



The importance of managing symptoms to improve the quality of life of persons with multiple sclerosis

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Importance of symptom management in MS clinical practice

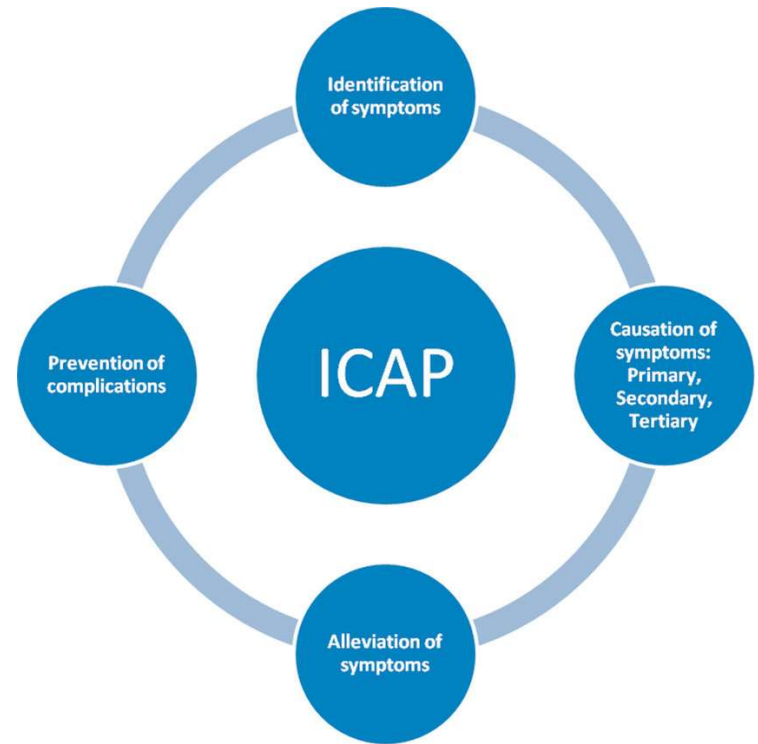
- Despite advances in DMT treatment, PwMS experience a variety of often progressive and disabling symptoms.¹
- Symptoms negatively impact many aspects of a PwMS life including activities of daily living, social relationships, jobs and HRQoL.¹⁻⁴
- Patient care should individualize symptom management by individual priorities.⁵

DMT, disease modifying therapy; HRQoL, health-related quality of life; MS, multiple sclerosis; PwMS, persons with multiple sclerosis;

1. Gil-González I, et al. *BMJ Open*. 2020;10(11):e041249; 2. Raggi, et al. *Disabil Rehabil*. 2016;38(10):936-44. 3. Buzaid A, et al. *Phys Med Rehabil Clin N Am*;2013;24(4):629-38; 4. Hakim EA, et al. *Disabil Rehabil*. 2000;22(6):288-93. 5. Ben-Zacharia AB, et al. *Mount Sinai Journal Of Medicine*. 2011;78:176-191.

Symptom management in MS clinical practice

- Symptoms can be recognized and managed using the ICAP method^{1,2}:
 - **I**dentification of symptoms.
 - **C**ausation of symptoms (primary, secondary or tertiary).
 - **A**lleviation of symptoms.
 - **P**revention of complications.



1. Cohen BA, et al. Neurology. 2008;71(24 Suppl 3):S14-20; 2. Ben-Zacharia AB, et al. Mount Sinai Journal Of Medicine. 2011;78:176-191.

