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# The effect of hydrotherapy on the symptoms and functional characteristics of multiple sclerosis patients

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**Abstract**
**Aim:** A review of the literature on the effect of hydrotherapy on the symptoms of fatigue, pain, spasticity as well as on the balance and gait of people with Multiple Sclerosis (MS).
**Method:** Search databases such as MEDLINE, Cochrane Library, Science Direct and PEDro were used to search the literature. The inclusion criteria were studies that included physiotherapy and mainly hydrotherapy as a means of rehabilitation in MS.
**Results:** Hydrotherapy programs significantly reduced the symptoms of fatigue, pain, spasticity as well as significantly improved balance and gait in patients with MS, as reflected in the evaluation tests.
**Conclusions:** Hydrotherapy is proposed as a safe, effective and enjoyable method of rehabilitation in patients with MS to reduce symptoms and improve balance and gait.

**Keywords:** Multiple sclerosis, hydrotherapy, fatigue, pain, spasticity, balance, gait

## 1. Introduction
Multiple Sclerosis (MS) is an inflammatory demyelinating disease of the Central Nervous System (CNS). The onset of the disease usually occurs in people aged 20-40 years. The prevalence ratio of the disease in women compared to men is reported to be 3: 1 [1]. It is the most common neurological disease in North America and Europe [2]. It is the third leading cause of neurological disorders in adults and affects approximately 2.5 million adults worldwide. About 400,000 young people get sick in the US and the incidence increases by about 10,000 people each year [3]. The global median prevalence of the disease increased from 30 per 100,000 in 2008 to 33 per 100,000 in 2013 [4].
The exact etiology of MS is unknown and a multifactorial cause is generally accepted where both genetic and environmental factors determine the morbidity risk of an individual in a complex interaction that is not yet fully understood [5]. Among the environmental factors reported is Epstein-Barr virus infection [6], smoking [7], latitude [8], low vitamin D levels and elevated Body Mass Index (BMI) during adolescence [5]. However, the causes of MS are still largely unknown and there are currently no documented risk factors for preventing the disease [9].
Because MS can affect any part of the CNS, symptoms range from cognitive, motor, sensory, visual to bladder and bowel dysfunction. However, some symptoms such as difficulty in walking, spasticity, pain, tremor, fatigue, cognitive decline, depression and sexual dysfunction can sometimes be the most harmful and are often not treated adequately [10, 11]. CNS damage results in a slowing of nerve conduction and a reduction in motor activation which leads to reduced motor performance [12]. Motor dysfunctions such as abnormal biomechanics of gait, changes in balance, muscle weakness and fatigue, are one of the most common parameters affected and associated with MS [13]. These physical limitations and neuropsychiatric disorders may affect the quality of life of patients with MS, which includes biological, economic, social and psychological needs [14].
Physiotherapy is a common rehabilitation strategy that can be effective in improving gait disorders in people with MS. Physiotherapy may include exercise (e.g. aerobic exercise, resistance exercise, neurophysiological approaches, and yoga), electrotherapy, orthotics,

massage, or hydrotherapy [15] and should be aimed at preventing the decline of physical condition and mental ability, as well as preventing the development of disability, balancing the loss of functioning, adapting the patient to changes in environmental conditions and creating appropriate conditions for maintaining independence [16].

Hydrotherapy is used to treat many diseases as the aquatic environment has unique properties such as buoyancy, resistance and hydrostatic pressure which can be used for the benefit of patients [17]. Water characteristics such as hydrostatic pressure, buoyancy, density, temperature and resistance have a positive effect. They allow the patient to exercise balanced and coordinated movements [18]. Buoyancy makes it possible to perform movements that are not possible on land [19]. The microgravity environment allows patients to actively participate in exercise. Due to the lack of a stable position of the body in the water, the muscles are constantly activated in order to stabilize it. This makes it possible to gain strength, flexibility and balance. Hydrostatic pressure provides proprioceptive and sensory feedback different from that on land. In addition, as patients with MS may experience symptoms on heat exposure, hydrotherapy helps reduce weakness and other neurological symptoms [20]. Elevated body temperature is also one of the main problems of patients with MS during physical activity and it is argued that water can partially prevent a rise in body temperature resulting in the patient exercising and cooperating more effectively [20].

There is a lack of literature on the effect of hydrotherapy on the various symptoms of MS. The aim of this review is to investigate the literature on the efficacy of hydrotherapy, as a physiotherapy tool, in the various symptoms of MS such as fatigue, pain, spasticity and functional characteristics such as gait and balance of people with MS.

