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U-turn speed is a valid and reliable smartphone-based measure of multiple sclerosis-related gait and balance impairment

Wei-Yi Cheng [a], Alan K. Bourke [a], Florian Lipsmeier [a], Corrado Bernasconi [a], Shibeshih Belachew [a,1], Christian Gossens [a,*], Jennifer S. Graves [b,c], Xavier Montalban [d,e], Michael Lindemann [a,f]

[a] F. Hoffmann-La Roche Ltd, Basel, 4070, Switzerland
[b] Department of Neurosciences, University of California, San Diego, San Diego, CA, 92093, USA
[c] University of California, San Francisco, San Francisco, CA, 94143, USA
[d] Division of Neurology, University of Toronto, Toronto, ON, M5S 1A1, Canada
[e] Department of Neurology-Neuroimmunology, Multiple Sclerosis Centre of Catalonia (CEMCAT), Vall d'Hebron University Hospital, Barcelona, 08035, Spain
[f] Department of Economics, Baden-Wuerttemberg Cooperative State University, Loerrach, 79539, Germany

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ABSTRACT

Background: People living with multiple sclerosis (MS) experience impairments in gait and mobility, that are not fully captured with manually timed walking tests or rating scales administered during periodic clinical visits. We have developed a smartphone-based assessment of ambulation performance, the 5 U-Turn Test (5UTT), a quantitative self-administered test of U-turn ability while walking, for people with MS (PwMS).
Research question: What is the test-retest reliability and concurrent validity of U-turn speed, an unsupervised self-assessment of gait and balance impairment, measured using a body-worn smartphone during the 5UTT?
Methods: 76 PwMS and 25 healthy controls (HCs) participated in a cross-sectional non-randomised interventional feasibility study. The 5UTT was self-administered daily and the median U-turn speed, measured during a 14-day session, was compared against existing validated in-clinic measures of MS-related disability.
Results: U-turn speed, measured during a 14-day session from the 5UTT, demonstrated good-to-excellent test-retest reliability in PwMS alone and combined with HCs (intraclass correlation coefficient [ICC] = 0.87 [95 % CI: 0.80–0.92]) and moderate-to-excellent reliability in HCs alone (ICC = 0.88 [95 % CI: 0.69–0.96]). U-turn speed was significantly correlated with in-clinic measures of walking speed, physical fatigue, ambulation impairment, overall MS-related disability and patients' self-perception of quality of life, at baseline, Week 12 and Week 24. The minimal detectable change of the U-turn speed from the 5UTT was low (19.42 %) in PwMS and indicates a good precision of this measurement tool when compared with conventional in-clinic measures of walking performance.
Significance: The frequent self-assessment of turn speed, as an outcome measure from a smartphone-based U-turn test, may represent an ecologically valid digital solution to remotely and reliably monitor gait and balance impairment in a home environment during MS clinical trials and practice.

1. Introduction

Symptoms of multiple sclerosis (MS), including impaired lower-extremity muscle strength, sensory, cerebellar, vestibular and cognitive disturbances [1], may contribute to gait and balance impairment. People with MS (PwMS) experience a higher incidence of falls [2], with over 50 % reporting a fall in a 3–6-month period [1]. Most falls take place at home while standing, walking or turning [2]. To turn while

* Correspondence author at: F. Hoffmann-La Roche Ltd, 124 Grenzacherstrasse, Basel, CH 4070, Switzerland.
E-mail addresses: wei-yi.cheng@roche.com (W.-Y. Cheng), alan.bourke@roche.com (A.K. Bourke), florian.lipsmeier@roche.com (F. Lipsmeier), corrado.bernasconi@roche.com (C. Bernasconi), belachew@me.com (S. Belachew), christian.gossens@roche.com (C. Gossens), jgraves@ucsd.edu (J.S. Graves), xavier.montalban@cem-cat.org (X. Montalban), michael.lindemann@roche.com (M. Lindemann).
[1] During completion of the work related to this manuscript, S. Belachew was an employee of F. Hoffmann-La Roche Ltd; his current affiliation is Biogen, Cambridge, MA, USA.

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walking, the body must reduce its forward momentum, rotate and then accelerate in the new direction [3]. The ability to adapt gait and balance, to perform a turn or change in direction safely, is thus an essential part of independent living [4]. Studies suggest that the neural systems involved in turning may be more vulnerable to impairments than during forward walking [5]. Characteristics of turning while walking have thus been shown to be important predictors of balance confidence, gait impairment and falls in PwMS [6].

