

A new digital measure to meaningfully assess daily-life ambulatory function of people with Multiple Sclerosis



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HIA
Percy



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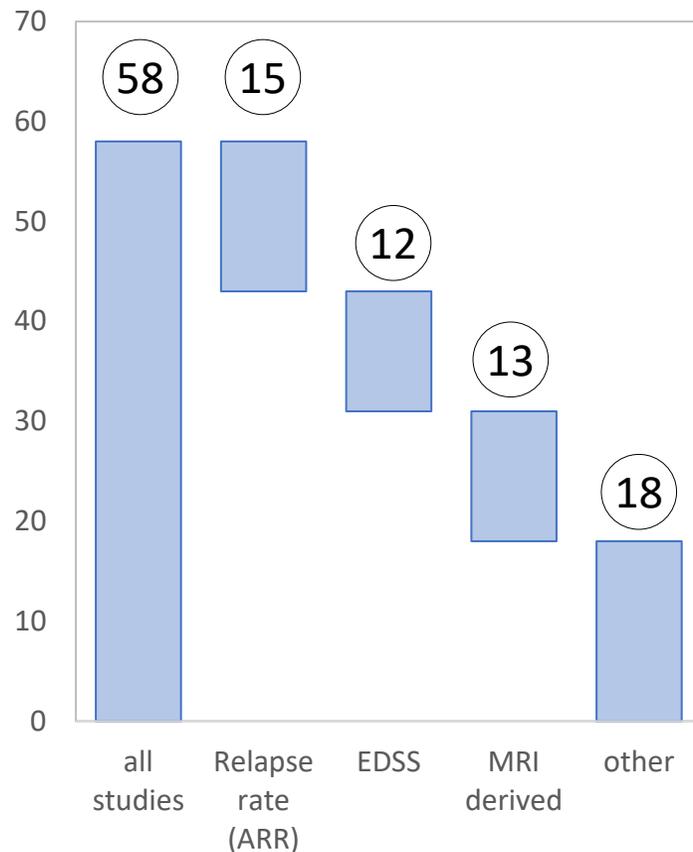
Disclaimer :

- **WS95C is still under development.**
- **This study is ongoing and the data are not fully clean.**

EDSS is the gold standard in MS functional assessment but has known limitations

EDSS is the most used functional assessment

Primary endpoints used for Phase II & III MS studies *



* As of clinicaltrials.gov, studies started since 2020

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First regulatory qualification of a digital primary endpoint to measure treatment efficacy in DMD

[Laurent Servais](#) , [Damien Eggenspieler](#), [Margaux Poleur](#), [Marc Grelet](#), [Francesco Muntoni](#), [Paul Strijbos](#) & [Mélanie Anoussamy](#)

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Committee for Medicinal Products for Human Use (CHMP)

Qualification Opinion for Stride velocity 95th centile as primary endpoint in studies in ambulatory Duchenne Muscular Dystrophy studies

Draft agreed by Scientific Advice Working Party (SAWP)	01 September 2022
Adopted by CHMP for release for consultation	15 September 2022 ¹
Start of public consultation	27 February 2023 ²
End of consultation (deadline for comments)	09 April 2023
Adopted by CHMP	20 July 2023

Keywords	Qualification of Novel Methodology, Duchenne Muscular Dystrophy studies, Digital Health Technology, efficacy endpoint, wearable sensor
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Digital endpoint development according to FDA / EMA digital endpoint standards & DiMe V3 framework

Concepts of Interest for MS:

- ✓ Walking speed
- ✗ Fatigue
- ✗ Activity
- ✗ Walking perimeter

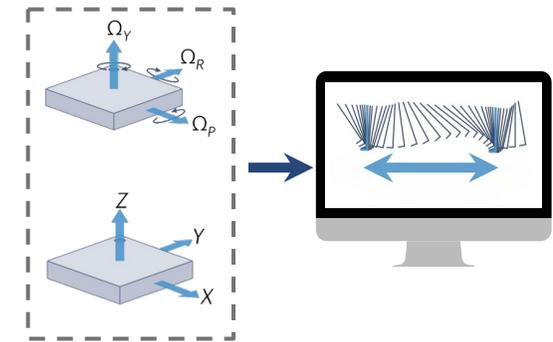
Validation:

- ✓ Verification
- ✓ Analytical validation
- 📍 Clinical validation

Variable: the velocity of the top 5% most rapid walking strides measured in patient daily life

Data acquisition according to the ActiMS protocol (N=78 patients)

Patients were equipped for 2 recording periods of 1 month with sensors with stride level data reconstruction capabilities



WS95C

is an objective and accurate real-world measure of gait impairment in MS

Development of this clinically meaningful endpoint was performed on ActiMS dataset

Items of clinical validation of an outcome

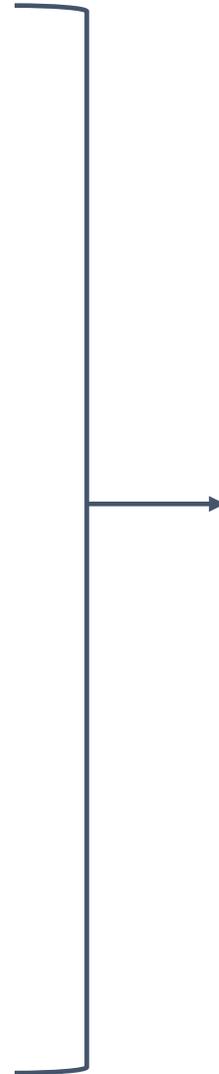
Adherence

Reliability

Known-group validity

Convergent validity

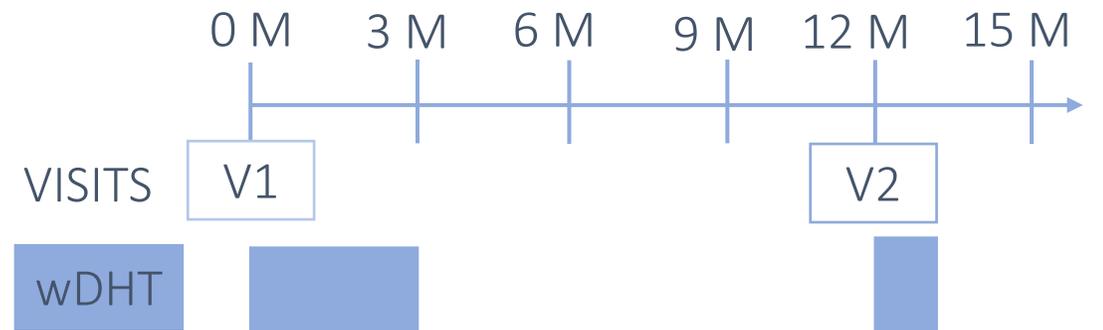
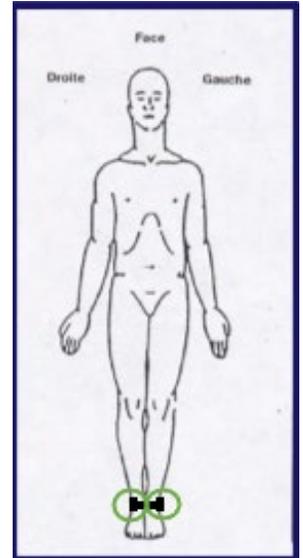
Ability to detect change



ACTiMS STUDY

Ongoing longitudinal natural history study

- 5 sites (in Belgium and France)
- Evaluation at baseline and at 1 year
- Subjects were asked to wear the DHT for 3 months after the 1st visit and 1 month after the follow-up visit



Baseline characteristics of patients in ActiMS

Number of patients	78
Age (years) : median \pm SD [range]	48.5 \pm 11.7 [22-65]
Sex: female (%)	43 (55.1%)
PMS / RRMS	17 / 61
EDSS: mean \pm SD [range]	3 \pm 1.4 [0-5.5]
T25FW (seconds): mean \pm SD [range]	6.5 \pm 6.7 [2.8-60.0]