## 2. Literature review

### 2.1 The effect of hydrotherapy on fatigue

Fatigue is one of the most common symptoms in patients with MS [21]. Fatigue in MS has been defined as a reversible, motor and cognitive impairment with reduced motivation and desire for relaxation, whether occurring spontaneously or caused by mental or physical activity, humidity, acute infection and ingestion of food. It may occur at any time, but usually worsens in the afternoon. In MS, fatigue can occur on a daily basis, usually coexisting for years and is more serious than any precursor fatigue [22]. It often leads to job loss [23], social isolation [24], affects mental health [25] and generally reduces the ability of the individual to perform their daily activities [26].

Fatigue can be primary and is the result of the effects of the disease itself and especially of the inflammation, demyelination or loss of the axis caused by MS, or secondary, which is due to other factors such as drugs, sleep and mood disorders [27]. The pathophysiological mechanisms of fatigue in MS have been extensively investigated and it is reported that fatigue is a central component of MS [28]. The biological complexity of these mechanisms also reflects the heterogeneity in the measurement scales of this common symptom [29]. Fatigue measurement scales include the Fatigue Severity Scale (FSS) [30], the Modified Fatigue Impact Scale (MFIS) [26], the Fatigue Assessment Scale (FAS) [31], the Fatigue Scale for Motor and Cognitive Functions (FSMC) [32] and the Unidimensional Fatigue Impact Scale (U-FIS) [33].

Hydrotherapy is recommended as a means of physiotherapy in patients with MS by the American Physical Therapy Association. Kargafard *et al.* [34] investigated the effect of hydrotherapy on the improvement of fatigue and the effect of an 8-week hydrotherapy program compared to a 4-week program in patients with MS. The hydrotherapy program consisted of three sessions per week, lasting 60 minutes each (10 minutes warm-up, 40 minutes exercise and 10 minutes recovery). The intensity of the exercises was prescribed at 50% -75% of the Maximal Heart Rate Reserve (HRRmax). The temperature of the pool was maintained between 28 °C and 30 °C while the patients were informed to report the possible presence of symptoms during the program such as some difficulty or excessive fatigue. The results showed that the intervention group at both four and eight weeks had lower scores on the MFIS. Furthermore, the score in the intervention group was lower at eight weeks compared to four weeks. The researchers suggest hydrotherapy as an effective and safe way to improve fatigue in patients with MS. No accidents, excessive fatigue or any other side effects related to the intervention program were reported. Moreover, further research with a larger number of participants and a higher degree of disability is proposed, as well as the comparison of hydrotherapy with aerobic-type programs on land.

### 2.2 The effect of hydrotherapy on pain

In people with MS symptoms such as headache, neuropathic limb pain, back pain, painful convulsions as well as the Lhermitte effect are common. Chronic pain can be defined as "pain that occurs continuously or intermittently for at least three months after treatment time" [35]. Pain in patients with MS can be a significant problem [36]. It is estimated that 42-90% of patients with MS experience pain as it manifests in all stages of the disease [37]. MS-related pain can cause both acute and chronic symptoms, is reported as one of the most severe symptoms in 8-32% of patients with MS [38] and often coexists as a combination of acute, paroxysmal and chronic pain in the same or different parts of the body [39].

According to the underlying pathophysiological mechanisms, pain is divided into five categories: (1) Neuropathic pain, defined as pain arising directly from an injury or condition affecting the somatosensory system [40], which may present as persistent limb pain and numbness, as trigeminal neuralgia, and as the Lhermitte phenomenon (defined as the transient sensation associated with movements of the neck, back, lower back, and other parts of the body) [41], (2) Nociceptive pain, whether inflammatory or non-inflammatory, which includes musculoskeletal and back pain that may be related to posture, optic neuritis [42], headaches and pain caused by treatment, (3) Psychogenic pain, which is difficult to identify and refers to somatoform pain associated with psychiatric conditions such as depression and anxiety or pain behaviors developed in patients with chronic, persistent pain, (4) Idiopathic pain, which includes diseases that are not fully understood, such as fibromyalgia, interstitial cystitis and atypical facial pain, and (5) Mixed pain, which includes a heterogeneous group of pain with different pathophysiological mechanisms, which are caused by MS, such as muscle spasms and spasticity pain.