Existing best practice methods of assessing ambulation in PwMS primarily involve clinical observations using trained clinical staff, with manual stopwatch-timed walking-based assessments (e.g., Timed Up and Go [TUG], Timed 25-Foot Walk [T25FW], Two-Minute Walk Test [2MWT] and Six-Minute Walk Test [6MWT]) [7]. However, such in-clinic assessments are administered infrequently and can be time-consuming, thus limiting their utility in some clinical practice settings and are prone to rater-dependent error. Furthermore, the biomechanical aspects of participants' mobility function remain uncaptured.

Recently, body-worn inertial sensor-based systems have been used to assess physical function in PwMS in laboratory and clinical settings, showing differences in mobility between PwMS and healthy controls (HCs) [6,8–11]. While performing a modified TUG test, PwMS had a longer U-turn duration [8]. A follow-up longitudinal study, conducted over 18 months, demonstrated that turning duration was important but not significant in separating HCs versus patients with mild and moderate MS disability [11]. The magnitude of turns measured during the TUG test was also a relevant feature in a regression model used to distinguish PwMS from HCs [9]. The inclusion of turn parameters collected during the TUG and 6MWT improved modelling of patient-reported balance confidence and walking limitations in PwMS [6]. A longitudinal study conducted by Chitnis et al. [10] reported significant moderate-to-good correlations between turn speed during the TUG and 2MWT, and conventional in-clinic MS disability metrics, including the Expanded Disability Status Scale (EDSS) and T25FW.

Advances in inertial-sensor technology, combined with the widespread adoption of smartphones, have made the ubiquitous monitoring of human body movement, using body-worn inertial sensors, in a free-living situation more feasible. Inertial sensor-based smartphones and body-worn sensors have facilitated the instrumentation of existing physical functional tests [12] and the harvesting of rare real-world events (e.g., falls) [13]. In the study "*Monitoring of Multiple Sclerosis (MS) Participants With the Use of Digital Technology (Smartphones and Smartwatches) - A Feasibility Study*" (NCT02952911) [14], we introduced a daily self-administered U-turn test that can be performed independently at home using a smartphone. The 5 U-Turn Test (5UTT) aims to examine a person's ability to perform five 180° turns (U-turns) while walking at a comfortable pace.

This study assessed the test-retest reliability and concurrent validity of the 5UTT to assess gait and balance impairment, a surrogate for disease state, in PwMS in both supervised and unsupervised settings, using inertial-sensor data from a preconfigured smartphone.

2. Materials and methods

This cross-sectional analysis examined the longitudinal intra-session test-retest reliability and concurrent validity of the 5UTT, a self-administered functional assessment of gait and balance impairment in PwMS.

2.1. Participants

In total, 76 PwMS and 25 HCs were enrolled in this study. PwMS were included if they had a diagnosis of MS (2010 revised McDonald criteria [15]; treated or untreated) and an EDSS score of 0–5.5 (inclusive). A maximum EDSS score of 5.5 was used to ensure any patient with relapsing or progressive MS would not have any significant difficulty in participating in the study protocol. Further details regarding the inclusion/exclusion criteria were previously published [14].

The trial protocol was approved by the institutional review board/ethics committee at each participating site. These include the Multiple Sclerosis Centre of Catalonia (CEMCAT), Vall d'Hebron University Hospital, Barcelona, Spain; and the University of California, San Francisco (UCSF), San Francisco, California, USA. The study protocol conformed to Good Clinical Practice guidelines and the principles outlined in the Declaration of Helsinki. The study is registered at ClinicalTrials.gov (NCT02952911) [14]. Written informed consent was obtained from all participants or participants' legally authorised representatives prior to assessment.

2.2. Protocol

Eligible PwMS and HCs were assessed clinically at three time points over the 24-week study duration. They were provided with a smartphone at enrolment and asked to perform the 5UTT once daily (Fig. 1).

2.3. The 5 U-Turn Test

The 5UTT is a self-administered test, where participants walk at a self-selected comfortable pace and perform five consecutive 180° turns (U-turns) at least 4 m apart within 60 s (Fig. 2a-c).

2.4. The in-clinic assessments

At the three in-clinic visits, all participants performed both the T25FW and the 5UTT, and were assessed using the Fatigue Scale for Motor and Cognitive Functions (FSMC) [16]. In addition, PwMS were assessed at each scheduled visit with the following disability rating scales and patient-reported outcomes: EDSS [17], Multiple Sclerosis Impact Scale-29 (MSIS-29; version 2) [18] and Patient Determined Disease Steps (PDDS) (Fig. 1) [19].

