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Original article

Improving our understanding of the most important items of the Multiple Sclerosis Walking Scale-12 indicating mobility dysfunction: Secondary results from a RIMS multicenter study

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ABSTRACT

Background: The 12-item Multiple Sclerosis Walking Scale (MSWS-12) is currently the most widely validated, patient-reported outcome measure assessing patients' perception of the impact of multiple sclerosis (MS) on walking ability. To date, the majority of previous studies investigating the MSWS-12 have focused on the total score despite individual items being potentially informative. Therefore, our objective was to examine the associations between the individual items of the MSWS-12 and mobility and whether these associations depend on disability level.

Methods: Participants completed the MSWS-12, Two-Minute Walk Test (2MWT), Timed 25-Foot Walk (T25FW), Timed Up and Go Test (TUG) and the Four Square Step Test (FSST). Subsequently, they were divided into two groups according to their disability level, classified as either "mildly" or "moderately-severely" disabled. The correlation between individual items of the MSWS-12 and clinical measures of mobility were separately examined by Spearman's correlation coefficients; linear regression analyses were performed for each disability group, with/without adjusting for cognition, age and gender.

Results: 242 people with MS (PwMS), 108 mildly and 134 moderately-severely disabled, were included. Stronger correlations between the MSWS-12 items and mobility tests were found in the mildly disabled compared to the moderately-severely disabled group. The linear regression analysis showed that in the mildly disabled, item 9 (use of support outdoors) explained 35.4%, 30.8%, and 23.7% of the variance related to the 2MWT, T25FW and TUG, respectively. As for the moderately-severely disabled, the linear regression analysis presented a model which included item 8 (use of support indoors), explaining 31.6%, 18.0%, 20.2% and 9.5% of the variance related to the 2MWT, T25FWT, TUG and FSST, respectively.

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Conclusions: Items 8 and 9 of the MSWS-12 focusing on the patient's use of walking support in and outdoors, provide a robust indicator of mobility capabilities for mildly and moderately-severely disabled PwMS.

1. Introduction

Mobility impairment is one of the most serious and frequent concerns of people with multiple sclerosis (PwMS) (Frohman, 2003). Based on a survey of 1011 patients, 70% stated mobility impairment as the most challenging aspect of multiple sclerosis (MS) (Larocca, 2011). Various quantitative scales have been developed to assess mobility in PwMS. However, the 12-item Multiple Sclerosis Walking Scale (MSWS-12) is currently the most widely, qualitative, patient-reported outcome measure assessing the patients' perception of the impact of MS on walking ability (Kieseier and Pozzilli, 2012). The MSWS-12 is frequently employed in clinical trials, particularly in trials where the interventions are targeted at alleviating walking impairment (McGuigan and Hutchinson, 2004).

The MSWS-12 was developed by Hobart et al. (2003) study of 30 patient interviews, expert opinions, and literature reviews. The initial psychometric evaluation was based on 602 PwMS recruited from the MS Society's UK database. Further psychometric evaluation was performed on two hospital-based samples: people with primary progressive MS ($n = 78$) and people with relapses admitted for steroid treatments ($n = 54$) (Hobart et al., 2003). The MSWS-12 was more responsive than the Functional Assessment of the MS mobility scale, the 36-Item Short Form Health Survey Physical Functioning Scale, the Expanded Disability Status Scale (EDSS), the Timed 25 Foot-Walk (T25FW), and Guy's Neurologic Disability Scale lower limb disability item. In 2004, validity and responsiveness of the MSWS-12 was confirmed in a community sample of 149 PwMS and in 53 hospital outpatients (McGuigan and Hutchinson, 2004). Additional validation studies have reported a significant association between the MSWS-12 and accelerometer data (Motl et al., 2010a), energy cost of walking (Motl et al., 2010b) and spatiotemporal parameters of gait (Pilutti et al., 2013). Furthermore, we previously reported that the MSWS-12 is superior to short walking tests in detecting clinically meaningful improvement after physical rehabilitation (Baert et al., 2014).

Interestingly, the majority of previous studies investigating the MSWS-12 have focused on the total MSWS-12 score, despite individual items being potentially informative. Moreover, it may provide further insights into key questions that should be asked during consultations in order to obtain as much information as possible. Aside from translation and validation purposes, only a few studies have analysed the individual MSWS-12 items (Nakhostin et al., 2015; Mokkink et al., 2016; Marengo et al., 2019; Nilsagard et al., 2007). Sidovar et al., by analysing the individual items, aimed at mapping the MSWS-12 for use as a health-utility measure (Sidovar et al., 2013, 2016). The authors found that the EuroQol 5-dimension health-utility index scores can be predicted with reasonable precision by utilizing the MSWS-12 individual item scores. Nilsagård et al. examined the relationship between the individual items of the MSWS-12 and three clinical mobility measures (Four Square Step Test (FSST); Timed-Up and Go Cognitive, and the Berg Balance Scale) Nilsagard et al., 2007). The authors reported relatively low correlations, however, their concurrent validity measures were primarily targeting balance rather than walking, which can possibly explain the generally weak reported relationships.

