

Cut-points of the 6-min walk test, the six spot step test, and the timed-25-foot walk test discriminating impaired from non-impaired walking capacity in persons with Multiple sclerosis

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Multiple Sclerosis Journal—
Experimental, Translational
and Clinical

January–March 2025, 1–11

DOI: 10.1177/
20552173251324600

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Abstract

Background: Assessing and interpreting walking capacity in persons with Multiple sclerosis (PwMS) is essential in clinical practice and research – and thus for PwMS themselves – yet research evaluating cut-points is limited. The present study aims to establish cut-points for 6-min walk test (6MWT), six spot step test (SSST), and timed 25-foot walk test (T25FWT) in PwMS.

Methods: Classification of PwMS having walking impairments and PwMS having limited or no walking impairments was based on distinct benchmarks for each walking test, as derived from the 12-item Multiple Sclerosis Walking Scale (MSWS-12) on a 5-point Likert scale. Cut-points, area under the curve (AUC), sensitivity (Se), and specificity (Sp) were established using receiver operating characteristic curve analyses.

Results: A total of $n = 211$ ambulatory PwMS were enrolled (68% females, 54 ± 11 years, patient-determined disease step 2.9 ± 1.9 [range; 0–7], 65.1% relapse-remitting Multiple sclerosis). The following cut-points between the two groups were established: 6MWT (446 m; AUC = 0.82, Se = 0.87, Sp = 0.78), SSST (0.121 rounds/s (corresponding to 8.3 s); AUC = 0.80, Se = 0.84, Sp = 0.75), and T25FWT (1.39 m/s (corresponding to 5.5 s); AUC = 0.79, Se = 0.89, Sp = 0.69).

Conclusion: Cut-points discriminating PwMS having walking impairments vs. PwMS having limited or no walking impairments were identified for 6MWT (446 m), SSST (8.3 s), and T25FWT (5.5 s).

Keywords: Multiple sclerosis, cut-points, walking, 6-min walk test, six spot step test, timed 25-foot walk test, 12-items Multiple Sclerosis Walking Scale, ROC curve, area under curve

Date received: 25 July 2024; accepted: 13 February 2025

Introduction

Multiple sclerosis (MS) is a chronic autoimmune, inflammatory, and degenerative neurological disease of the central nervous system.¹ While persons with MS (PwMS) often experience a wide range of symptoms, impairments in walking capacity are particularly prevalent.^{2,3} Walking capacity is strongly associated with both the level of physical function during daily activities and with independent living.⁴ Furthermore, walking is considered one of the most important bodily functions by patients both early and late in the course of the disease.⁵

Because of the fundamental role of walking in PwMS, regular walking assessments are essential for both treatment decisions and research. Walking capacity is usually assessed using a battery of performance tests, covering different aspects of walking. Specifically, three of the most commonly used objective walking measures are the timed 25-foot walk test (T25FWT, e.g. speed), the 6-min walk test (6MWT, e.g. endurance) and the six spot step test (SSST, e.g. walking balance/coordination).⁶ In addition to these objective walking capacity tests, the 12-item MS walking scale (MSWS-12) is a patient-reported

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outcome measure, proposed as a screening tool for lower-extremity physical functioning and mobility in PwMS.⁷ The MSWS-12 assesses self-perceived limitations in walking ability.^{8,9} Incorporating the clinical interpretation of walking capacity with the patient perspective on walking ability thus seems highly relevant but is currently lacking. Moreover, establishing cut-points that distinguish between patients with or without walking limitations would provide an easy and immediate interpretation of physical performance related to specific walking aspects, making cut-points a useful tool for both clinicians and researchers – and through here also for PwMS. Interestingly, numerous ‘aging’ studies have established various cut-points across different walking capacity tests, proven useful for risk prediction of specific diseases, fall tendency, mobility disability, and mortality rates.^{10–12} To the best of our knowledge, only one study has investigated cut-points for a walking outcome (T25FWT) in PwMS.¹³ To expand on this knowledge, the present study aimed to identify cut-points on the T25FWT, 6MWT, and SSST that reflect functionally relevant walking limitations in PwMS, using patient-reported outcomes from the MSWS-12 as the defining anchor.

Methods

The current study is a secondary analysis based on data from an ongoing pragmatic cross-sectional study performed at the Danish MS Hospitals, investigating walking capacity in Danish PwMS. The original study was approved by the relevant ethical committee and data protection agency (Local Ethics Committee in the Central Denmark Region reference: 39/2021, project number 1-10-72-1-21). One paper has been published investigating the extent of impairments in PwMS vs. healthy controls across T25FWT, 6MWT, and SSST.³

Participants underwent a test battery consisting of walking tests, patient-reported outcomes, and assessment of motor function and cognitive performance. All functional assessments and patient-reported outcomes were completed at baseline (i.e. at admission to inpatient rehabilitation) and repeated approximately 1 year after. In the present study, only baseline data was analysed from the following walking capacity tests: 6MWT, SSST, and T25FWT and patient-reported walking ability: MSWS-12.