The T25FW test score was calculated as the average time of two successive timed walking bouts over 25 feet (7.62 m) and has demonstrated reliability, validity and clinical meaningfulness in MS [20].

FSMC is a validated 20-item scale developed for the assessment of MS-related motor and cognitive fatigue [16]. Here we examined the 10-item subscale related to motor fatigue, specifically items 2–3, 5–6, 9–10, 12, 14, 16 and 19 (FSMC motor subscale, range 10 [no fatigue]–50 [severe fatigue]).

MSIS-29 is a 29-item MS-specific questionnaire to assess patient-reported quality of life [18]. Scores were summed to form a physical subscale (20 items, range 20–80) and psychological impact subscale (9 items, range 9–36), with higher values indicating lower perceived quality of life. The physical MSIS-29 subscale was used (items 1–20), along with the ambulation summed items, which include items 4 and 5. All scales and summed items were transformed to a 0–100 scale.

PDDS is a validated ordinal scale that ranks MS severity from 0 (normal) to 8 (bedridden) [21] according to patients' perceptions, primarily based on physical motor function and gait impairment.

2.5. Equipment

Participants were provided with a Samsung Galaxy S7 smartphone. The inertial-sensor embedded in the smartphone contained tri-axial accelerometer and gyroscope sensors and sampled using a variable sampling rate of approximately 50 Hz. The sensor data were encrypted before wireless transmission to a secure server for subsequent data analysis [22].

2.6. Sensor data analysis

Data analysis was performed in Python 2.7 and 3.6. The inertial-sensor data were first resampled, using linear interpolation, to a fixed

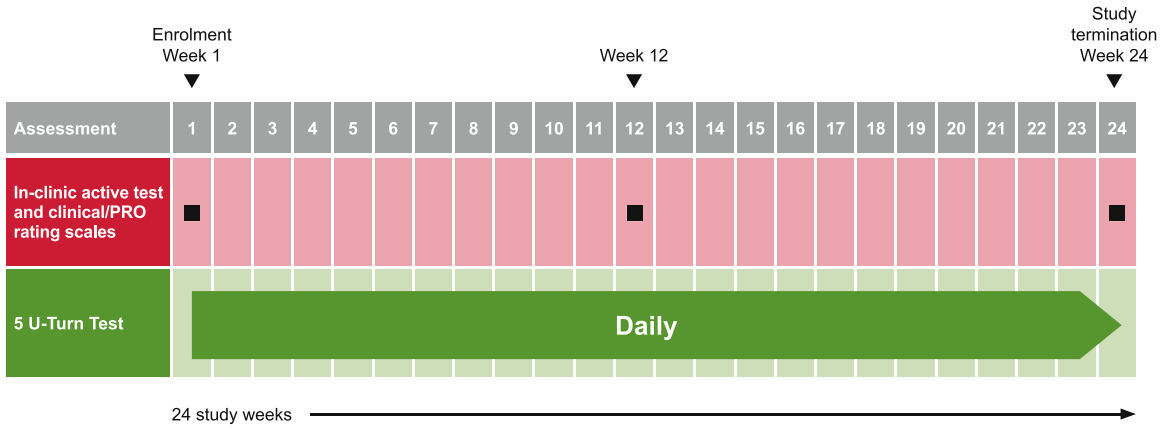

Fig. 1. Study protocol. PwMS and HCs were assessed clinically at baseline (enrolment), Week 12 and study termination/early discontinuation (Week 24). At the enrolment visit, PwMS and HCs were provided with a preconfigured smartphone. Participants were requested to attach the smartphone and perform the 5UTT once daily, at approximately the same time, during the entire 24-week study duration [15].
5UTT = 5 U-Turn Test; HC = healthy control; PRO = patient-reported outcome; PwMS, people with multiple sclerosis.

Fig. 2. The 5UTT is a self-administered test, which can be activated by the participant through the touchscreen interface. The test is recorded using the same smartphone attached to the body. After answering safety questions, reading the instructions (a) and attaching the smartphone, participants were requested to walk at a self-selected comfortable pace and perform five consecutive 180° turns (U-turns) at least 4 m apart within 60 s (a-b). Audio and vibration cues indicate the start and the end of the test. Feedback on how participants perform the test is not provided. A 4m distance was chosen to allow a clear separation between U-turns while also reducing the risk of dizziness and fatigue. The test was performed on a flat level surface, either indoors or outdoors. Participants were allowed to wear regular footwear and an assistive and/or orthotic device as needed. The smartphone was carried at the front of the waist in a belt bag or alternatively in a trouser pocket (c). (a) Instruction screens presented to the participant prior to completing the 5UTT. (b) Participants are instructed to walk safely and perform five successive U-turns going back and forth between two points at least 4 m apart, safely and at a normal comfortable walking speed within 60 s. (c) The attachment methods. The smartphone is either worn at the front of the waist, in a waist-worn belt bag (provided to the participant) or in a trouser pocket. 5UTT = 5 U-Turn Test.