Consequently, the aim of the present study was to further examine the construct validity of the MSWS-12 items according to disability level by performing a secondary analysis of data from a previous multicentre study (Baert et al., 2018). Specifically, our goal was to clarify whether certain items demonstrate a stronger relationship with objective mobility measures than others and whether this is dependent on patient disability level.

2. Material and methods

The present study reports a secondary analysis of Baert et al. (2018) previous study encompassing PwMS from 17 global MS centres in Europe and the United States. The authors previously reported on the responsiveness and clinically meaningful improvement of PwMS according to the disability level of 13 walking measures, including the MSWS-12 (Baert et al., 2018). The participating centres were all members of the European Rehabilitation in Multiple Sclerosis (RIMS) network. The Ethics Committee of the primary investigator (Hasselt University, Belgium) as well as the local ethics committees from each participating centre, approved this study.

2.1. Participants

Inclusion criteria included a definite diagnosis of MS (Polman et al., 2011) and an Expanded Disability Status Scale (EDSS) (Kurtzke., 1983) score of ≥ 2 and ≤ 6.5 as determined by neurologists or trained clinicians. Exclusion criteria included relapses and/or changes in disease-modifying treatment, and/or corticoid therapy within the last month, other medical conditions interfering with mobility (e.g., pregnancy or fractures), other neurological conditions causing permanent damage (e.g., stroke or Parkinson's disease), MS-like syndromes such as neuromyelitis optica, or the inability to understand and execute simple instructions related to physical testing or completion of the questionnaires. All subjects provided written informed consent.

2.2. MSWS-12

The MSWS-12, a valid questionnaire assessing walking ability in PwMS, is the most widely used patient-reported measure of perceived limitation in walking due to MS. Many studies recommend the use of the MSWS-12 due to its psychometric properties (Hobart et al., 2003; McGuigan and Hutchinson, 2004; Baert et al., 2014, 2018; Learmonth et al., 2013; Langeskov-Christensen et al., 2017). Each of the 12 items are rated on a scale ranging from 1 ('not at all') to 5 ('extremely'). Items cover different aspects of walking function and quality such as the ability to walk, walking speed, ability to run, ability to climb and descend stairs, ability to stand, balance, endurance, smoothness of gait, need for support (in and outdoors), effort and concentration required. Total calculated scores range from 12 to 60 and are converted into scores ranging from 0 to 100. Higher scores reflect a higher level of walking disability. Langeskov-Christensen et al. recently reported that the MSWS-12 captures impairments more gradually than the 2MWT and 6MWT in people with mild MS, thus, suggesting that the MSWS-12 is sensitive to impairments when evaluating walking even in people with mild MS (Langeskov-Christensen et al., 2017).

2.3. Cognitive status

All patients completed the Symbol Digit Modalities Test (SDMT), a neuropsychological test examining attention and speed of processing. Research studies have clearly supported the reliability and validity of the SDMT as a screening tool for cognitive impairment in PwMS (Benedict et al., 2017).

2.4. Clinical mobility tests

In addition to the MSWS-12 scale, four clinical walking and balance tests were completed: the Two-Minute Walk Test (2MWT), Timed Up and Go Test (TUG), Timed 25-Foot Walk (T25FW) and Four Square Step Test (FSST). The selected tests reflect a representative and relevant array of mobility performance in PwMS.

Two-Minute Walk Test (2MWT). The participants were instructed to perform the test ‘at their fastest speed’ and to cover as much distance as possible by walking up and down a 30-meter hallway. Participants were allowed to use their own walking aid. The 2MWT has been validated and used extensively in PwMS (Gijbels et al., 2010).

Timed Up and Go Test (TUG). The participants' starting point was determined after the subject had been seated in a standard height chair, with their back flush against the chair and their arms resting on the arm rests. The participant was then instructed to stand up, walk 3 m, turn around, walk back to the chair and sit down again. Timing began when the individual started to rise and ended when the person returned to the chair and sat down. The TUG is a valid measure of functional mobility in PwMS (Sebastiao et al., 2016).

Timed 25-Foot Walk (T25FW). The participants were instructed to walk a clearly marked 25-foot course as quickly and safely as possible. The T25FW has been validated as one of the three components of the Multiple Sclerosis Functional Composite (Fisher et al., 1999).

