

ACE BRIEF FOR NEW AND EMERGING HEALTH TECHNOLOGIES

Portable Neuromodulation Stimulator (PoNS) for treating gait deficit due to multiple sclerosis

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This briefing presents independent research by the ACE. It reflects the evidence available at the time of writing based on a limited literature search. It does not involve critical appraisal and is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered. The views expressed are those of the author and not necessarily those of the ACE, or the Ministry of Health.



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Summary of Key Points

- Multiple sclerosis (MS) is a chronic autoimmune condition affecting the central nervous system, causing motor impairment underpinned by balance and gait difficulties in patients with MS.
- Standard of care (SOC) for these patients includes corticosteroids, disease-modifying therapies and symptomatic management such as physiotherapy, to improve motor impairment. However, treatment success with physiotherapy is limited by lower physical capability of patients with MS which challenges their adherence to outpatient rehabilitation appointments.
- Portable Neuromodulation Stimulator (PoNS) is a non-implantable neurostimulator that delivers electrical impulses translingually to cranial nerves to upregulate cerebral cortical activity in areas that mediate motor function to provide treatment of motor deficits. It is indicated for short-term treatment of gait deficit due to mild to moderate symptoms from MS in patients ≥ 22 years as an adjunct to a supervised exercise programme.
- Key evidence included two small randomised controlled trials (RCTs; total $n=34$; up to 14 weeks follow-up) comparing PoNS plus physiotherapy (PoNS arm) to physiotherapy plus a sham device (control arm). The trials suggest that PoNS was safe with some benefits in improving motor outcomes.
 - No serious adverse events (AEs) were reported, with all AEs resolved without complications.
 - Using the sensory organisation test to assess balance, one trial demonstrated improvements from baseline at 14 weeks for both arms, with statistically significant improvement detected only for the PoNS arm ($p<0.001$) but not for the control arm ($p<0.06$). No between arms difference in improvement in balance was reported in the study.
 - Using dynamic gait index, improvement from baseline was demonstrated for gait in both arms. However, inconsistent findings were reported for between arms comparison, with one trial showing statistically greater improvement at week 14 ($p<0.001$) in the PoNS arm compared to the control arm and no between arms difference in the other.
- Key limitations include the small sample sizes of the RCTs, with baseline imbalances in disease-specific factors such as MS duration between arms, short follow-up time, and limited between-group comparisons reported.
- Cost-effectiveness of PoNS remains unclear. In the US, the cost of the PoNS system is estimated to be USD\$25,700 (SGD\$34,960) while in Canada, PoNS programme costs between CAD\$10,000 (SGD\$9,479) and CAD\$15,000 (SGD\$14,219), depending on the clinic where treatment is provided. It is not clear what the programme cost entails or if this cost includes the PoNS system.
- While local clinical experts indicated the clinical need given the debilitating nature of MS, they opined that uptake of the technology would be guided by strength of recommendations from clinical practice guidelines (CPGs). As of June 2025, no CPGs have mentioned PoNS use in patients with MS.

I. Background

Multiple sclerosis (MS) is a chronic autoimmune condition where the immune system attacks myelin, the protective sheath around nerve fibres in the brain and spinal cord. The loss of myelin forms scar tissue known as sclerosis and disrupts nerve signals, affecting brain-body communication.¹ There are four types of MS, relapsing-remitting (RRMS), where patients experience relapses with new or worsening symptoms followed by periods of recovery; primary progressive MS (PPMS), characterised by steady disability progression without relapses; secondary progressive MS (SPMS), where patients may develop progressive disability after initial RRMS; and clinically isolated syndrome (CIS), where patients experience first-time symptoms but do not meet full MS diagnostic criteria.² Locally, a diagnosis of MS is based on the McDonald 2017 criteria, which combine clinical, imaging and laboratory evidence.³ Patients with MS experience various symptoms, including fatigue, vision problems, memory issues, numbness, and motor issues (underpinned by poor balance and coordination, and gait dysfunction).¹