sampling rate of 50 Hz. The vertical axis of the sensor coordinate frame, attached to the body, was aligned with gravity via matrix rotation [23], and the yaw gyroscope signal was integrated to calculate the turn angle. Individual turns were included if they exceeded 90°. The turn speed was calculated as the turn angle divided by the duration of the turn event [23]. Using the algorithm by El-Gohary et al. [5], the beginning and end of each turn was identified using thresholds of ±5°/s on the angular velocity profile. If turns were less than 0.05 s apart and in the same direction, they were considered part of the same turn. The median turn speed of the recorded turns was taken for each test, with a minimum of one turn required per test.

2.7. Statistical analysis

A session consists of a 14-day non-overlapping period, chosen to reduce intra-day, day-to-day/weekend-weekday fluctuations and variations in the daily test schedule/location, which may be considered irrelevant to the chronic temporal pattern of MS disability progression. A minimum of three tests performed during this 14-day period was required to register a valid session. The median turn speed during each valid session was compiled for each participant. Test-retest reliability was assessed using the second (baseline session excluded to allow familiarisation) and subsequent complete 14-day session per participant. A two-way analysis of variance using a mixed-effects model with absolute agreement (intraclass correlation coefficient [ICC]; ICC [2,1]) was chosen [24].

The standard error of measurement (SEM) provides an absolute index of reliability and is used to quantify the precision of the measurement instruments [25]. The SEM was calculated, where SD is the standard deviation of all turn speed values as:

$$SEM = SD.\sqrt{1 - ICC}$$

The minimal detectable change, with a 95 % confidence interval (CI) (MDC_{95}), was calculated to determine how much measured change is likely to reflect true change [25]. The MDC_{95} [4] was calculated as:

$$MDC_{95} = z - score\ (95\%\ CI)SEM.\sqrt{2}$$

The SEM and MDC_{95} provide a longitudinal assessment of the sensitivity to change in signal versus noise from repeated tests.

The SEM and MDC_{95} can be expressed as percentages that are independent of the units of measurement, calculated as:

$$SEM\% = 100.\frac{SEM}{\bar{x}}$$

$$MDC_{95}\% = 100.\frac{MDC_{95}}{\bar{x}}$$

This allows comparison of the amount of random error between measurements using the above two equations, where $\bar{x}$ is the mean for all observations [26].

To examine concurrent validity, the median turn speed during 14-day sessions from 7 days before to 7 days after each of the three clinical visits (baseline, Week 12 and Week 24), and during all three visits ('All visits'), was correlated against the in-clinic disability outcome measures and patient-reported quality-of-life and fatigue scales (EDSS, T25FW, PDDS, MSIS-29 ambulation summed items, MSIS-29 physical subscale and FSMC motor subscale) using non-parametric Spearman's correlation. The two-sided p-value, for significant correlation, was adjusted using Holm–Bonferroni correction applied across all primary outcome measures, with statistical significance set at $p < 0.05$.

3. Results

A total of 9628 tests were recorded, with an average of 90.46 (SD: 56.01) tests recorded per participant. Average 5UTT turn speed was 77.91°/s ± 3.27°/s (mean ± 95 % CI, $n = 76$) for PwMS and 80.63°/s ± 3.72°/s (mean ± 95 % CI, $n = 25$) for HCs. Participants' baseline demographics are described in Table 1.

3.1. Test-retest reliability

Test-retest reliability data were available for 85 participants (67 PwMS, 18 HCs). ICC values demonstrated good-to-excellent reliability for the PwMS alone (ICC [2,1] [95 % CI]: 0.87 [0.80–0.92]) and combined with HCs (ICC [2,1] [95 % CI]: 0.87 [0.81–0.91]). Moderate-to-excellent reliability was demonstrated for the HCs (ICC [2,1] [95 % CI]: 0.88 [0.69–0.96]) (Table 2). Low MDC_{95} (10.40°/s–15.36°/s) and MDC_{95}% (12.97 %–19.42 %) values were found along with low SEM (3.75°/s–5.54°/s) and SEM% (4.68 %–7.00 %) values.

