovenia* Slovenia Pre-Post	**Population:** *MS participants (n=225):* Mean age=50yr; Gender: males=74, females=151; Disease course: unspecified; Disease severity: unspecified; Disease duration: unspecified. **Intervention:** MS participants received comprehensive rehabilitation at the University Rehabilitation Institute in Ljubljana. Patients were divided into two groups based on time-period of admission: during 1999-2000, or from 2004-2006. Assessments were performed at admission and discharge. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Functional Independence Measure (FIM).	1. Admission motor and cognitive FIM subscale scores were on average 5 points lower in the 2004-2006 period, the average total score being approximately 10 points lower. The average difference between discharge and admission scores (rehabilitation gain) increased over time, in total by about 3 points in MS patients. 2. Progress on FIM scores at discharge was significantly different between the groups of MS patients in terms of FIM total (p<0.001), motor (p=0.001), and cognitive (p=0.001).

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
$N_{Initial}=225$, $N_{Final}=225$	**Other Outcome Measures:** None.	3. Significant differences in MS patients were observed between the time-period groups in terms of efficiency (calculated from FIM scores): total ($p<0.001$), motor ($p=0.002$), and cognitive ($p<0.001$), and effectiveness (calculated from FIM scores): total ($p<0.001$), motor ($p<0.001$), and cognitive ($p=0.003$). Both efficiency and effectiveness significantly increased over the time period observed.
Khan et al. 2010 *Clinical practice improvement approach in multiple sclerosis rehabilitation: a pilot study* Australia Case Series $N_{Initial}=24$, $N_{Final}=24$	**Population:** Mean age=51.54yr; Gender: males=10, females=14; Disease course: RRMS=5, PPMS=5, SPMS=14; Disease severity: unspecified; Mean disease duration=11.1yr. **Intervention:** Records for 24 consecutive MS patients presenting in a 14mo period and receiving inpatient rehabilitation were selected for data extraction with the goal of addressing the functional gains after rehabilitation. Each patient received a customized program incorporating physiotherapy, occupational therapy, speech pathology, social work, dietetics, and neuropsychology. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Barthel Index (BI); Functional Independence Measure (FIM). **Other Outcome Measures:** Neurological Impairment Set (NIS); Rehabilitation Complexity Scale (RCS); Northwick Park Therapy Dependency Assessment (NPTDA); Hospital Length of Stay (LOS); discharge destination.	1. Functional gains from admission to discharge for the FIM (motor: $p<0.001$; cognitive: $p=0.005$; total: $p<0.001$) and BI ($p<0.001$) were significant. 2. All patients in the rehabilitation program improved in function (FIM, BI) ($p<0.001$ for both) from admission to discharge, and returned home.
Grasso et al. 2009 *Prognostic factors in multiple sclerosis rehabilitation* Italy Pre-Post $N_{Initial}=230$, $N_{Final}=200$	**Population:** Mean age=49.7yr; Gender: unspecified; Disease course: unspecified; Mean EDSS=6.93; Mean disease duration=17.3yr. **Intervention:** MS patients were admitted to a rehabilitation ward who followed an individualized, goal-oriented, multidisciplinary rehabilitation program. Patients were grouped according to EDSS scores of 2-5.5, 6-6.5, 7-8.5. Assessments were performed at admission and discharge. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Barthel Index (BI); Rivermead Mobility Index (RMI). **Other Outcome Measures:** EDSS; Functional Systems.	1. Following treatment, a significant improvement in both BI and RMI values ($p<0.001$) was observed at discharge. 2. The mean effectiveness value of the whole sample was 16.00 on the BI and 8.60 on the RMI. 3. The BI score improved in 48% of patients, while the RMI score improved in 43.4% of patients. 4. Patients with mild and moderate MS showed an effectiveness on activities of daily living and mobility that was significantly higher compared to patients with the severe form of MS ($p=0.001$, $p<0.05$, respectively).

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Self-Care Activity Results**
Khan et al. 2009 *Multiple sclerosis rehabilitation outcomes: analysis of a national casemix data set from Australia* Australia Case Series $N_{Initial}$=1010, N_{Final}=1010	**Population:** *Whole Population (n=1010):* Mean age=52.0yr; Gender: males=29.8%, females=70.2%; Disease course: unspecified; Disease severity: Australian National Subacute and Non Acute Patient (ANSNAP) casemix classification system classes 216, 217, 218, and 219 which are defined by FIM functional motor scores: 216 (FIM motor (m) scores range 63–91), 217 (FIM m=49–62), 218 (FIM m=18–48), and 219 (FIM m=14–17); Disease duration: unspecified. A*NSNAP 216 (n=404):* Mean age=49.2yr; Gender: males=25.7%, females=74.3%. *ANSNAP 217 (n=222):* Mean age=54.1yr; Gender: males=26.6%, females=73.4%. *ANSNAP 218 (n=360):* Mean age=53.8yr; Gender: males=34.4%, females=65.6%. *ANSNAP 219 (n=24):* Mean age=51.2yr; Gender: males=58.3%, females=41.7%. **Intervention:** De-identified data from MS patients in the Australian Rehabilitation Outcomes Centre (AROC) database were analyzed for all rehabilitation admissions to examine outcomes of inpatient rehabilitation for persons with MS. **Primary Outcome Measures:** Functional Independence Measure (FIM); Hospital Length of Stay (LOS); discharge destination. **Self-Care Outcome Measures:** FIM. **Other Outcome Measures:** None.	1. Classes 216–218 all showed significant improvements in FIM scores from admission to discharge (p<0.001); although class 219 showed a trend towards improvement, this was not significant. 2. FIM improvement differed significantly among the four ANSNAP classes, (p<0.001). 3. Post hoc analyses indicated that ANSNAP 216 had a smaller FIM change compared with 217 (p<0.001) and 218 (p<0.001). (These findings are expected, given that FIM admission scores are higher (indicating better function) in ANSNAP 216 and therefore have less potential for improvement). 4. FIM efficiency was also significantly higher in class 217 than in any of the other classes (p<0.001). 5. There was no significant change in FIM improvement or FIM efficiency from the first to last yr of the study.
Khan et al. 2008 *Use of goal attainment scaling in inpatient rehabilitation for persons with multiple sclerosis* Australia Pre-Post $N_{Initial}$=24, N_{Final}=24	**Population:** Mean age=52.0yr; Gender: males=10, females=14; Disease course: RRMS=5, PPMS=5, SPMS=14; Disease severity: unspecified; Disease duration: unspecified. **Intervention:** MS patients receiving comprehensive inpatient rehabilitation were assessed for clinically important functional changes. Functional assessments were performed within 48hr of admission and discharge. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Functional Independence Measure (FIM); Barthel Index (BI). **Other Outcome Measures:** Goal Attainment Scaling (GAS); Clinical Global Impression (CGI).	1. For the sample as a whole, there was a statistically significant change from admission to discharge on BI and FIM scores (BI: p<0.001; FIM: p<0.001). 2. There was no significant or clinically important difference in responder and non-responder scores for the BI or the FIM.
Vikman et al. 2008	**Population:** *Cohort A (n=40):* Mean age=56.3yr; Gender: males=8, females=32; Disease course: RRMS=2, PPMS=15, SPMS=21, unclassified=2; Mean EDSS=5.8;	1. No significant changes were observed in any cohort for personal care ability as measured by the BI.

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Self-Care Activity Results**
Effects of inpatient rehabilitation in multiple sclerosis patients with moderate disability Sweden Pre-Post $N_{Initial}$=58, N_{Final}=58	Mean disease duration=20.4yr. *Cohort B (n=18):* Mean age=54.7yr; Gender: males=4, females=14; Disease course: PPMS=4, SPMS=14; Mean EDSS=5.6; Mean disease duration=17.0yr. **Intervention:** MS patients with moderate disability received 3wks of inpatient neurorehabilitation in two cohorts, A and B. Rehabilitation consisted of physiotherapy, occupational therapy, and consultation by speech therapist, social worker, and psychologist. Cohort A was assessed on admission and discharge during a rehabilitation period. Cohort B was assessed 3wks before admission, on admission and at discharge. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Barthel Index (BI). **Other Outcome Measures:** 36 Item Short-Form questionnaire (SF-36); Functional Assessment of Multiple Sclerosis (FAMS); Fatigue Severity Scale (FSS); Beck Depression Inventory (BDI); Multiple Sclerosis Functional Composite (MSFC); Grippit; Box and Block Test (B&B); Nine Hole Peg Test (9HPT); Clinical Outcome Variables (COVS); Berg Balance Scale (BBS); Timed 25-Foot Walk Test (T25FWT).	
Grasso et al. 2005 *Prognostic factors in multidisciplinary rehabilitation treatment in multiple sclerosis: an outcome study* Italy Pre-Post $N_{Initial}$=230, N_{Final}=230	**Population:** Mean age=49.42yr; Gender: male/female ratio=1:1:7 (not specified further); Disease course: unspecified; Mean EDSS=6.93; Mean disease duration=16.90yr. **Intervention:** All patients were enrolled in an individualized, goal oriented, multidisciplinary inpatient program based on activities of daily living (ADL). The program took place twice-daily, each session being 45min long, for 6d/wk, for 10wks. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Barthel Index (BI); Rivermead Mobility Index (RMI). **Other Outcome Measures:** EDSS; Functional Systems.	1. Both BI and RMI scores increased significantly from admission to discharge ($p<0.001$). 2. All patient subgroups (basal EDSS score < 6, score 6-6.5, and score > 6.5) showed significant differences between basal and discharge functional values as well as in treatment effectiveness, on the BI and RMI ($p<0.002$). 3. The basal EDSS score was negatively associated with the effectiveness of the treatment, both on BI and RMI ($p<0.001$). 4. Patients without severe cognitive impairment had a probability of improvement in RMI twice as high compared to other patients ($p<0.05$). 5. Patients without severe sphincteric disturbances had probability of improvement in ADL nearly twice as high as that of other patients ($p<0.01$).

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Self-Care Activity Results**
Liu et al. 2003 *Does neurorehabilitation have a role in relapsing-remitting multiple sclerosis?* UK Case Series $N_{Initial}$=90, N_{Final}=90	**Population:** *RRMS group (n=90):* Mean age=33.4yr; Gender: unspecified; Mean EDSS=6.9; Mean disease duration=6.4yr. *PPMS group (n=80):* Mean age=46.0yr; Gender: unspecified; Mean EDSS=7.3; Mean disease duration=10.3yr. *SPMS group (n=402):* Mean age=45.5yr; Gender: unspecified; Mean EDSS=7.1; Mean disease duration=18.4yr. **Intervention:** MS patients received relatively short-stay, goal-orientated, patient-centred multidisciplinary inpatient rehabilitation. The primary study group of RRMS patients were compared to PPMS and SPMS groups. Assessments were performed at admission and after rehabilitation. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Barthel Index (BI); Functional Independence Measure (FIM). **Other Outcome Measures:** EDSS; Visual Analog Scale (VAS).	1. Disability scores in RRMS patients were significantly better at discharge than admission (p<0.0001 all comparisons; mean change of +4.5 points for BI and +15.6 points for FIM), which was significantly greater than the other MS subtypes.
Freeman et al. 1999 *Inpatient rehabilitation in multiple sclerosis: Do the benefits carry over into the community?* UK Pre-Post $N_{Initial}$=50, N_{Final}=44	**Population:** Mean age=44.8yr; Gender: males=21, females=29; Disease course: PPMS=7, SPMS=42; Mean EDSS=6.7; Mean disease duration=11.6yr. **Intervention:** Patients with progressive MS undergoing inpatient rehabilitation were followed for 12mo after discharge. Assessments were undertaken on admission (A), at discharge, and subsequently at 3mo intervals for 1yr (1Y). **Primary Outcome Measures:** Functional Independence Measure (FIM); London Handicap Scale (LHS). **Self-Care Outcome Measures:** FIM. **Other Outcome Measures:** EDSS; Kurtzke's Functional Systems; 36-item Short Form Health Survey Questionnaire (SF-36); 28-item General Health Questionnaire (GHQ).	1. Improvement was seen across all measures during the inpatient stay. These gains declined in varying patterns after discharge. 2. The FIM scores steadily lowered, remaining only marginally above baseline at the 9 and 12mo assessments. 3. No tests of statistical significance were reported in this study.
Di Fabio et al. 1998 *Extended outpatient rehabilitation: Its influence on symptom frequency, fatigue, and functional status for persons with progressive multiple sclerosis*	**Population:** *Treatment group (n=20)***:** Mean age=49yr; Gender: males=5, females=15; Disease course: PPMS or SPMS; EDSS range: 5-8; Mean disease duration=17yr. *Waiting List group (n=26)*: Mean age=50yr; Gender: males=7, females=19; Disease course: PPMS or SPMS; EDSS range=5-8; Mean disease duration=15yr. **Intervention:** Participants were non-randomly assigned to either the treatment or waiting list group. The treatment group received outpatient rehabilitation services for 5hr,	1. When adjusted for the functional level at the initial assessment, the mean RIC-FAS score for the treatment group at the 1yr assessment was 60% compared with 57% for the waiting list group. 2. Mean effect sizes at the 1yr follow-up, adjusted for differences in baseline values, indicated less loss of functional status in the treatment group compared with the waiting list group (-0.07 vs. -0.70 for treatment and waiting list groups, respectively).