In Singapore, based on data from public hospitals in 2020, there were approximately 260 adults and three children living with MS.⁴ The disease burden is significant, with global MS-related disability-adjusted life years increasing by 59.7% in the 30 years between 1990 and 2019.⁵ Moreover, patients with MS have an 80% higher risk of mortality than individuals without MS, after adjusting for other demographic and clinical factors.⁶ In particular, motor impairment is prevalent, presenting in 50% to 80% of patients with MS through balance and gait dysfunction.⁷ Within 10 to 15 years of an initial diagnosis, about 80% of people with MS develop gait problems.⁸

The current standard of care (SOC) for MS includes corticosteroids for acute relapses, disease-modifying therapies (DMT) to reduce relapses and disability,^{4,9} and may also include physiotherapy for patients with motor issues.¹⁰ While physical therapy shows evidence for improving functional outcomes,¹¹ its effectiveness as a standalone intervention is constrained by the lower physical capability of patients with MS which challenges their adherence to outpatient rehabilitation.¹² There is thus a need for more effective management strategies for people with MS, especially those aimed at improving balance and gait dysfunction.

II. Technology

Portable Neuromodulation Stimulator (PoNS; Solana Company, previously as Helius Medical Technologies) is a non-implantable device that triggers neural impulses to brain structures that control motor function to alleviate functional deficits due to MS.¹³ Specifically, the PoNS device delivers electrical impulses translingually to cranial nerves, to upregulate cerebral cortical activity in areas that mediate motor function such as the left motor cortex, the bilateral anterior cingulate and the dorsolateral prefrontal cortex areas. With sustained neuromodulation of these regions via the PoNS device during physiotherapy, the brain may consolidate exercise-induced changes and 'learn' (through neuroplasticity) to employ mechanisms and pathways to improve motor functional deficits.¹³

PoNS is a three-component device (Figure 1) comprising a controller – that rests on the patient's neck, a mouthpiece – that rests on top of the patient's tongue and a charger – that

connects to the controller.¹⁴ Patients can use the controller to regulate the degree of electrical stimulation being delivered by the mouthpiece. The controller also records usage data, including session duration and activities, through an accelerometer. The treating clinical team can connect the controller to a computer to view the usage data through PoNS proprietary software. The manufacturer's website did not provide information on the intended intensity of the treatment regime using PoNS. According to Canada's Drug Agency (CDA-AMC), each session should last for approximately 20 minutes and be used in conjunction with physiotherapy over a period of 14 weeks.¹³ After this time, the controller ceases stimulation and requires a healthcare professional to reset it, and the mouthpiece must be disposed of. The devices cannot be reused by another patient after 14 weeks, although it may be possible for the regimen to be repeated in the same patient using the same controller but with a new mouthpiece.¹⁴



Figure 1: The PoNS device (left); Illustration of the stimulation pathway triggered using PoNS during physiotherapy (right)

PoNS represents a novel, non-invasive technology that allows patients to improve their lost motor function through incorporation into existing physiotherapy regimens.

III. Regulatory and Subsidy Status

In May 2020, PoNS was granted the breakthrough device designation by the US Food and Drug Administration (FDA). Subsequently, in March 2021, it was granted De Novo clearance (DEN200050) by the FDA for short-term treatment of gait deficit due to mild to moderate symptoms from MS in patients ≥ 22 years.¹⁴ PoNS is a prescription-only device intended for use as an adjunct to a supervised therapeutic exercise programme.¹⁴

In the US,¹⁵ Anthem Blue Cross Blue Shield became the first major private healthcare insurer to provide reimbursement for the PoNS device in March 2025, with a reimbursement of USD\$15,420 (SGD\$20,976)¹ covering both the controller and mouthpiece.¹⁶

IV. Stage of Development in Singapore

¹ Based on Monetary Authority of Singapore's 2024 to 2025 exchange rate: USD\$1=SGD\$1.3603 and CAD\$1=SGD\$0.9479

- | | |
|--|--|
| ☒ Yet to emerge | ☐ Established |
| ☐ Investigational / Experimental
(subject of clinical trials or deviate
from standard practice and not
routinely used) | ☐ Established <i>but</i> modification in
indication or technique |
| ☐ Nearly established | ☐ Established <i>but</i> should consider for
reassessment (due to perceived
no/low value) |

V. Treatment Pathway

The clinical pathway for the management of patients with MS experiencing gait deficit is summarised in Appendix A. It is based on the Agency for Care Effectiveness (ACE)'s health technology assessment (HTA) on the use of DMTs for patients with MS and the National Institute for Health and Care Excellence (NICE)'s guidance on MS management in adults (NG220).^{4,17} The pathway has been validated by local clinical experts (Personal Communication: Senior Principal Physiotherapist from Singapore General Hospital, April 2025).