Table 1
Cohort demographics and characteristics for PwMS and HCs at baseline.

Parameter	PwMS ($N = 76$)	HCs ($N = 25$)	p-value
Age, mean ± SD, years	39.5 ± 7.9	34.9 ± 9.3	0.043
Female, n (%)	53 (69.7)	7 (28.0)	NA
MS diagnosis (PPMS, SPMS, RRMS), %	3.9, 5.3, 90.8	NA	NA
Time since MS symptom onset, mean ± SD, years	11.3 ± 7.0	NA	NA
EDSS, mean ± SD	2.4 ± 1.4	NA	NA
9HPT, mean ± SD, seconds			
Dominant hand	22.1 ± 4.6	18.9 ± 2.1	<0.001
Non-dominant hand	22.8 ± 4.9	19.5 ± 2.0	<0.001
T25FW, mean ± SD, seconds	6.0 ± 2.1	5.0 ± 1.0	0.19
BBS, mean ± SD	52.5 ± 5.7	56.0 ± 0	<0.001
PDDS, mean ± SD	1.5 ± 1.6	NA	NA
FSMC total score, mean ± SD	59.1 ± 22.7	25.5 ± 6.0	<0.001
PHQ-9, mean ± SD	8.3 ± 6.1	2.4 ± 2.9	<0.001
MSIS-29 (version 2), mean ± SD			
Physical subscale	26.2 ± 24.4	NA	NA
Psychological subscale	36.4 ± 26.5	NA	NA

9HPT = 9-Hole Peg Test. BBS = Berg Balance Scale. EDSS = Expanded Disability Status Scale. FSMC = Fatigue Scale for Motor and Cognitive Functions. HC = healthy control. MS = multiple sclerosis. MSIS-29 = Multiple Sclerosis Impact Scale-29. NA = not applicable. PDDS = Patient Determined Disease Steps. PHQ-9 = Patient Health Questionnaire-9. PPMS = primary progressive multiple sclerosis. PwMS = people with multiple sclerosis. RRMS = relapsing-remitting multiple sclerosis. SD = standard deviation. SPMS = secondary progressive multiple sclerosis. T25FW = Timed 25-Foot Walk.

Table 2
Test-retest reliability for the turn speed (°/s) of the 5UTT for PwMS and HCs.

Category	ICC (95 % CI)	SEM	SEM %	MDC_{95}	MDC_{95}%
14-day session median					
PwMS & HC	0.87 (0.81–0.91)	5.24	6.60	14.51	18.29
PwMS	0.87 (0.80–0.92)	5.54	7.00	15.36	19.42
HC	0.88 (0.69–0.96)	3.75	4.68	10.40	12.97

ICC(2,1) calculated for the 14-day session median. Reliability is indicated using the ICC values classified as poor (ICC < 0.5), moderate (ICC = 0.5–0.75), good (ICC = 0.75–0.9) and excellent (ICC > 0.9) [24]. SEM and MDC_{95} can be expressed as percentages that are independent of the units of measurement.
5UTT = 5 U-Turn Test. CI = confidence interval. HC = healthy control. ICC = intraclass correlation coefficient. MDC_{95} = minimal detectable change with a 95 % CI. PwMS = people with multiple sclerosis. SEM = standard error of measurement.

3.2. Concurrent validity

Median turn speed was correlated against in-clinic disability outcome measures and patient-reported quality-of-life and fatigue scales using Spearman's rho correlation. All correlations were statistically significant at all study time points (baseline, Week 12 and Week 24) individually and collectively, and varied between fair and moderate-to-good (r=–0.331 to –0.603, all p-values from $p < 0.001$ to $p < 0.025$). Examining across all three time points collectively ('All visits'), median turn speed produced significant moderate-to-good negative correlations with the T25FW and MSIS-29 ambulation summed items (r=–0.506 to –0.516, $p < 0.001$). The strength of correlations with the EDSS, PDDS, MSIS-29 physical summed items and the FSMC motor subscale was fair, approaching moderate-to-good (r=–0.452 to –0.498, $p < 0.001$). The details of the observed correlations are summarised in Table 3 and Fig. 3.

4. Discussion

This study provides evidence of the reliability and concurrent validity for PwMS to self-assess gait and balance impairment through a novel smartphone sensor-based outcome measure of turn speed, the 5UTT.

A recent study demonstrated that turning is an important marker of balance confidence and walking limitation in PwMS. They promote the inclusion of turning in tests of longer durations with multiple turns, as performed in the 5UTT, which may be used to model longitudinal change more accurately [6].