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
US PCT $N_{Initial}$=46, N_{Final}=33	1d/wk, over 1yr. Both groups received comparable pharmacologic management. **Primary Outcome Measures:** MS-Related Symptom Checklist; Rehabilitation Institute of Chicago Functional Assessment Scale (RIC-FAS). **Self-Care Outcome Measures:** RIC-FAS. **Other Outcome Measures:** None.	3. With regard to functional status, the waiting list subjects who dropped out of the study had significantly lower RIC-FAS scores compared with those who completed the study.
Rossiter et al. 1998 *Integrated care pathways in multiple sclerosis rehabilitation: completing the audit cycle* UK Pre-Post $N_{Initial}$=125, N_{Final}=125	**Population:** *Cohort 1 (n=39)*: Gender: males=41%, females=59%. *Cohort 2 (n=43)*: Gender: males=36%, females=64%. *Cohort 3 (n=42)*: Gender: males=27%, females=73%. For total study sample: Mean age: unspecified for all groups, but participants were similar in age status; Disease course: unspecified, but the majority were SPMS; Mean EDSS=7; Mean disease duration: unspecified. **Intervention:** Participants were divided into three cohorts and each received a comprehensive process of care that was being audited within the structure of an Integrated Care Pathway (ICP), so that episodes of clinical care could be documented for each of the three main sections: the process pathway, the goal categorization sheet, and the variation tracking sheet. Variations from the expected pathway of clinical care (ICP for neurorehabilitation) were documented and analyzed for each cohort in order to evaluate the effectiveness of the goal-directed therapy implementation. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Barthel Index (BI); Functional Independence Measure (FIM); Handicap Assessment Scale (HAS). **Other Outcome Measures:** Mean variations from process pathway; Mean length of stay; Mean number of goals set by discharge for each patient (goal achievement).	1. All three cohorts showed a mean improvement in BI, HAS, and FIM motor and cognitive subscale scores between admission and discharge, but no significant differences were found between cohorts. 2. No significant correlation between level of goal achievement and changes on outcome measure scores was found. An increase in carer involvement was recognized.
Di Fabio et al. 1997 *Health-related quality of life for patients with progressive multiple sclerosis: influence of rehabilitation* US	**Population:** *Treatment group (n=12):* Mean age=44.5yr; Gender: males=2, females=10; Disease course: PPMS or SPMS; EDSS range: 5-8; Mean disease duration=17.6yr. *Wait-listed group (n=19):* Mean age=49.2yr; Gender: males=4, females=15; Disease course: PPMS or SPMS; EDSS range: 5-8; Mean disease duration=14.2yr. **Intervention:** MS patients received either outpatient care for 1yr or did not receive rehabilitation (wait-listed control).	1. Over the course of the year, both groups showed a decrease in physical function, as demonstrated by negative effect sizes for the RIC-FAS composite scores (including bed mobility, wheelchair propulsion, bed transfers, ambulation, and skin status). However, functional status in the wait-listed group declined more than in the treatment group (effect sizes = -0.52 vs. -0.33, respectively).

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
PCT $N_{Initial}=44$, $N_{Final}=31$	**Primary Outcome Measures:** Rand 36-Item Health Survey 1.0 (SF-36). **Self-Care Outcome Measures:** Rehabilitation Institute of Chicago Functional Assessment Scale (RIC-FAS). **Other Outcome Measures:** MS Quality of Life 54 Item (MSQoL-54).	
Aisen et al. 1996 *Inpatient Rehabilitation for Multiple Sclerosis* US Case Series $N_{Initial}=37$, $N_{Final}=37$	**Population:** Mean age=46.87yr; Gender: males=4, females=33; Disease course: RRMS=6, SPMS=26, PRMS=5; Mean EDSS=7.47; Mean disease duration=11.84yr. **Intervention:** MS patients receiving inpatient rehabilitation for functional decline were assessed retrospectively. Patients received one or two follow-up telephone assessments at intervals ranging from 6mo to 3yr after discharge. Assessment scores at admission, discharge, and follow-up were analyzed. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Functional Independence Measure (FIM). **Other Outcome Measures:** Kurtzke Functional Systems; EDSS.	1. For all groups combined, significant improvements between admission and discharge were seen in FIM (p=0.0001) scores. Gains were partly maintained between discharge and follow-up. 2. Significant improvements also occurred in FIM subgroupings: self-care (eating, dressing, grooming, bathing) (p=0.0001), sphincter control (bladder, bowel) (p=0.0222), and locomotion (ambulation, stair climbing, wheelchair management) (p=0.0001) for all patients. 3. Follow-up assessments obtained in 28 patients at 12 to 24mo showed statistically insignificant changes in FIM compared to the end of rehabilitation. 4. Twelve patients were assessed 24 to 36mo after discharge, whose FIM performance significantly deteriorated (p=0.008) compared to the end of rehabilitation.
Kidd et al. 1995 *The benefit of inpatient neurorehabilitation in multiple sclerosis* UK Pre-Post $N_{Initial}=79$, $N_{Final}=79$	**Population:** Mean age=48.8yr; Gender: males=30, females=49; Disease course: RRMS, SPMS, PPMS; Median DSS=7.0; Mean disease duration=12.1yr. **Intervention:** MS patients admitted over a 16mo period for multidisciplinary rehabilitation were studied using assessment scales as measures of disability and handicap. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Barthel Index (BI). **Other Outcome Measures:** Kurtzke's Disability Status Scale; Environmental Status Scale (ESS).	1. The median BI on admission was 14.0 and increased (improved) by a median of 1.0 overall (p<0.0001). It increased in 51 patients (65%), diminished in one patient (1%) and was unchanged in 27 (34%). 2. Improvement on the BI was most marked in patients in whom a reduction in impairment occurred, but also increased in progressive and stable patients. The difference in terms of changes in BI between patients in whom a reduction in impairment occurred, and progressive and stable patients, was not statistically significant (p=0.13). 3. When the BI on admission was subdivided into mild (20-16), moderate (15-11), severe (10-6) and very severe disability (5-0) the greatest change in disability occurred in the severely and moderately disabled patients.
Carey et al. 1988	**Population:** *MS participants (n=196):* Mean age=46yr; Gender: unspecified; Disease	1. MS patients had mean gain scores of 16 and 20 on the ADL and mobility aspects

Author Year Title Country Research Design PEDro Sample Size	Methods	Self-Care Activity Results
Who makes the most progress in inpatient rehabilitation? An analysis of functional gain US Case Series $N_{Initial}$=6194, N_{Final}=6194	course: unspecified; Disease severity: unspecified; Disease duration: unspecified. **Intervention:** MS patients in rehabilitation facilities were assessed in functional gains over their stay. **Primary Outcome Measures:** Revised Level of Rehabilitation Scale (LORS-II). **Self-Care Outcome Measures:** LORS-II. **Other Outcome Measures:** None.	of the LORS-II, respectively (no significance reported).
Greenspun et al. 1987 *Multiple sclerosis and rehabilitation outcome* US Case Series $N_{Initial}$=28, N_{Final}=28	**Population:** Mean age=42yr; Gender: males=27%, females=73%; Disease course: unspecified; Severity: unspecified; Mean disease duration=12.2yr. **Intervention:** Patients with severe MS were admitted to an inpatient rehabilitation center, and treatment included physical, occupational, and speech therapy, as well as recreational therapy. Patients were seen daily by a physiatrist who coordinated all aspects of care. Data was gathered on admission, at discharge, and at 3mo post-discharge follow-up, over a 4yr period. **Primary Outcome Measures:** Not specified. **Self-Care Outcome Measures:** Study used an assessment which was designed to measure activities of daily living (comprised of dressing, bathing, eating, and toileting). Assessment name was not provided. **Other Outcome Measures:** Mobility assessment instrument (comprised of ambulating, transferring, stair climbing). Assessment name was not provided.	1. After completion of rehabilitation, the proportion of patients independent in dressing, eating, toileting, and bathing increased. 2. At 90d follow-up, 82%, 73%, 85%, and 91% of patients were independent in dressing, bathing, toileting, and eating.

Table 2. Summary of Self-Care Activity Outcomes within RCTs Examining Team-Based Rehabilitation for Multiple Sclerosis

Author, Year	Outcome Measure(s)	Results	Quality of RCT
Nedeljkovic et al. 2016***[1]	FIM	Not Significant	Fair
Pappalardo et al. 2016[2]	FIM	Positive	Good
Rietberg et al. 2014[1]	FIM	Not Significant	Good
Salhofer-Polanyi et al. 2013	RMI	Not Significant	Fair
Khan et al. 2010*	GNDS – bladder subscale	Positive	Excellent
Khan et al. 2008	FIM	Positive	Good

Storr et al. 2006	GNDS	Not Significant	Good
Craig et al. 2003***[1]	GNDS, AMCA, BI	Positive	Fair
Patti et al. 2003**[2]	FIM	Positive	Good
Pozzilli et al. 2002[1]	FIM	Not Significant	Fair
Guagenti-Tax et al. 2000	ISS	Not Significant	Fair
Freeman et al. 1997[2]	FIM	Positive	Fair
Francabandera et al. 1988[1]	ISS	Positive	Fair

Positive indicates a statistically significant finding; *Not Significant* indicates a non-statistically significant finding
AMCA: Amended Motor Club Assessment; BI: Barthel Index; FIM: Functional Independence Measure; GNDS: Guy's Neurological Disability Scale; ISS: Incapacity Status Scale; RCT: Randomized Controlled Trial; RMI: Rivermead Mobility Index
[1] Studies involved only an active control group as the control group also received an intervention
[2] Studies included only participants with a progressive MS disease course
*Khan et al. 2010 is a substudy of Khan et al. 2008 (overlapping samples)
**Patti et al. 2003 is a substudy of Patti et al. 2002 (overlapping samples)
***Included Relapsing Remitting MS with acute MS relapse only

Discussion

Thirteen randomized controlled trials (RCTs) were found which examined the effect of team-based rehabilitation on self-care outcomes in comparison to usual care, a waitlist control group, or an active control group. From these studies, numerous observations can be made to help PwMS and their health care providers create care plans that may best meet their needs. Seven studies used the FIM while the remaining studies applied other outcome measures which included at least some aspects of self-care function to evaluate the effect of team-based rehabilitation strategies (Table 2). Significant improvements were observed on total FIM scores or FIM motor sub-scores in four of the seven studies utilizing the FIM. Improvements on the FIM were seen following inpatient, outpatient, or a mix of inpatient/outpatient team-based rehabilitation approaches (Freeman, Langdon, Hobart, & Thompson, 1997; Khan, Pallant, Brand, & Kilpatrick, 2008; Patti et al., 2003).

According to the studies with improvements in FIM outcomes, team-based interventions were especially effective for certain aspects of self-care. For example, moderate and large effect sizes were reported by Khan et al. (2008) and Patti et al. (2003) for the FIM motor domains of transfers (1.04 and 0.65, respectively), locomotion (0.69 and 0.76, respectively) and other self-care (0.95 and 0.73, respectively). Smaller effect sizes were also reported by Patti et al. (2003) for the FIM domain sphincter function (0.40). In the inpatient study by Freeman et al. (1997), FIM motor effect sizes for improvement were smaller, yet the median change on the FIM motor score was still an improvement in the treatment group (+4; range -10 to +19) versus a worsening in the control group (-2.5; range -16 to +5).