Participants

Participants were randomly recruited and contacted by email from the patient admission list prior to their 2- or 3-week inpatient rehabilitation stay at one

of the two Danish MS-hospitals in the period between March 2022 and February 2023. Participants were included without any interference to their planned rehabilitation.

Participants had to have a definite diagnosis of MS according to the international McDonald 2017 criteria.¹⁴ Participants were excluded if they had cognitive limitations or any other illness hindering participation or made them unable to perform at least one of the included short walking tests within reasonable time limits (i.e. <180 s; SSST and T25FWT), and if they had failed to complete the MSWS-12. All participants provided written informed consent.

Outcome measures

Assessment of walking capacity in PwMS. To limit measurement bias, only trained assessors undertook functional assessments. Tests instructions were strictly followed, and testing were completed in an appropriate environment using conventional equipment. All three walking tests have previously shown good validity and reliability.^{15–18} For safety reasons, participants were allowed to use their habitual walking aids during the walking tests. MSWS-12 was completed at home prior to inpatient rehabilitation admission (on average 12 days before performing the objective walking tests).

6-min walk test. Participants were instructed to walk as far as possible in 6 min on a 30 m indoor corridor, pivoting at each end.¹⁷ Each minute the tester announced the remaining test time and noted the distance covered. Standing (but not sitting) breaks were allowed during the test.

Six spot step test. The SSST was performed based on the procedure described by Nieuwenhuis and colleagues.¹⁵ Participants were instructed to safely walk as fast as possible down a 1 × 5 m test lane in a criss-cross pattern, kicking five small, wooden cylinder blocks off each spot alternating between the lateral and the medial side of the foot. Two trials were performed with each leg, and the time was manually recorded in seconds. The mean time of the four trials was used in the analysis.¹⁵

Timed 25-foot walk test. From a standing position behind the starting line, participants were instructed to walk 25-feet (7.62 m) as fast as possible. The test was performed twice, and the time was manually recorded in seconds.¹⁸ The mean time of the two trials was used in the analysis.

Patient-reported walking ability

12-Item Multiple sclerosis walking scale. The MSWS-12 contains 12 items evaluating the subjective perception of the impact of MS on walking ability. Each item focuses on a different aspect of walking ability (e.g. item 6: walking endurance, item 5: walking balance, and item 10: walking speed).⁸ Items are rated on a 5-point Likert scale ranging from 1: 'not at all' to 5: 'extremely', resulting in a sum score between 12 and 60 points. Higher scores indicate greater impact of MS on walking.¹⁹ Finally, the MSWS-12 was converted to a 0–100 score:

$$\text{MSWS-12} = \frac{(\text{participant score} - 12)}{48} \times 100$$

Statistical analysis

Descriptive statistics were used to report participant characteristics within the included sample. Initially, data from the walking tests and MSWS-12 was examined for normal distribution based on visual inspection of histograms and scatter plots. Due to violations to the distributional assumptions of the T25FWT and SSST, these were transformed to meter/second (m/s) for the T25FWT and rounds/second (r/s) for SSST using the following equations:

$$\frac{7.62 \text{ m}}{\text{T25FWT in seconds}} = \text{m/s and } \frac{1}{\text{SSST in seconds}} = \text{rounds/s}$$

Of note, to support the interpretability of the cut-points for both clinicians and patients, identified cut-points for these walking measures were back transformed into seconds.

An anchor-based approach was used for the estimation of the cut-points for the 6MWT, SSST, and T25FWT. The strength of the association between the MSWS-12 and the three walking tests (6MWT, SSST, and T25FWT) was estimated using Spearman's Rank-order Correlation (r_s). Additionally, the correlation between item 6, 5, and 10 and the walking tests (6MWT, SSST, and T25FWT) was also estimated using r_s , as these items correspond well with the 6MWT, SSST, and T25FWT, respectively (i.e. walking endurance, balance, and speed). Correlation values were interpreted as weak <0.40 , moderate $0.40\text{--}0.69$, and strong ≥ 0.70 .²⁰

Establishing cut-points using an anchor-based approach

In the present work, the MSWS-12 average item score was used as an anchor discriminating PwMS with 'limited or no walking impairments' from those

with 'walking impairments'. By using the MSWS-12 item responses (1 ('Not at all'), 2 ('A little'), 3 ('Moderately'), 4 ('Quite a lot'), and 5 ('Extremely')), we initially explored three different classification benchmark approaches to categorise PwMS into those having 'limited or no walking impairments' or those having 'walking impairments'. Specifically, inclusion into the category 'limited or no walking impairments' was done based on the MSWS-12 average item score of either ≤ 2 , ≤ 2.5 , or ≤ 3 (corresponding to MSWS-12 scores of ≤ 25 , ≤ 37.5 , and ≤ 50 points on a 0–100 scale). The classification benchmark (≤ 2 , ≤ 2.5 , or ≤ 3) with the highest proportion of true positives and lowest proportion of false positives among the three different classification benchmarks was used for further analysis. To compare subgroups, we used a linear mixed model. Participant ID was set as a random effect and subgroups (limited or no walking impairments and walking impairments) as fixed effects. A significance level of $p < 0.05$ was applied to all analyses.

