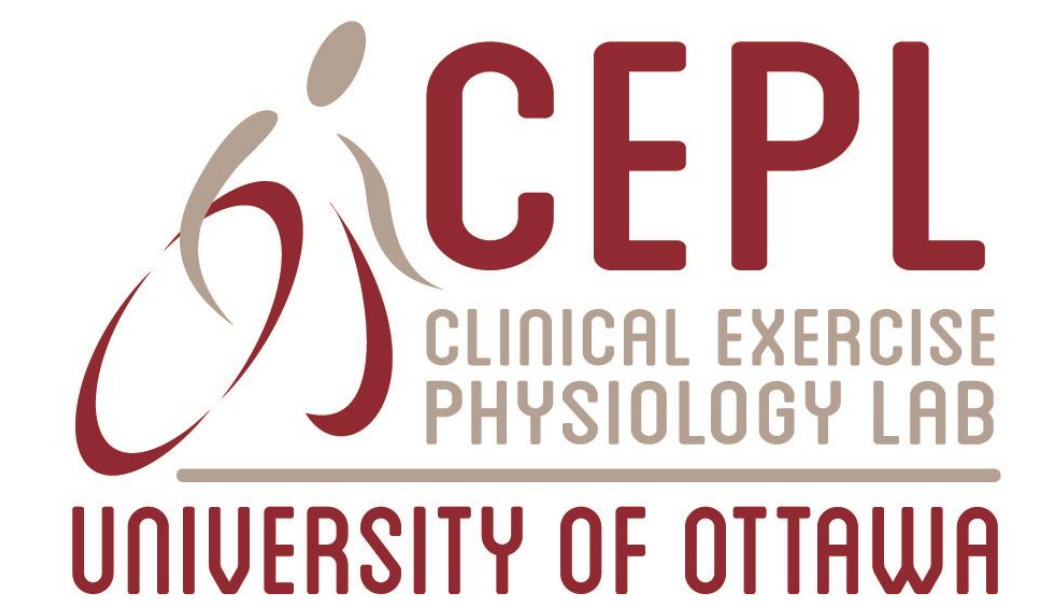




# Exploring Wellness-Based Interventions in People with Progressive Multiple Sclerosis: An Evidence-Based Review

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## BACKGROUND

- Progressive multiple sclerosis (MS) is characterized by gradual accumulation of neurological disability without recovery, or following an initial relapsing course.
- While there are now many disease-modifying therapies approved for the treatment of relapsing MS, similar progress has not been made in the development of therapies for patients with progressive MS.<sup>1</sup>
- Lifestyle-based interventions can be used to target and modify wellness behaviours, and may provide an alternative approach for managing outcomes in patients with progressive MS.

## OBJECTIVES

- To explore the role of wellness-based interventions in patients with progressive MS;
- To summarize the current evidence for the efficacy of exercise training, emotional well-being therapies, and dietary modification in patients with progressive MS.

## METHODS

- Five electronic databases were searched for relevant articles: Pubmed, EMBASE, Web of Science, OvidMEDLINE, and PsycINFO.
- Studies included patients with PPMS or SPMS who participated in a wellness-based intervention of exercise training, emotional well-being, or dietary modification.
- Level of evidence was rated for each study using the American Academy of Neurology criteria.<sup>2</sup>
- The final search retrieved 21 articles reporting on 16 studies of wellness-based interventions in patients with progressive MS.
- Ten studies examined exercise training, three examined emotional well-being therapies (primarily mindfulness), two examined dietary modification, and one was a combined wellness intervention.
- Considering the limited number of records identified, the focus of this review was primarily on exercise training, with an exploration of mindfulness, dietary modification, and combined wellness therapies for patients with progressive MS.

