<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Type of intervention (E = experimental, C = control)</th>
</tr>
</thead>
</table>
| Graham 2006 |      | To assess the effectiveness of three resistance-based exercise rehabilitation interventions on physical functioning. All three interventions were based on quantitative progressive exercise rehabilitation (QPER) principles and the duration on training was 12 weeks, 3 days per week for 30–60 minutes per day.  
  (E1) Supervised exercise [SE]: unilateral isotonic and endurance contractions against 10% up to 60% of the individual’s maximum voluntary isometric contraction (MVC); 12 weeks, 3 days per week for 30–60 minutes per day.  
  (E2) home exercise [HE]: adjustable ankle weights, dumbbells and theraband; 12 weeks, at home 2 times per week and supervised exercise 1 time per week, 30–60 min each session  
  (E3) functional training [FT]: body-weight exercises that are fundamental components of daily functional activities (e.g. body squats, step-ups, lunges, modified push-ups and seated triceps extensions)  
  (C) non-exercise control [MSC]: not to begin any new exercise or physical activities during 12 weeks follow-up period; 12 weeks, at home 2 times per week and supervised exercise 1 time per week, 30 min each session |
| Harvey 1999 |      | To evaluate the influence on function of two different exercise programmes compared with a programme of supportive phone calls but no exercise.  
  (E1) weighted leg exercise (specifically to strengthen the quadriceps); seated leg extension exercises with ankle weights according to their strength; 5 sets of 10 leg extensions on both legs, twice a day.  
  (E2) general mobility exercises; an individual daily programme of exercise aiming to improve patient’s physical function (stretching and general balance and mobility exercises, swimming and sessions on an exercise bike  
  (C) non-exercise control; a programme of supportive phone calls but no exercise |
| Jackson 2008 |      | To evaluate the acute effects of a brief exposure to whole-body vibration (WBV) on quadriceps and hamstrings muscle performance (isometric muscle torque)  
  (E1) high frequency; 26 Hz WBV (6-mm amplitude, 30 seconds)  
  (E2) low frequency; 2 Hz WBV (6-mm amplitude, 30 seconds) |
| Romberg 2004, 2005 and Surakka 2004 |      | To evaluate the effects of a progressive 6-month exercise program, the main aim was to improve muscular strength:  
  (E) 3 weeks inpatient rehabilitation program (supervised training in groups) and 23 weeks home exercise;  
  Weeks 1–3 inpatient supervised training in groups including 5 circuit type resistance exercise sessions (strength training using pressurized air resistance machines; 10 exercises with 10–15 repetitions in two sets; 50–60% of the 1 RM) and 5 aerobic exercise sessions in pool |
Weeks 4–26 exercise at home: combined resistance training 3–4 times/week (theraband) with aerobic endurance training once a week

(C) control group received no intervention

*Resistance exercises / respiratory training*

**Fry 2007**
To assess the effectiveness of home exercise inspiratory training program (E) inspiratory muscle strength training (IMT); daily for 10 weeks training with inspiratory muscle threshold trainer, 3 sets of 15 repetitions. Initial resistance 3 H2O of the IMT was set at 30% of the subjects pretest MIP. Progression: IMT pressure resistance was progressed weekly according to the subject’s baseline IMP pressure and RPE as well as subject’s symptom

(C) non-exercise control

**Gosselink 2000**
To evaluate the contribution respiratory muscle training (part 2) to pulmonary function, cough efficacy, and functional status in patients with advanced MS. (E) The training group performed three series of 15 contractions against an expiratory resistance (60% maximum expiratory pressure [PEmax]) two times a day for 3 months

(C) breathing exercises to enhance maximal inspirations routinely part of the physiotherapy treatment and breathing exercises were not supervised.