Four Square Step Test (FSST) has been validated in PwMS (Kalron and Givon, 2016). The FSST measures dynamic balance and clinically assesses the person's ability to step over objects while proceeding forward, sideways and backwards. Four canes, resting flat on the floor, formed a square. The participants were instructed to complete the sequence as fast as possible without touching the canes with both feet, making contact with the floor in each square. The participants performed two trials and the better time was taken as the final score.

2.5. Statistical analysis

The sample group was divided into two groups according to their disability level, either “mildly” (EDSS ≤4) or “moderately-severely” disabled (EDSS >4), in line with our previous publication (Baert et al., 2018). All data followed a normal distribution according to the Kolmogorov-Smirnov test. Box plots determined outliers for each outcome. Descriptive statistics were employed for demographic, clinical characteristics, and mobility measures. The chi-square test examined the differences between the disability groups by MS type and gender, and by one-way analysis of variance tests (ANOVA) for age, disease duration, EDSS, height, weight, BMI, cognition (SDMT) and mobility measures.

The relationship between each of the MSWS-12 items and clinical measures of mobility were examined by Spearman's correlation coefficients. The analyses were performed separately for each disability group. Using the Fisher r-to-z transformation, we assessed the significance (two-tailed) of the difference between the correlation scores according to disability group (mild vs. moderate/severe). Furthermore, an exploratory linear regression analysis (stepwise method) for each mobility measure was performed. The mobility parameter was defined as the dependent variable. The individual MSWS-12 items were integrated into the analysis as independent variables. The linear regression analysis was performed twice for each disability group, with/without adjusting for cognition (represented by the SDMT), age and gender.

Based on the output of the linear regression analysis, ANOVA tests were performed, focusing on selected items for each disability group. For each item, the differences were examined in terms of mobility metrics, according to the five possible answers (not at all, a little, moderately, quite a bit, extremely). The Bonferroni post hoc test compared multiple comparisons between answers. All analyses were carried out using the SPSS software (version 25.0 for Windows; SPSS Inc., Chicago, Illinois, USA). Reported P values were two-tailed and the level of significance was set at $p<0.05$.

Table 1
Demographic, clinical and mobility characteristics of the MS sample.

Variable	Total group	Mild disability EDSS ≤ 4	Moderate-severe disability EDSS > 4	Mild vs. Moderate-severe p-Value
Number	242	108	134	—
Age (years)	49.2 (10.4)	47.7 (9.9)	50.5 (10.7)	0.042*
Gender (F/M)	156/86	73/35	83/51	0.248
Disease duration (years)	12.2 (8.3)	10.8 (7.6)	13.5 (8.6)	0.014*
MS type (RR/P)	196/46	89/19	107/27	0.012*
Height (cm)	169.8 (14.4)	168.6 (18.8)	170.7 (9.7)	0.281
Weight (kg)	71.5 (15.6)	71.4 (15.0)	71.3 (16.1)	0.973
BMI (kg/m^2)	24.6 (4.9)	24.6 (4.8)	24.5 (5.1)	0.825
EDSS (score)[a]	4.5 (2.0–7.0)	3.0 (2.0–4.0)	6.0 (4.5–7.0)	< 0.001*
SDMT (score)	40.9 (14.4)	44.9 (13.0)	37.7 (14.8)	< 0.001*
Mobility measures				
MSWS-12 (score)	37.8 (13.3)	31.9 (12.3)	42.5 (12.2)	< 0.001*
2MWT (m)	123.7 (53.2)	156.3 (46.8)	97.2 (42.4)	< 0.001*
T25FW (s)	8.6 (6.3)	6.1 (2.7)	10.7 (7.5)	< 0.001*
TUG (s)	12.4 (7.7)	8.8 (4.4)	15.3 (8.6)	< 0.001*
FSST (s)	15.7 (11.1)	10.4 (4.8)	20.5 (12.9)	< 0.001*

Data are reported as mean (SD).
F, Female; M, Male; RR, Relapsing-remitting; P, Progressive; BMI, Body mass index; EDSS, Expanded disability status scale; SDMT, Symbol digit modalities test; MSWS, Multiple sclerosis walking scale; 2MWT, 2-minute walk test; T25FW, Timed 25-foot walk; TUG, Timed up and go; FSST, Four square step test.
[a] data reported as median/range.
* $P<0.05$.