Common MS symptoms and their impact

Spasticity

(up to 85% PwMS)

Impact: contributes to gait disorders, falls, fatigue, spasms, pain¹

Fatigue

(90% PwMS)

Impact: leading cause of decreased HRQoL³

Bladder dysfunction

(70% PwMS)

Impact: Increased incidence of UTI⁶

Emotional issues

(13–50% PwMS)

including depression and anxiety

Impact: suicidality, drug abuse⁶

Chronic pain

(~45% PwMS)

Impact: short term: daily activities and mood; Long term: increased disability²

Sleep problems

(25–54% PwMS)⁴

Impact: contributes to fatigue, pain and the development of comorbidities^{4,5}

Cognitive issues

(50% PwMS)

Impact: deficits in processing speed, attention, memory, language⁶

PwMS, persons with multiple sclerosis; MS, multiple sclerosis; HRQoL, health-related quality of life; UTI, urinary tract infections

1. Rizzo MA, et al. *Mult Scler* 2004;10:589-595; 2. Ehde DM, et al. *Mult Scler*. 2003;9:605-11; 3. Janardhan V, Bakshi R. *J Neurol Sci*. 2002;205:51-8. 4. Brass AD, et al. *Sleep Med Rev*. 2010;14(2):121-9. 5. Krupp L, et al. *Mult Scler*. 2006;12:367-8; 6. Sammarco AG, et al. *J Neurol Neurophysiol* 2014;5:3. 7. Silveira C, et al. *Psychiatry Investig*. 2019;16(12):877-888.

Challenges of symptom management in MS clinical practice

- MS symptoms can present in well-recognized clusters, or as interrelated or individual symptoms.^{1,2}
 - This can lead to difficulty distinguishing the cause of symptoms and prioritizing treatment.
- Personalized care is challenging:
 - Most symptoms are invisible, difficult to describe and hard to distinguish from the disease.
 - Outcome measures are frequently generic and not individualized.³
 - There can be mismatch between patient and clinician priorities for symptom management.⁴
 - There are few biomarkers to guide treatment decisions.⁵

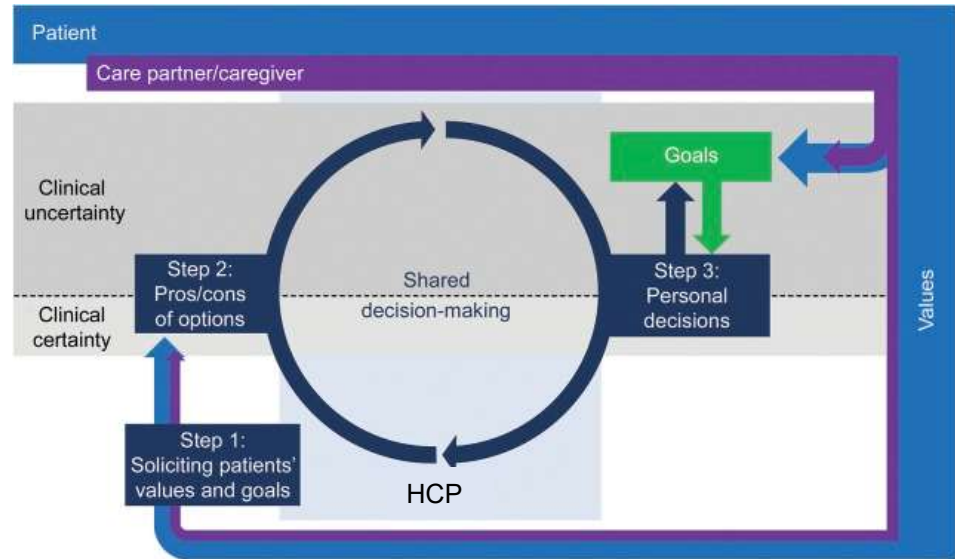
Example clusters ¹
Leg weakness
Gait imbalance
Spasticity
Bladder and bowel
Sexual dysfunction
Interrelated ¹
Fatigue
Individual ¹
Blurred vision
Diplopia
Nystagmus

MS, multiple sclerosis.

1. Crabtree-Hartman E. *Neurol Clin.* 2018;36:197–218; 2. Fernández O, et al. *Front Neurol.* 2020;17:11:152. 3. D'Amico E, et al. *Mult Scler Relat Disord.* 2019. 33:61-66; 4. Tintore M, et al. *Patient Prefer Adherence.* 2017;11: 33–45.; 5. Gafson A, et al. *Multi Scler.* 2017;23(3):362-369.