Defining clinically meaningful effectiveness for self-care function is both germane and challenging in MS since decline in function over time is often inherent to the natural history. Among the four studies reporting improvement on the FIM in relation to the comparator group, the mean disease duration from MS onset ranged from nine to seventeen years. Baseline impairment levels were also heterogeneous. These positive studies support that improvement on the FIM is possible across different disease durations and impairment levels. However, three of the seven RCTs reporting on the FIM did not report significant

FIM improvements. The negative studies for FIM improvement could be explained by many factors, including lack of effectiveness and methodological limitations discussed below. However, a lack of improvement on the FIM may not necessarily indicate that the intervention was without a clinically meaningful effect. Future studies could more consistently include defining effectiveness as it relates to slowing down the rate of deterioration on the FIM.

Freeman et al. (1997) reported both improved FIM outcomes in the treatment group and fewer participants in the treatment group showed deterioration on their FIM scores (25%) compared to the control group (62%). This slower rate of decline in function is likely clinically relevant in progressive MS. This study included a heterogeneous sample of participants with progressive MS (baseline motor FIM sub-scores ranged from 13 to 87). A sub-group analysis of only the wheelchair users demonstrated a statistically significant improvement specifically in the FIM motor locomotion sub-score which was not observed in the ambulatory group. Findings from other RCTs also support the contention that individuals with at least moderate mobility restrictions may have the most to benefit from team-based rehabilitation in terms of self-care activities (Francabandera, Wiesel-Levison, & Scheinberg, 1988; Pappalardo et al., 2016). It is conceivable that people with moderate mobility restrictions may have greater challenges with self-care and have more room to improve independence with self-care compared to people with less physical impairment. All three studies which included only people with a progressive MS reported improved outcomes on the FIM in favour of the intervention group. These findings support the role of team-based rehabilitation for improving self-care activities on the FIM in progressive forms of MS.

These improvements on the FIM in people with progressive MS occurred even in the absence of a mean improvement on the Expanded Disability Status Scale (EDSS), supporting the known distinction between impairment and activity restrictions. Activity improvement may be attainable in the absence of a changed impairment level. However, the exact mechanisms by which self-care improvements occurred in the trials involving people with progressive MS requires further study. It is also possible that the EDSS is not sufficiently sensitive to capture subtle changes in impairment in progressive MS which could influence more obvious gains with self-care function. In particular, the EDSS does not focus on capturing upper extremity impairments which may be most critical for independence with self-care activities. In the setting of progressive impairment, it is also possible to improve independence with self-care through the use of assistive equipment and technologies. Irrespective of the mechanism, the observed improvements in self-care are important for people with progressive MS for whom there are few other effective treatment interventions.

The evidence for team-based rehabilitation approaches for improving self-care activities in relapsing-remitting MS is less consistent. Two RCTs (Craig, Young, Ennis, Baker, & Boggild, 2003; Nedeljkovic et al., 2016) examined only people with relapsing-remitting MS who had a recent acute MS relapse. In both studies, all participants received intravenous steroids and the intervention groups also received MS multidisciplinary rehabilitation. Craig et al. (2003) reported a statistically significant outcome on the GNDS favouring the multidisciplinary rehabilitation intervention group while Nedeljkovic et al. (2016) reported non-significant differences in the FIM between the multidisciplinary intervention group and their active control group. It is challenging to compare across studies when, firstly, the intensity of therapy is not consistently described for both the intervention and control groups. Secondly, after an acute MS relapse, it may be expected that self-care function improves as PwMS experience recovery of their impairment after the relapse, regardless of treatment. When both groups improve considerably, this may diminish the power to detect between-group differences. In the Craig et al. (2003) study, participants were older and the severity of relapses was more clearly described (the majority experienced a moderate to severe relapse). In determining the need for team-based rehabilitation services after MS relapse, consideration should be given to the severity of the relapse and the impact the relapse has had on self-care function. More research is needed to determine the optimal selection of people and setting for rehabilitation services after acute MS relapses for improving self-care specifically.

Other RCTs included participants with a clinically-stable, relapsing-remitting course (i.e., no recent relapse) in addition to people with a progressive MS course (Khan et al., 2008; Pappalardo et al., 2016; Rietberg, Van Wegen, Eyssen, & Kwakkel, 2014). Results were not stratified to examine the impact of team-based rehabilitation on people with relapsing-remitting MS separately. However, overall, improvement on the FIM favouring the multidisciplinary intervention was reported in the Khan et al. (2008) study, where approximately 30% of the sample had relapsing-remitting MS. In the study by Rietberg et al. (2014) which failed to detect a statistically significant between-group difference, it is noteworthy that all participants were ambulatory at baseline and greater than 50% of the sample had relapsing-remitting MS. Improvement on the FIM may occur following team-based care in relapsing-remitting MS independent of recovery from acute relapses; however, results are difficult to interpret and compare when studies involve a different mix of study participants.

Studies with non-statistically significant findings provide opportunity for learning about team-based rehabilitation interventions. In some cases, the control groups were active in that they also received multidisciplinary care which was structured in a different format from the intervention group (Nedeljkovic et al., 2016; Pozzilli et al., 2002). While there are many possible reasons for a negative study, including lack of treatment effectiveness, it is also possible that there is more than one effective format for delivering team-based rehabilitation services. In fact, the recent well-designed RCT in progressive MS compared a wait-list control group with both inpatient and outpatient multidisciplinary care (Pappalardo et al., 2016). Inpatient and outpatient services were similarly effective for improving self-care and both groups were superior to the wait-list control group.

One study with a statistically negative outcome included a 3-week multidisciplinary intervention period (Salhofer-Polanyi et al., 2013). However, self-care trended towards improvement in the intervention group compared to the wait list control group at 15 weeks. Self-care was measured as a secondary outcome according to the RMI and was assessed only at the 15-week post-intervention time point. In the case of a known progressive disease course, it may be that measurements at multiple time points are needed to detect change in the rate of functional decline over time and the power to detect these changes needs to be considered.

Importantly, Storr et al. (2006) proposed that differences in the degree of blinding to group allocation (control vs. intervention group) may partially account for differences in study outcomes. Participants who know they are in the treatment group may have a desire and motivation for the treatment to work, thus awareness of group allocation, as well as other potential motivational factors, may impact self-care performance and study outcomes. Blinding is not often possible in rehabilitation studies and rarely are participants' attitudes regarding independence with self-care known. In clinical practice, a person's motivation for independence with self-care may be a complex and changing balance between a strong desire to be independent and the benefits of accepting assistance for personal care in order to conserve energy for other valued life activities.

The longest duration RCT involved two years of follow-up (Guagenti-Tax, DiLorenzo, Tenteromano, LaRocca, & Smith, 2000). This study was also statistically negative for self-care outcomes as measured by the ISS. The authors reported a decline in self-care function that was similar for both the intervention and control groups. The longer intervention and follow-up period is considerably different from the six- to twelve-week end points usually reported in other trials. Given that MS is a life-long disease, evaluation of the impact of team-based interventions on self-care function across several years may be more clinically meaningful to PwMS and their families. The Guagenti-Tax et al. (2000) study also assessed caregiver burden and found that in spite of the decline in self-care function over time among people with progressive MS, caregivers reported that they found the team-based intervention helpful.

Non-RCT study designs may offer further insights into who might be likely to benefit from team-based interventions for self-care function. The majority of these study designs involving team-based rehabilitation care reported improvements on the BI or the FIM (Grasso, Troisi, Rizzi, Morelli, & Paolucci, 2005; Rossiter, Edmondson, al-Shahi, & Thompson, 1998). Non-RCT studies utilizing the RMI (Grasso et al., 2005), and HAS (Rossiter et al., 1998) similarly demonstrated improved self-care outcomes. It is noteworthy that PwMS across all levels of disability may improve in self-care function (Grasso, Pace, Troisi, Tonini, & Paolucci, 2009). However, people with cognitive impairment (Grasso et al., 2005) or severely advanced levels of disability (Grasso et al., 2009; Khan, Turner-Stokes, Stevermuer, & Simmonds, 2009) may be the least likely to experience improvement. Those with moderate levels of disability at baseline may experience the greatest improvements (Khan et al., 2009). Further, improvement in self-care function may not be sustainable over longer periods (Aisen, Sevilla, & Fox, 1996; Freeman, Langdon, Hobart, & Thompson, 1999).

In summary, short-term improvements in self-care function were observed with team-based rehabilitation for PwMS on a variety of outcome measures. These improvements in self-care function were especially apparent in studies where participants had a progressive MS disease course and when the study was powered to assess change in FIM motor scores. Typically, the duration of treatment was at least three weeks, suggesting that time is needed to improve self-care function perhaps through practice, learning, and training effects. The mechanisms leading to improvement or sustained self-care function remain unclear. Fewer studies examined the impact of team-based care for improving specifically self-care function after acute MS relapses and only one study examined caregiver burden as an outcome of interest. Maintaining or slowing the loss of independence for self-care activities over the longer term through multidisciplinary team-based rehabilitation and the impact this may have on caregivers warrants more systematic evaluation.

Conclusion

There is level 1a evidence (from three randomized controlled trials; Pappalardo et al. 2016; Patti et al. 2003; Freeman et al. 1997) that team-based rehabilitation is an effective intervention for improving basic self-care activities as measured by the Functional Independence Measure in progressive MS.

There is conflicting evidence (from five randomized controlled trials; Nedeljkovic et al. 2016; Rietberg et al. 2014; Craig et al. 2003; Pozzilli et al. 2002; Francabandera et al. 1988) regarding whether or not team-based rehabilitation improves basic self-care activities compared to an active control group in persons with MS.

There is conflicting evidence (from two randomized controlled trials; Nedeljkovic et al. 2016; Craig et al. 2003) regarding whether or not team-based rehabilitation improves basic self-care activities for persons with MS who have had an acute MS relapse.

Team-based rehabilitation may result in improved self-care as measured by the Functional Independence Measure in progressive MS. However, the evidence is conflicting regarding whether or not team-based rehabilitation improves self-care for persons with relapsing remitting MS as studies involve both relapsing and progressive disease courses. The evidence is also conflicting for the acute MS relapse population.

2.2 Participation

The World Health Organization defines participation as "involvement in a life situation"[1]. Ideally, team-based rehabilitation approaches assist in maintaining participation in meaningful and purposeful activities and social roles over the lifespan of MS. Outcome measures commonly employed to assess participation outcomes within studies examining team-based rehabilitation for MS include the following:

- The Human Activity Profile [HAP; (Daughton, Fix, Kass, Bell, & Patil, 1982)] is a 94-item questionnaire designed to assess ADLs. On the HAP, respondents indicate if they are currently able to perform the activity, if they have stopped performing the activity, or if they have never performed it. For example, the HAP includes some participation activities such as dining at a restaurant, shopping by oneself, and dancing.
- The London Handicap Scale [LHS; (Harwood, Rogers, Dickinson, & Ebrahim, 1994)] is a self-report measure of mobility, physical independence, occupation, social integration, orientation, and economic self-sufficiency.
- The Multiple Sclerosis Impact Scale-29 [MSIS-29; (Hobart, Lamping, Fitzpatrick, Riazi, & Thompson, 2001)] is a 29-item self-report measure of the physical and psychological impacts of MS. Items are rated on a 5-point Likert-type scale. In particular, some items assess the impact of MS on home social and leisure activities, work or daily activities, and doing things spontaneously. Several items assess the impact of symptoms.
- The Canadian Occupational Performance Measure [COPM; (Law, Baptiste, & McColl, 1990)] is a client-centred, patient-derived outcome measure where respondents identify, prioritize, and measure their performance on activities in three broad categories: self-care, leisure, and productivity. Participants rate on a visual analog scale their performance and their satisfaction with performance for each self-identified and prioritized activity.
- The Impact on Participation and Autonomy scale [IPA; (Cardol, de Haan, van den Bos, De Jong, & de Groot, 1999)] is a generic outcome measure used to assess the perceived impact of the disease (and related symptoms) on five life domains (interior and exterior autonomy, family role, social relations, and job and education). Subjects rate their perception of limitations affecting participation and autonomy and the extent to which these limitations are experienced as problematic.
- The Environmental Status Scale [ESS; (International Federation of Multiple Sclerosis Societies, 1984)] is a component of the Minimal Record of Disability devised by the International Federation of MS societies and deals with seven areas of handicap including work status and the

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[1] The International Classification of Functioning, Disability and Health

need for domestic help. Each area is scored from 0 to 5 for increasing handicap with a maximum score of 35.