WS95C measures the ability of MS patients to walk fast in their daily life

WS95C

Walking Speed 95th centile is:

- the velocity of the top 5% most rapid walking strides measured in the daily life of a patient
 - derived from data collected over a 1 month period (minimum of 50h of data and 1000 strides)
- an under development digital measure assessing MS patients continuously and passively in one of the most important concept of health

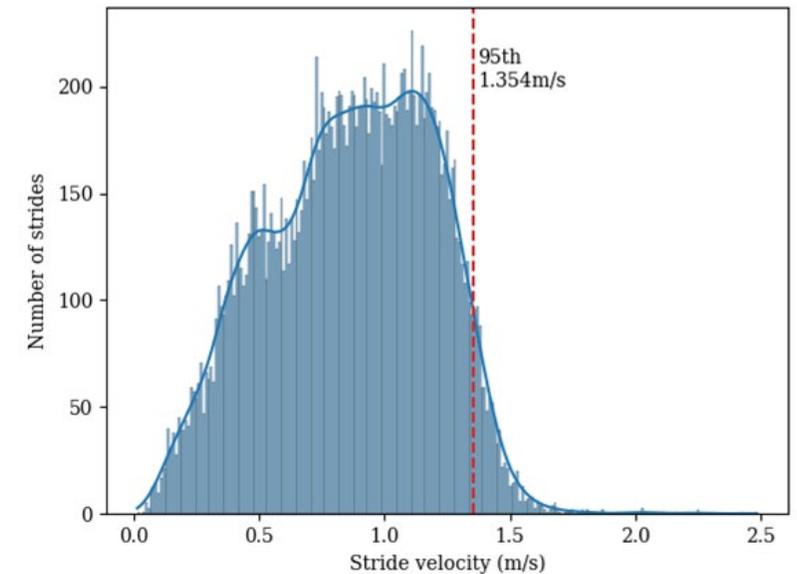


Illustration of strides reconstruction with Syde during a 6MWT

Over all completed recording periods, patients show good adherence with DHT wear

Adherence

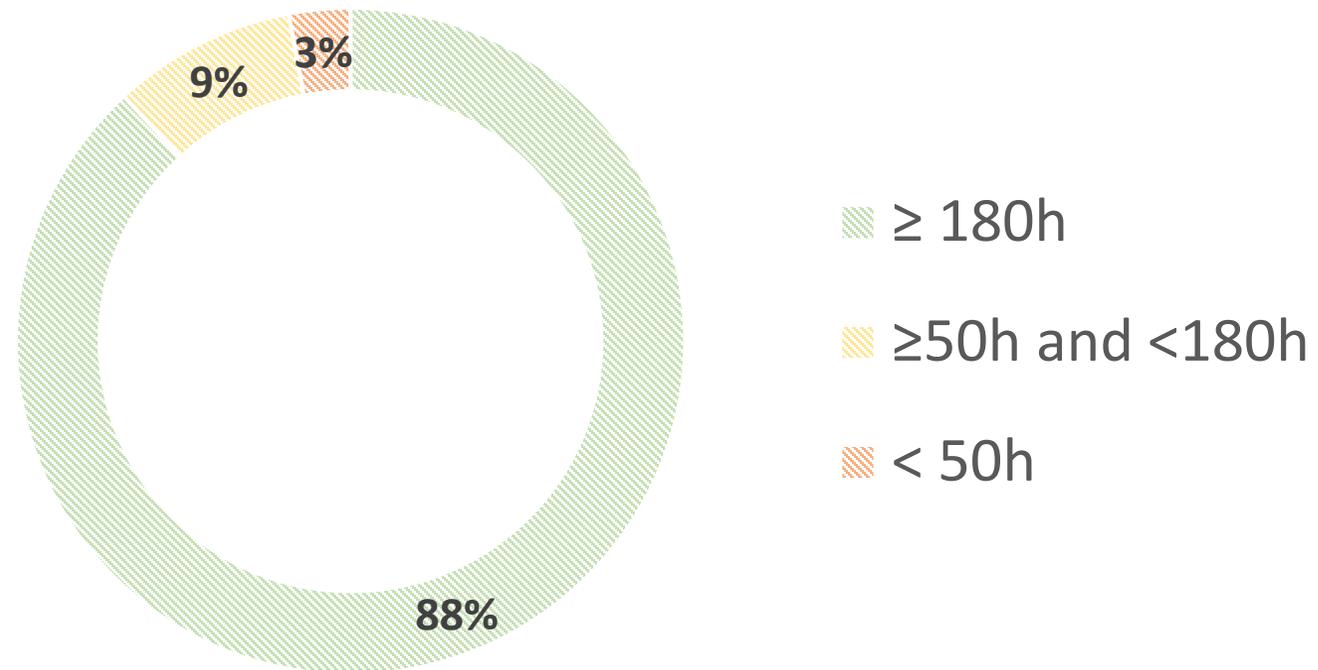
Reliability

Known-group validity

Convergent validity

Ability to detect change

Percentage of patients by amount of DHT data recorded



Notes: 14 patients withdrew and 7 patients had no follow-up visit due to the departure of an investigator in one site