Briefly, in patients diagnosed with MS with gait deficit, MS relapses are managed with acute management strategies that include corticosteroids during relapses. For chronic management, patients might undergo both DMTs and symptomatic management. Typically, the latter includes physiotherapy (e.g. supervised aerobic and moderate progressive resistance activity), the use of mobility aids and/or assistive devices, as well as pharmacological interventions. Physiotherapy is conducted with the aim of improving functional outcomes, including mobility and muscular strength through strengthening, gait and balance training (Personal Communication: Senior Principal Physiotherapist from Singapore General Hospital, April 2025).¹¹

Local clinical expert opined that PoNS can be used in conjunction with physiotherapy, and may be introduced to patients experiencing any impairment that limits daily activities. Patients would not have to fail conventional physiotherapy before being considered for PoNS (Personal Communication: Senior Principal Physiotherapist from Singapore General Hospital, May 2025).

VI. Summary of Evidence

This assessment was conducted based on the Population, Intervention, Comparator and Outcome (PICO) criteria in Table 1. Literature searches were conducted using HTA databases, Cochrane Library and Embase. Key evidence includes two small prospective, double-blind, randomised controlled trials (RCTs) by Tyler, et al (2014)¹⁸ and Leonard, et al (2017)¹⁹. Both RCTs compared PoNS plus physiotherapy (PoNS arm) to physiotherapy with a sham device

(control arm), and assessed the effectiveness of PoNS on changes in motor function and functional neural imaging. In both studies, subjects underwent an intensive two-week in-lab phase requiring twice-daily training sessions five days per week. In Leonard et al, sessions were 90 minutes each and included warm-up, balance, gait, motor control exercises, and breathing and awareness techniques.¹⁹ In Tyler et al, subjects performed 20 minutes each of gait, balance and relaxation training with the device, as well as movement isolation exercises without the device.¹⁸ The in-lab phase was followed by a 12-week at-home phase with three sessions daily. In Leonard, et al¹⁸, five patients in the control arm crossed over to the PoNS group following the initial 14-week follow-up period (rollover arm) and were followed up for a further 14 weeks.¹⁹

It is worth noting that at baseline, MS duration differed significantly between the arms in both studies, with patients in the PoNS arm having a longer MS duration (24.1 years vs 13.1 years, $p=0.01$) in Tyler, et al¹⁸ but shorter duration (11.2 vs 22.3 years, $p=0.045$) in Leonard, et al.¹⁹ As MS duration is an important indicator for disease progression, it may confound the study results. Both trials were sponsored by the manufacturer, with the author of one of these trials being the co-inventor of PoNS.¹⁸ Detailed study characteristics of the key evidence sources are presented in Appendix B.

Table 1: Summary of PICO criteria

Population	Patients (≥ 22 years) with gait deficit due to MS
Intervention	PoNS + physiotherapy
Comparator	Physiotherapy
Outcome	Safety, clinical effectiveness (changes in motor function e.g. gait (gait speed, walking endurance), balance, neural imaging assessment, neuropsychological assessments, disability scores, QoL, other patient-related outcomes), cost and cost-effectiveness
Abbreviations: MS, multiple sclerosis; PoNS, Portable Neuromodulation Stimulator; QoL, quality of life.	

Safety

Safety outcomes were reported by Tyler, et al.¹⁸ Compared to the control arm, patients in the PoNS arm had higher rates of MS relapse (PoNS vs control, 20% vs 0%) but lower rates of minor illness (PoNS vs control, 10% vs 20%) that led to temporary suspension of training (Table 2). No formal statistical test was reported to compare the adverse event (AE) rate between the two arms, but all patients were able to resume training without complications. It is also unclear if these AEs were related to the use of the device.

Across both arms, all patients experienced salivation and 25% experienced mild headache and temporo-mandibular joint pain, which resolved following adoption of alternative swallowing strategies and placement of the PoNS or sham devices.