Table 3. Studies Examining Team-Based Rehabilitation on Participation Outcomes in Multiple Sclerosis

Author Year Title Country Research Design PEDro Sample Size	Methods	Participation Results
Papeix et al. 2015 *Evaluation of an integrated multidisciplinary approach in multiple sclerosis care: A prospective, randomized, controlled study* France RCT PEDro=5 $N_{Initial}$=50, N_{Final}=42	**Population:** *Control group (n=25):* Median age=50yr; Gender: males=18, females=7; Disease course: RRMS=5, PPMS=6, SPMS=14; Median EDSS=6; Median disease duration=17yr. *Integrated multidisciplinary (IMD) group (n=25):* Mean age=52yr; Gender: males=20, females=5; Disease course: RRMS=3, PPMS=3, SPMS=19; Median EDSS=6; Median disease duration=17yr. **Intervention:** MS patients were allocated to one of two treatment strategies: (i) an IMD approach, consisting of a half-day individually tailored comprehensive assessment in the MS clinic; (ii) standard care. Assessments were performed at baseline and after 6 (M6) and 12 (M12) mo. **Primary Outcome Measures:** MS Impact Scale (MSIS-29). **Participation Outcome Measures:** MSIS-29. **Other Outcome Measures:** EDSS; Hospital Anxiety and Depression Scale (HADS); Modified Fatigue Impact Scale (MFIS); QUALIVEEN; Visual Analog Scale (VAS).	1. Median MSIS-29 score (higher score corresponding to greater impact of MS) of over 6mo decreased in the control group, and increased in the IMD group. The difference between the two groups was significant (p<0.03). However, in the multivariate analysis, after adjustment of HADS-D and INTERMED score, this difference was no longer significant. 2. Changes in MSIS-29 from baseline to M12 (0 and -5 in the control and the IMD group, respectively) were not significantly different between the two groups.
Rietberg et al. 2014 *Effects of multidisciplinary rehabilitation on chronic fatigue in multiple sclerosis: a randomized controlled trial* The Netherlands RCT PEDro=7 $N_{Initial}$=48, N_{Final}=44	**Population:** *Multidisciplinary outpatient rehabilitation (MDR) group (n=23):* Mean age=45yr; Gender: males=9, females=14; Disease course: RRMS=16, PPMS=2, SPMS=5; Median EDSS=3; Mean disease duration=7yr. *Nurse consultation (NC) group (n=25):* Mean age=47yr; Gender: males=8, females=17; Disease course: RRMS=12, PPMS=6, SPMS=7; Median EDSS=4; Mean disease duration=8yr. **Intervention:** MS patients with chronic fatigue were randomized to MDR or to MS-NC groups. Assessments were performed at baseline and after intervention. **Primary Outcome Measures:** Checklist Individual Strength (CIS-20R). **Participation Outcome Measures:** Impact on Participation and Autonomy (IPA); MS Impact Scale (MSIS-29). **Other Outcome Measures:** Functional Independence Measure (FIM); Modified Fatigue Impact Scale (MFIS); Fatigue Severity Scale (FSS); Disability and Impact Profile (DIP).	1. At 12–24wks, the IPA problem experience subscale 'mobility' (p=0.03) showed a significant difference in favour of the MDR group, but there were no significant between-group differences for the other IPA subscales. 2. No significant between-group differences were found for the MSIS-29. 3. No significant within-group effects were found for multidisciplinary rehabilitation or nurse consultation with respect to the primary and secondary outcome measures from baseline to 12 or 24wks.

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Participation Results**
Khan et al. 2008 *Effectiveness of rehabilitation intervention in persons with multiple sclerosis: a randomised controlled trial* Australia RCT PEDro=8 $N_{Initial}$=101, N_{Final}=98	**Population:** *Treatment Group (n=49)*: Mean age=49.5yr; Gender: males=18, females=31; Disease course: RRMS=13, PPMS=7, SPMS=29; EDSS: 0-3=7, 3.5-6.0=27, 6.5+=15; Mean disease duration=10.69yr. *Control Group (n=52)*: Mean age=51.1yr; Gender: males=11, females=41; Disease course: RRMS=18, PPMS=7, SPMS=27; EDSS: 0-3=12, 3.5-6.0=32, 6.5+=8; Mean disease duration=9.73yr. **Intervention:** The treatment group underwent multidisciplinary rehabilitation and received either individualized patient (IP) or outpatient (OP) rehabilitation. IP rehabilitation: 3-6wks, 3 or more times/wk, 3h therapy/d, 2 blocks of 45min physiotherapy and occupational therapy with other blocks comprised of speech pathology, neuropsychology and social work. OP rehabilitation: Up to 6wks, 2-3times/wk, 30min sessions for physiotherapy, occupational therapy, social work and speech pathology in addition to doing stretching home exercises. The control group received no intervention, only an 8 weekly monitoring phone call for information about medical hospital visits in the previous month and received no other information. **Primary Outcome Measures:** Functional Independence Measure (FIM) motor subscale. **Participation Outcome Measures:** Multiple Sclerosis Impact Scale (MSIS-29). **Other Outcome Measures:** General Health Questionnaire (GHQ-28).	1. There were no differences between the treatment and control group scores on the MSIS-29.
Kos et al. 2007 *Multidisciplinary fatigue management programme in multiple sclerosis: a randomized clinical trial* Belgium RCT PEDro=6 $N_{Initial}$=51, N_{Final}=40	**Population:** *Group A (n=28):* Mean age=42.9yr; Gender: males=8, females=20; Disease course: RRMS=20, PPMS=2, CPMS=2; Disease severity: unspecified; Mean disease duration=6.1yr. *Group B (n=23):* Mean age=44.5yr; Gender: males=8, females=15; Disease course: RRMS=14, PPMS=3, CPMS=4; Disease severity: unspecified; Mean disease duration=8.2yr. **Intervention:** MS patients were randomly allocated to group A, who only received the 4wk multidisciplinary fatigue management programme (MFMP), or group B receiving a placebo intervention programme first and the MFMP after 6mo. In both groups, assessment was performed at baseline, 3wks and 6mo after the programmes.	1. No significant impact of treatment on IPA was reported.

Author Year Title Country Research Design PEDro Sample Size	Methods	Participation Results
	Primary Outcome Measures: Modified Fatigue Impact Scale (MFIS). **Participation Outcome Measures:** Impact on Participation and Autonomy (IPA). **Other Outcome Measures:** Fatigue Severity Scale (FSS); Multiple Sclerosis Self-Efficacy Scale (MSSE); Mental Health Inventory (MHI).	
Craig et al. 2003 *A randomised controlled trial comparing rehabilitation against standard therapy in multiple sclerosis patients receiving intravenous steroid treatment* UK RCT PEDro=5 $N_{Initial}$=41, N_{Final}=40	**Population:** *Control group (n=20)*: Mean age=42yr; Gender: males=4, females=16; Disease course: active relapsing; Mean EDSS=5.1; Mean disease duration=5.69yr. *Intervention group (n=20)*: Mean age=38yr; Gender: males=9, females=11, Disease course: active relapsing; Mean EDSS=5.4; Mean disease duration=7.42yr. **Intervention:** All MS participants were randomized to either the control group and received standard ward routine care and 3d of intravenous methylprednisolone (IVMP), or to the intervention group and received planned coordinated multidisciplinary team treatment and 3d of IVMP. Participants were assessed at baseline upon receiving IVMP treatment, at 1mo and at 3mo after the first day of IVMP. **Primary Outcome Measures:** Guy's Neurological Disability Scale (GNDS); Amended Motor Club Assessment (AMCA). **Participation Outcome Measures:** Human Activity Profile (HAP). **Other Outcome Measures:** Barthel Index (BI); 36-Item Short Form Health Survey (SF-36).	1. The difference in the mean scores from baseline to 3mo between treatment and control groups was significant for the HAP (both maximum scores and adjusted score; p=0.004, p=.019).
Freeman et al. 1997 *The impact of inpatient rehabilitation on progressive multiple sclerosis* UK RCT PEDro=5 $N_{Initial}$=70, N_{Final}=66	**Population:** *Rehabilitation group (n=32)*: Mean age=43.2yr; Gender: males=11, females=21; Disease course: PPMS=2, SPMS=30; Median EDSS=6.5; Mean disease duration=9.6yr. *Waitlist group (n=34)*: Mean age=44.6yr; Gender: males=13, females=21; Disease course: PPMS=4, SPMS=30; Median EDSS=6.5; Mean disease duration=11.4yr. **Intervention:** Patients were randomized to either the rehabilitation or the waitlist groups. The rehabilitation program consisted of a multidisciplinary team approach, interventions tailored to meet the individual's needs and a patient centered functional goal setting approach. The waitlist group continued with their normal routine. Interventions were 6wks. Patients were tested at baseline and at 6wks. **Primary Outcome Measures:** Not specified.	1. The rehabilitation group had significantly greater improvements compared to the waitlist group in overall level of handicap (p<0.01).

Author Year Title Country Research Design PEDro Sample Size	Methods	Participation Results
	Participation Outcome Measures: London Handicap Scale (LHS). **Other Outcome Measures:** EDSS; Functional Independence Measure (FIM).	
Lexell et al. 2014 *Self-perceived performance and satisfaction with performance of daily activities in persons with multiple sclerosis following interdisciplinary rehabilitation* Pre-Post Sweden $N_{Initial}$=43, N_{Final}=43	**Population:** Mean age=51yr; Gender: males=16, females=27; Disease course: RRMS=16.3%, PPMS=9.3%, SPMS=74.4%, PRMS=unspecified; Mean EDSS=6.5; Mean disease duration=16.5yr. **Intervention:** Participants took part in an individualized, goal-oriented, and interdisciplinary rehabilitation program. **Primary Outcome Measures:** Canadian Occupational Performance Measure (COPM). **Participation Outcome Measures:** COPM. **Other Outcome Measures:** None.	1. At admission, participants reported a variety of problems with daily activities on the COPM subgroups of self-care, productivity, and leisure. 2. At discharge, performance on those activities increased significantly in 42% of the participants (significance is inferred at a 2 or more point increase in score). 3. At discharge, satisfaction with performing those activities increased by 2 or more score points in 56% of the participants.
Freeman et al. 1999 *Inpatient rehabilitation in multiple sclerosis: Do the benefits carry over into the community?* UK Pre-Post $N_{Initial}$=50, N_{Final}=44	**Population:** Mean age=44.8yr; Gender: males=21, females=29; Disease course: PPMS=7, SPMS=42; Mean EDSS=6.7; Mean disease duration=11.6yr. **Intervention:** Patients with progressive MS undergoing inpatient rehabilitation were followed for 12mo after discharge. Assessments were undertaken on admission (A), at discharge, and subsequently at 3mo intervals for 1yr (1Y). **Primary Outcome Measures:** Functional Independence Measure (FIM); London Handicap Scale (LHS). **Participation Outcome Measures:** LHS. **Other Outcome Measures:** EDSS; Kurtzke's Functional Systems; 36-item Short Form Health Survey Questionnaire (SF-36); 28-item General Health Questionnaire (GHQ).	1. Improvement was seen across all measures during the inpatient stay. These gains declined in varying patterns after discharge. 2. The LHS scores steadily lowered, remaining only marginally above baseline at the 9 and 12mo assessments. 3. No tests of statistical significance were reported in this study.
Kidd et al. 1995 *The benefit of inpatient neurorehabilitation in multiple sclerosis* UK Pre-Post $N_{Initial}$=79, N_{Final}=79	**Population:** Mean age=48.8yr; Gender: males=30, females=49; Disease course: RRMS, SPMS, PPMS; Median DSS=7.0; Mean disease duration=12.1yr. **Intervention:** MS patients admitted over a 16mo period for multidisciplinary rehabilitation were studied using assessment scales as measures of disability and handicap. **Primary Outcome Measures:** Not specified. **Participation Outcome Measures:** Environmental Status Scale (ESS).	1. The ESS was scored in 52 patients. It improved in 23 patients (44%), worsened in 13 (25%) and was unchanged in 16 (31%). The median ESS was 19.0 on admission and on discharge although overall the degree of change was significant (p=0.05). 2. Improvement was greatest in those in whom a reduction in impairment occurred, and was less marked in stable and progressive patients. The difference in terms of changes in ESS between

Author Year Title Country Research Design PEDro Sample Size	Methods	Participation Results
	Other Outcome Measures: Kurtzke's Disability Status Scale; Barthel Index (BI).	patients in whom a reduction in impairment occurred, and progressive and stable patients, was statistically significant (p=0.01).