Subsequently, a receiver operating characteristic (ROC) curve was used to identify cut-points between two subgroups. For each analysis, the sensitivity (Se), specificity (Sp), and area under the curve (AUC) was determined based on Youden's index calculations. Additionally positive predictive values were calculated for each test as done previously.^{21,22} Furthermore, a histogram plot was generated for the dichotomous outcome for the 6MWT, SSST, and T25FWT, respectively. The cut-point identified using ROC analysis was visually plotted onto histograms (Figure 1). All analyses were performed using STATA 17.0 (StataCorp LLC, College Station, USA).

Results

Participant characteristics

While a total of $n = 228$ PwMS performed at least one of the three walking tests (see Skerbjæk and colleagues³), $n = 17$ PwMS did not fill in the MSWS-12 questionnaire and were excluded. Hence, a total of $n = 211$ PwMS were included in the present analyses, with participant characteristics being displayed in Table 1.

Correlations (r_s) between the 6MWT, SSST, and T25FWT and MSWS-12. Strong correlations were observed between MSWS-12 and 6MWT, SSST, or T25FWT (ranged from $r = -0.76$ to $r = -0.73$) (Table 2). In contrast, only moderate correlations were

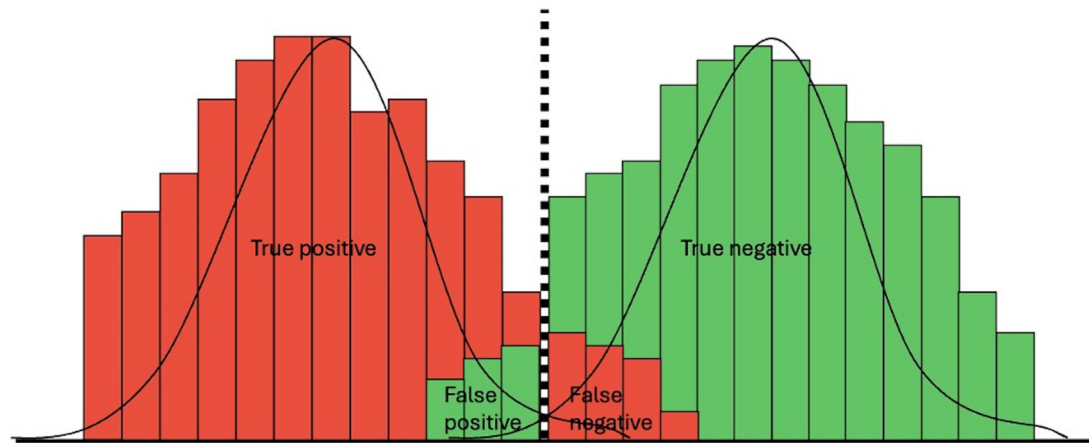


Figure 1. Conceptual visualisation of the histogram plot and cut-point identification. The figure does not represent specific quantitative results. The solid line represents the normal distribution of each group, while the dotted vertical line represents the identified cut-point.

Table 1. Participant characteristics.

<i>n</i>	211
Age, years, mean (SD)	53.5 (11.4)
Sex, <i>n</i> (%)	
Female	143 (67.8)
Male	68 (32.2)
Height, m, mean (SD)	1.73 (0.9)
Weight, kg, mean (SD)	79.4 (18.5)
BMI, kg/m ² , mean (SD)	26.6 (5.9)
PDDS, median (IQR)	3 (1–4)
Type of MS, <i>n</i> (%)	
Relapse-remitting	136 (65.1)
Secondary progressive	36 (17.2)
Primary progressive	37 (17.7)
Time since diagnosis, years, mean (SD)	12.4 (9.6)
Time since first symptoms, years, mean (SD)	16.4 (11.6)
Co-morbidities, <i>n</i> (%)	
Yes	73 (34.6)
No	138 (65.4)

SD: standard deviation; IQR: interquartile range (25th–75th percentile); PDDS: patient-determined disease steps, BMI: body mass index; MS: multiple sclerosis.

observed between MSWS-12 items 6, 5, or 10 and the respective walking test (range from $r = -0.68$ to $r = -0.53$) and were therefore disregarded as external criteria for further analysis. There is a slightly lower sample size for each test compared to the total sample size ($n = 211$). This is because not all participants completed all three walking capacity tests.