3. Results

A total of 242 PwMS were included in the final analysis: 108 (44.6%) mildly disabled and 134 (55.4%) moderately-severely disabled (Table 1)[1]. Participants in the moderate to severe group were older, with longer disease duration and included more patients with progressive MS. According to the clinical mobility tests, people with moderate to severe MS walked slower and scored lower compared to people with mild MS. The MSWS-12 overall score for the total group was 37.8 (S.D. = 13.3). Mildly disabled PwMS scored lower compared to moderately- severely disabled PwMS, 31.9 (S.D. = 2.3) vs. 42.5 (S.D. = 12.2), respectively. The SDMT overall score for the total group was 40.9 (S.D. = 14.5). Mildly disabled PwMS scored higher compared to moderately-to severely disabled PwMS, 44.9 (S.D. = 13.0) vs. 37.7 (S.D. = 14.8), respectively. Table 2 provides a full overview of the distribution of the MSWS-12 responses for each item. The most frequent answers were "*Quite a bit*" and "*Extremely*" in PwMS who were moderately-severely disabled. Item 2 (running) was the only item in the mildly disabled group where the response "*Extremely limited*" was the most frequent answer (44.4%).

Table 3[2] presents Spearman's coefficient correlation scores between each of the MSWS-12 items and the clinical mobility tests. In general, stronger correlations between the MSWS-12 items and mobility tests were found in the mildly disabled compared to the moderately- severely disabled. However, when compared statistically, differences between groups were found only for items 2, 10, 11 and 12. Furthermore, stronger correlations between the MSWS-12 items and mobility tests were demonstrated in the 2MWT, TUG and T25FW compared to the FSST. For the mildly disabled group, the linear regression analysis

[1] According to the proof version the colmns should be stretched (wider) a bit (especially the "Total group") in order for the place all rows in line with each other.

[2] Same note as presented for table 1. The first columns should be wider in order for all rows to be in line with each other.

Table 2
Distribution (percentage) of the MSWS-12 responses according to disability groups.

MSWS-12 item	Mild (EDSS ≤ 4) (n = 108)					Moderate-severe (EDSS > 4) (n = 134)				
	Not at all	Little	Moderately	Quite a bit	Extremely	Not at all	Little	Moderately	Quite a bit	Extremely
1. Limited your ability to walk	22.2	26.9	**31.5**	14.8	4.6	8.2	14.2	26.1	**38.1**	13.4
2. Limited your ability to run	10.2	11.1	7.4	26.9	**44.4**	4.5	3.0	0.7	9.0	**82.8**
3. Limited your ability to climb up and down stairs	23.1	25.9	**28.7**	14.8	7.4	6.7	16.4	23.9	**29.9**	23.1
4. Made standing when doing things more difficult.	25.0	**35.2**	25.9	9.3	4.6	14.2	17.9	25.4	**27.6**	14.9
5. Limited your balance when standing or walking	18.5	30.6	**32.4**	11.1	7.4	6.7	19.4	22.4	**32.8**	18.7
6. Limited how far you are able to walk	15.7	21.3	23.1	**24.1**	15.7	7.5	14.9	20.1	**31.3**	26.1
7. Increased the effort needed for you to walk	14.8	**26.9**	24.1	25.9	8.3	10.4	14.9	17.9	**33.6**	23.1
8. Made it necessary for you to use support when walking indoors	**48.1**	29.6	8.3	8.3	5.6	22.2	14.9	17.2	**26.1**	19.4
9. Made it necessary for you to use support when walking outdoors	**53.7**	18.5	11.1	10.2	6.5	14.9	11.9	8.2	26.9	**38.1**
10. Slowed down your walking	15.7	**32.4**	19.4	24.1	8.3	7.5	12.7	17.2	28.4	**34.3**
11. Affected how smoothly you walk	16.7	**32.4**	18.5	23.1	9.3	9.0	13.4	17.2	27.6	**32.8**
12. Made you concentrate on your walking	26.9	19.4	17.6	**27.8**	8.3	8.2	15.7	14.9	29.9	**31.3**

Maximum percentage for each item is highlighted in bold.

Table 3
Spearman's coefficient correlation scores between the MSWS-12 items and mobility tests according to disability groups.