**Klefbeck 2003**
To evaluate whether inspiratory muscle training (IMT) improves inspiratory muscle strength, respiratory capacity, fatigue, and subjective perception of physical endurance in patients with advanced MS. (E) Threshold inspiratory muscle trainer; twice every other day, with 3 sets of 10 loaded inspirations (40%–60% of patients’ maximal inspiratory pressure [Pimax]) over a 10-week period. (C) no intervention, but deep-breathing exercises were a routine part of their ordinary physiotherapy.

**Mutluay 2007**
To explore the effectiveness of breathing-enhanced upper extremity exercises on the respiratory function.

(E) A six-week home training program designed to strengthen accessory respiratory muscles; a six-week home training program, once a day. All the relevant procedures involving arm, shoulder and trunk motions.

(C) no exercises.

**Smeltzer 1996**
To compare the effects of expiratory muscle training and sham training on respiratory muscle strength in patients with MS. (E) expiratory training using a threshold training device (3 months, 7 days a week, 2 sessions per day separated by a minimum of 4 hours between session), 3 sets of 15 repetitions with 5 minutes of rest between each set. The threshold load was increased periodically weekly home visits by the therapist

(C) sham training using the same device than intervention group but without an expiratory training threshold load (to train the inspiratory muscles) for 3 months.
**Aerobic training**

**Bjarnadottir 2007**

To determine the effect of aerobic and strength exercise on physical fitness and quality of life.  
(E) outpatient exercise training (cycle-ergometer plus resistance exercise plus stretching and relaxation) 60 minutes, three times a week for 5 weeks (or a total of 15 hours).  
The exercise period was divided in:  
i) cycle ergometer 15–20 minutes at the subject’s aerobic threshold (55% of the subject’s VO₂peak)  
ii) 13 resistance exercise involving the major muscle groups, 15–20 repetitions per exercise  
iii) stretch and relaxation (last 5 minutes in session)  
(C) no exercise: a diary of all physical activity exceeding 20 minutes and occurring more than twice a week.

**Davis 2003**

The effects of aerobic exercise training on resting antioxidant mechanisms and markers of oxidative damage.  
(E) Supervised training sessions by air resistance arm and leg cycle ergometer; 15 weeks, 30 minutes three times per week (60% VO₂peak (with a 5-minute warm-up at 30% of VO₂peak and 5-minute cool down at 30% of VO₂peak). Training workloads were adjusted through the programs based on GXT results.  
(C) No exercise

**Malec 2002**

The effectiveness of a self-care lifestyle modification program  
(E1) a health seminar (the Bridging Self-Care with Health Care program); 14 week Health Seminar (1 hour/week) by a multidisciplinary team  
(E2) Exercise training; 14 week moderate effort Exercise Program (1 hour / twice a week)  
(E3) Combined E1 & E2  
(C) Wait-list control

**McAuley 2007**

To determine the effects of an efficacy enhancement intervention on adherence and perceptions of well-being. Both groups participated 3 months physical activity program, 3 times a week for 1 hour per session including aerobic exercise 50% up to 60–75% of subject’s age-predicted maximum heart rate (treadmills, stationary cycles, elliptical trainers) and stretching exercises at end.  
(E1) enhancement exercise condition; bi-weekly workshops focused on the provision of efficacy-based information relative to physical activity participation  
(E2) standard care exercise condition; bi-weekly workshops of general health topics.

**McCullagh 2008**

To assess both the short- and long-term effects of exercise on quality of life and fatigue  
(E) Aerobic exercise group:  
i) Supervised twice weekly over 12 weeks and consisted of a 5-minute warm-up and cool-down and 40 minutes of exercise. Each participant completed four stations, each lasting 10 minutes (treadmill walking/running, cycling, stair-master training,
arm-strengthening exercises, volleyball and outdoor walking including steps and slopes). Intensity target between 11 and 13 on the RPE

ii) Home exercise once a week lasting between 40 minutes and 1 hour

Intensity target between 11 and 13 on the RPE

(C) No exercise.

Mostert 2002
To assess effects of 4 week inpatient rehabilitation program
(E) an exercise training; Training intervention consisted of 5 x 30 min sessions per week of bicycle exercise with individualised intensity for 4 weeks
(C) non-training group; took part of the normal physical therapy of the rehabilitation program but agreed not to increase their physical activity level.