Walking performance across MSWS-12 subgroups.

The optimal classification (i.e. highest proportion of true positives and lowest proportion of false positives) between ‘Limited or no walking impairments’ and ‘Walking impairments’ for 6MWT and T25FWT was obtained when based on an average response of ≤ 2.5 (corresponding to ≤ 37 points on the 0–100 scale in MSWS-12), and an average response of ≤ 2.0 (corresponding to ≤ 25 points on the 0–100 scale in MSWS-12) for the SSST (see supplementary materials for further details). Therefore, all further analyses use these classifications.

Walking capacity outcomes for the whole group and the two subgroups are presented in Table 3. The PwMS subgroup ‘Limited or no walking impairments’ showed superior performance on all walking tests compared to the PwMS subgroup ‘Walking impairments’: 6MWT +197 [160;234] m ($p < 0.001$), SSST +0.064 [0.049;0.078] r/s ($p < 0.001$), and T25FWT +0.63 [0.50;0.75] m/s ($p < 0.001$).

Cut-points discriminating between the subgroups ‘Limited or no walking impairments’ and ‘Walking impairments’ are presented in Table 4 and Figures 2–5, and corresponded to 446 m, 0.121 r/s (corresponding to 8.3 s), and 1.39 m/s (corresponding to 5.5 s) for the 6MWT, SSST, and T25FWT, respectively. AUC values ranged from 0.79 to 0.82.

The frequency of true positives was $n = 98$, $n = 90$, and $n = 117$ whereas the frequency of false positives was $n = 10$, $n = 9$, and $n = 8$ PwMS for the 6MWT, T25FWT, and the SSST, respectively. The positive

Table 2. Correlation between 6MWT, SSST, T25FWT, and MSWS-12.

Walking capacity	MSWS-12	Item 6	Item 5	Item 10
6MWT ($n = 203$)	−0.76 ^a	−0.65 ^a		
SSST ($n = 205$)	−0.73 ^a		−0.53 ^a	
T25FWT ($n = 210$)	−0.73 ^a			−0.68 ^a

^aStatistical significance at $p < 0.05$, 6MWT: 6-minute walk test; SSST: six spot step test; T25FWT; timed 25-foot walk test; MSWS-12; 12-Item Multiple Sclerosis Walking Scale (0–100); MSWS-12 questions related to Item 6: *Limited how far you are able to walk*; Item 5: *Limited your balance when standing or walking*; Item 10: *Slowed down your walking*.

predictive values were 90.7%, 90.9% and 93.6% for the 6MWT, the T25FWT and the SSST, respectively (Table 4).

Discussion

The present study established cut-points for three commonly used walking capacity tests for PwMS, using the MSWS-12 as the defining anchor. Specifically, the cut-off scores corresponded to 446 m for 6MWT, 0.121 r/s (corresponding to 8.3 s) for SSST, and 1.39 m/s (corresponding to 5.5 s) for T25FWT.

Validity of the applied anchor (MSWS-12)

MSWS-12 was chosen as the defining external anchor for the present study as it has displayed good psychometric properties^{23–25} and satisfactory face validity (i.e. adhering to the assumption that the three walking tests and the MSWS-12 measure-related constructs), making it a valuable tool for understanding how patients experience their walking difficulties.²⁶ In line with previous research, the MSWS-12 was chosen as the defining anchor, thus including the participants' subjective perception of walking ability when classifying walking impairments.²⁷ Ideally, the outcome measure and the anchor should be related, implying that both instruments measure a related construct. Whereas the objective measurements identify quantitative variables of interest related to PwMS' walking capacity, the MSWS-12 is considered a reflection of walking ability during daily life.^{7,28} This may lead to a disparity in the classification derived from patient-reported walking ability and the actual objective assessments of walking capacity in PwMS. In line with this it can be challenging to apply both subjective and objective outcome measures in combination when assessing such associations. In addition, MSWS-12 specifically captures walking difficulties attributed to MS, without accounting for impairments caused by other comorbidities or conditions that may influence walking performance independently of MS. As shown in Table 1, a third of our sample population reported

having comorbidities, which could partly explain the presence of false positives. Of note, however, in some cases, it might be difficult to separate the consequences of MS per se from those of comorbidities. Nevertheless, we observed strong correlations between MSWS-12 and all three walking tests. This confirms the face validity of MSWS-12 as a measure that sufficiently measures the construct(s) it purports to measure (i.e. walking ability).²⁹ Altogether, this suggests that MSWS-12 is a valid and reliable anchor.