MSWS-12 item	Mild (EDSS ≤ 4) (n = 108)				Moderate-severe (EDSS > 4) (n = 134)			
	2MWT	TUG	T25FW	FSST	2MWT	TUG	T25FW	FSST
1. Limited your ability to walk	−0.504	0.419	0.359	0.381	−0.509	0.408	0.447	0.201
2. Limited your ability to run	−0.537*	0.558*	0.449*	0.464*	−0.290	0.281	0.262	**NS**
3. Limited your ability to climb up and down stairs	−0.492	0.432	0.464	0.394	−0.449	0.420	0.448	0.277
4. Made standing when doing things more difficult.	−0.482	0.453	0.37	0.401	−0.405	0.412	0.410	0.274
5. Limited your balance when standing or walking	−0.474	0.473	0.375	0.371	−0.389	0.384	0.421	0.287
6. Limited how far you are able to walk	−0.496	0.447	0.401	0.383	−0.309	0.256	0.267	0.220
7. Increased the effort needed for you to walk	−0.481	0.412	0.405	0.334	−0.320	0.277	0.287	0.225
8. Made it necessary for you to use support when walking indoors	−0.526	0.545	0.551	0.352	−0.548	0.495	0.535	0.359
9. Made it necessary for you to use support when walking outdoors	−0.612	0.595	0.595	0.374	−0.480	0.467	0.465	0.352
10. Slowed down your walking	−0.572*	0.539*	0.533*	0.418	−0.337	0.309	0.305	0.224
11. Affected how smoothly you walk	−0.569*	0.522*	0.475	0.418	−0.332	0.274	0.289	0.244
12. Made you concentrate on your walking	−0.535*	0.556*	0.511	0.443*	−0.366	0.313	0.318	**NS**

* Significant difference (two-tailed) in correlation score between disability groups (using Fisher r-to-z transformation).

output produced a model which included item 9 (*"Made it necessary for you to use support when walking outdoors"*), which explained 35.4%, 30.8%, and 23.7% of the variance related to the 2MWT, T25FW and TUG, respectively. Item 2 *("Limited your ability to run")* explained 16.2% of the variance related to the FSST. All other independent variables were non-significant. As for the moderately-severely disabled group, the linear regression analysis output produced a model which included item 8 (*"Made it necessary for you to use support when walking indoors"*), which explained 31.6%, 18.0%, 20.2% and 9.5% of the variance related to the 2MWT, T25FW, TUG and FSST, respectively. The addition of the SDMT, and age and gender to the independent variables, did not have any significant effect on the linear regression analysis results (Table 4).

Mobility performance according to the responses to item 9 in the mildly disabled group, are illustrated in Fig. 1 (note that the FSST scores are based on item 2). Distributions of mobility performance according to the responses of item 8 in the moderately-severely disabled group are illustrated in Fig. 2.

4. Discussion

The present paper present data from a secondary analysis of a RIMS multicenter study, which primarily aimed to determine the responsiveness of mobility measures, and provide reference values for clinically meaningful improvements in PwMS following physical rehabilitation. The aim of the present report was to explore the construct validity of the individual items of the MSWS-12. Specifically, we sought to determine the relationship between the individual items of the MSWS-12 with clinical mobility tests in PwMS.

According to the regression analysis, item 9 of the MSWS-12′s scale (*"During the past two weeks, to what extent has your disease made it necessary for you to use support when walking outdoors?"*) provided the strongest associations with mobility difficulties in people with mild MS. In those who were moderately- severely disabled, MSWS-12′s item 8 (*"During the past two weeks, to what extent has your disease made it necessary for you to use support when walking indoors?")* was the stronger correlate of mobility difficulties. Of note, these items are the only items in the questionnaire asking about apparent consequences of walking limitations due to MS in an environmental context. Furthermore, the use of support to assist walking in PwMS is common in the MS population (Hobart et al., 2003) where 60.5% of the MS working-age population living in the USA, own at least one mobility aid (Iezzoni et al., 2010).

We propose several explanations for why the two items which included the phrase "use of support" provided a stronger correlation compared with the other items. Firstly, there is a possibility that certain items listed in the MSWS-12 are more influenced by confounders than others. For instance, the use of walking aids is related to increased fatigue and energy expenditure (Devasahayam et al., 2019), which are related with a slower performance on the TUG and a shorter distance on the 2MWT (Valet et al., 2019). Additionally, an increased risk of falling is related with use of walking aids in PwMS (Carling et al., 2018), and is associated with a slower performance score on the TUG (Kalron et al., 2017).

In a slightly different context, a cohort study of 132 PwMS reported a significant relationship between the overall MSWS-12 score and depressive symptoms (Kalron and Aloni, 2018). Regardless of age, gender,

Table 4
Exploratory linear regression analysis (stepwise method) for the clinical mobility tests (dependent variable) based on the MSWS-12 items (independent variables).