Table 2: Summary of adverse events

Adverse event	PoNS (n=10)	Control (n=10)
Salivation	100% (10/10)	100% (10/10)
Mild headache and temporo-mandibular joint pain	25% (5/20) ^a	
MS relapse leading to suspension of training	20% (2/10)	0% (0/10)
Minor illness leading to suspension of training	10% (1/10)	20% (2/10)

Abbreviation: PoNS, Portable Neuromodulation Stimulator.

Notes

a. Incidence per arm was not reported

Table adapted from Tyler (2014)¹⁸

Effectiveness

The effectiveness of PoNS therapy on motor function was assessed through balance and gait changes across both trials.^{18,19} Neural imaging of areas in the brain associated with motor function was also assessed in one study.¹⁹ No studies assessing disability scores and quality of life were identified. The details of measurement tools used, and their scoring systems can be found in Appendix C.

Balance

Leonard, et al¹⁸ used the sensory organisation test (SOT) to assess balance.¹⁹ While both groups showed improvement in scores over time, only the PoNS arm demonstrated significant improvement in SOT at 14 weeks compared to baseline ($p < 0.001$). However, the magnitude of change was not reported. For the five patients in the rollover arm, continued improvements in SOT scores were reported from week 14 (no PoNS) to final testing (14 weeks following rollover with PoNS). No between-group difference in improvement in balance was reported in the study.

Gait

In both included studies, improvement in gait from baseline was assessed by the dynamic gait index (DGI) score.^{18,19} Compared to baseline, findings from Tyler, et al¹⁷ showed both statistically and clinically significant improvements in DGI scores (≥ 4 DGI score improvement between baseline and that timepoint) by six weeks in the PoNS arm, with continued improvements until week 14 (mean DGI score at baseline: 8.90, week 14: 16.85; Table 3).¹⁸ In contrast, no statistically significant improvement in DGI scores from baseline was reported in the control arm, although a clinically significant improvement was reported at week 10. Compared to the control arm, the PoNS arm showed statistically greater improvement from baseline at week 14 (7.95 vs 3.45, $p < 0.001$).

In Leonard, et al¹⁸, no significant differences in DGI scores were reported between study arms. A non-significant increase in DGI score over time was reported for the PoNS arm (DGI score not reported). There was no difference in DGI score in the rollover arm during the three timepoints (baseline: 13.0, week 14: 13.6, final testing: 14.2).¹⁹

Table 3: Summary of gait outcome

Week	PoNS (DGI score ^a)			Control (DGI score ^a)			Difference between arms $\pm$ SD ^e
	Mean $\pm$ SD	Difference ^b	p-value	Mean $\pm$ SD	Difference ^b	p-value	
0 (baseline)	8.90 $\pm$ 2.85	—	—	11.95 $\pm$ 4.04	—	—	-3.05 $\pm$ 4.94
2	13.30 $\pm$ 3.92	4.40 ^c	0.056	14.95 $\pm$ 4.29	3.00	0.610	-1.65 $\pm$ 5.81

6	15.05 ± 3.53	6.15 ^c	0.003 ^d	15.63 ± 4.73	3.68	0.471	-0.58 ± 5.90
10	16.60 ± 3.95	7.70 ^c	<0.001 ^d	16.75 ± 5.20	4.80 ^c	0.166	-0.15 ± 6.53
14	16.85 ± 3.40	7.95 ^c	<0.001 ^d	15.40 ± 5.03	3.45	0.745	+1.45 ± 6.07
Abbreviations: DGI, Dynamic Gait Index; PoNS, Portable Neuromodulation Stimulator; SD, standard deviation. Notes: a. Eight item test assessing ability to modify gait in response to task demands. Scores range 0 to 24, with higher scores indicating better function b. Difference from baseline and that timepoint for DGI scores. c. Clinically significant (≥ 4) between baseline and that timepoint for DGI scores d. Statistically significant difference ($p < 0.05$) between baseline and that timepoint for DGI scores e. Difference in mean DGI score between PoNS and control arm, at each time point Table adapted from Tyler (2014) ¹⁸							

Other motor skills

As reported by Leonard, et al¹⁸, assessment of motor ability using the grooved pegboard test and movement sequencing showed no significant differences between arms.¹⁹