Additionally, we investigated individual MSWS-12 items as the external anchor for our analysis and identification of cut-points on the three objective walking capacity outcomes (Table 3). We assumed that individual items directly probing specific aspects of walking ability assessed by the three tests, respectively, exhibit greater face validity and stronger correlations. Contrary to our expectations, we observed moderate correlations only between individual items (item 6, 5, and 10) on MSWS-12 and the three walking tests, respectively. The total MSWS-12 score may capture nuances in self-perceived walking ability that individual items do not capture. As a result, the overall score could provide a stronger, more stable and more reliable correlation with the objective tests compared to any single item.

Reference values for cut-point identification

Identification of cut-points is often based on ROC analysis.^{10,30} By delineating specific cut-points for two subgroups (i.e. 'Limited or no walking impairments' and 'Walking impairments'), we aimed to reduce ambiguity and ultimately obtain a more robust statistical approach by using ROC-curve analyses. Previous research suggests a cut-point of 450 m for the 6MWT in patients with atrial fibrillation,³¹ which is in line with our findings of 446 m. Interestingly, Goldman and colleagues reported cut-points for the T25FWT in PwMS ($n = 159$) to be 6.0 s and 8.0 s (median: 5.4 s) discriminating between three subgroups; 'Need no help', 'Need

Table 3. Whole group and group comparisons of walking capacity.

	Whole group Mean $\pm$ SD Median (IQR)	Limited or no walking impairments Mean $\pm$ SD	Walking impairments Mean $\pm$ SD	Mean difference [95%-CI]	p-value
6MWT ^a	420.8 $\pm$ 162.7 m 432 (321–541) m	543 $\pm$ 92.8 m	346 $\pm$ 150.3 m	197 [160;234] m	<0.001
SSST ^b	0.121 $\pm$ 0.050 r/s 9.25 (7.13–15.1) s	0.158 $\pm$ 0.045 r/s	0.094 $\pm$ 0.046 r/s	0.064 [0.049;0.078] r/s	<0.001
T25FWT ^a	1.38 $\pm$ 0.5 m/s 5.35 (4.20–7.45) s	1.78 $\pm$ 0.37 m/s	1.15 $\pm$ 0.50 m/s	0.63 [0.50;0.75] m/s	<0.001
MSWS-12	49.2 $\pm$ 28.6 50 (10.4–72.9)	—	—	—	—

6MWT: 6-minute walk test; SSST: six spot step test; T25FWT: timed 25-foot walk test; MSWS-12: 12-Item Multiple Sclerosis Walking Scale (score 0–100); Class: classification benchmark; SD: standard deviation; IQR: interquartile range (25th–75th percentile); m/s: meter per second; r/s: rounds per second; s: seconds; 95%-CI: 95%-confidence interval.

^aBenchmark classification = 2.5.

^bBenchmark classification = 2.0.

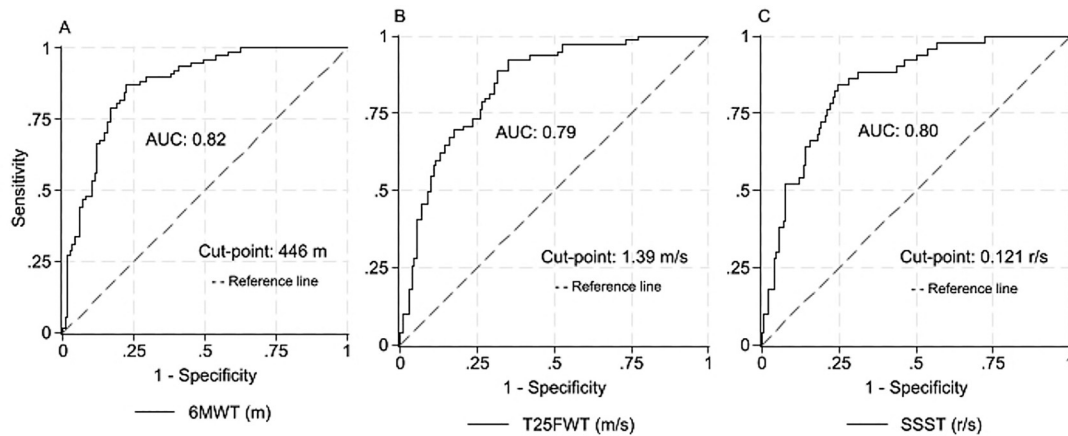


Figure 2. Receiver operating characteristic (ROC) curve of walking capacity in relation to self-perceived walking ability (MSWS-12). (A) and (B) are using a benchmark classification of 2.5, while (C) is using a benchmark classification of 2.0. The cut-point on each ROC-curve distinguishes between the two subgroups 'limited or no walking impairments' and 'walking impairments'. The identified cut-point is estimated based on Youden's Index. SSST: six spot step test; 6-min walk test; T25FWT: timed 25-foot walk test; AUC: area under curve; m: meters; m/s: meters per second; r/s: rounds per second; MSWS-12: 12-item Multiple Sclerosis Walking Scale.