Oken 2004
To determine the effect of yoga and of aerobic exercise on cognitive function, fatigue, mood, and quality of life in MS.
(E1) weekly Iyengar yoga class along with home practice; weekly class á 90 min along with home practice for 6 months
(E2) weekly exercise class using a stationary bicycle along with home exercise; one class per week along with home exercise; Very light to moderate intensity on the RPE scale.
(C) a waiting-list control group.

Petajan 1996
To study the effects of aerobic training.
(E) 15 weeks of aerobic training; 3 supervised training session á 40 minute per week of combined arm and leg ergometry (5-min warm-up + 30 minutes at 60% of VO₂max + 5-min cooldown) plus 5–10 min stretching. Workloads were calculated from the workload / VO₂ relationship and were updated at weeks 5 and 10.
(C) No treatment.

Rampello 2007
To study the effects of aerobic training.
(E1) aerobic training program consisting of tree training sessions per week on a leg cycle ergometer for 8 weeks. Each training session consisted of a warm-up, at 60% of maximum work rate training and a cool-down. Subjects performed stretching exercise of their lower limbs and trunk muscles
(E2) neurological rehabilitation consisting of three sessions per week for 8 weeks, each session lasted 60 minutes. Consisted of exercises aimed at improving respiratory- motor synergies and of stretching exercises.

Schulz 2004
To study immunological, endocrine and neurotrophic factors during aerobic training.
(E) an aerobic bicycle training; Training was performed twice a week with an interval-training schedule for 30 min at a maximal intensity of 75% of the maximal watts for 8 weeks.
(C) a waitlist control.

Sutherland 2001
To assess the effects of an exercise program on HRQOL.
(E) water aerobics three times per week for 10 weeks; three supervised training sessions a week á 45 minute in water (Water aerobics, water jogging and deep water
running) for 10 weeks. Stretching.
(C) control (no-special-activity).

**Mobility**

**Armutlu 2001**
To investigate the efficacy of neuromuscular rehabilitation and Johnstone Pressure Splints in the patients who had ataxic MS.
(E) neuromuscular rehabilitation with Johnstone Pressure Splints in addition (The splint was applied for 20 min to both lower extremities before exercise sessions and were used during crawling, kneeling, half-kneeling and single-limb stance)
(C) neuromuscular rehabilitation alone including PNF, Frenkel Coordination Exercises, postural stability and balance training and walking exercises.

**Baker 2007**
To investigate the effects of standing exercise. Interventions were sequential and crossed after 3 weeks.
(E1) Daily standing in a standing frame for 30 minutes
(E2) A daily exercise program

**Beer 2008**
To evaluate feasibility and perform explanatory analysis of the efficacy of robot-assisted gait training (RAGT) during an inpatient stay. 15 x 30 min sessions over three weeks, 5 times/week; 1 hour/session with an effective treatment time of 30 min. All patients participated additionally in a multimodal rehabilitation program
(E1) RAGT
(E2) conventional walking training (CWT) during an inpatient stay.

**Cattaneo 2007**
To evaluate the effects of balance retraining.
(E1) balance rehabilitation to improve motor and sensory strategies; 10–12 sessions spread over 3 weeks, 45 min/session.
(E2) balance rehabilitation to improve motor strategy; 10–12 sessions spread over 3 weeks, 45 min/session.
(C) conventional therapy not specifically aimed at improving balance; 10–12 sessions spread over 3 weeks, 45 min/session.

**Fuller 1996**
To determine whether mobility at home improved after hospital inpatient physiotherapy and if there was benefit in activities of daily living.
(E) 2 week inpatient rehabilitation; Average admission duration 13.5 days with an average of 6.9 hours of physiotherapy contact time (38 minutes on average per working day).
(C) Wait-list control.