Neural activity from functional MRI

In the Leonard, et al study¹⁸, functional imaging analyses for a gait imagery task (i.e. mental imitation of different gait conditions displayed) showed increased activation in the bilateral premotor and motor regions of the brain. These areas are known to be involved in coordinating and executing movements.¹⁹ Neural activity was assessed using blood oxygen level-dependent (BOLD) signal. At 14 weeks, the PoNS arm showed significant increases from baseline in the left motor cortex ($p=0.024$) and left pre-motor cortex. In the control arm, significant BOLD changes were only observed in the bilateral premotor regions (left: $p=0.02$; right: $p=0.006$).

Cost-effectiveness

No economic analysis was identified for PoNS.

Ongoing trials

Additional studies including RCTs of larger sample size and longer follow-up period would be useful to validate the benefit of PoNS. Based on a scan of ongoing trials conducted on ScanMedicine database (NIHR Innovation Observatory; Table 4) as of March 2025, two ongoing trials were identified assessing the efficacy of PoNS, although their status is unknown.

A manufacturer-sponsored trial (PoNSTEP; NCT05437276) enrolling 38 patients (≥ 22 to 65 years) with gait deficit due to mild-to-moderate MS released early results (via press release) in end January 2025.²⁰ This trial demonstrated that use of PoNS improved gait compared to baseline. While this trial addresses some previously identified limitations through its larger sample size ($n=43$ planned) and extended follow-up period (six months), its single-arm design means that the relative benefit of adding PoNS to physiotherapy remains uncertain.

Another trial (NeuroMSTraLS; NCT05275049) identified was due to report results by mid-2023 according to the University of Oxford's FDA Amendments Act (FDAAA) trial tracker,²¹ but did not.

Table 4: Ongoing trials assessing efficacy of PoNS

Study (Trial ID)	Population & estimated enrolment	Brief description	Estimated study completion date	Remarks
PoNSTEP (NCT05437276)	Adults aged ≥22 to 65 years with a demonstrated gait deficit but can walk at least 10 metres with/without walking aids (n=43)	Prospective (six months follow-up), open-label, single-arm, observational study with all patients undergoing 14-weeks of physiotherapy combined with PoNS to assess adherence to PoNS.	July 2024	Sponsored by the manufacturer. Early results via press release released in end January 2025
NeuroMSTraLS (NCT05275049)	Adults aged 18 to 70 years with gait deficit due to MS but still able to walk (n=52)	Prospective randomised, blinded, controlled trial with active arm patients having physiotherapy with PoNS and patients in the control arm having physiotherapy with a control device. Study aims to assess the effect of additional PoNS therapy in improving walking and balance in patients with MS.	December 2022 Current status: Unknown ^a	Did not submit results to FDA, as of data reviews in February 2024. Study not sponsored by manufacturer
Abbreviation: PoNS, Portable Neuromodulation Stimulator. <u>Note:</u> a. According to the University of Oxford's FDA Amendments Act (FDAAA) trial tracker, the study was required to report results by mid-2023, but did not do so. ²¹				

Summary

The overall evidence base comprised two very small RCTs (sample sizes of 10 to 20 patients), with significant differences in MS duration at baseline between the groups detected. The studies were further limited by the short follow-up and limited reporting on between-group comparisons.

The studies showed that PoNS was generally safe, with all AEs resolved without complication. It is unclear whether any of the AEs were device-related. Both studies reported improvements in balance and gait for PoNS and control arms. One trial demonstrated statistically greater improvement from baseline at week 14 (7.95 vs 3.45, $p < 0.001$) in gait for the PoNS arm compared to the control arm, and no between-arms difference in improvement for balance. Increases in neural activities of brain regions associated with motor function over the 14-week period was also observed. The cost-effectiveness of PoNS remains uncertain.

Due to the short follow-up period, the sustained effect of these improvements is unclear. Moreover, with the sparse reporting of between-group comparisons, it is uncertain if PoNS with physiotherapy is superior to physiotherapy alone, as patients in both arms showed

improvements in some measures. The intense training program applied in the trials also creates potential adherence issues.