Table 4. Summary of Participation Outcomes within RCTs Examining Team-Based Rehabilitation for Multiple Sclerosis

Author, Year	Outcome Measure(s)	Results	Quality of RCT
Papeix et al. 2015	MSIS-29	Not Significant	Fair
Rietberg et al. 2014	IPA, MSIS-29	Not Significant	Good
Khan et al. 2008	MSIS-29	Not Significant	Good
Kos et al. 2007	IPA	Not Significant	Good
Craig et al. 2003	HAP	Positive	Fair
Freeman et al. 1997	LHS	Positive	Fair

Positive indicates a statistically significant finding; *Not Significant* indicates a non-statistically significant finding
HAP: Human Activity Profile; IPA: Impact on Participation and Autonomy; LHS: London Handicap Scale; MSIS-29: Multiple Sclerosis Impact Scale; RCT: Randomized Controlled Trial

Discussion

Six relatively short-duration RCTs (<15 weeks) were found which reported on outcomes related to participation, of which four included follow-up evaluations (≤1 year) (Khan et al., 2008; Kos, Duportail, D'Hooghe, Nagels, & Kerckhofs, 2007; Papeix et al., 2015; Rietberg et al., 2014). Three RCTs included the MSIS-29 as a participation outcome measure, two used the IPA, and the HAP and LHS were each used once by two separate RCTs. All outcome measures included some aspect of self-reported participation in life situations, yet it remains unclear which outcomes are most sensitive and specific for which life situations (i.e., vocational, social, or other roles). Studies included a wide variety of team-based rehabilitation interventions.

At the time of MS relapse, Craig et al. (2003) compared coordinated multidisciplinary inpatient treatment versus standard inpatient ward care. Both groups also received three days of intravenous methylprednisolone (IVMP). The multidisciplinary treatment group improved significantly more on the HAP at the planned three-month follow-up, although effect sizes were not reported. The multidisciplinary intervention group received more physical therapy (PT) time (mean 2.62 hr for intervention vs. 0.26 hr for control group) and occupational therapy (OT) time (mean 1.49 hr vs. 0.075 hr). A larger proportion of participants in the intervention arm also accessed additional service providers as compared to the control group: speech therapy (15% vs. 0%, respectively); nurse specialists (100% vs. 45%) and orthoptist (15% vs. 0%). Finally, a greater proportion of people in the multidisciplinary intervention group were referred for follow-up outpatient PT (65% vs. 15%, respectively) and OT (50% vs. 10%, respectively). Mean length of inpatient stay was short for both groups and shorter for the multidisciplinary intervention group (mean 3.45 days vs. mean 4.8 days with standard care). The inpatient short-stay setting for relapses warranting steroid treatment may be less applicable to clinical practice today. Outpatient high-dose oral steroids have become standard care in many centres. However, multidisciplinary services may still be made available through outpatient settings. It would appear that the intensity and follow-up with a variety of services may be relevant to participation outcomes.

Freeman et al. (1997) found a significant improvement in participation as measured by the LHS following multidisciplinary inpatient rehabilitation compared to a waitlist control group (effect size 0.23 in the treatment group and -0.27 in the control group). This study was remarkable in that it included only people with progressive MS and improvement on the LHS as well as the FIM occurred even though there was no change in neurological status as measured by the EDSS. Treatment duration averaged 20 days (SD 3; range 17-31) and included medical, nursing and on average, twice daily 45-minute PT sessions and a single OT session. Eighty-five percent of patients were assessed by neuropsychology, 64% by speech and language therapy, and 48% by social work. Consultation was also available as needed from psychiatric, urological, and dietetic services. It is noteworthy that Freeman et al. (1999) also later conducted a single-group study examining participation outcomes on the LHS for up to one year after discharge from inpatient multidisciplinary rehabilitation. In this single-group study, the gains in LHS scores tended to be maintained for 6 months after discharge, declining at the 9- and final 12-month follow-up. The authors suggest a 6-month patient review to help address the decline in scores after six months. However, they noted that flexibility and responsiveness to individual needs is necessary as individual data showed that the pattern of performance and duration of carry-over differed for each individual. In clinical practice, review by a multidisciplinary team able to meet the individual needs of PwMS is recommended at least annually, however it is unclear when repeat admission for intensive team-based rehabilitation may be indicated.

In contrast to the Freeman et al. (1997) study above, Khan et al. (2008) found no differences on participation outcomes which were evaluated as secondary outcomes using the MSIS-29 and the GHQ-28. Khan et al. (2008) compared team-based rehabilitation care to a waitlist control group. The intervention group received three to six weeks of multidisciplinary rehabilitation. Despite no significant between-group differences at the planned 12-month follow-up on the MSIS-29 or the GHQ-28, the FIM was maintained or improved to a greater extent in the intervention group. Khan and colleagues (2008) suggested that participation outcomes in particular may be subject to a response shift whereby individuals reset their expectations regarding perceived participation. In clinical practice, PwMS may share different levels of satisfaction with changing vocational and social participation roles over time. Outcome measures which assess perceived satisfaction with participation may not reliably capture actual time- or role-based changes. The authors also proposed that the longer 12-month follow-up may have missed earlier positive impacts on participation. Finally, they proposed that community re-integration factors (which may serve as barriers for participation) may not have been adequately addressed.

Papeix at al. (2015) aimed to compare differing approaches for team-based rehabilitation utilizing the MSIS-29 as the primary outcome. While the authors considered the MSIS-29 a QoL outcome, the measure also includes self-reported leisure and vocational participation. The integrated multidisciplinary treatment group received a half-day of individually-tailored comprehensive assessments integrated within the MS clinic visit. In this treatment group, participants saw various medical specialists and allied health professionals based on their individual needs. Standard care involved referral to different specialists and allied health professionals on different days and in different locations. Median MSIS-29 scores at the planned primary six-month follow-up were not significantly different between groups after adjusting for the Hospital and Anxiety Depression Scale (HADS) scores within the multivariate analysis. The results suggest that multidisciplinary approaches may be delivered in an integrated fashion at a single visit or in a successive format (at later times and different sites). PwMS may become fatigued at clinical appointments. It may not always be feasible or necessary to address barriers impacting participation at one visit, provided that appropriate services are later made accessible. The study by Papeix et al. (2015) also noted that lower mood, as measured by the HADS, impacted participation, suggesting that mood symptoms may be important to address in order to maximize participation.

Kos et al. (2007) found no significant between-group differences comparing a 4-week multidisciplinary fatigue management programme to a control group who received only general education about MS. Participation was a secondary outcome measured at three and six weeks by the IPA scale. This scale has a larger focus on family, work, and educational roles. Both groups received four weekly sessions of two hours each, but the treatment group received a focus on energy saving strategies involving medical treatments, psychosocial support, and physiotherapeutic approaches. The authors noted that implementation of fatigue management strategies after the intervention was poor. However, it is noteworthy that both groups improved on the primary outcome of fatigue as measured by the Modified Fatigue Impact Scale. The authors suggested that future research should examine individually-tailored programs rather than group-based sessions to allow more concrete and individualized action plans. This study also demonstrates that fatigue levels may change (in this case improve) even when no measured improvement in participation is appreciated. It is possible that PwMS may restrict participation in order to conserve energy and experience less fatigue.

Rietberg et al. (2014) found that multidisciplinary outpatient rehabilitation had no significant effect on the total IPA score or the MSIS-29 compared to an MS-nurse consultation group. The multidisciplinary group included an individually-tailored program focusing on optimizing self-management behaviours related to physical fitness, fatigue, and energy conservation including PT, OT, and/or social work. The authors noted the multidisciplinary group received much of the same information as those randomized to the MS nurse consultation group, perhaps explaining the lack of between-group differences. Unlike the Kos et al. (2007) study, however, there was no improvement in either group compared to their baseline in the primary fatigue outcomes as well as the secondary IPA and MSIS-29 participation outcomes. The authors proposed that the lack of a within-group change over time may be due to the fact that the small study sample included only people with known chronic fatigue who were ambulatory. They argued for finding a different approach to minimize the impact of fatigue in people with chronic fatigue and mild physical disability, although they did not suggest a particular approach. Interestingly, the IPA mobility participation experience sub-score and the Disability and Impact (DIP) symptom sub-score were statistically significant in favour of the multidisciplinary group. The authors noted that the latter may be spurious findings. However, given the positive effects rehabilitation may have on mobility-related outcomes as seen in other studies, it is possible that improved mobility could influence aspects of participation.

In summary, there is conflicting evidence from six RCTs and from other study designs concerning participation outcomes after team-based rehabilitation interventions. A significant limitation is that participation was not identified as a primary outcome in the majority of studies. Secondly, among the participation outcome measures chosen, often only select aspects of participation roles are evaluated together with the impact of other MS symptoms. Participation, while related to MS symptoms, may also change independent of symptom severity. A complex relationship likely exists, particularly between fatigue, mood, and participation. The actual time spent participating in vocational, volunteer, social, leisure, or other roles was not clearly reported in the studies. Future research should aim to include both objective time-based participation outcomes as well as self-reported satisfaction with participation since expectations may change over the course of the disease. Future interventions could also explore the role of additional team members with potential for enhancing participation such as recreational therapists, vocational therapists, counsellors, and peer supports. Individualized and goal-orientated approaches have been recommended to meet the needs of PwMS. Lexell et al. (2014) recommend an individualized approach in particular for maximizing meaningful participation outcomes to PwMS. However, no studies reporting on participation outcomes compared individualized and group-based approaches directly. Finally, the assessment of participation should occur after there is opportunity for reintegration into the community since participation is defined by involvement in life situations and social roles.

Conclusion

There is conflicting evidence (from six randomized controlled trials; Papeix et al. 2015; Rietberg et al. 2014; Khan et al. 2008; Kos et al. 2007; Craig et al. 2003; Freeman et al. 1997) regarding whether or not team-based rehabilitation approaches improve participation outcomes in persons with MS.

Team-based rehabilitation may result in improved participation outcomes in persons with MS; however, the evidence is conflicting. More standardized approaches for including and measuring participation outcomes are needed.

2.3 Quality of Life

The World Health Organization defines QoL as follows:

> […] (A)n individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment.[2]

The term 'health-related' is sometimes added to denote a subset of QoL. Outcome measures used to assess QoL outcomes within studies examining team-based rehabilitation for PwMS include the following:

- The 36-Item Short Form Health Survey [SF-36; (Ware & Sherbourne, 1992)] is a generic self-report measure of perceived health.
- The Multiple Sclerosis Quality of Life-54 [MSQoL-54; (Vickrey, Hays, Harooni, Myers, & Ellison, 1995)] is a self-report measure that includes the generic SF-36 as well as 18 MS-specific items.
- The Functional Assessment in Multiple Sclerosis [FAMS; (Cella et al., 1996)] is a 59-item self-report measure of QoL. Only 44 items contribute to the score. Six domains are included: mobility, symptoms, emotional well-being, general contentment, thinking/fatigue, and family/social well-being.
- The Disability and Impact Profile [DIP; (Lankhorst et al., 1996)] is intended to measure disability and impact of mobility, self-care, social activities, communication, and psychological status. It

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[2] WHOQOL: Measuring Quality of Life

includes three symptom items and 36 disability items and each disability item is followed by a question concerning its importance or impact. Items are rated on 11-point scales (0-10). For disability items, zero denotes maximal disability; ten denotes no disability. For the importance/impact items, zero denotes ‘not important at all’; ten denotes ‘most important of all.’

- The Incontinence Impact Questionnaire [IIQ7; (Uebersax, Wyman, Shumaker, McClish, & Fantl, 1995)] is a self-report measure assessing the impact of urine leakage upon engagement in household chores, physical activity, entertainment activities, travel, and social activities, as well as on emotional health and frustration.
- The American Urological Association Symptom Index & Quality of Life Questionnaire [AUA QoL; (Barry et al., 1992)] is a self-report measure of frequency of bladder symptoms in the previous month. In addition, there is a single item concerning QoL if the urinary condition did not change for the rest of life.
- The General Health Questionnaire [GHQ-28; (Goldberg & Hillier, 1979)] is a self-report screen for psychiatric disorders (i.e., somatic symptoms, anxiety and insomnia, social dysfunction, severe depression).
- The Nottingham Health Profile [NHP-1; (Hunt et al., 1980)] is intended to measure subjective health status in the physical, social, and emotional domains. It is a self-report measure containing three to nine statements concerning emotional reactions, pain, mobility, social isolation, sleep, and energy level. Respondents answer ‘yes’ or ‘no’ to indicate whether each statement applies to them in general.
- The Life Appreciation and Satisfaction Questionnaire [LASQ; (Ravnborg, Storr, & Sorensen, 2001)] is purported to assess perspectives of being; however, we were not able to obtain any further information about this measure.