To the best of our knowledge, this is the first study to demonstrate excellent test-retest reliability for turn-speed, derived from a smartphone-based self-assessment of gait and balance impairment, in an MS population using the embedded inertial sensors. Attaching the smartphone using a belt bag at the waist, or in a trouser pocket, allows for the approximation of the body's centre-of-mass movement and therefore a better indication of general body movement. It is anticipated that these convenient sensor attachment options will ensure adherence for future 5UTT implementations.

An analysis of the ICC results demonstrated excellent intra-session test-retest reliability in both PwMS and HCs. In addition to demonstrating acceptable ICC values, a measurement tool should exhibit small measurement error and be capable of identifying real changes within a group and in individuals [27]. The absolute reliability analysis performed in this study corroborates the good relative reliability of the 5UTT from the 14-day session median. Specifically, the low SEM and SEM% values together with low MDC_{95} and MDC_{95}% values indicate good precision of the measurement tool. In particular, the MDC_{95}%

Table 3
Spearman's correlations between the turn speed (°/s) of the 5UTT and in-clinic disability and patient-reported outcome measures in PwMS at baseline, Week 12, Week 24 and for all three visits ('All visits').

In-clinic outcome measures	*r*	*p*-value*	*n*
T25FW			
All visits	–0.506	<0.001	70
Baseline	–0.525	<0.001	53
Week 12	–0.501	<0.001	55
Week 24/early discontinuation	–0.416	0.008	50
EDSS			
All visits	–0.452	<0.001	70
Baseline	–0.529	<0.001	54
Week 12	–0.546	<0.001	57
Week 24/early discontinuation	–0.347	0.025	51
PDDS			
All visits	–0.498	<0.001	70
Baseline	–0.582	<0.001	54
Week 12	–0.591	<0.001	57
Week 24/early discontinuation	–0.463	0.003	51
MSIS-29 ambulation summed items			
All visits	–0.516	<0.001	70
Baseline	–0.576	<0.001	54
Week 12	–0.529	<0.001	57
Week 24/early discontinuation	–0.490	0.002	51
MSIS-29 physical subscale			
All visits	–0.470	<0.001	70
Baseline	–0.603	<0.001	54
Week 12	–0.556	<0.001	57
Week 24/early discontinuation	–0.331	0.018	51
FSMC motor subscale			
All visits	–0.496	<0.001	70
Baseline	–0.564	<0.001	53
Week 12	–0.537	<0.001	56
Week 24/early discontinuation	–0.416	0.010	51

5UTT = 5 U-Turn Test. EDSS = Expanded Disability Status Scale. FSMC = Fatigue Scale for Motor and Cognitive Functions. MSIS-29 = Multiple Sclerosis Impact Scale-29. *n* = number of participants. PDDS = Patient Determined Disease Steps. PwMS = people with multiple sclerosis. *r* = Spearman's correlation. T25FW = Timed 25-Foot Walk.

* Significant correlation after Holm–Bonferroni adjusted *p*-values with an alpha value of 0.05 for 24 statistical significance tests. The strengths of the correlations were classified as good-to-excellent ($r>0.75$), moderate-to-good ($r = 0.5$–0.75), fair ($r = 0.25$–0.49) or no correlation ($r<0.25$) [25].

value was 19.42 % for PwMS, which compares favourably with values of 36 % for the in-clinic T25FW [28]. More precisely, for 95 % of PwMS, differences in repeated session measurements of ≥15.36°/s would reflect a real difference, reflective of a change in disease status.

The concurrent validity [27] of turn speed measured during the self-administered 5UTT was demonstrated against conventional in-clinic MS disability outcome measures (EDSS and T25FW), patients' perception of their disability (PDDS), physical impact of MS (physical subscale and ambulation summed items of the MSIS-29) and physical fatigue (motor subscale of the FSMC).

Our results compare favourably with a recent longitudinal study conducted by Chitnis et al. [10]. They reported fair and moderate-to-good significant correlations for turn speed measured at the chest, with the EDSS (r=–0.563 to –0.588, $p < 0.05$, for maximum, mean and standard deviation) and with the T25FW ($r = 0.476$, $p < 0.05$, for standard deviation and $r = 0.552$ for maximum, $p < 0.05$). Similarly, in this study, we observed fair and moderate-to-good significant correlations with the EDSS (r=–0.347 to –0.546, $p < 0.05$) and with the T25FW (r=–0.416 to –0.525, $p < 0.05$). However, Chitnis et al. [10] analysed turns recorded during clinically based assessments in a smaller cohort of PwMS ($n = 23$). In our study, by comparison, we analysed turns recorded during a novel self-administered U-turn test, the 5UTT, performed independently at home using a smartphone, in a larger cohort of PwMS ($n = 76$).