In the literature only one study has investigated the effect of hydrotherapy on pain in patients with MS [43]. The researchers used a structured Ai-Chi exercise program in the water. The individuals of the intervention group participated in the hydrotherapy program twice per week for a total duration of 20 weeks. The researchers used different scales to assess pain and found that the intervention group showed a statistically significant reduction in the Visual Analog Scale (VAS) for pain score, which was maintained for up to 30 weeks. No statistically significant differences were observed in the

control group at any time point. Additionally, the intervention group exhibited a significant decrease in the VAS score, in terms of convulsions, during the 20th week. The authors report that an Ai-Chi-based hydrotherapy program reduces pain in patients with MS, an effect that is maintained for 10 weeks after the end of treatment. It also improves other symptoms associated with MS, such as disability, depression and fatigue. The results of this study are superior to or equivalent to those of an exercise program in a treatment room.

### 2.3 The effect of hydrotherapy on spasticity

Spasticity is one of the symptoms of MS [44] and is a major problem for 60-80% of patients with MS [45]. The most commonly used definition of spasticity is that of Lance [46], who states that: "Spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes ('muscle tone') with exaggerated tendon jerks resulting from hyperexcitability of the stretch reflex". Spasticity can predict future falls [47] and is reported to affect quality of life by increasing fatigue, pain, disability and posture deficits [48, 49].

Non-pharmacological treatment of spasticity in patients with MS generally includes the avoidance of activating agents and regular physiotherapy [50]. Treatment includes a wide range of physiotherapy approaches such as exercise, therapeutic postures, electrostimulation and vibration. It is reported that physiotherapy is the most appropriate treatment for spasticity [51]. Physiotherapy interventions aim to maintain muscle length, prevent contractions and change the mechanical properties of the musculoskeletal system and plasticity within the CNS [52].

Hydrotherapy may have a positive effect on spasticity in patients with MS [53], however to date there is no study in the literature on the effect of hydrotherapy on spasticity in patients with MS. This hypothesis is supported by a recent relatively systematic review of non-pharmacological approaches to spasticity in MS, which does not include any reference to hydrotherapy programs [54].

### 2.4. The effect of hydrotherapy on balance

Balance is one of the components of physical condition [55]. Balance disorders or imbalance are common symptoms of MS [56]. Overall, 50-80% of people with MS experience balance problems [57]. Motor problems and balance disorders are due to decreased muscle strength, exercise tolerance, coordination and reaction time that may increase the risk of falls [58]. Balance requires many CNS-controlled functions and many or all of these functions can be affected by MS, which is the reason why balance is considered to be regularly affected in people with MS. MS can cause damage to vestibular function, proprioception, vision, eye movement, coordination, cognitive function and strength. Balance dysfunction in MS is often perceived as three interrelated problems: reduced ability to maintain position, limited and slow motion at the limits of stability, and delayed responses to shifts and disturbances. In addition, the performance of functional balance can be affected in cases of simultaneous work, as in many real situations, balance is required when performing other motor or cognitive work [59].

Various evaluation tools have been used to assess balance in patients with MS, such as the Timed Up-and-Go (TUG) test [60], the Berg Balance Scale (BBS) [61], the Tinetti Performance Oriented Mobility Assessment (POMA) [62], the Dynamic Gait Index (DGI) test [60] and the Guralnik Test Battery [63]. There is a lack in the literature on the effect of physiotherapy interventions on the balance of patients with MS. In particular, few studies have examined the efficacy of hydrotherapy programs on the balance of people with MS. Kargarfard *et al.* [64] studied the effect of an 8-week hydrotherapy program on the gait of patients with MS. Participants were 32 women with a mean age of 36.4 ± 8.2 years, who were randomly divided into two groups, the intervention group consisting of 17 women and the control group consisting of 15 women. The hydrotherapy protocol included three sessions per week for 8 weeks. Each session had a duration of 60 minutes at an intensity of 50-75%HRRmax. Each session consisted of 10 minutes warm-up, 40 minutes hydrotherapy exercises and 10 minutes recovery. Exercises aimed at mobilizing the joints, functional exercises, balance exercises and walking at different intensities were used. The program was performed in cycles in stations and each exercise included 10-12 repetitions. The BBS was used to assess balance. The results showed that the intervention group score on the BBS improved significantly while in the control group it decreased. The interaction of group-time factors was statistically significant on the BBS score.