## RESULTS

Reference	Design (AAN Class)	Disability	Intervention	Study Findings
<b>EXERCISE TRAINING</b>				
Bricken et al 2014/ Bricken et al 2016	RCT (II)	5.2±0.9 4.7±0.8 5.0±0.8 4.9±0.9	8-10 weeks, AET Arm-cycle ergometer Rowing Leg-cycle ergometer Waitlist control	*↑ CRF (VO <sub>2peak</sub> ), walking endurance (6MW), cognition (attention, tonic alertness, verbal learning) *↓ Depression (IDS), fatigue (MFIS) *↑ Serum BDNF (acute exercise response) ↔ Serum Irisin, IL-6 (acute exercise response) ↔ Serum BDNF, Irisin, IL-6 (post-intervention)
Skjerbaek et al 2014	RCT (III)	6.5-8.0 6.5-8.0	4 weeks, upper-body AET 4 weeks, standard MS rehabilitation	↑ CRF (VO <sub>2peak</sub> ) ↔ Upper-extremity function (9HPT, handgrip power, Box and Block Test), aerobic endurance (6-minute wheelchair-test), fatigue (FSMC), depression (MDI), QoL (MSIS)
Fornusek et al 2014	Pre-Post (IV)	6.5-8.5	18 sessions, electrical stimulation assisted cycling	*↑ Thigh circumference ↑ Perceived muscle strength, leg circulation, spasticity and transfer ability
Giesser et al 2007	Pre-Post (IV)	7.0-7.5	40 sessions, BWSTT	↑ Muscle strength (MMT), walking speed (10-MWT), walking endurance (6MW), balance (BBS), spasticity (MAS), QoL (MSIS) ↔ EDSS (no formal statistics performed)
Pilutti et al 2011	Pre-Post (IV)	6.0-8.0	12 weeks, BWSTT	*↑ QoL (MSQoL-54) ↓ Fatigue (MFIS), MSFC ↔ EDSS
Pilutti et al 2016	Randomized clinical trial (IV)	7.0 (mdn) 7.0 (mdn)	12 weeks, TBRST 12 weeks, BWSTT	*↓ Fatigue (MFIS) ↑ QoL (MSQoL-54) ↔ EDSS or MSFC
Ratchford et al 2010	Pre-Post (IV)	6.0-6.5	6 months, FES cycling	↑ Strength in muscles stimulated, MSFC scores, walking speed (T25FW), walking endurance (2MW), agility (TUG), QoL (SF-36) ↔ EDSS, spasticity (LLSMS), psychiatric functioning (SCL-90) Analysis of 120 cytokines, chemokines, and growth factors in CSF (*↓ MCP-1 only)
Roehrs et al 2010	Pre-Post (IV)	6.1±1.2 5.1±2.6	12 weeks, aquatic exercise Women Men	*↑ Social functioning, fatigue domains of QoL (SF-36 & MSQoL), perceived social support (MSSS) ↔ Pain, sexual satisfaction, bladder control, bowel control, visual impairment, perceived deficits, mental health (domains of QoL)
Straudi et al 2013	Pre-Post (IV)	4.5-6.5 4.5-6.5	6 weeks, BWSTT Conventional therapy	*↑ Walking speed (T25FW), walking endurance (6MW), gait ↑ Agility (TUG) ↓ Fatigue (FSS)
Szelesi et al 2009	Pre-Post (IV)	4.0-8.0	2 weeks, FES cycling	*↓ Acute spasticity (MAS) ↔ Strength, walking speed (T25FW), spasticity (MAS; post-intervention)
<b>EMOTIONAL WELL-BEING</b>				
Bogosian et al 2015/ Bogosian et al 2016	RCT (I)	6.8±1.6 6.2±1.4	8 weeks, Skype-delivered mindfulness intervention Wait list control	*↓ Distress (GHQ-12), depression and anxiety (HADS), pain (non-specific numerical scale), QoL (MSIS psychological) ↓ Fatigue (FSS), QoL (MSIS physical), service use and costs (CSRI) ↑ QoL (ED-5D)
Mills et al 2000	RCT (III)	NR	6 individualized, one-to-one mindfulness sessions Waitlist control	*↑ Timed single-leg balance task ↑ Symptom management (SRQ)
Hoogerwerf 2017	Pre-Post (IV)	3.9±1.7	10-week mindfulness-based cognitive therapy	*↓ Fatigue (CIS-20), depression and anxiety (HADS), cognitive symptoms (CFQ) *↑ Emotion-oriented coping (CISS), mindfulness (FFMQ-SF) ↓ Self-reported fatigue, negative emotions, and negative thoughts
<b>DIETARY MODIFICATION</b>				
Mauriz et al 2013	Randomized clinical trial (III)	>6.5 >6.5	42-day, low-fat diet 42-day, low-fat diet with antioxidant supplementation	*↓ Serum CRP, 8-iso-PGF2α, IL-6 *↑ Catalase antioxidant activity ↓ Glutathione peroxidase ↑ SOD activity increase ↔ Glucose, total cholesterol, total lipids, protein (albumin & prealbumin), mineral concentrations, total antioxidant status
Riccio et al 2016	Pre-Post (IV)	4.2±0.7	Calorie restricted, modified Mediterranean diet with vitamin D, fish oil, lipoic acids, omega-3 polyunsaturated fatty acids, resveratrol, and multivitamin complex	↑ Serum PUFA concentration ↓ Serum MMP-9, fatigue (FSS), waist and hip circumference, and body weight ↔ Vitamin D levels, total cholesterol, triglycerides, fibrinogen, creatinine, depression (HAM-D), QoL (SF-36), EDSS
<b>COMBINED</b>				
Bisht et al 2014	Pre-Post (IV)	6.2±0.3	Modified Paleolithic diet + stretching and resistance exercises with NMES + meditation and massage	*↓ Fatigue (FSS)
Bisht et al 2015/ Bisht et al 2017/ Lee et al 2017	Pre-Post (IV)	6.2±1.0	Modified Paleolithic diet + stretching and resistance exercises with NMES + meditation and massage	*↓ Fatigue (FSS) *↑ QoL (SF-36) *↑ Mood (BDI & BAI), cognition (DKEFS, FSIQ, WAIS) ↔ Gait (TUG, T25FW) and balance (BBS)