Table 5. Studies Examining the Effect of Team-Based Rehabilitation on Quality of Life Outcomes in Multiple Sclerosis

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Quality of Life Results**
Nedeljkovic et al. 2016 *Multidisciplinary rehabilitation and steroids in the management of multiple sclerosis relapses: a randomized controlled trial* Serbia RCT PEDro=5 $N_{Initial}$=49, N_{Final}=37	**Population:** *Intervention Group (IG; n=17):* Mean age=41.3yr; Gender: males=6, females=11; Disease course: RRMS; Mean EDSS=4.5; Mean disease duration=104.5mo. *Control Group (CG; n=20):* Mean age=39.4yr; Gender: males=5, females=15; Disease course=RRMS; Mean EDSS=4.0; Mean disease duration=80.6mo. **Intervention:** Subjects were randomized to a multidisciplinary inpatient rehabilitation program (IG) or standard care (CG) after receiving intravenous methylprednisolone (1g/d, 5d). Rehabilitation was comprised of physiotherapy (1h/d, 5d/wk) and occupational therapy (30min/d, 3d/wk) for a total of 3wks. Outcomes were assessed at baseline, 1mo, and 3mo. **Primary Outcome Measures:** Not specified.	1. On the MSQoL-54 at 1mo, the intervention group showed significantly greater improvement on the ‘physical role limitations’ subscale than the control group (p=0.015). 2. On the MSQoL-54 at 3mo, the intervention group showed significantly greater improvement on the ‘physical role limitations’ (p=0.016), ‘emotional role limitations’ (p=0.010), and ‘mental health composite’ (p=0.017) subscales than the control group.

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Quality of Life Results**
	Quality of Life Outcome Measures: Multiple Sclerosis Quality of Life-54 (MSQoL-54). **Other Outcome Measures:** Functional Independence Measure (FIM); EDSS; Beck Depression Inventory (BDI).	
Rietberg et al. 2014 *Effects of multidisciplinary rehabilitation on chronic fatigue in multiple sclerosis: a randomized controlled trial* The Netherlands RCT PEDro=7 $N_{Initial}$=48, N_{Final}=44	**Population:** *Multidisciplinary outpatient rehabilitation (MDR) group (n=23):* Mean age=45yr; Gender: males=9, females=14; Disease course: RRMS=16, PPMS=2, SPMS=5; Median EDSS=3; Mean disease duration=7yr. *Nurse consultation (NC) group (n=25):* Mean age=47yr; Gender: males=8, females=17; Disease course: RRMS=12, PPMS=6, SPMS=7; Median EDSS=4; Mean disease duration=8yr. **Intervention:** MS patients with chronic fatigue were randomized to MDR or to MS-NC groups. Assessments were performed at baseline and after intervention. **Primary Outcome Measures:** Checklist Individual Strength (CIS-20R). **Quality of Life Outcome Measures:** Disability and Impact Profile (DIP). **Other Outcome Measures:** Functional Independence Measure (FIM); MS Impact Scale (MSIS-29); Impact on Participation and Autonomy (IPA); Modified Fatigue Impact Scale (MFIS); Fatigue Severity Scale (FSS).	1. At 12–24wks, the DIP subscale “symptoms” showed a significant difference in favour of the MDR group (p=0.03). 2. No significant within-group effects were found for multidisciplinary rehabilitation or nurse consultation with respect to the primary and secondary outcome measures from baseline to 12 or 24wks.
Salhofer-Polanyi et al. 2013 *Benefits of inpatient multidisciplinary rehabilitation in multiple sclerosis* Austria RCT PEDro=5 $N_{Initial}$=21, N_{Final}=19	**Population:** *Intervention Group (n=10):* Mean age=53.8yr; Gender: males=5, females=5; Disease course: RRMS=2, PPMS=2, SPMS=6; Median EDSS=6; Mean disease duration=17.6yr. *Control Group (n=9):* Mean age=52.9yr; Gender: males=3, females=6; Disease course: RRMS=2, SPMS=7; Median EDSS=5.5; Mean disease duration=15.9yr. **Intervention:** Subjects were randomized to a multidisciplinary inpatient rehabilitation program (intervention) or a waiting list (control). Rehabilitation was provided 5d/wk with 4-5 sessions/d, for a total of 3wks. Outcomes were assessed at baseline and after 15wks. **Primary Outcome Measures:** Timed 50m Walk (T50MW); 2-min Walk Test (2MW); 6-min Walk Test (6MW); Walking Speed. **Quality of Life Outcome Measures:** Functional Assessment in Multiple Sclerosis (FAMS). **Other Outcome Measures:** EDSS; Rivermead Mobility Index (RMI); Berg Balance Scale (BBS); Tinetti Test (TT); MS Functional	1. There was no significant difference between the intervention group and the control group in mean improvement on the FAMS (+7.5 vs. +3.5, p=0.372) after treatment.

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Quality of Life Results**
	Composite: 9 Hole Peg Test (9HPT), Timed 25ft Walk (T25FW), Paced Auditory Serial Addition Test (PASAT); MS Self-Efficacy Scale (MSSE); Global Clinical Impression Scale (GCIS).	
Khan et al. 2010 *A randomised controlled trial: outcomes of bladder rehabilitation in persons with multiple sclerosis* Australia RCT PEDro=9 $N_{Initial}$=74, N_{Final}=58	**Population:** *Treatment group (n=24):* Mean age=49.9yr; Gender: males=9, females=15; Disease course: RRMS=6; PPMS=4; SPMS=14; EDSS: 0-3=5, 3.5-6.0=9, 6.5 or greater=10; Mean disease duration=12.2yr. *Control group (n=34):* Mean age=51.1yr; Gender: males=5, females=29; Disease course: RRMS=14, PPMS=4, SPMS=16; EDSS: 0-3=9, 3.5-6.0=21, 6.5 or greater=4; Mean disease duration=10.0yr. **Intervention:** Patients were randomized to either the intervention group where they received a multifaceted, individualized, bladder rehabilitation programme, or to the control group (no intervention). Ten participants randomized to control group required some treatment during the study. **Primary Outcome Measures:** Urogenital distress inventory (UDI6); Incontinence impact questionnaire (IIQ7). **Quality of Life Outcome Measures:** Incontinence impact questionnaire (IIQ7); AUA Symptom Index. **Other Outcome Measures:** Guy's Neurological Disability Scale (GNDS – bladder subscale only).	1. In comparison to the control group, the treatment group showed statistically significant within-group differences in IIQ7 (p<0.001) change scores before-and-after treatment. The effect size was large (0.5 or greater), as per Cohen's criteria. 2. In the control group, a larger proportion of patients deteriorated compared to the treatment group as measured by the IIQ7 ($\varkappa^2$=14.47, df=2, p=0.001) scores. 3. There were statistically significant differences in change scores between the treatment and control groups with respect to the AUA total and AUA Quality of Life scores (all p<0.001). The effect sizes of these differences in change scores were large (0.5 or greater), as per Cohen's criteria. 4. In the treatment group, within-group differences in AUA total scores from baseline to post-treatment were statistically significant (p=0.03); this was indicated by higher symptom levels at baseline compared to post-treatment.
Khan et al. 2008 *Effectiveness of rehabilitation intervention in persons with multiple sclerosis: a randomised controlled trial* Australia RCT PEDro=8 $N_{Initial}$=101, N_{Final}=98	**Population:** *Treatment Group (n=49)*: Mean age=49.5yr; Gender: males=18, females=31; Disease course: RRMS=13, PPMS=7, SPMS=29; EDSS: 0-3=7, 3.5-6.0=27, 6.5+=15; Mean disease duration=10.69yr. *Control Group (n=52)*: Mean age=51.1yr; Gender: males=11, females=41; Disease course: RRMS=18, PPMS=7, SPMS=27; EDSS: 0-3=12, 3.5-6.0=32, 6.5+=8; Mean disease duration=9.73yr. **Intervention:** The treatment group underwent multidisciplinary rehabilitation and received either individualized patient (IP) or outpatient (OP) rehabilitation. IP rehabilitation: 3-6wks, 3 or more times/wk, 3h therapy/d, 2 blocks of 45min physiotherapy and occupational therapy with other blocks comprised of speech pathology, neuropsychology and social work. OP rehabilitation: Up to 6wks, 2-3times/wk,	1. There were no differences between the treatment and control group scores on the GHQ-28.

Author Year Title Country Research Design PEDro Sample Size	Methods	Quality of Life Results
	30min sessions for physiotherapy, occupational therapy, social work and speech pathology in addition to doing stretching home exercises. The control group received no intervention, only an 8 weekly monitoring phone call for information about medical hospital visits in the previous month and received no other information. **Primary Outcome Measures:** Functional Independence Measure (FIM) motor subscale. **Quality of Life Outcome Measures:** General Health Questionnaire (GHQ-28). **Other Outcome Measures:** Multiple Sclerosis Impact Scale (MSIS-29).	
Storr et al. 2006 *The efficacy of multidisciplinary rehabilitation in stable multiple sclerosis patients* Denmark RCT PEDro=8 $N_{Initial}$=106, N_{Final}=90	**Population:** *Control group (n=52)*: Mean age=50.1yr; Gender: males=16, females=36; Disease course: RRMS=12 (23%), PPMS=11 (21%), SPMS=29 (56%); Median EDSS=6.5; Median disease duration=9.0yr. *Intervention group (n=38)*: Mean age=53.0yr; Gender: males=16, females=22, Disease course: RRMS=5 (13%), PPMS=9 (24%), SPMS=24 (63%); Median EDSS=6.5; Median disease duration=9.0yr. **Intervention:** Individuals were randomized either to the control group and received no rehabilitation treatment, or to the intervention group and received rehabilitation treatment from the MS rehabilitation hospital in Haslev Denmark. **Primary Outcome Measures:** Functional Assessment in Multiple Sclerosis (FAMS). **Quality of Life Outcome Measures:** FAMS; Life Appreciation and Satisfaction Questionnaire (LASQ). **Other Outcome Measures:** Guy's Neurological Disability Scale (GNDS); Multiple Sclerosis Impairment Scale (MSIS); EDSS; Visual Analog Scale for symptoms (VAS); 10 meter walk test (TW10); Nine-Hole Peg Test (9HPT).	1. No significant difference was found between the control and the intervention groups on any of the outcome measures.
Craig et al. 2003 *A randomised controlled trial comparing rehabilitation against standard therapy in multiple sclerosis patients*	**Population:** *Control group (n=20)*: Mean age=42yr; Gender: males=4, females=16; Disease course: active relapsing; Mean EDSS=5.1; Mean disease duration=5.69yr. *Intervention group (n=20)*: Mean age=38yr; Gender: males=9, females=11, Disease course: active relapsing; Mean EDSS=5.4; Mean disease duration=7.42yr. **Intervention:** All MS participants were randomized to either the control group and	1. Changes in SF-36 scores did not differ between groups from baseline to 3mo.