In another study, Majdinasab *et al.* [65] while researching the effect of hydrotherapy on balance in women with MS found that there was a significant improvement in balance in the experimental group for the Forward Reach, Left Reach and Right Reach tests but not for the TUG test. The study involved 40 women, who were randomly divided into two groups, intervention and control. Each group consisted of 20 women. The hydrotherapy program had a duration of eight weeks and a total of 24 sessions were held, three each week. Each session lasted 60 minutes and consisted of 10 minutes warm-up, 40 minutes hydrotherapy exercises and 10 minutes recovery. Stretching exercises, balance exercises, walking and cycling were used. The exercises were performed in three sets of 10 repetitions for the first four weeks and in three sets of 20 repetitions for the next four weeks.

Salem *et al.* [66], studied, among other things, the effect on the balance of a hydrotherapy program in the community. The study involved 11 patients with MS, while only 10 completed the program, of which eight were women and two men. The study did not have a control group. The hydrotherapy program had a total duration of five weeks and took place in a swimming pool with a constant temperature of 31°C. There were two sessions per week and each session lasted 60 minutes and consisted of warm-up, hydrotherapy exercises and recovery (the times were not mentioned). The warm-up included moderate-intensity aerobic exercise, flexibility exercises and neck, upper and lower limb exercises. The hydrotherapy exercises included activities aimed at joint mobility, muscle strength, balance, posture, as well as functional activities. The BBS and the TUG test were used to assess balance. The results showed that the score on the BBS increased statistically significantly, while there was a significant decrease in the score on the TUG test. During the intervention, there was no change in the level of fatigue, and no side effects related to the program were observed. The percentage of patient satisfaction for the experience, quality and organization of the program reached 100%. The researchers concluded that a community hydrotherapy program has significant benefits and is necessary for the rehabilitation of patients with MS.

### 2.5 The effect of hydrotherapy on gait

Walking is one of the most basic and oldest functions of the

human species [67] and is strongly related to the autonomy and quality of life of individuals [68]. Gait is one of the functions most affected in patients with MS [69] at 89% as assessed by the Expanded Disability Status Scale (EDSS) [70]. In patients with MS, gait disorders are considered to be one of the leading causes of disability [68]. People with MS walk more slowly, with fewer, smaller and wider steps. have increased variability in time between steps and spend more time on double support compared to healthy individuals [71, 72]. MS is also highly associated with reduced levels of walking in everyday life as reflected by accelerometers or pedometers [73], resulting in reduced levels of physical activity compared to the recommended levels [74].

In the study of Salem *et al*. [66], which is briefly described in the balance section, the results showed a significant improvement in gait speed in patients with MS after the end of the hydrotherapy program. From the literature review, no other study was identified on the effect of hydrotherapy on gait in people with MS.

## 3. Discussion

The main purpose of this study was to review the literature on the effect of hydrotherapy on characteristic symptoms of MS such as fatigue, pain and spasticity as well as on functional characteristics such as balance and gait. The results show that there is a relative lack of literature on the use of hydrotherapy as a physiotherapy tool in MS and its effect on all the aforementioned factors. The few studies that have been conducted either include a small number of participants, do not report detailed results, or the control group is absent. However, hydrotherapy is proposed as an effective and enjoyable rehabilitation method for patients with MS, which can reduce the levels of fatigue, pain and spasticity and improve both balance and gait parameters.

The effect of hydrotherapy on fatigue in people with MS can be explained by two mechanisms. The first one is that because MS patients are sensitive to heat and symptoms worsen in hot environments, pool water can lower body temperature and increase exercise tolerance compared to land exercise programs. The second is that water buoyancy reduces gravity and resistance to body movements and helps MS patients engage in physical activity for longer periods of time with less fatigue [34].

Regarding pain, hydrotherapy programs can reduce pain in patients with MS and this effect is reported to be maintained up to 10 weeks after the end of the programs [75, 76]. Spasticity, which has a significant impact on overall disability in MS, is significantly improved with hydrotherapy due to the fact that patients are able to perform more movements as they immerse themselves in water [77]. Increasing the level of exercise also has a positive effect on fatigue [78].

In patients with MS, loss of balance is a major problem due to reduced power and motor control [79]. Therefore, the risk of fractures from falls in patients with MS increases by 2 to 3.5 compared to healthy individuals [80]. Hydrotherapy programs can improve balance as evidenced by BBS scores [64, 66]. However, no studies longer than eight weeks are available [64]. A limitation of the BBS is that it does not assess the vertical axis or cognitive factors that affect balance, thus affecting the risk of falling [81].

Targeted hydrotherapy programs that include specific exercises can improve gait speed in patients with MS [66]. This improvement may be due to the appropriate combination of exercises and the properties of water as well as the fact that exercises can be performed by patients with MS in water, which cannot be performed on land [82].