**Johnson 1999**
To determine whether a course of Feldenkrais bodywork would result in significant improvement in physical, mood symptoms and functioning in MS patients beyond the effects observed using a sham condition (nontherapeutic bodywork). 8 week cross-over.
(E) Feldenkrais sessions; weekly one 45 min session
(C) sham sessions; weekly one 45 min session.

**Lo 2008**
To determine whether physiotherapy can improve mobility. Cross-over: 2
times/week for 3 weeks (a total of 6 sessions per phase); 40 min/session. Normal physical activities, not to begin any new exercise programs outside the protocol
(E1) Body weight supported treadmill training (BWSTT)
(E2) Body weight supported treadmill training (BWSTT) with robotic assistance (R)

Lord 1998
To compare two physiotherapy approaches to improve walking in patients with gait disturbance due to MS; for a minimum of 15 treatments over a 5–7-week period (15–19 times), 1 hour/session
(E1) a facilitation (impairment-based) approach; passive and active techniques
(E2) a task-oriented (disability-focused) approach; functional exercises

Schuhfried 2005
To examine whether a whole-body vibration (mechanical oscillations) in comparison to a placebo administration leads to better postural control, mobility and balance. One-time term of nine minutes treatment or placebo application. Follow-up 2 weeks
(E) 9 min a whole-body vibration at low frequency (2.0–4.4 Hz oscillations at 3-mm amplitude) in 5 series of 1 min each with a 1-min break between the series
(C) 9 min placebo treatment (TENS on the nondominant forearm).

Solari 1999
To examine the efficacy of an inpatient physical rehabilitation program on impairment, disability, and quality of life of MS patients
(E1) 3 weeks of inpatient physical rehabilitation (study treatment) Twice-daily exercise periods, each 45 min long; passive (stretching, mobilization) and active interventions. Goals were normalization of postural control, facilitation of normal gait patter, increasing range of movement, and maximizing muscle power and endurance. Plus self-executed exercise program at home for 12 weeks.
(E2) 1-day session of individual instruction from a physiotherapist as well as written instructions, exercises performed at home for 15 weeks.

Stephens 2001
To examine the effectiveness of a structured group motor learning process on balance, balance confidence, and self-efficacy
(E1) Awareness Through Movement (ATM); (Feldenkrais); 8 classes, 2 to 4 hours each for a total of 20 hours, over a period of 10 weeks.
(E2) educational sessions (EDU)

van den Berg 2006
To evaluate the effects of aerobic exercise (treadmill training) on walking performance (mobility) and levels of fatigue.
(E) Supervised treadmill training, 3 sessions/week for 4 weeks, walking duration up to a maximum of 30 minutes/session with a maximum of three rest periods, goal intensity of 55–85% of age predicted maximum heart rate (APMHR).
(C) Delayed intervention group acted as control group; 4 session, 90-min each, over a period of 10 weeks.

Wiles 2001
To determine whether physiotherapy can improve mobility in chronic MS. Cross-over; Each patients received three 8 weeks periods of treatment. Treatment periods were separated by 8 weeks.
(E1) Hospital outpatient physiotherapy (2 sessions of 45 min each week for 8
weeks). Focus was on specific facilitation techniques.

(E2) Home physiotherapy (2 sessions of 45 min each week for 8 weeks). Focus was on specific functional activities.

(C) No physiotherapy

Physical therapy for bladder dysfunction

Klarskov 1994  
To study the effectiveness of biofeedback:

(E) biofeedback using bladder pressure and simultaneous EMG registration via surface electrodes; 30–60 min every 2 weeks during the hospital stay (median 3 times) using display of bladder pressure and EMG signal.

(C) No biofeedback

All the patients (E and C groups) had behavioural modification, pharmacological adjustment and pelvic floor training instructions of 40 min twice a week (median 6 times) by a physiotherapist.