WS95C is reliable and separates patient subgroups

Adherence

Reliability

Known-group validity

Convergent validity

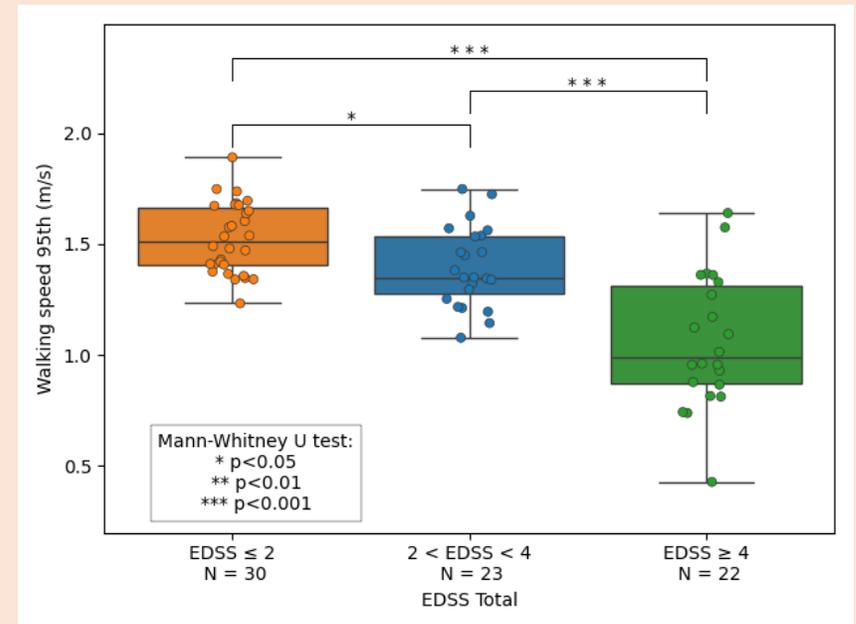
Ability to detect change

Very good test-retest reliability

Variable	ICC(2,1)*	SEM*
WS95C	0.98	0.04

*N=77

WS95C is significantly different between 3 EDSS subgroups