## 4. Conclusions

Hydrotherapy is proposed as a safe, effective and enjoyable method of rehabilitation in patients with MS to improve fatigue, pain, spasticity, balance and gait as evidenced by studies. Furthermore, no hydrotherapy-related injuries, accidents or side effects have been reported. However, longer studies are needed with a larger number of participants that will include, in addition to hydrotherapy programs, land exercise programs in order to produce comparable results.

## 5. References


1. Ford H. Clinical presentation and diagnosis of multiple sclerosis. Clinical medicine (London, England) 2020;20(4):380-3.
2. Hughes CM, Smyth S, Lowe-Strong AS. Reflexology for the treatment of pain in people with multiple sclerosis: a double-blind randomised sham-controlled clinical trial. Mult Scler 2009;15(11):1329-38.
3. Corvillo I, Varela E, Armijo F, Alvarez-Badillo A, Armijo O, Maraver F. Efficacy of aquatic therapy for multiple sclerosis: a systematic review. Eur J Phys Rehabil Med 2017;53(6):944-52.
4. Belbasis L, Bellou V, Evangelou E, Ioannidis JPA, Tzoulaki I. Environmental risk factors and multiple sclerosis: an umbrella review of systematic reviews and meta-analyses. The Lancet Neurology 2015;14(3):263-73.
5. Amato MP, Derfuss T, Hemmer B, Liblau R, Montalban X, Soelberg Sorensen P *et al*. Environmental modifiable risk factors for multiple sclerosis: Report from the 2016 ECTRIMS focused workshop. Mult Scler 2018;24(5):590-603.
6. Handel AE, Williamson AJ, Disanto G, Handunnetthi L, Giovannoni G, Ramagopalan SV. An updated meta-analysis of risk of multiple sclerosis following infectious mononucleosis. PLoS One, 2010, 5(9).
7. Handel AE, Williamson AJ, Disanto G, Dobson R, Giovannoni G, Ramagopalan SV. Smoking and multiple sclerosis: an updated meta-analysis. PLoS One 2011;6(1):e16149.
8. Simpson S, Jr., Blizzard L, Otahal P, Van der Mei I, Taylor B. Latitude is significantly associated with the prevalence of multiple sclerosis: a meta-analysis. J Neurol Neurosurg Psychiatry 2011;82(10):1132-41.
9. Ramagopalan SV, Dobson R, Meier UC, Giovannoni G. Multiple sclerosis: risk factors, prodromes, and potential causal pathways. The Lancet Neurology 2010;9(7):727-39.
10. Schiess N, Calabresi PA. Multiple Sclerosis. Semin Neurol 2016;36(4):350-6.
11. Buchanan RJ, Minden SL, Chakravorty BJ, Hatcher W, Tyry T, Vollmer T. A pilot study of young adults with multiple sclerosis: demographic, disease, treatment, and psychosocial characteristics. Disabil Health J 2010;3(4):262-70.
12. Petajan JH, White AT. Recommendations for physical activity in patients with multiple sclerosis. Sports medicine (Auckland, NZ) 1999;27(3):179-91.
13. Larocca NG. Impact of walking impairment in multiple sclerosis: perspectives of patients and care partners. The patient 2011;4(3):189-201.
14. Algahtani HA, Shirah BH, Alzahrani FA, Abobaker HA, Alghanaim NA, Manlangit JS, Jr. Quality of life among