McClurg 2006  
To study the effectiveness of a combined 9 weeks programme for bladder dysfunction:

(E1) pelvic floor muscle training and advice (PFTA): information for preventing incontinence and suppressing urge plus pelvic floor muscle contractions at home without the assistance of any device. Education at week 1 plus PFM contractions five times a day (regimen was reviewed weekly according to the PERFECT scheme; weekly visit at clinic).

(E2) PFTA and EMG biofeedback (home training): PFTA identically outlined for group E1 plus EMG biofeedback training

(E3) PFTA, EMG biofeedback and neuromuscular electrical stimulation (NMES) (weekly at clinic plus daily home treatment): PFTA identically outlined for group E1 and EMG biofeedback identically outlined for group E2 plus intravaginal NMES (initially for 5 min increasing to a maximum of 30 min).

McClurg 2008a  
To evaluate the efficacy of pelvic floor muscle training, EMG biofeedback and neuromuscular electrical stimulation (NMES) and to establish the benefit of NMES above and beyond that of EMG biofeedback and pelvic floor muscle training.

9 weeks training including for all participants daily home exercises with a weekly visit at a clinic, daily pelvic floor muscle exercises according to the initial vaginal assessment using the OERFECT scheme and the modified Oxford Scale and EMG biofeedback (performed for 15 min at each clinic visit: warm-up of five contractions and five relaxations and endurance exercise by Neurotrack).

At week 1 all participants were taught skills and strategies for preventing incontinence and suppressing urge and were provided with an information booklet

(E1) pelvic floor muscle training (PFMT), EMG biofeedback and placebo neuromuscular electrical stimulation (NEMS): placebo NMES (2 Hz frequency, 50 μsec pulse width, 2 sec stimulation and 60 sec of no stimulation with a ramp of 8 sec) used at home with a gradual increase to a daily maximum of 30 min.

(E2) pelvic floor muscle training (PFMT), EMG biofeedback and active neuromuscular electrical stimulation: Weekly at clinic: bi-phasic constant current at a frequency of 40 Hz, a pulse width 250 μsec, a stimulation time of 5 sec with 10 sec
of no stimulation, and a ramp of 1 sec (at maximum tolerated intensity with active assisted exercises). At home with a gradual increase to a daily maximum of 30 min: at a frequency of 10 Hz, a pulse width 450 μsec, a stimulation time of 10 sec, and a rest time of 3 sec, with a ramp of 2 sec, at maximum tolerated intensity.

**McClurg 2008b**

NA

**Prasad 2003**

To investigate the effect of ‘abdominal vibration’ in reducing residual volume measured; three separate two week periods of treatment, treatment periods were separated by a week:

- (E1) *abdominal vibration*
- (E2) *abdominal pressure*
- (C) *no treatment*

All participants were given practical advice on the management of continence, such as toileting regimes, and continence aids were provided.

**Vahtera 1997**

To determine the effect of pelvic floor muscle exercises combined with electrical stimulation of pelvic floor on lower urinary tract dysfunction in MS patients with near normal (< 100 ml) post-void residual volumes:

- (E) *pelvic floor muscle exercises combined with electrical stimulation*:
  - i) 6 electrical stimulation treatment sessions during a period of 2 weeks; carrier frequency of 2000 Hz, treatment frequencies 5–10 Hz, 10–50 Hz and 50 Hz (7 s pulse / 25 s pause), 10 min of each frequency followed by 3 min rest, at maximal tolerated intensity
  - ii) 1–2 sessions of biofeedback for instructions in pelvic floor exercise
  - iii) same exercises in the sitting and standing positions as well as during their normal daily activities 3–5 times a week for at least 6 months
- (C) *no treatment*

**Electrical stimulation for pain**

**Al-Smadi 2003**

To investigate the hypoalgesic effects of transcutaneous electrical nerve stimulation (TENS) upon low back pain (LBP)

- (E1) **TENS 1** (4 Hz, 200 micros)
- (E2) **TENS 2** (110 Hz, 200 micros)
- (E3) placebo TENS

All treatments was applied for 45 minutes three times a week for six weeks with a four-week follow-up.
The main target of the electrode placement was the lumbar and sacral nerve roots (E1 and E2) The intensity of the unit was increased until a “strong but comfortable” sensation was experienced.