WS95C shows good correlations with other clinical outcomes at baseline

Adherence

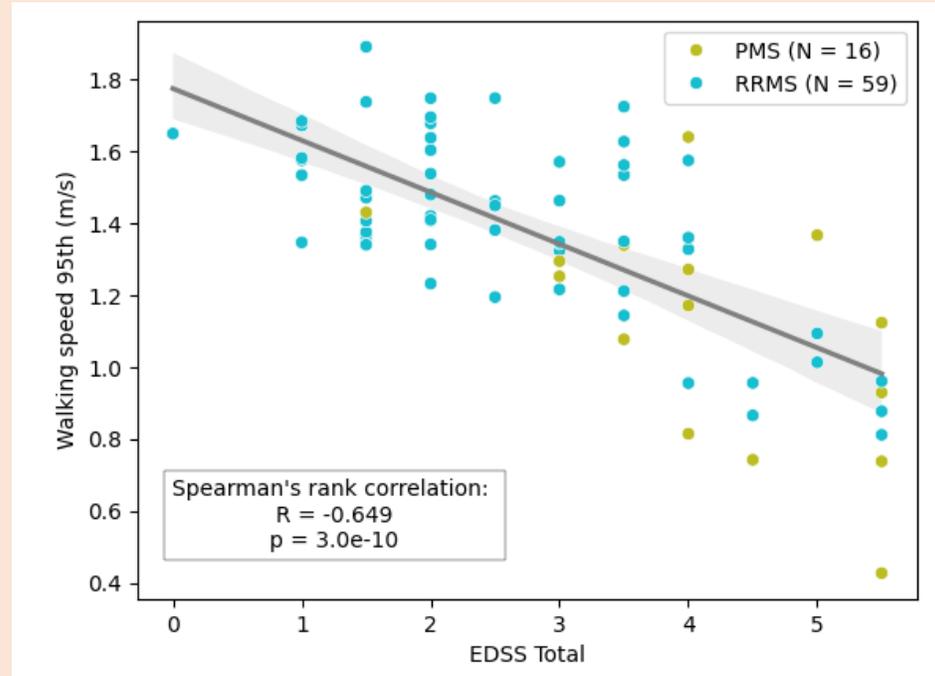
Reliability

Known-group validity

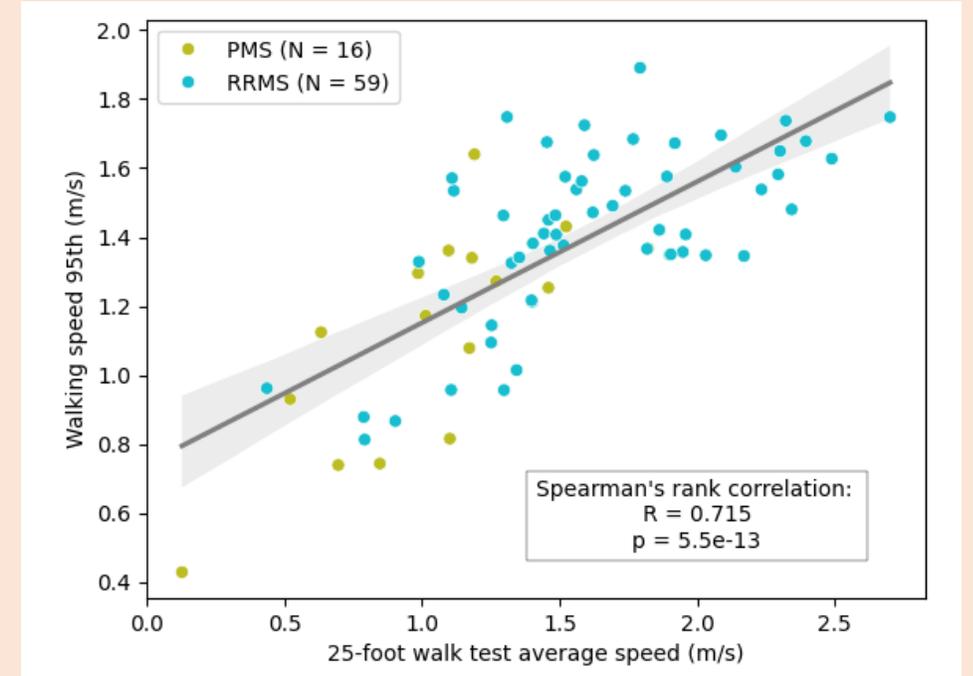
Convergent validity

Ability to detect change

EDSS



T25FW speed



WS95C shows a significant decline at 1 year in both progressive and non progressive patients