VII. Estimated Costs

In the US, the PoNS system costs approximately USD\$25,700 (SGD\$34,960)^a, with the mouthpiece costing USD\$7,900 (SGD\$10,746)^a and the controller costing USD\$17,800 (SGD\$24,213)^{a, 15}

In Canada, it was reported that a 14-week PoNS programme costs between CAD\$10,000 (SGD\$9,479)^a and CAD\$15,000 (SGD\$14,219),^a depending on the clinic where treatment is provided.¹³ It is not clear what the programme entails, and if this cost includes the PoNS system.

VIII. Implementation Considerations

There may be minimal implementation issues associated with integrating PoNS into existing healthcare practices, given that it is intended to be used as an adjunct to physiotherapy, which is already well-established for patients with MS. While initial training takes place in a clinical setting, the main considerations for adoption focus on ensuring proper training for home use, especially for patients with mobility limitations. The intensive nature of the training programme may present some challenges for patient adherence.

Additionally, healthcare providers will need to implement appropriate data protection and privacy measures to safeguard patient information stored in PoNS' proprietary software.

IX. Concurrent Developments

No other non-invasive neuromodulation technologies intended to be used as an adjunct to physiotherapy were identified to address gait deficit due to MS.

X. Additional Information

PoNS has also been approved for use in Australia and Canada to treat gait or balance deficits arising from mild to moderate traumatic brain injury and stroke.

Drawing from experience with robotic therapy in stroke rehabilitation, local clinical experts indicated that there is a strong patient preference for having access to new technology-based treatment options. This is particularly relevant for patients with MS who are likely to seek access to all available treatment options that could potentially reduce their disabilities, given the debilitating nature and progressive impact of the condition. However, it was shared that the adoption of new technologies such as PoNS by local care teams is typically influenced by the strength of clinical practice guidelines (CPG) recommendations (Personal Communication: Senior Principal Physiotherapist from Singapore General Hospital, May 2025). To date (June 2025), no CPGs for patients with MS include recommendations for the use of PoNS.

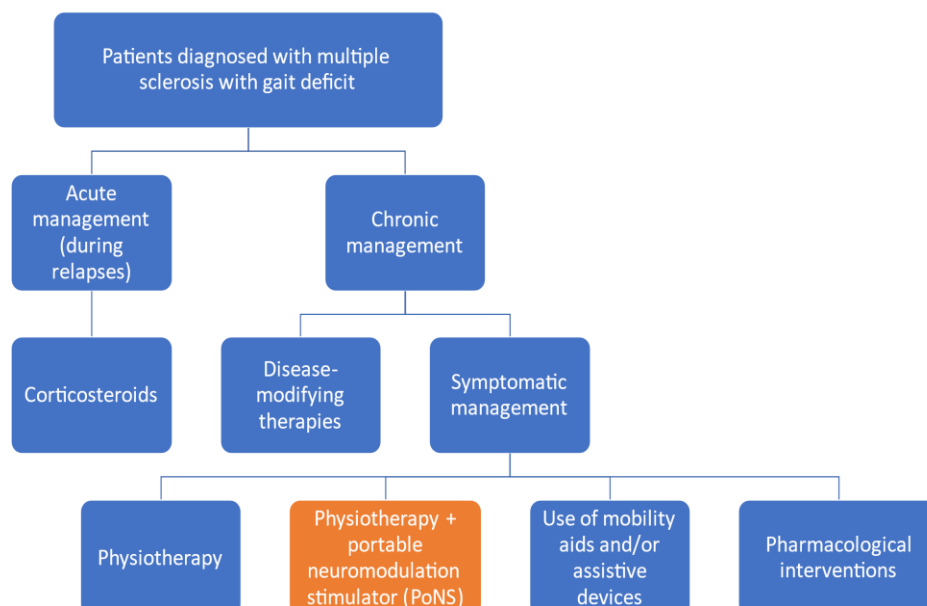
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Appendix

Appendix A: Clinical pathway for the use of PoNS, with current pathway in blue, and proposed pathway in orange