Author Year Title Country Research Design PEDro Sample Size	Methods	Quality of Life Results
receiving intravenous steroid treatment UK RCT PEDro=5 $N_{Initial}$=41, N_{Final}=40	received standard ward routine care and 3d of intravenous methylprednisolone (IVMP), or to the intervention group and received planned coordinated multidisciplinary team treatment and 3d of IVMP. Participants were assessed at baseline upon receiving IVMP treatment, at 1mo and at 3mo after the first day of IVMP. **Primary Outcome Measures:** Guy's Neurological Disability Scale (GNDS); Amended Motor Club Assessment (AMCA). **Quality of Life Outcome Measures:** 36-Item Short Form Health Survey (SF-36). **Other Outcome Measures:** Barthel Index (BI); Human Activity Profile (HAP).	
Patti et al. 2002 *The impact of outpatient rehabilitation on quality of life in multiple sclerosis* Italy RCT PEDro=8 $N_{Initial}$=111, N_{Final}=111	**Population:** *Outpatient rehabilitation (n=58)*: Mean age=45.2yr; Gender: males=24, females=34; Disease course: PPMS or SPMS; Mean EDSS=6.2; Mean disease duration=17.2yr. *Home exercise (n=53)*: Mean age=46.1yr; Gender: males=23, females=30; Disease course: PPMS or SPMS; Mean EDSS=6.1; Mean disease duration=17.2yr. **Intervention:** Patients were randomized to a comprehensive rehabilitation program and a home exercise group. The patients in the comprehensive rehabilitation group received an individualized, goal-oriented program involving an interdisciplinary team, addressing a wide range of areas for 6wks (6x/wk) and a home exercise program for a further 6wks. The home exercise group received the home exercise program for 12wks. Both groups were assessed at baseline and at 12wks. **Primary Outcome Measures:** 36-Item Short Form Health Survey (SF-36); EDSS. **Quality of Life Outcome Measures:** SF-36. **Other Outcome Measures:** Fatigue Impact Scale (FIS); Social Experience Tempelaar Checklist (SET); Beck Depression Inventory (BDI).	1. All health related quality of life domains of the SF-36 improved significantly in the rehabilitation group ($p<0.001$ in physical functioning, role physical, bodily pain, general health, social functioning; $p<0.05$ in vitality, role emotional, mental health).
Pozzilli et al. 2002 *Home based management in multiple sclerosis: results of a randomised controlled trial*	**Population:** *Intervention group (n=133):* Mean age=47yr; Gender: males=47, females=86; Disease course: RRMS=26, PPMS=27, SPMS=80; Mean EDSS=6.0; Mean disease duration=18.4yr. *Control group (n=68):* Mean age=46.7yr; Gender: males=21, females=47; Disease course: RRMS=14, PPMS=14, SPMS=40; Mean EDSS=6.0; Mean disease duration=18.6yr.	1. The intervention group had a significant improvement in bodily pain ($p=0.0001$), general health ($p=0.0001$), social functioning ($p=0.001$), and role, emotional ($p=0.0001$) compared to the control group. 2. The intervention group showed more favourable changes than the control group in terms of both physical

Author Year Title Country Research Design PEDro Sample Size	Methods	Quality of Life Results
Italy RCT PEDro=5 $N_{Initial}$=201, N_{Final}=188	**Intervention:** MS patients were randomized to receive either individually tailored multidisciplinary home-based medical care with regular phone support available 5d/wk (intervention group) or routine care involving multidisciplinary care coordinated through a hospital-based MS centre (control group). Assessments were performed at baseline and at 12mo. **Primary Outcome Measures:** Not specified. **Quality of Life Outcome Measures:** 36 item short form health survey questionnaire (SF-36). **Other Outcome Measures:** Functional Independence Measure (FIM); EDSS; Mini-Mental State Examination (MMSE); Fatigue Severity Scale (FSS); State Trait Anger Expression Inventory (STAXI); State Trait Anxiety Inventory (STAI); Clinical Depression Questionnaire (CDQ); cost resource assessment.	component score (p=0.0001) and mental component score (p=0.0001) of the SF-36. 3. The intervention group displayed an improvement in eight SF-36 scales, while the control group had increased scores on four SF-36 scales. However, the improvement was less consistent than in the intervention group.
Guagenti-Tax et al. 2000 *Impact of a comprehensive long-term care program on caregivers and persons with multiple sclerosis* US RCT PEDro=5 $N_{Initial}$=73, N_{Final}=59 (patient-caregiver units)	**Population:** *Patients (n=59)*: *Experimental*: Mean age=44.0yr; Gender: males=8 (13.3%), females=51 (86.7%); Disease course: CPMS=39 (66.7%); Mean EDSS=7.06; Mean disease duration=8.9yr. *Control*: Mean age=49.0yr; Gender: males=18 (31.0%), females=41 (69.0%); Disease course: CPMS=51 (86.2%); Mean EDSS=7.24; Mean disease duration=14.2yr. *Caregivers (n=59)*: *Experimental*: Mean age=44.9yr; Gender: males=43.3%, females=56.7%. *Control*: Mean age=51.8yr; Gender: males=48.3%, females=51.7%. **Intervention:** Patient-caregiver units were randomized to a comprehensive rehabilitation program or a standard care group. The comprehensive rehabilitation program consisted of 4 coordinated components: 1) twice-monthly medical day-care program, 2) a series of semi-annual workshops for persons with MS and family caregivers, 3) monthly home visits by social workers, nurses, and volunteers, 4) case management and liaison services. Patients and caregivers were assessed at baseline, 12 and 24mo. **Primary Outcome Measures:** Not specified.	1. A significant interaction was found on the SF-36 general health subscale, with the control patient group and their caregivers reporting significantly greater decline in perceived health compared to the rehabilitation group (p=0.039, p=0.01). 2. Control patients reported significantly greater satisfaction with getting help with their daily routine compared to the rehabilitation patients (p=0.004).

Author Year **Title** **Country** **Research Design** **PEDro** **Sample Size**	**Methods**	**Quality of Life Results**
	Quality of Life Outcome Measures: 36-Item Short Form Health Survey (SF-36). **Other Outcome Measures:** EDSS; Incapacity Status Scale (ISS); Number of acute hospital admissions; Perceived deficits questionnaire (PDQ); Hopkins Verbal Learning Test (HVLT); Mental Health Inventory (MHI); Sickness Impact Profile (SIP); Revised UCLA Loneliness-Companionship Scale; Questionnaire on Resource and Stress (QRS); Satisfaction with care; Length of stay.	
Pappalardo et al. 2016 *Inpatient versus outpatient rehabilitation for multiple sclerosis patients: Effects on disability and quality of life* Italy RCT – Pre-Post for Quality of Life analyses PEDro=6 $N_{Initial}$=146, N_{Final}=146	**Population:** *Group A outpatient (n=49):* Mean age=48.0yr; Gender: males=18, females=31; Disease course: PPMS=18, SPMS=31; Mean EDSS=6.5; Disease duration: unspecified. *Group B inpatient (n=49):* Mean age=46.0yr; Gender: males=17, females=32; Disease course: PPMS=17, SPMS=32; Mean EDSS=6.5; Disease duration: unspecified. *Group C control (n=48):* Mean age=45.0yr; Gender: males=18, females=30; Disease course: PPMS=18, SPMS=30; Mean EDSS=6.4; Disease duration: unspecified. **Intervention:** MS patients were randomized to three groups: the outpatient treatment group (Group A), the inpatient treatment group (Group B) and the control waiting list (Group C). Assessments were performed at baseline (T0) and at 6mo follow-up (T1). **Primary Outcome Measures:** Functional Independence Measure (FIM). **Quality of Life Outcome Measures:** 36-Health Survey Questionnaire (SF-36). **Other Outcome Measures:** None.	1. Significant intragroup differences in SF-36 were observed at T1 compared to T0 only in Group A. In particular, the most significant change was found in physical role functioning (p<0.0001), vitality (p<0.0001), social role functioning (p<0.0001) and mental health (p<0.0001). 2. The authors did not conduct inter-group analyses for the SF-36.
Bjerre et al. 2011 *Self-reported changes in quality of life among people with multiple sclerosis who have participated in treatments based on collaboration between conventional healthcare providers and CAM practitioners* Denmark PCT $N_{Initial}$=173, N_{Final}=142	**Population:** *Intervention group (n=142):* Mean age=51.1yr; Gender: males=46, females=96; Disease course: RRMS=47, PPMS=21, SPMS=65; Mean EDSS=5.5; Mean disease duration=16.2yr. *Comparison group (n=142):* Mean age=52.1yr; Gender: males=54, females=88; Disease course: RRMS=52, PPMS=13, SPMS=72; Mean EDSS=5.2; Mean disease duration=17.1yr. **Intervention:** MS patients were treated with combined interventions by a team of 5 healthcare practitioners and 5 complementary and alternative medicine practitioners for 18mo. A comparison group treated with conventional therapy was included as a control. Assessments were performed before and after the intervention.	1. The average change in FAMS total score was significantly different in the intervention group compared to the comparison group (p<0.01). People with MS in the intervention group experienced an increase in quality of life whereas patients in the comparison group experienced a decrease in quality of life. 2. The intervention group and the comparison group differed in terms of change scores for the following FAMS subscales, when measured over the period of 18mo: emotional well-being, thinking/fatigue. 3. No significant difference was found in terms of change scores on the other

Author Year Title Country Research Design PEDro Sample Size	Methods	Quality of Life Results
	Primary Outcome Measures: Functional Assessment of Multiple Sclerosis (FAMS). **Quality of Life Outcome Measures:** FAMS. **Other Outcome Measures:** None.	FAMS subscales: mobility, symptoms, general contentment, family/social well-being. 4. Treatment group allocation was significant in all analyses when confounding factors were accounted for (gender, age, EDSS, diagnosis).
Vikman et al. 2008 *Effects of inpatient rehabilitation in multiple sclerosis patients with moderate disability* Sweden Pre-Post $N_{Initial}=58$, $N_{Final}=58$	**Population:** *Cohort A (n=40):* Mean age=56.3yr; Gender: males=8, females=32; Disease course: RRMS=2, PPMS=15, SPMS=21, unclassified=2; Mean EDSS=5.8; Mean disease duration=20.4yr. *Cohort B (n=18):* Mean age=54.7yr; Gender: males=4, females=14; Disease course: PPMS=4, SPMS=14; Mean EDSS=5.6; Mean disease duration=17.0yr. **Intervention:** MS patients with moderate disability received 3wks of inpatient neurorehabilitation in two cohorts, A and B. Rehabilitation consisted of physiotherapy, occupational therapy, and consultation by speech therapist, social worker, and psychologist. Cohort A was assessed on admission and discharge during a rehabilitation period. Cohort B was assessed 3wks before admission, on admission and at discharge. **Primary Outcome Measures:** Not specified. **Quality of Life Outcome Measures:** 36 Item Short-Form questionnaire (SF-36); Functional Assessment of Multiple Sclerosis (FAMS). **Other Outcome Measures:** Barthel Index (BI); Fatigue Severity Scale (FSS); Beck Depression Inventory (BDI); Multiple Sclerosis Functional Composite (MSFC); Grippit; Box and Block Test (B&B); Nine Hole Peg Test (9HPT); Clinical Outcome Variables (COVS); Berg Balance Scale (BBS); Timed 25-Foot Walk Test (T25FWT).	1. Cohort A improved significantly in the SF-36 domains of general health (p<0.05), vitality (p<0.05) and mental health (p<0.05) between admission and discharge. 2. Cohort B improved significantly in the FAMS domain emotional well-being between the first assessment (3wks before admission) and the second assessment at admission (mean score 19.2 to 21.6, p<0.05), but not between admission and discharge.
Freeman et al. 1999 *Inpatient rehabilitation in multiple sclerosis: Do the benefits carry over into the community?* UK Pre-Post $N_{Initial}=50$, $N_{Final}=44$	**Population:** Mean age=44.8yr; Gender: males=21, females=29; Disease course: PPMS=7, SPMS=42; Mean EDSS=6.7; Mean disease duration=11.6yr. **Intervention:** Patients with progressive MS undergoing inpatient rehabilitation were followed for 12mo after discharge. Assessments were undertaken on admission (A), at discharge, and subsequently at 3mo intervals for 1yr (1Y). **Primary Outcome Measures:** Functional	1. Improvement was seen across all measures during the inpatient stay. These gains declined in varying patterns after discharge. 2. Improvements in emotional well-being (GHQ) were maintained, on average, for 7mo. Improvements in SF-36 physical scores were maintained for nearly 10mo and SF-36 mental scores for nearly 6mo. However, there was considerable variability.