Adherence

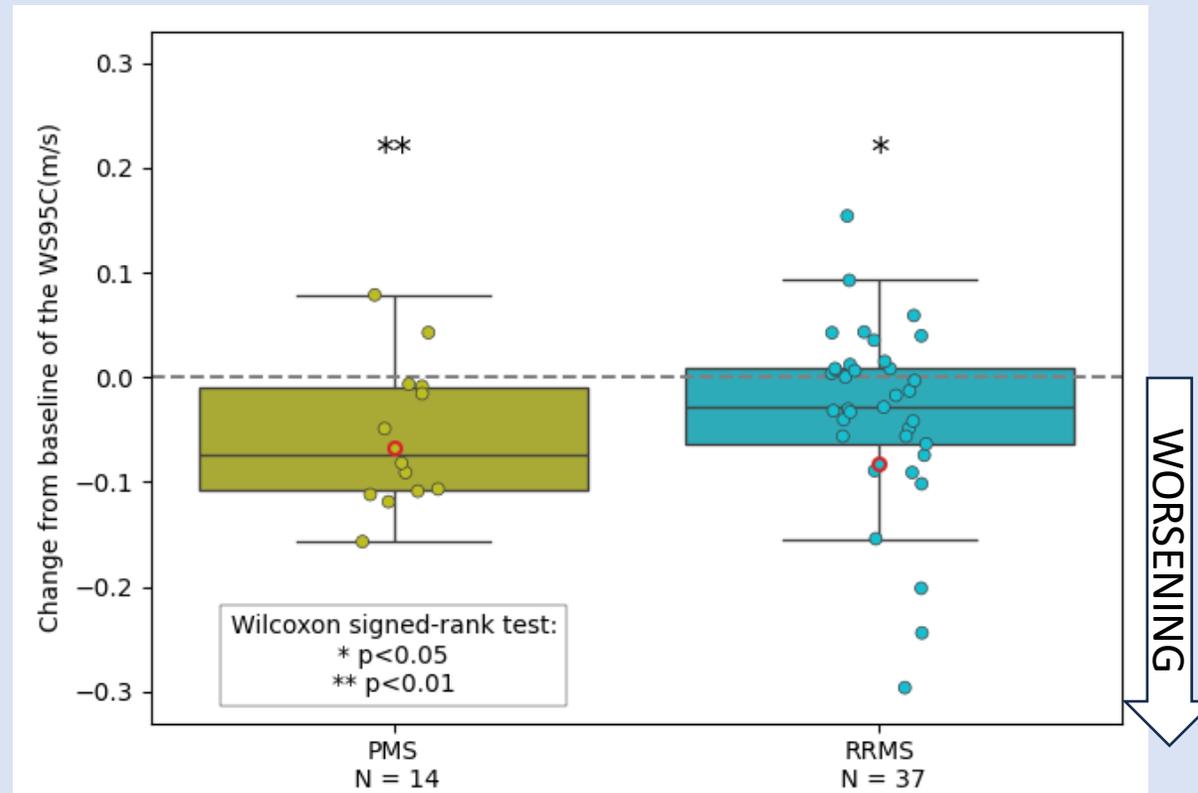
Reliability

Known-group validity

Convergent validity

Ability to detect change

Walking Speed 95th centile



○ Participants who experienced relapse(s) between visits

While EDSS total score detects change only for progressive patients & T25FW does not capture change