multiple sclerosis patients in Saudi Arabia. Neurosciences (Riyadh) 2017;22(4):261-6.
15. Learmonth YC, Ensari I, Motl RW. Physiotherapy and walking outcomes in adults with multiple sclerosis: systematic review and meta-analysis. Physical Therapy Reviews 2016;21(3-6):160-72.
16. Łuszczyńska A, Kuliński W. Physiotherapy in multiple sclerosis. Medical Studies 2015;3:168-77.
17. Kottaras A, Lytras D, Kottaras S, Iakovidis P. Effect of Aquatic Physiotherapy on Functioning, Balance Performance, Motor Performance, and Health-Related Quality of Life in Patients with Parkinson's Disease: A Review of Structure and Dosimetry of Aquatic Exercise Programs. Critical Reviews™ in Physical and Rehabilitation Medicine 2021;33(1):65-84.
18. Kim EK, Lee DK, Kim YM. Effects of aquatic PNF lower extremity patterns on balance and ADL of stroke patients. Journal of physical therapy science 2015;27(1):213-5.
19. Alikhajeh Y, Hosseini SRA, Moghaddam A. Effects of Hydrotherapy in Static and Dynamic Balance Among Elderly Men. Procedia - Social and Behavioral Sciences 2012;46:2220-4.
20. Roehrs TG, Karst GM. Effects of an Aquatics Exercise Program on Quality of Life Measures for Individuals with Progressive Multiple Sclerosis. Journal of Neurologic Physical Therapy, 2004, 28(2).
21. Kargarfard M, Eetemadifar M, Mehrabi M, Maghzi AH, Hayatbakhsh MR. Fatigue, depression, and health-related quality of life in patients with multiple sclerosis in Isfahan, Iran. European journal of neurology 2012;19(3):431-7.
22. Mills RJ, Young CA. A medical definition of fatigue in multiple sclerosis. QJM: monthly journal of the Association of Physicians 2008;101(1):49-60.
23. Jackson MF, Quaal C, Reeves MA. Effects of multiple sclerosis on occupational and career patterns. Axone (Dartmouth, NS) 1991;13(1):16-7, 20-2.
24. Iriarte J, Katsamakis G, de Castro P. The Fatigue Descriptive Scale (FDS): a useful tool to evaluate fatigue in multiple sclerosis. Mult Scler 1999;5(1):10-6.
25. Fisk JD, Pontefract A, Ritvo PG, Archibald CJ, Murray TJ. The impact of fatigue on patients with multiple sclerosis. The Canadian journal of neurological sciences Le journal canadien des sciences neurologiques 1994;21(1):9-14.
26. Fisk JD, Ritvo PG, Ross L, Haase DA, Marrie TJ, Schlech WF. Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. Clinical infectious diseases: An official publication of the Infectious Diseases Society of America 1994;18(1):S79-83.
27. Rottoli M, La Gioia S, Frigeni B, Barcella V. Pathophysiology, assessment and management of multiple sclerosis fatigue: an update. Expert Rev Neurother 2017;17(4):373-9.
28. Roelcke U, Kappos L, Lechner-Scott J, Brunnschweiler H, Huber S, Ammann W *et al*. Reduced glucose metabolism in the frontal cortex and basal ganglia of multiple sclerosis patients with fatigue: a 18F-fluorodeoxyglucose positron emission tomography study. Neurology 1997;48(6):1566-71.
29. Bakshi R, Shaikh ZA, Miletich RS, Czarnecki D, Dmochowski J, Henschel K *et al*. Fatigue in multiple sclerosis and its relationship to depression and neurologic disability. Mult Scler 2000;6(3):181-5.
30. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Archives of neurology 1989;46(10):1121-3.
31. Michielsen HJ, De Vries J, Van Heck GL. Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. Journal of psychosomatic research 2003;54(4):345-52.
32. Penner IK, Raselli C, Stöcklin M, Opwis K, Kappos L, Calabrese P. The Fatigue Scale for Motor and Cognitive Functions (FSMC): validation of a new instrument to assess multiple sclerosis-related fatigue. Mult Scler 2009;15(12):1509-17.
33. Doward LC, Meads DM, Fisk J, Twiss J, Hagell P, Oprandi NC *et al*. International development of the Unidimensional Fatigue Impact Scale (U-FIS). Value in health: the journal of the International Society for Pharmacoeconomics and Outcomes Research 2010;13(4):463-8.
34. Kargarfard M, Etemadifar M, Baker P, Mehrabi M, Hayatbakhsh R. Effect of aquatic exercise training on fatigue and health-related quality of life in patients with multiple sclerosis. Arch Phys Med Rehabil 2012;93(10):1701-8.
35. Merskey H, Bogduk N. Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms. 2nd ed. Seattle: IASP Press, 1994.
36. Khan F, Pallant J. Chronic pain in multiple sclerosis: prevalence, characteristics, and impact on quality of life in an Australian community cohort. The journal of pain: official journal of the American Pain Society 2007;8(8):614-23.
37. Heckman-Stone C, Stone C. Pain management techniques used by patients with multiple sclerosis. The journal of pain: official journal of the American Pain Society 2001;2(4):205-8.
38. Stenager E, Knudsen L, Jensen K. Acute and chronic pain syndromes in multiple sclerosis. Acta neurologica Scandinavica 1991;84(3):197-200.
39. Foley PL, Vesterinen HM, Laird BJ, Sena ES, Colvin LA, Chandran S *et al*. Prevalence and natural history of pain in adults with multiple sclerosis: systematic review and meta-analysis. Pain 2013;154(5):632-42.
40. Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW *et al*. Neuropathic pain: redefinition and a grading system for clinical and research purposes. Neurology 2008;70(18):1630-5.
41. Al-Araji AH, Oger J. Reappraisal of Lhermitte's sign in multiple sclerosis. Mult Scler 2005;11(4):398-402.
42. Truini A, Barbanti P, Pozzilli C, Cruccu G. A mechanism-based classification of pain in multiple sclerosis. Journal of neurology 2013;260(2):351-67.
43. Castro-Sanchez AM, Mataran-Penarrocha GA, Lara-Palomo I, Saavedra-Hernandez M, Arroyo-Morales M, Moreno-Lorenzo C. Hydrotherapy for the treatment of pain in people with multiple sclerosis: a randomized controlled trial. Evid Based Complement Alternat Med 2012;2012:473963.
44. Compston A, Coles A. Multiple sclerosis. Lancet (London, England) 2002;359(9313):1221-31.
45. Rizzo MA, Hadjimichael OC, Preiningerova J, Vollmer TL. Prevalence and treatment of spasticity reported by multiple sclerosis patients. Mult Scler 2004;10(5):589-95.
46. Lance JW. The control of muscle tone, reflexes, and