↑ Indicates increase in outcome measure; ↓ Indicates decrease in outcome measure, ↔ Indicates no increase or decrease in outcome. \*Indicates statistically significant difference, p<.05; \*\*Indicates statistically significant difference, p<.001.

## RESULTS (continued)

- Exercise training:**  
Level C classification (i.e., possibly effective) for the efficacy of aerobic exercise training on cardiorespiratory fitness.  
Level U classification (i.e., data inadequate or conflicting) for other outcomes.
- Emotional well-being:**  
Level B classification (i.e., probably effective) for the efficacy of mindfulness-based training on psychological distress, depression, anxiety, pain, and QoL.
- Dietary modification:**  
Level U classification (i.e., data inadequate or conflicting) for the efficacy of dietary modification and supplementation.
- Combined:**  
Level U classification (i.e., data inadequate or conflicting) for the efficacy of combined wellness therapies.

## DISCUSSION

- 21 articles reporting on 16 wellness-based interventions were identified in patients with progressive MS.
- Current evidence suggests possible benefits of exercise training and mindfulness therapies for patients with progressive MS, although this literature is limited.
- There is inconclusive evidence for dietary modification or combined wellness interventions in progressive MS.
- Collectively, the current level of evidence points to the need for high-quality research to determine the feasibility and efficacy of wellness-based approaches in progressive MS.
- Better characterization of wellness behaviours in progressive MS will be critical to design, test, and implement the most effective therapies for patients living with progressive MS.

### References

- Mott RW, Mowry EM, Ehde DM, LaRocca NG, Smith KE, Costello K, et al. Wellness and multiple sclerosis: The National MS Society establishes a Wellness Research Working Group and research priorities. *Mult Scler*. 2017; doi: 10.1177/1352458516687404 [Epub ahead of print].
- Haselkorn JK, Hughes C, Rae-Grant A, Henson LJ, Bever CT, Lo AC, et al. Summary of comprehensive systematic review: Rehabilitation in multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2015;85:1896-903.