Appendix B: Details of evidence base

Study ID	Study type	Population	Follow-up	Intervention	Comparator
Leonard (2017) ¹⁹	Prospective, randomised, double-blind RCT	Adults with gait deficits due to MS (subtype NR) n= 7 active arm n=7 control arm	14 weeks	Physiotherapy with PoNS device	Physiotherapy with sham device
Tyler (2014) ¹⁸		Adults with gait deficits due to MS (subtypes: RRMS, PPMS, and SPMS) n= 5 active arm n=5 control arm			
Abbreviations: EDSS, Expanded Disability Status Scale; NR, not reported; PoNS, portable neuromodulation stimulator; PPMS, primary progressive multiple sclerosis ; RCT, randomised controlled trial; RRMS, relapsing–remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.					
<u>Notes:</u>					
a. For patient populations, Leonard (2017): PoNS arm had lower EDSS scores (4.2 ± 0.8) than in the control arm (4.8 ± 0.9) and had been living significantly longer with MS (22.3 years vs. 11.2 years). In Tyler (2014) PoNS arm had a higher EDSS score (5.3 ± 1.0) compared to the control arm (4.6 ± 1.1) and had been living significantly shorter with MS (24.1 ± 11.0 years versus 13.1 ± 6.7 years)					
b. For both studies, patients in both arms had a two-week in-lab phase followed by 12 weeks at home where patients continued exercises learned during the initial phase					

- c. Tyler (2014) implemented two standardised sessions daily with a structured program (including gait training with treadmill, balance training on floor/foam, and relaxation training) while Leonard (2017) conducted three daily sessions with patient-specific regimens. Leonard (2017) did not report on the general structure of each session
- d. Leonard (2017) conducted working memory re-training to assess the effect of working memory training with PoNS versus working memory training alone during the same time period as physiotherapy training using COGMED – a commercial computer-based working memory training software.²²

Appendix C: Effectiveness outcomes and corresponding measurement tools

Study ID	Outcome	Measurement tool	Definition/Description	Assessment timepoints	Clinical meaningfulness
Functional motor changes					
Leonard (2017) ¹⁹	Gait	DGI	Eight item test assessing ability to modify gait in response to task demands. Scores range 0 to 24, with higher scores indicating better function	Baseline, 2, 4, 6, 8, 10, 12, and 14 weeks	No data on MCID found for patients with MS. Information on MCID found for community-dwelling older adults. ²³ MCID for total study population was found to be 1.90. For patients with an initial score of <21, the MCID was 1.80, and for patients with an initial score >21, the MCID was 0.60.
Tyler (2014) ¹⁸				Baseline, 2, 6, 10, and 14 weeks	
Leonard (2017) ¹⁹	Balance	SOT	Stability measurement under six progressively difficult conditions. Easiest condition: patients standing on a fixed platform with their eyes open. Most difficult condition: swaying the patient's visual surround and platform surface.	Baseline, 2, 4, 6, 8, 10, 12, and 14 weeks	MCID was NR and no literature identified on this.
	Fine motor skills	Grooved Pegboard ²⁴	A pegboard test requiring complex visual-motor coordination where subjects must insert 25 pegs into holes with randomly positioned slots. Each peg has a ridge along one side that must be aligned properly with a groove in the hole before insertion.	Baseline and 14 weeks	
	NR	Movement sequencing	NR, and no literature found		

Neural activity					
Leonard (2017) ¹⁹	Neural activity	fMRI BOLD signal	Assess BOLD signals to quantify changes in brain activity in areas associated with motor function (bilateral premotor cortex and motor cortex) through measuring blood oxygen levels. ²⁵	Baseline, 14 weeks	MCID was NR and no literature identified on this
Abbreviations: BOLD, blood oxygenation level dependent; DGI, Dynamic Gait Index; fMRI, functional magnetic resonance imaging; MCID, minimally clinically important difference; NR, not reported; SOT, Sensory Organisation Test.					

Appendix D: Effectiveness of PoNS on working memory

Study ID	Outcome	Effect estimates
Leonard (2017) ¹⁹	COGMED score	- Both arms demonstrated significant improvements on COGMED scores ($p < 0.0001$) - No significant difference between arms with time - Trend for PoNS arm to benefit more, but this was not statistically significant ($p = 0.15$)
Abbreviations: PoNS, Portable Neuromodulation Stimulator.		
Notes:		
The authors describe that this training used the COGMED package, a commercial computer-based working memory training software.²²		