The 5UTT is a quick and convenient smartphone-based test that can be incorporated into the daily routine of PwMS, as it does not require a laboratory setting, external timing/camera-based measurement equipment or trained clinical/technical staff. Instead, it can be performed remotely on an even walking surface, either indoors at home or outdoors. In addition, the test enables patients to self-assess gait and balance impairment at a comfortable pace and therefore does not increase the risk of falling. Consequently, this self-administered test allows clinicians to perform continuous longitudinal monitoring of MS disease state.

4.1. Limitations and future work

PwMS from this study encompassed mostly patients with relapsing forms of MS, with mild levels of overall disability and minimal

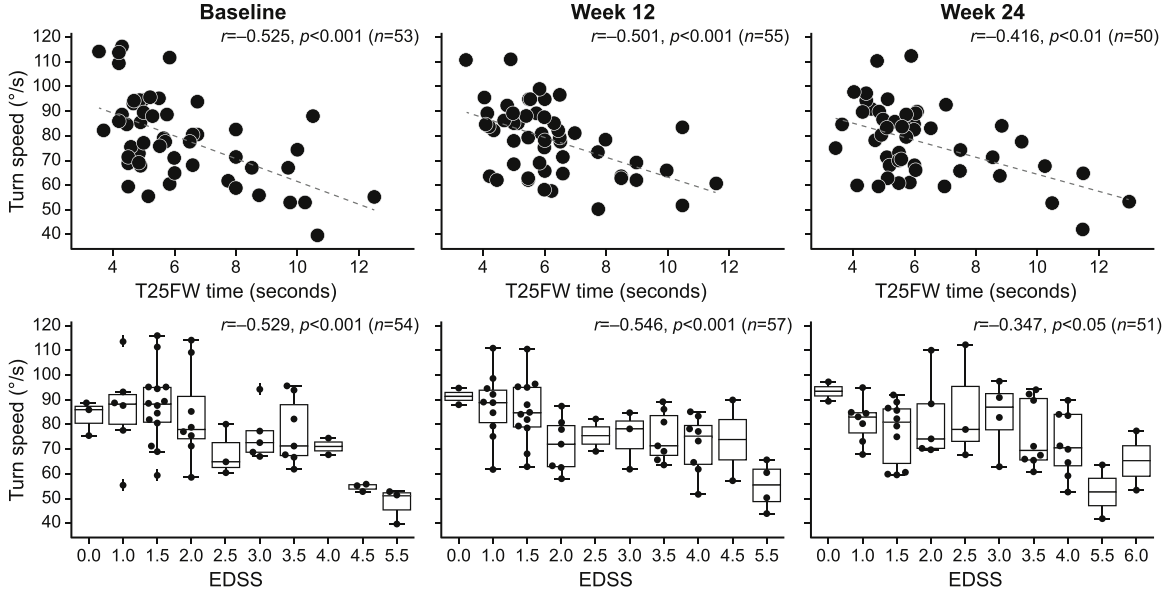

Fig. 3. A graphical representation of the Spearman's correlations between the turn speed and in-clinic disability outcome measures in PwMS. Spearman's correlations between the turn speed and EDSS and T25FW at baseline, Week 12 and Week 24 (or early discontinuation).
EDSS = Expanded Disability Status Scale. *n* = number of participants. PwMS = people with multiple sclerosis. *r* = Spearman's correlation. s = seconds. T25FW = Timed 25-Foot Walk.

ambulatory impairment. Correlations observed in this preliminary work, between 5UTT turn speed and all in-clinic disability and patient-reported outcome measures, need to be further substantiated across the complete spectrum of MS clinical phenotypes. The longitudinal sensitivity to change of turn speed and its responsiveness to treatment intervention, will be investigated in the ongoing Phase III CONSONANCE trial (NCT03523858). Finally, by construction, the 5UTT turn speed assesses only the speed of turning while walking at a self-selected comfortable pace (due to safety concerns) and may not fully capture aspects of gait ataxia that could be better reflected by other combinations of 5UTT sensor-based features.

In addition to motor skills, participant-specific confounding factors, such as motivation, may impact test performance [29], which may explain the decrease in correlations observed at Week 24.