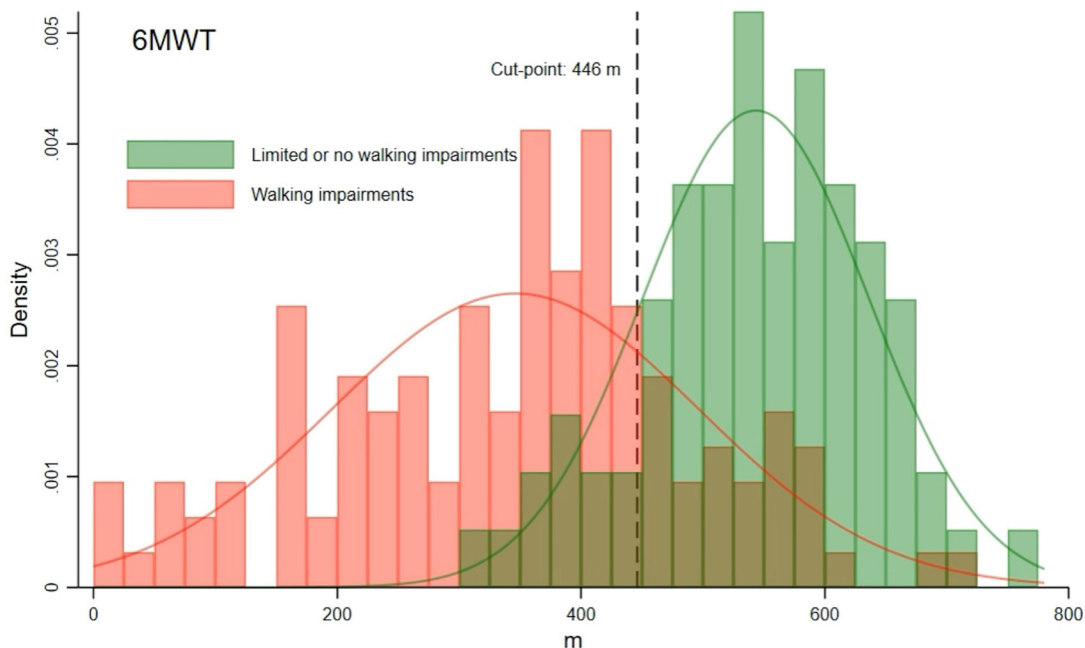


Figure 3. Histogram plot and identification of cut-point for the two subgroups ('limited or no walking impairments' and 'walking impairments') using benchmark classification: 2.5. The dotted line depicted on the graph represents the identified cut-point for 6MWT determined through ROC analysis. 6MWT: 6-min walk test; m: meter. Y-axis: density shows the distribution of participants within a specific walking distance range for each of the two groups. X-axis: represents the walking distance in meters. ROC: receiver operating characteristic.

some help' and 'Unable to do task' in relation to instrumental activities of daily living.¹³ Despite the differences in statistical methods and demographic

properties (nationality, disease severity etc.), their results are somewhat in line with our results (5.5 s). However, our approach uses the MSWS-12 to