Shared decision-making to optimize the management of MS symptoms

- In shared decision-making, clinicians and patients discuss available efficacy and safety evidence and make a decision together based on the patient's values and preferences.¹
- PwMS have unmet information needs and desire more education about MS symptoms, prognosis, and management than they currently receive.^{2,3}



Framework for patient engagement in clinical encounters⁴

HCP, healthcare practitioner; MS, multiple sclerosis; PwMS, persons with MS;

1. Frosch DL, Kaplan RM. *Am J Prev Med* 1999;17:85–294; 2. Forbes A, et al. *J Adv Nurs* 2007;58:11–22; 3. Lorefice L, et al. *BMC Neurol* 2013; 3:177.

4. Armstrong MJ, et al. *Neurol Clin Pract*. 2016; 6(2):190–197.

Management of multiple sclerosis symptoms in clinical practice

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Symptom management differs from disease modification in MS care

- DMTs are used to reduce inflammatory disease activity and its long-term clinical consequences.¹
- Symptomatic treatments are used for the amelioration of MS symptoms affecting functional abilities and HRQoL.¹
- However, for most symptomatic therapies, the evidence base for clinical efficacy in patients with MS is weak.¹
- There are a limited number of FDA-approved symptomatic therapies in MS.
- Several different pharmacological agents are used off-label to treat the symptoms of MS.²

DMT, disease-modifying therapy; HRQoL health-related quality of life; MS, multiple sclerosis;

1. Filippi M, et al. Nat Rev Dis Primers. 2018;8;4:43; 2. Murphy KL, et al. Multiple Sclerosis: Perspectives in Treatment and Pathogenesis [Internet]. Brisbane (AU): Codon Publications; 2017. Chapter 4.

Examples of pharmacologic and non-pharmacologic management of MS symptoms

Fatigue

Stimulants

Modafinil, amantadine, methylphenidate had similar efficacy to placebo in the TRIUMPHANT-MS RCT.¹

Exercise and CBT

A SLR found that exercise improves HRQoL and activities of daily living vs no exercise.²

An SLR found that CBT has a moderately positive short-term effect.³

Spasticity

Muscle relaxants

Small-scale (n=15–22) RCTs indicated that gabapentin improved measures of spasticity vs placebo,^{4,5} with larger RCTs of baclofen⁶ and botulinum^{7,8} also demonstrating benefit.

Cannabinoids

An RCT of oral cannabinoids has indicated some self-reported spasticity improvement,⁹ and RCTs of oromucosal spray of CBD and THC have indicated some self-reported spasticity improvement.^{10,11}

Neuropathic pain

Anti-depressants

TCAs, SSRIs and SNRIs, including duloxetine have all shown efficacy in treating neuropathic pain.^{12,13}

Anti-convulsants

Small clinical trials indicate incomplete pain relief with anti-convulsants and tolerance issues.¹²

Cannabinoids

A small-scale (n=24) RCT demonstrated dronabinol treatment significantly reduced pain.¹⁴

Symptom management is important even in the age of DMTs

- DMTs may lessen symptoms, reduce relapses, and delay disability progression in MS. However, many DMTs produce only modest improvements in function and HRQoL.^{1,2}
- In PwMS receiving DMTs, symptoms and HRQoL may improve with additional therapies that treat specific symptoms, with the aim of improving patient function and the ability to perform the activities of daily life.³
 - For example, mobility impairment has been reported as one of the worst aspects of MS.^{3,4}
 - However, almost half of patients treated with DMTs reported no improvement in mobility.³

What is the future of symptom management in MS?

- As most pharmacological therapies are being used off-label to manage MS symptoms, there is a clear need for novel FDA-approved symptomatic therapies in MS.
- Non-pharmaceutical therapies are available that can improve the symptoms of fatigue, poor functionality, balance, and HRQoL but further evidence to support them is required.¹
 - Physical activity
 - Rehabilitation
 - Resistance training

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