movement: Robert Wartenberg Lecture. Neurology 1980;30(12):1303-13.
47. Gunn H, Creanor S, Haas B, Marsden J, Freeman J. Risk factors for falls in multiple sclerosis: an observational study. Mult Scler 2013;19(14):1913-22.
48. Milinis K, Tennant A, Young CA. Spasticity in multiple sclerosis: Associations with impairments and overall quality of life. Mult Scler Relat Disord 2016;5:34-9.
49. Zettl UK, Henze T, Essner U, Flachenecker P. Burden of disease in multiple sclerosis patients with spasticity in Germany: mobility improvement study (Move I). The European journal of health economics: HEPAC: health economics in prevention and care 2014;15(9):953-66.
50. Galea MP. Physical modalities in the treatment of neurological dysfunction. Clinical neurology and neurosurgery 2012;114(5):483-8.
51. Barnes M, Kocer S, Murie Fernandez M, Balcaitiene J, Fheodoroff K. An international survey of patients living with spasticity. Disabil Rehabil 2017;39(14):1428-34.
52. Adams MM, Hicks AL. Spasticity after spinal cord injury. Spinal cord 2005;43(10):577-86.
53. Currie R. Spasticity: a common symptom of multiple sclerosis. Nursing standard (Royal College of Nursing (Great Britain): 1987) 2001;15(33):47-52. quiz 4-5.
54. Amatya B, Khan F, La Mantia L, Demetrios M, Wade DT. Non pharmacological interventions for spasticity in multiple sclerosis. Cochrane Database Syst Rev 2013(2):CD009974.
55. Huxham FE, Goldie PA, Patla AE. Theoretical considerations in balance assessment. The Australian journal of physiotherapy 2001;47(2):89-100.
56. Kalron A, Dvir Z, Achiron A. Effect of a cognitive task on postural control in patients with a clinically isolated syndrome suggestive of multiple sclerosis. Eur J Phys Rehabil Med 2011;47(4):579-86.
57. Mazumder R, Murchison C, Bourdette D, Cameron M. Falls in people with multiple sclerosis compared with falls in healthy controls. PLoS One 2014;9(9):e107620.
58. Daubney ME, Culham EG. Lower-extremity muscle force and balance performance in adults aged 65 years and older. Physical therapy 1999;79(12):1177-85.
59. Prosperini L, Giannì C, Fortuna D, Marchetti MR, Pozzilli C. Oral dalfampridine improves standing balance detected at static posturography in multiple sclerosis. Multiple sclerosis international 2014;2014:802307.
60. Cattaneo D, Regola A, Meotti M. Validity of six balance disorders scales in persons with multiple sclerosis. Disabil Rehabil 2006;28(12):789-95.
61. Cattaneo D, Jonsdottir J, Zocchi M, Regola A. Effects of balance exercises on people with multiple sclerosis: a pilot study. Clinical rehabilitation 2007;21(9):771-81.
62. Silkwood-Sherer D, Warmbier H. Effects of hippotherapy on postural stability, in persons with multiple sclerosis: a pilot study. Journal of neurologic physical therapy: JNPT 2007;31(2):77-84.
63. Rogers ME, Rogers NL, Takeshima N, Islam MM. Methods to assess and improve the physical parameters associated with fall risk in older adults. Preventive medicine. 2003;36(3):255-64.
64. Kargarfard M, Shariat A, Ingle L, Cleland JA, Kargarfard M. Randomized Controlled Trial to Examine the Impact of Aquatic Exercise Training on Functional Capacity, Balance, and Perceptions of Fatigue in Female Patients With Multiple Sclerosis. Arch Phys Med Rehabil 2018;99(2):234-41.
65. Majdinasab N, Nakhostin-Mortazavi A, Bahadoram M, Pouretezad M, Afraz PJ *et al*. Effect of Aquatic Therapy on Functional Balance in Patients with Multiple Sclerosis: A Randomized Controlled Trial, 2016, 3.