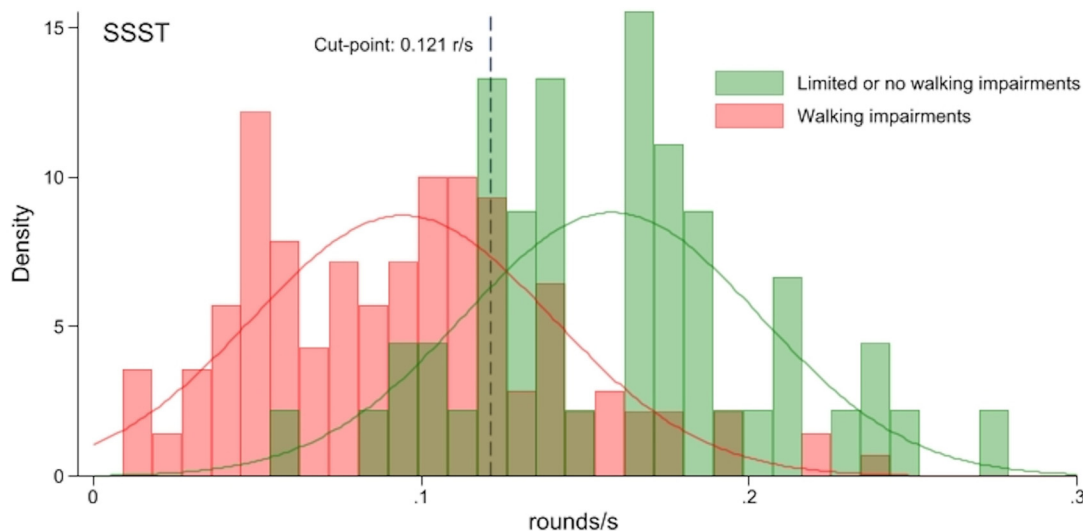


Figure 4. Histogram plot and identification of cut-point for the two subgroups ('limited or no walking impairments' and 'walking impairments') using benchmark classification: 2.0. The dotted line depicted on the graph represents the identified cut-point for SSST determined through ROC analysis. SSST: six spot step test; r/s: rounds per second. Y-axis: density shows the distribution of participants within a specific walking speed range for each of the two groups. X-axis: represents the walking speed in rounds/s. ROC: receiver operating characteristic.

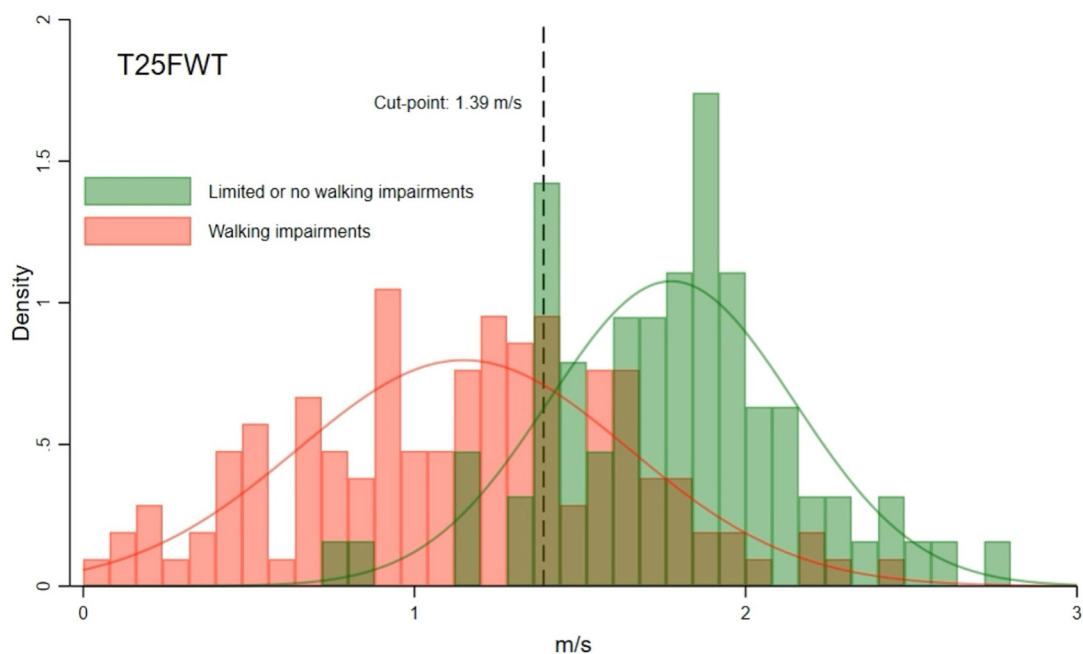


Figure 5. Histogram plot and identification of cut-point for the two subgroups ('limited or no walking impairments' and 'walking impairments') using benchmark classification: 2.5. The dotted line depicted on the graph represents the identified cut-point for T25FWT determined through ROC analysis. T25FWT: timed 25-foot walk test; m/s: meter per second. Y-axis: density shows the distribution of participants within a specific walking speed range for each of the two groups. X-axis: represents the walking speed in m/s. ROC: receiver operating characteristic.

anchor the cut-points to patient-perceived limitations in walking ability, offering a more personalised, simple and subjective perspective. We also see it as

a strength to identify cut-points for three different walking tests within the same study population, offering therapists better flexibility, accessibility and

Table 4. Outcomes of ROC-curve analysis.

	Cut-point	AUC	Sensitivity	Specificity	PPV
6MWT ^a	446 m	0.82	0.87	0.78	90.7%
SSST ^b	0.121 r/s [8.26 s]	0.80	0.84	0.75	93.6%
T25FWT ^a	1.39 m/s [5.48 s]	0.79	0.89	0.69	90.9%

6MWT: 6-minute walk test; SSST: six spot step test; T25FWT: timed 25-foot walk test; AUC: area under the curve; m/s: meter per second; r/s: rounds per second; PPV: positive predictive value; ROC: receiver operating characteristic.

^aBenchmark classification = 2.5.