Dependent variable	Independent variable (Model 1)	β	95% CI	*P*-value	R Square
Mild disability (EDSS ≤ 4)					
2MWT	Question 9	−0.595	−27.3, −16.0	< 0.001	0.354
T25FWT	Question 9	0.555	0.82, 1.48	< 0.001	0.308
TUG	Question 9	0.487	1.10 2.26	< 0.001	0.237
FSST	Question 2	0.369	0.65, 1.93	< 0.001	0.162
Moderate-severe disability (EDSS > 4)					
2MWT	Question 8	−0.562	−20.74, −12.33	< 0.001	0.316
T25FWT	Question 8	0.424	1.39, 3.02	< 0.001	0.180
TUG	Question 8	0.450	1.76, 3.61	< 0.001	0.202
FSST	Question 8	0.308	1.16, 4.33	0.001	0.095
Adjusted for cognition (SDMT), age and gender					
Mild disability (EDSS ≤ 4)					
2MWT	Question 9	−0.535	−25.1, −13.4	< 0.001	0.357
T25FWT	Question 9	0.495	0.67, 1.37	< 0.001	0.286
TUG	Question 9	0.416	0.86 2.06	< 0.001	0.281
FSST	Question 2	0.407	0.61, 1.64	< 0.001	0.172
Moderate-severe disability (EDSS > 4)					
2MWT	Question 8	−0.520	−19.9, −11.3	< 0.001	0.369
T25FWT	Question 8	0.407	1.31, 3.05	< 0.001	0.184
TUG	Question 8	0.421	1.63, 3.54	< 0.001	0.251
FSST	Question 8	0.234	0.42, 3.54	0.014	0.181

EDSS, Expanded disability status scale; 2MWT, 2-minute walk test; T25FW, Timed 25-foot walk; TUG, Timed up and go; FSST, Four square step test; SDMT, Symbol digit modalities test.

and EDSS score, PwMS with depressive symptoms showed elevated MSWS-12 scores compared to non-depressed PwMS (40.8 (S.D. = 15.9) vs. 26.6 (S.D. = 13.7); $p = 0.002$, respectively). In the same context, Sikes et al. (2019) found that self-efficacy (the belief that one can competently cope with a challenging situation) explained 45% and 48% of the variance in MSWS-12 scores in young and older adults with MS, respectively (Sikes et al., 2019). Both of these studies referred to the overall score of the MSWS-12. However, it is reasonable to assume that the effect of mood conditions varies between the MSWS-12 items. Mood and mental symptoms, such as anxiety and depressive symptoms were not assessed in our cohort. Therefore, only future research focusing on the relationship between the MSWS-12 items and mood symptoms can confirm this assumption.

Another interesting finding was that according to the linear regression the importance of items 8 and 9 were of similar magnitude, regardless of the patient's cognitive processing speed measured by the SDMT. Similarly, Motl et al. reported that the cognitive processing speed minimally influenced the construct validity of the total MSWS-12 scores in 96 PwMS (Motl et al., 2013). One may argue that it is relatively easy to comprehend the issue of using support for walking, as it is a visual external element. In contrast, several of the other items are less clear. For instance, items such as "*affected how smoothly you walk*" (item 11) or "*made you concentrate on your walking*" (item 12) might be more difficult to interpret.

In the present study, the correlation coefficients for items 11 and 12 were significantly stronger in people with mild MS who demonstrated better cognitive capabilities (mean SDMT = 44.9) compared with the correlation scores of the moderately-severely disabled, with poorer cognitive capabilities (mean SDMT = 37.7). Cognition was not the focus of the present study, nevertheless, we believe that the relationship between the MSWS-12′s individual items and cognition is worthy of further investigation.

Interestingly, previous studies evaluating the Italian, Dutch, and Persian version of the MSWS-12, emphasized items 8 and 9