**Warke 2004**

To evaluate the use of self-applied transcutaneous nerve stimulation (TENS) for low back pain.

- (E1) **TENS 1** (4 Hz, 200 μs)
- (E2) **TENS 2** (110 Hz, 200 μs)
- (C) placebo TENS
All treatment involved self-application of TENS on a daily basis for 6 weeks. The treatment for a total of 45 minutes twice a day and at any time painful episode occurred at a strong but comfortable intensity or at the midpoint of the dial.

**Warke 2006**

To evaluate the hypoalgesic effects of self-applied transcutaneous electrical nerve stimulation (TENS) on chronic low-back pain (LBP)

- **(E1)** low-frequency TENS (4 Hz, 200 µs);
- **(E2)** high-frequency TENS (110 Hz, 200 µs);
- **(C)** placebo TENS

TENS at home for 45 min, a minimum twice daily for 6 weeks and at any time painful episode occurred

All treatment involved self-application of at a strong but comfortable intensity or at the midpoint of the dial.

---

**Physiotherapy for spasticity**

**Brar 1991**

To assess the effects of low-dose baclofen and stretching exercises, both singly and combination on MS-related spasticity (cross-over, 2 weeks):

- **(E1)** baclofen alone
- **(E2)** stretching exercise with placebo
- **(E3)** stretching exercises with baclofen
- **(E4)** placebo treatment without exercises

Stretching exercises (E2 and E3) included stretch of hamstrings, quadriceps, adductor and plantarflexor musculature.

**Giovannelli 2007**

To investigate the potential efficacy of botulium toxin type A in combination with neurological rehabilitation to treat multiple sclerosis-related spasticity

- **(E)** a physiotherapy programme after botulium toxin type A injection

Daily for 15 consecutive days after botulium toxin type A injection including weekends

Activity was designed to maintain muscle lengthly through passive or active exercise and stretching regimen on the injected area (40 min) for each session

- **(C)** botulium toxin type A injection but no physiotherapy

---

**Cooling therapy**

**Beenakker 2001**

To investigate the effects of head-vest cooling garment; 2 weeks cross-over 1 week apart. A single session wearing a head-vest cooling garment.

- **(E)** active cooling: A single session for 60 minutes at 7 degrees C
- **(C)** sham cooling: A single session for 60 minutes at 26 degrees C

**Mayer-Heim 2007**

To investigate the efficiency, clinical benefit and handling of the newly developed cooling device (a thigh-cuff cooling-garment).

- **(E)** active cooling: A single session over a period approximately 60 min.
- **(C)** inoperable cooling: A single session over a period approximately 60 min.
Nilsagård 2006  To evaluate a single session with cooling garment; A single session, cross-over, wash-out period at ≥ 7 days
(E) active cooling: A single session over a period of 45 min
(C) Placebo cooling: A single session over a period of 45 min

Schwid 2003  To determine the effects of a single acute dose of cooling therapy and to determine whether effects are sustained during daily cooling garment use. Cross-over, 1 week wash-out period.
Acute phase (1st randomization): a single session
(E1) Active cooling: high-dose (55°F) cooling with a liquid cooling garment
(C1) Sham cooling: low-dose (70°F) cooling with a liquid cooling garment
Chronic phase (2nd randomization)
(E2 Active cooling: Daily cooling for a month: the use the cooling garment 1 hour each day at home (high-dose)
(C2) no treatment: observation for a month

**Acupuncture**

Donnellan 2008  To compare the effect of Chinese medical acupuncture and minimal acupuncture on the perceived quality of life.
10 acupuncture treatments of 25 minutes duration over 5 consecutive weeks.
(E) Chinese medical acupuncture according to the individualized plan.
(C) minimal acupuncture (sham) involving the insertion of acupuncture needles just through the skin and away from the acupuncture sites

NA = not available.