The work presented here formed part of a pilot study, which aimed to evaluate the feasibility of conducting remote patient monitoring, using digital technology in PwMS [14]. As the primary aims of this study were considered exploratory in nature, a duration of 24 weeks was deemed adequate to assess the feasibility of performing smartphone- and smartwatch-based assessments. It is also sufficient to assess the test-retest reliability of the 5UTT and its correlation with in-clinic disability and patient-reported outcome measures at three clinical time points.

We noted significant inter-patient differences in turn speed in PwMS, who otherwise had similar performance-based disability scores, such as the ambulation speed captured by the T25FW (Fig. 3). This suggests that sensor-grade measures of turn speed, recorded in a patient's own environment, may capture valuable incremental dimensions in characterising MS-related disability. A similar phenomenon, of higher separation of performance distribution in inertial sensor-based measures of physical function, within EDSS subgroups, was also observed by Block et al. [30] when measuring daily step count in PwMS. Turn speed thus warrants further evaluation as an outcome measure in longitudinal MS clinical trials and could provide an assessment of gait and balance impairment at higher temporal resolution, compared to the relatively infrequent periodic snapshots of function, currently captured by in-clinic assessments.

Future work will further establish the qualitative and quantitative validity of the 5UTT for assessing gait and balance impairment using data from CONSONANCE and explore the application of this algorithm to turns performed during free-living activity. The longitudinal analysis of turn speed recorded during walking in a free-living situation, may expose potential subtle insidious changes in MS state that may occur early in disease onset. Two types of turning strategy while walking, namely the spin turn and the step turn [3], are typically described. Further biomechanical investigation is required to assess which turn strategy is adopted by PwMS, and what is the relationship to speed and smoothness of turns in the 5UTT and during free-living gait. The algorithm for turn speed measurement, implemented here, was validated in a Parkinson's disease cohort by El-Gohary et al. [5] using a motion capture system. Future work will determine the accuracy of this algorithm, using ground truth data, harvested from an MS cohort.

In conclusion, turn speed collected from a smartphone-based self-assessment in PwMS, demonstrated excellent intra-session test-retest reliability and correlates significantly with all in-clinic MS disability and patient-reported outcome measures. The 5UTT is reliable and showed concurrent validity to assess gait and balance impairment in PwMS.

CRediT authorship contribution statement

Wei-Yi Cheng: Methodology, Software, Validation. **Alan K. Bourke:** Conceptualization, Methodology, Software, Validation, Formal analysis, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration. **Florian Lipsmeier:** Conceptualization, Methodology, Writing - review & editing. **Corrado Bernasconi:** Conceptualization, Formal analysis, Writing - review & editing. **Shibeshih Belachew:** Conceptualization, Methodology, Investigation, Writing - review & editing, Supervision. **Christian Gossens:** Conceptualization, Resources, Writing - review & editing, Supervision, Funding acquisition. **Jennifer S. Graves:** Conceptualization, Methodology, Investigation, Resources, Writing - review & editing. **Xavier Montalban:** Conceptualization, Validation, Investigation, Supervision, Writing - review & editing. **Michael Lindemann:** Conceptualization, Methodology, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: W. Y.C. is an employee of F. Hoffmann-La Roche Ltd. A.K.B. is an employee of F. Hoffmann-La Roche Ltd. F.L. is an employee of F. Hoffmann-La Roche Ltd. C.B. is a contractor for F. Hoffmann-La Roche Ltd. S.B. was an employee of F. Hoffmann-La Roche Ltd during the completion of the work related to this manuscript. S.B. is now an employee of Biogen (Cambridge, MA, USA), which was not in any way associated with this study. C.G. is an employee and shareholder of F. Hoffmann-La Roche Ltd. J.S.G. has received grants or research support from Biogen, Genentech, Inc. and S3 Group, and has received compensation for a non-branded resident and fellow education seminar supported by Biogen. X. M. has received speaker honoraria and travel expense reimbursement for participation in scientific meetings, and has been a steering committee member of clinical trials or served on advisory boards of clinical trials for Actelion, Biogen, Celgene, Merck, Novartis, Oryzon, Roche, Sanofi Genzyme and Teva Pharmaceutical. M.L. is a consultant for F. Hoffmann-La Roche Ltd via Inovigate.

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Qualified researchers may request access to individual patient level data through the clinical study data request platform (https://vivli.org/). Further details on Roche's criteria for eligible studies are available here (https://vivli.org/members/ourmembers/). For further details on Roche's Global Policy on the Sharing of Clinical Information and how to request access to related clinical study documents, see here (https://www.roche.com/research_and_development/who_we_are_how_we_work/clinical_trials/our_commitment_to_data_sharing.htm).

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