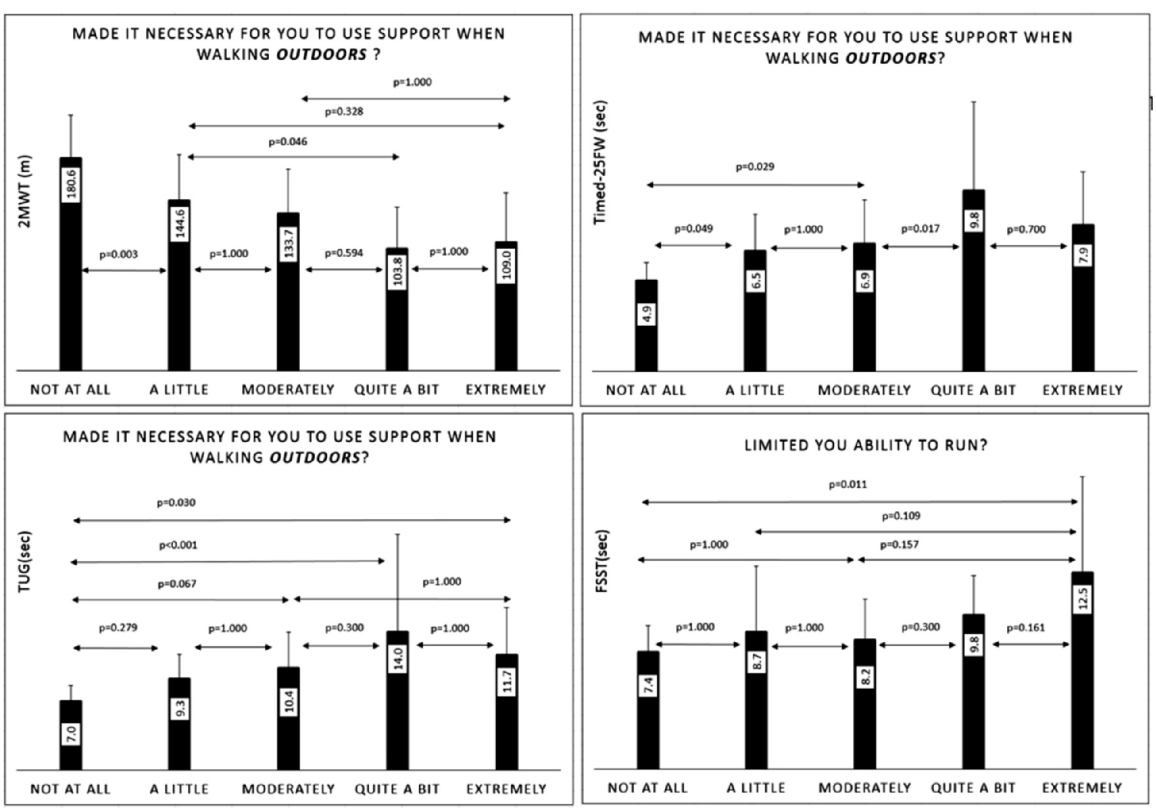

Fig. 1. Mobility scores according to MSWS-12 item 9 in people with mild MS.

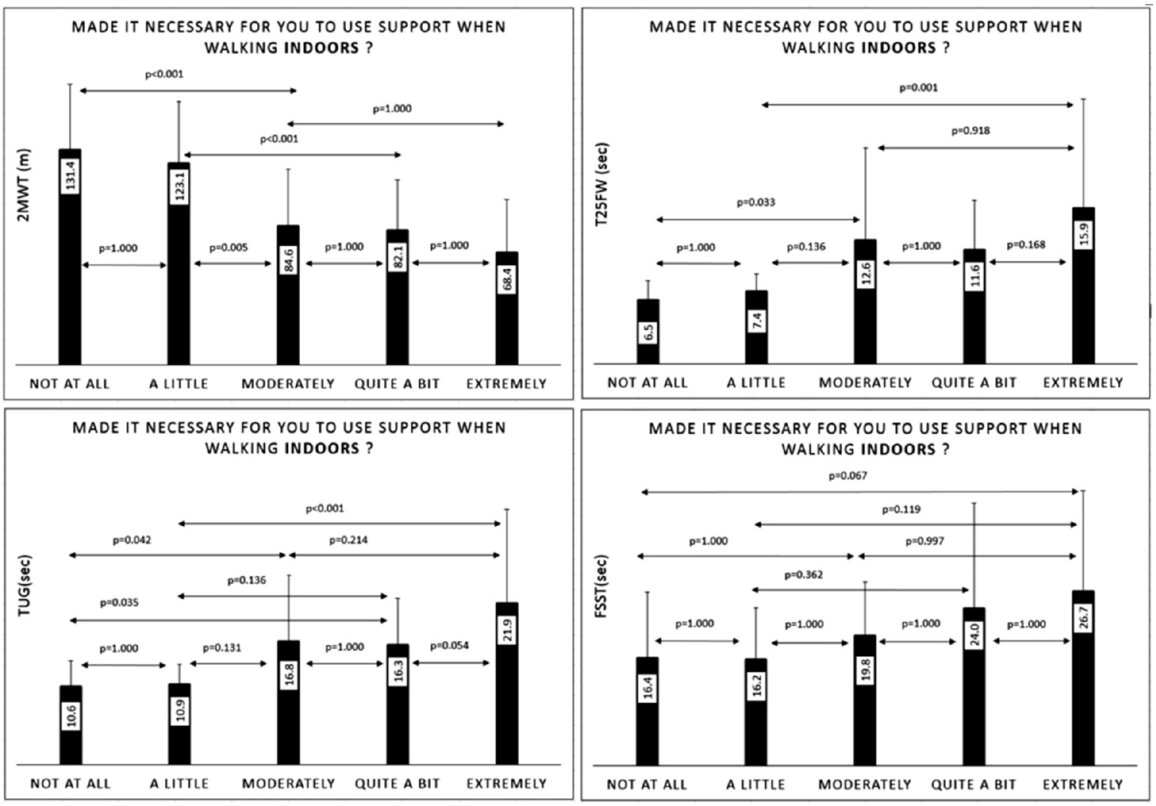

Fig. 2. Mobility scores according to MSWS-12 item 8 in people with moderate to severe MS.