Author Year Title Country Research Design PEDro Sample Size	Methods	Quality of Life Results
	Independence Measure (FIM); London Handicap Scale (LHS). **Quality of Life Outcome Measures:** 36-item Short Form Health Survey Questionnaire (SF-36); 28-item General Health Questionnaire (GHQ). **Other Outcome Measures:** EDSS; Kurtzke's Functional Systems.	3. No tests of statistical significance were reported in this study.
Sitzia et al. 1998 *Evaluation of a nurse-led multidisciplinary neurological rehabilitation programme using the Nottingham Health Profile* UK Pre-Post $N_{Initial}$=42, N_{Final}=33	**Population:** *MS participants (n=33):* Mean age=49.0yr; Gender: males=11, females=31; Disease course: unspecified; Disease severity: unspecified; Disease duration: unspecified. **Intervention:** MS patients received an individually adapted, multidisciplinary rehabilitation programme. The programmes lasted from 5-10d. Assessments were performed at baseline and after rehabilitation. **Primary Outcome Measures:** Nottingham Health Profile Part 1 (NHP-1). **Quality of Life Outcome Measures:** NHP-1. **Other Outcome Measures:** None.	1. The multiple sclerosis group showed a significant improvement in the dimensions 'emotional reactions' (p<0.01), 'pain' (p<0.01), and 'physical mobility' (p<0.05), and in the total NHP-1 score (p<0.01). 2. Overall improvement was not significantly associated with either gender or age.
Di Fabio et al. 1997 *Health-related quality of life for patients with progressive multiple sclerosis: influence of rehabilitation* US PCT $N_{Initial}$=44, N_{Final}=31	**Population:** *Treatment group (n=12):* Mean age=44.5yr; Gender: males=2, females=10; Disease course: PPMS or SPMS; EDSS range: 5-8; Mean disease duration=17.6yr. *Waitlist group (n=19):* Mean age=49.2yr; Gender: males=4, females=15; Disease course: PPMS or SPMS; EDSS range: 5-8; Mean disease duration=14.2yr. **Intervention:** MS patients received either outpatient care for 1yr or did not receive rehabilitation (waitlist control). **Primary Outcome Measures:** Rand 36-Item Health Survey 1.0 (SF-36). **Quality of Life Outcome Measures:** SF-36; MS Quality of Life 54 Item (MSQoL-54). **Other Outcome Measures:** Rehabilitation Institute of Chicago Functional Assessment Scale (RIC-FAS) version 2.	1. The treatment group showed improvements in 6 health status measures on the SF-36 that were not improved in the wait-listed group: physical health, bodily pain, energy/fatigue, social support, cognitive ability, and overall positive change in general health from the previous year. 2. No significant effect of treatment on the MSQoL-54 was observed in either group. 3. Health status improved for both groups in the areas of role limitations due to physical problems, general health, emotional wellness, and health distress.

Table 6. Summary of Quality of Life Outcomes within RCTs Examining Team-Based Rehabilitation for Multiple Sclerosis

Author, Year	Outcome Measure(s)	Results	Quality of RCT
Nedeljkovic et al. 2016	MSQoL-54	Mixed	Fair
Rietberg et al. 2014	DIP	Not Significant	Good

Salhofer-Polanyi et al. 2013	FAMS	Not Significant	Fair
Khan et al. 2010	AUA QoL, IIQ7	Positive	Excellent
Khan et al. 2008	GHQ-28	Not Significant	Good
Storr et al. 2006	LASQ, FAMS	Not Significant	Good
Craig et al. 2003	SF-36	Not Significant	Fair
Patti et al. 2002	SF-36	Positive	Good
Pozzilli et al. 2002	SF-36	Mixed	Fair
Guagenti-Tax et al. 2000	SF-36	Mixed	Fair

Positive indicates a statistically significant finding; *Not Significant* indicates a non-statistically significant finding
AUA QoL: American Urological Association Symptom Index & Quality of Life Questionnaire; DIP: Disability and Impact Profile; FAMS: Functional Assessment in Multiple Sclerosis; GHQ-28: General Health Questionnaire; IIQ7: Incontinence Impact Questionnaire; LASQ: Life Appreciation and Satisfaction Questionnaire; MSQoL-54: Multiple Sclerosis Quality of Life-54; RCT: Randomized Controlled Trial; SF-36: 36-Item Short Form Health Survey

Discussion

Ten RCTs examined the effectiveness of team-based rehabilitation on QoL outcome measures. While MS-specific QoL outcomes exist and have been previously validated, the majority of the RCTs utilized generic QoL measures, most commonly the SF-36. Studies included a wide variety of team-based rehabilitation interventions, delivered in a variety of settings. Similarly, control conditions varied from waitlists to active care.

Patti et al. (2002) found significant improvement in all domains of the SF-36 (i.e., physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-functioning emotional, and mental health) in patients with progressive MS following outpatient team-based rehabilitation compared to a control group. This consisted of PT, OT, speech therapy, symptom management, and others, such as music, mirror/video therapy, and group PT. Guagenti-Tax et al. (2000) studied the effects of a comprehensive care program that included group-based PT, OT, recreational therapy, group counselling with a social worker, socialization, and nursing services. Ten semi-annual workshops for PwMS and family caregivers addressed coping with social, psychological, and medical aspects of MS. The authors noted a significant interaction between group and time on the SF-36 general health subscale. No other significant differences were found between the intervention and control groups.

Craig et al. (2003) randomized participants at the time of relapse to standard ward care or coordinated multidisciplinary team inpatient treatment. The SF-36 scores did not differ between groups from baseline to three months even though improvements were observed in the activity and participation outcomes. In a similar study, Nedeljkovic et al. (2016) randomized participants to receive five days of IVMP with either standard ward care or three weeks of multidisciplinary outpatient rehabilitation. There was a significant difference between groups in change in physical role limitations score on the MSQoL-54. In addition, the intervention group showed significantly greater improvement in MSQoL-54 physical role limitations, emotional role limitations, and mental health composite scores compared to the control group from baseline to the third month. In addition to differences in samples, interventions, and other methodological aspects, the different measures (SF-36 vs. MSQoL-54) may at least partially explain differences in results between these studies.

Khan et al. (2008) assessed QoL outcomes with the GHQ-28. Participants with baseline EDSS scores between 2 and 8, and without severe cognitive impairment (Cognitive Kurtzke Functional System score range 0–2) were randomized to individualized rehabilitation treatment (inpatient or outpatient) or a control group. While FIM motor scores improved significantly, GHQ-28 scores did not improve in the primary analysis. Of note, the GHQ-28 is a measure of somatic, anxiety, and depressive symptoms as well as social dysfunction; it is not an MS-specific QoL outcome measure.

Recognizing the negative impact of bladder symptoms in MS, Khan et al. (2010) later performed an RCT sub-study evaluating a multifaceted individualized bladder rehabilitation management program in addition to usual team-based rehabilitation versus wait-list controls in people with baseline bladder symptoms or issues. The individualized bladder program resulted in large favourable effect sizes on the IIQ7. In addition, a single question from the AUA Symptom Index was referenced to further address the complex construct of QoL related to continence. The study found significantly improved change scores on this AUA QoL question.

Pozzilli et al. (2002) found significant improvements on four subscales of the SF-36 related to daily living and social routines following multidisciplinary home-based medical care versus routine hospital care over a year. Home-based care involved observation, administration of intravenous drugs, nurse care, home rehabilitation, education, psychological support, and “the services of the social secretariat” (Pozzilli et al., 2002, p.251). The authors suggested that home-based care may complement hospital care and noted that it is an appropriate model for more disabled persons still living at home.

Storr et al. (2006) and Salhofer-Polanyi et al. (2013) utilized the disease-specific FAMS QoL measure and found no beneficial effect of inpatient multidisciplinary rehabilitation interventions. However, it is of note that both studies had low recruitment and low power. The larger of the two studies also found no effect on the LASQ.

Rietberg et al. (2014) compared the effects of multidisciplinary outpatient rehabilitation to those of MS-nurse consultation on fatigue in persons with MS, finding no significant difference in their QoL measure (DIP).

Overall, study results from RCTs are inconsistent regarding QoL despite the fact that some of the same studies demonstrated improved self-care and/or participation outcomes. There was no evidence of a detrimental effect from this intervention. These findings highlight the fact that QoL is a different construct from self-care and other activity level outcomes. There is a lack of sufficiently powered studies that include validated MS health-related QoL outcome measures. A previous meta-analysis on the effects of specific clinical interventions on health-related QoL in MS suggested that QoL in MS may be improved (Kuspinar, Rodriguez, & Mayo, 2012), as moderate to large effect sizes were reported for cognitive training, exercise, and/or psychological interventions aimed to improve mood. However, the individual studies included in the Kuspinar et al. (2012) meta-analysis did not detail team-based interventions specifically. For interventions targeting QoL as a primary outcome, it is reasonable to strategically consider the involvement of exercise therapists and psychologists on the team. These roles were often not mentioned or emphasized among the team-based rehabilitation studies meeting our inclusion criteria.

QoL and even health-related QoL are broad constructs with variable definitions (Post, 2014). As noted previously in this module, team-based rehabilitation is not a singular intervention; rather, in both research and clinical practice, it is often individualised and tailored to the needs/goals of the patient. Given the breadth and variability of QoL and team-based rehabilitation, it may not be reasonable to expect unanimity in the research literature regarding the effects of team-based rehabilitation on QoL amongst those with MS. The research picture may eventually be clarified with careful attention to definitions of QoL, targeted interventions, and appropriate measures and control groups. In any case, in clinical practice, it may be helpful to work with patients to move beyond global QoL goals toward the constituent health, self-care, and participation goals.

Conclusion

There is conflicting evidence (from ten randomized controlled trials; Nedeljkovic et al. 2016; Rietberg et al. 2014; Salhofer-Polanyi et al. 2013; Khan et al. 2010; Khan et al. 2008; Storr et al. 2006; Craig et al. 2003; Patti et al. 2002; Pozzilli et al. 2002; Guagenti-Tax et al. 2000) regarding whether or not team-based rehabilitation improves quality of life in persons with MS.

It is unclear whether or not team-based rehabilitation is effective in improving quality of life in persons with MS as assessed by various outcome measures.

3.0 Summary

Overall, team-based rehabilitation may result in gains in the area of self-care activities, and short-term improvements may occur for independence with self-care even for persons with progressive disease. These improvements are noteworthy given the paucity of effective interventions for persons with progressive disease. The evidence is more conflicting for longer-term outcomes and outcomes related to participation and QoL.

Descriptions of the elements of team-based rehabilitation (i.e., setting, intensity, team composition, timing, and goal setting) are often not well detailed in the current literature. In addition, some studies that reported positive outcomes for participation or QoL outcomes involved team-based programming that may not be feasible to implement across healthcare systems. Ongoing team-based care that crosses rehabilitation settings and the community must respond to changing needs over time. Yet, PwMS may be challenged to access appropriate coordinated rehabilitation services at the right time to meet their needs (O'Hara, Cadbury, De, & Ide, 2002). More research is needed to determine which team members and elements are most critical to include at which time points during the disease course. The limitations of RCT designs for the study of team-based rehabilitation in MS also warrant consideration. Different approaches to team-based rehabilitation may be better evaluated by delivering specific approaches to various MS cohorts and comparing these cohorts to a “treatment as usual” cohort (Relton, Torgerson, O'Cathain, & Nicholl, 2010). Research is also needed to evaluate the efficiency and cost effectiveness of different team-based rehabilitation approaches over the longer term. In the shorter term, based upon the findings of studies focused upon progressive MS, team-based rehabilitation approaches may be effective in improving self-care function on the FIM. In clinical practice, these improvements in self-care function may be critical for maintaining independent living or reducing the burden of care.

There is level 1a evidence (from three randomized controlled trials; Pappalardo et al. 2016; Patti et al. 2003; Freeman et al. 1997) that team-based rehabilitation is an effective intervention for improving basic self-care activities as measured by the Functional Independence Measure in progressive MS.

There is conflicting evidence (from five randomized controlled trials; Nedeljkovic et al. 2016; Rietberg et al. 2014; Craig et al. 2003; Pozzilli et al. 2002; Francabandera et al. 1988) regarding whether or not team-based rehabilitation improves basic self-care activities compared to an active control group in persons with MS.

There is conflicting evidence (from two randomized controlled trials; Nedeljkovic et al. 2016; Craig et al. 2003) regarding whether or not team-based rehabilitation improves basic self-care activities for persons with MS who have had an acute MS relapse.

There is conflicting evidence (from six randomized controlled trials; Papeix et al. 2015; Rietberg et al. 2014; Khan et al. 2008; Kos et al. 2007; Craig et al. 2003; Freeman et al. 1997) regarding whether or not team-based rehabilitation approaches improve participation outcomes in persons with MS.

There is conflicting evidence (from ten randomized controlled trials; Nedeljkovic et al. 2016; Rietberg et al. 2014; Salhofer-Polanyi et al. 2013; Khan et al. 2010; Khan et al. 2008; Storr et al. 2006; Craig et al. 2003; Patti et al. 2002; Pozzilli et al. 2002; Guagenti-Tax et al. 2000) regarding whether or not team-based rehabilitation improves quality of life in persons with MS.

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