^bBenchmark classification = 2.0.

comparability options when choosing the appropriate test. Furthermore, cut-points from other patient populations add further support to our results.^{10,11,30,31}

Of interest, cut-points may also be valuable in assessing a patient's independence when performing community ambulation. Andrews and colleagues predicted benchmarks for distance and speed requirements for community ambulation; defined as 'independent mobility outside the home'.³² Additionally, a minimum 6MWT-distance of 380 m is reported to allow grocery shopping independently, while a maximum walking speed of 1.32 m/s is required to safely cross the street. Compared to the cut-points identified in the present study, the subgroup classified as 'Walking impairments' closely corresponds to the established benchmarks by Andrews et al.,³² suggesting that being classified as impaired likely implies a greater probability of facing difficulties in performing community ambulation. Importantly, balance and coordination are also crucial objectives in community ambulation,³³ which is likely better captured by the SSST. Nevertheless, relevant and comparable outcomes and cut-points are lacking in the existing SSST literature.

Methodological considerations

Several methodological aspects warrant cautious consideration. The two subgroups were based on an average response of 2.0 and 2.5 (or 25 and 37.5) on MSWS-12. Since no gold standard method exists on how to identify cut-points, preliminary analyses were carried out (see supplementary materials) to help guide us reach this 'pragmatic' choice. Furthermore, our MSWS-12 grouping aligns with Goldman et al. (2017), making benchmarks of 25 and 37.5 reasonable for dividing participants into 'limited or no walking impairments' and 'walking impairments'. Goldman's categories (0–24.99, 25–49.99, 50–74.99, and 75–100) reflect increasing walking difficulties, making

our cut-points comparable and appropriate for distinguishing between minimal and more significant impairments.⁷ The established cut-points/classification is obviously a simplification of reality, especially since walking impairments caused by MS are highly complex and can rarely be captured by a dichotomous outcome.³⁴ Had we chosen other approaches, it is likely we would have observed slightly different results. We did consider conducting extended analyses with a larger number of subgroups, yet this would lead to small subgroup sample sizes, weakening the strength and external validity of the results. Furthermore, managing numerous cut-points becomes increasingly complex for clinicians, researchers, and PwMS.

The ROC analysis results in our study (AUC: 6MWT 0.82, SSST 0.80, T25FWT 0.79) align with Zeren et al. (2022), who reported a 6MWT AUC of 0.74 in atrial fibrillation patients.³⁰ This similarity likely stems from both studies comparing objective and subjective measures, which generally results in a weaker association than between two objective measures. In addition, Paltamaa et al. (2008) also reported similar AUC values for the 6MWT on deterioration with both participant and clinicians' perception as external criteria (AUC: 0.76 for both approaches).³⁵

The large sample of participants appears to span the adult lifespan and most disease severity levels (PDSS, types of MS, and time since diagnosis), suggesting that the sample might not differ substantially from the general MS population. However, our sample population primarily consists of PwMS with mild impairments (PDDS IQR: 1–4) and those completing the T25FWT in less than 8 s, which limits the generalisation of our findings. As a result, caution is advised when applying these cut-points to more impaired populations, as they may not fully reflect the clinical profile of individuals with more severe walking impairments.

Adjustment for confounders (e.g. age, gender, walking aids, etc.) was not conducted, raising the possibility that unaccounted variables may have influenced the outcome, warranting future studies.

Clinical implications

The applicability of cut-points for walking capacity in PwMS is multifold. Previous aging studies have displayed cut-points for walking velocity and its association with mobility disability, falls, and mortality.^{10,12,36–38} The utilisation of these evidence-based cut-points can help clinicians in classifying individuals into different risk groups, based on the patients' self-perceived walking impairments, enabling them to conduct further evaluations and/or implement targeted interventions. Hence, the present study provides evidence-based cut-points of the 6MWT, SSST, and T25FWT applicable as a screening tool for clinicians and providing individuals with MS clear and understandable feedback on their walking ability. While cut-points can be utilised as a screening tool, they should be viewed and used as a supplement to existing clinical and practical assessment to achieve a nuanced understanding of each individual PwMS.

Conclusion

In a heterogeneous sample of PwMS, cut-points discriminating PwMS with or without walking impairments were identified for the 6MWT (446 m), SSST (8.3 s) and T25FWT (5.5 s) using the MSWS-12 as an external criterion. These cut-points may assist clinicians and researchers in identifying walking impairments and subsequently initiate rehabilitation interventions in PwMS. Future studies should validate the cut-points in larger heterogeneous samples of PwMS, investigate cut-points' relation to function, disease progression and risk of fall, and build upon the applied methodological approach.

Acknowledgements

This study was only possible due to the engagement of our patients and the invaluable help from colleagues at the Danish MS Hospitals, Ry and Haslev, who helped administer patient recruitment and carried out study assessments.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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Supplemental material

Supplemental material for this article is available online.

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