Adherence

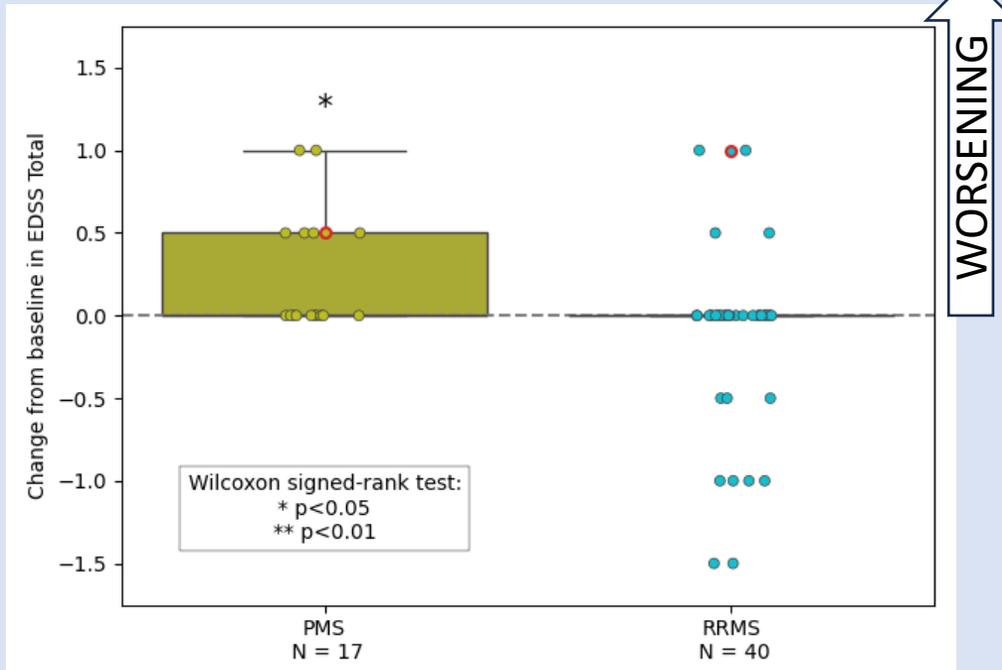
Reliability

Known-group validity

Convergent validity

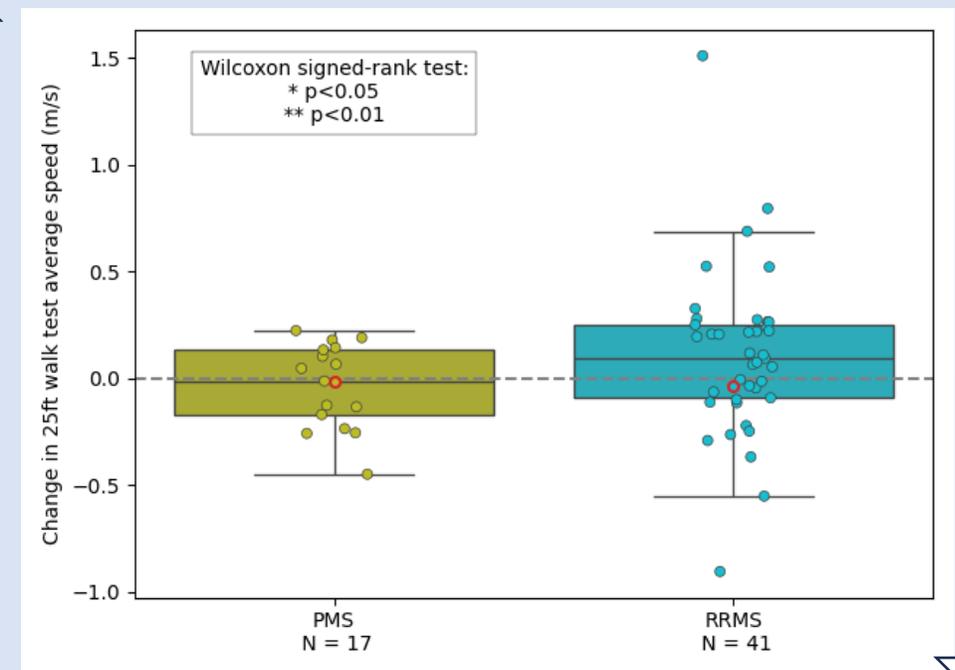
Ability to detect change

EDSS



↑
WORSENING

T25FW speed



↓
WORSENING

○ Participants who experienced relapse(s) between visits

Conclusion and next steps

WS95C

Adherence :

Sufficient data in 97% of recording periods

Reliability :

Excellent reliability (ICC = 0.98)

Construct validity :

Good known-group and convergent validity

Ability to detect change :

Able to detect change at 1 year in PMS & RRMS

NEXT STEPS

- Study extension for 2 years
- Validation required on a separate dataset