(Nakhostin et al., 2015; Mokkink et al., 2016; Marengo et al., 2019). Mokkink et al., reported that these items demonstrate better psychometric properties once patients with an EDSS score >5.5 are excluded from the analysis (Mokkink et al., 2016). This finding is in partial agreement with the current results. The results from the present linear regression models suggest that the relationship of these specific items with objective mobility measures, depend on the level of disability. In a similar context, Marengo et al. examined the validity of the MSWS-12 using the Rasch model to analyze the MSWS-12 items. The authors found that items 2 (running), 8 and 9 raise concern due to signs of multidimensionality and poor differential item functioning (Marengo et al., 2019). This finding might explain the present results found in the mild MS group. We observed that approximately half of these individuals selected a single response (not at all/extremely), causing the distribution of responses to narrow. Notably, this observation was not reported by Engelhard et al. who examined the MSWS-12′s items using the item response theory. Their conclusions focused on items 2 and 11, demonstrating that these specific items provide scarce information (Engelhard et al., 2016).

From a clinical standpoint, our findings have several implications for professionals engaged in the management of mobility in PwMS. Firstly, clinicians are advised to focus on questions relating to the patient's use of walking support devices. Our results indicate that information from items 8 or 9 (dependent on the patient's level of disability), provide a reasonable overview of the patient's mobility capabilities. Secondly, according to our data, people with mild MS who responded that they did not need any type of support when walking outdoors (~50% of the mild MS group), walked a distance of 180 m on the 2MWT, completed the T25FW <5 s, and performed the TUG test <7 s. These scores are on average well within the normative range (Langeskov-Christensen et al., 2017; Kalron et al., 2017; Goldman et al., 2013), indicating normal walking capabilities in the majority of this sample. Moreover, there is justification to utilize this item as an inclusion (or exclusion) criteria in trials involving mobility in MS. Finally, low correlation scores were observed between the FSST and the MSWS-12′s items, which is in agreement with the findings of Nilsagård et al. (2007), thus, indicating that in the MS population, the relationship between perceived walking ability and dynamic balance is weaker compared with objective walking tests. One more novel contribution of our study involves item 2, the ability to run. Significant differences in the correlation scores were demonstrated between disability groups. Correlation scores were significantly higher in the mild group compared with lower scores in the moderate-severe group. Interestingly, 44.4% of the individuals with mild MS reported that their running was extremely limited. In fact, item 2 was the only item in the mild group where the response "extremely limited" was the most frequent answer (out of the 5 options). This finding suggests that for many MS patients without significant walking difficulties, the ability to run is important. Fortunately, a recent study found that a 12-week community-located running training program can improve aerobic capacity, functional mobility, visuospatial memory, fatigue, and quality of life in PwMS during the early phases of the disease, emphasizing the benefits of running in PwMS (Feys et al., 2019).

Combining data from 17 MS rehabilitation centres is a major strength of this study. Nevertheless, our study does have limitations. Firstly, mobility was evaluated by clinical walking tests. Utilizing instrumented gait devices that provide definite gait characteristics might have further expanded our knowledge. However, only a few centres of the current consortium possessed these tools when the study was conducted. Secondly, our analysis did not include other factors related to mobility, such as spasticity, postural stability, muscle strength and endurance of the lower limbs.

In conclusion, we confirm that items 8 and 9 of the MSWS-12 focusing on the patient's use of walking support in/outdoors, provides a robust indicator of the MS individual's objective mobility capabilities.

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CRediT authorship contribution statement

Alon Kalron: Conceptualization, Methodology, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Rainer Ehling:** Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Ilse Baert:** Conceptualization, Methodology, Data curation. **Tori Smedal:** Data curation. **Kamila Rasova:** Writing - original draft, Writing - review & editing. **Adnan Heric-Mansrud:** Data curation. **Iratxe Elorriage:** Data curation. **Una Nedeljkovic:** Data curation. **Andrea Tachino:** Data curation. **Leszek Gargul:** Conceptualization, Methodology, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Klaus Gusowski:** Data curation. **Davide Cattaneo:** Data curation. **Sophie Borgers:** Data curation. **Jeffrey Hebert:** Data curation. **Ulrik Dalgas:** Conceptualization, Methodology, Data curation, Writing - original draft, Writing - review & editing, Formal analysis. **Peter Feys:** Conceptualization, Methodology, Data curation, Writing - original draft, Writing - review & editing, Formal analysis.

Declaration of Competing Interest

The authors declare that there is no conflict of interest.

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