66. Salem Y, Scott AH, Karpatkin H, Concert G, Haller L, Kaminsky E *et al*. Community-based group aquatic programme for individuals with multiple sclerosis: a pilot study. Disabil Rehabil 2011;33(9):720-8.
67. Johanson DC, Taieb M. Plio-Pleistocene hominid discoveries in Hadar, Ethiopia. Nature 1976;260(5549):293-7.
68. Fritz S, Lusardi M. White paper: walking speed: the sixth vital sign. Journal of geriatric physical therapy 2001-2009;32(2):46-9.
69. Heesen C, Böhm J, Reich C, Kasper J, Goebel M, Gold SM. Patient perception of bodily functions in multiple sclerosis: gait and visual function are the most valuable. Mult Scler 2008;14(7):988-91.
70. Hobart J, Lamping D, Fitzpatrick R, Riazi A, Thompson A. The Multiple Sclerosis Impact Scale (MSIS-29): a new patient-based outcome measure. Brain 2001;124(5):962-73.
71. Sosnoff JJ, Sandroff BM, Motl RW. Quantifying gait abnormalities in persons with multiple sclerosis with minimal disability. Gait & posture. 2012;36(1):154-6.
72. Comber L, Galvin R, Coote S. Gait deficits in people with multiple sclerosis: A systematic review and meta-analysis. Gait & posture. 2017;51:25-35.
73. Block VJ, Lizée A, Crabtree-Hartman E, Bevan CJ, Graves JS, Bove R, *et al*. Continuous daily assessment of multiple sclerosis disability using remote step count monitoring. Journal of neurology 2017;264(2):316-26.
74. Neven A, Vanderstraeten A, Janssens D, Wets G, Feys P. Understanding walking activity in multiple sclerosis: step count, walking intensity and uninterrupted walking activity duration related to degree of disability. Neurological sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology 2016;37(9):1483-90.
75. Kamioka H, Tsutani K, Okuizumi H, Mutoh Y, Ohta M, Handa S *et al*. Effectiveness of aquatic exercise and balneotherapy: a summary of systematic reviews based on randomized controlled trials of water immersion therapies. Journal of epidemiology 2010;20(1):2-12.
76. Hall J, Swinkels A, Briddon J, McCabe CS. Does aquatic exercise relieve pain in adults with neurologic or musculoskeletal disease? A systematic review and meta-analysis of randomized controlled trials. Arch Phys Med Rehabil 2008;89(5):873-83.
77. Barnes MP, Kent RM, Semlyen JK, McMullen KM. Spasticity in multiple sclerosis. Neurorehabilitation and neural repair 2003;17(1):66-70.
78. Conklyn D, Stough D, Novak E, Paczak S, Chemali K, Bethoux F. A home-based walking program using rhythmic auditory stimulation improves gait performance in patients with multiple sclerosis: a pilot study. Neurorehabilitation and neural repair 2010;24(9):835-42.
79. Leroux A, Pinet H, Nadeau S. Task-oriented intervention in chronic stroke: changes in clinical and laboratory measures of balance and mobility. American journal of physical medicine & rehabilitation 2006;85(10):820-30.
80. Dias Quiterio AL, Carnero EA, Baptista FM, Sardinha LB. Skeletal mass in adolescent male athletes and nonathletes: relationships with high-impact sports. Journal of strength and conditioning research

2011;25(12):3439-47.
81. Sibley KM, Beauchamp MK, Van Ooteghem K, Straus SE, Jaglal SB. Using the systems framework for postural control to analyze the components of balance evaluated in standardized balance measures: a scoping review. Arch Phys Med Rehabil 2015;96(1):122-32.e29.
82. Gabilan YP, Perracini MR, Munhoz MS, Gananç FF. Aquatic physiotherapy for vestibular rehabilitation in patients with unilateral vestibular hypofunction: exploratory prospective study. Journal of vestibular research: equilibrium & orientation 2008;18(2-3):139-46.