

Continuous Real-World Assessment of Ambulation in Amyotrophic Lateral Sclerosis Using Digital Health Technology

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BACKGROUND

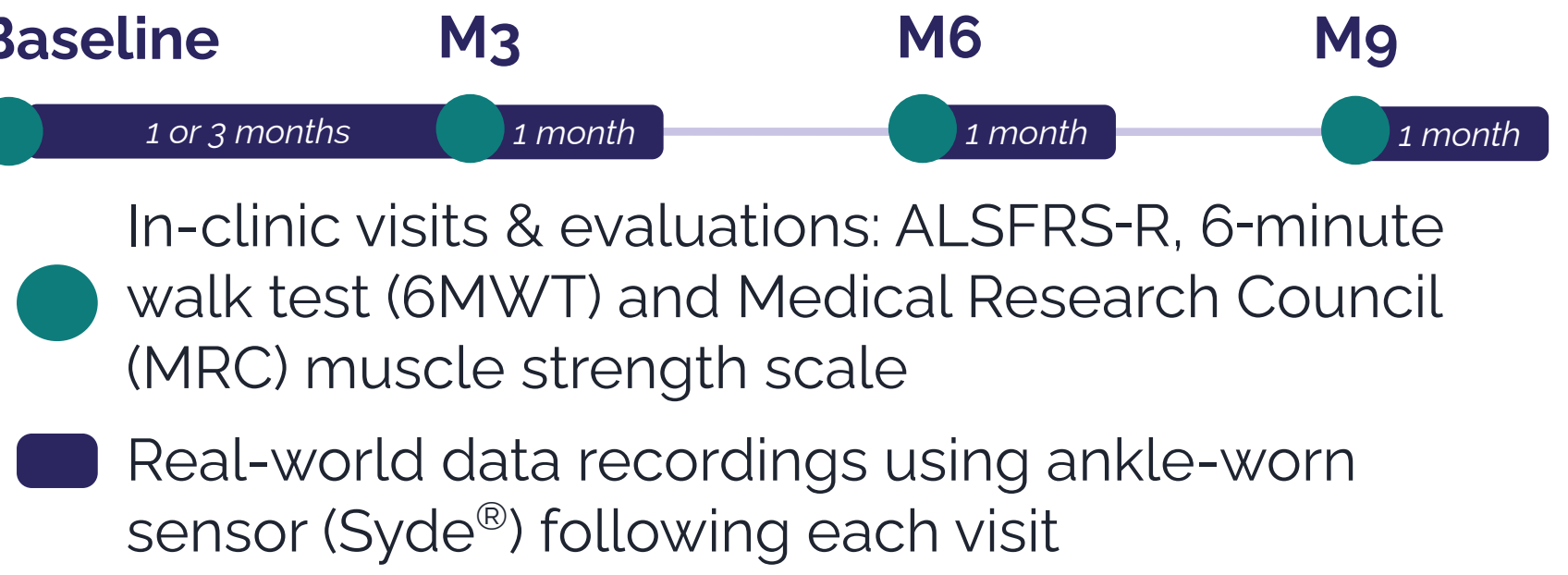
- Progressive **loss of ambulation** is a major contributor to **disability** in **amyotrophic lateral sclerosis** (ALS)
- Current measures** — the ALS Functional Rating Scale-Revised (ALSFRS-R) item 8 (Q8) and in-clinic walking tests — provide only **snapshots of ambulatory function** lacking the **granularity**, **sensitivity** and **ecological validity** needed to **detect change**

OBJECTIVE

Evaluate the **feasibility**, **reliability**, **convergent validity** and **sensitivity** of **DHT-derived outcomes** from real-world assessment to **quantify ambulation in people with ALS**

STUDY DESIGN

Data pooled from **three longitudinal studies** using a harmonized protocol, in **Belgium** and the **United States**



SV95C (m/s)
Stride velocity 95th centile — the top daily-life ambulation speed

Nb strides/h
Number of strides per hour of recording

PARTICIPANTS

CHARACTERISTIC	n	VALUE
Age, years	45	59.50 [26–79]
Sex, male, %	45	57
Time since onset, years	45	1.60 [0.70–10.80]
ALSFRS-R total	44	37.80 (5.3) [23–47]
ALSFRS-R Q8, 2 / 3 / 4	44	20 / 10 / 14
Baseline SV95C, m/s	43	1.05 (0.33) [0.40–1.60]
Baseline Nb strides/h, 1/h	44	109 [0.10–406.30]

Mean [range], median (IQR) [range] or %. n = participants with available data

FEASIBILITY

Recordings meeting the analysis criteria (≥ 50 hours and ≥ 1000 strides), among participants still equipped.

Baseline
98%
44 of 45

M3
93%
37 of 40

M6
91%
32 of 35

M9
80%
24 of 30

15 of 45 withdrew: clinical worsening (8), death (3), caregiver or patient burden (2), competing trial (1), difficulty using the ActiMyo® — the former version of Syde® (1)

**One USB drive containing an M3 recording was lost during shipment*

KEY FINDINGS & NEXT STEPS

- 1 Feasibility** is supported by **good-to-excellent** participant **adherence**, remaining ≥ 80% at every timepoint
- 2 SV95C** and **Nb strides/h** show **excellent reliability** (ICC 0.99 and 0.90), **align** with **ALSFRS-R GMS**, **6MWT** and **MRC**, and **discriminate independent ambulation** from walking requiring assistance
- 3 Digital outcomes** are **sensitive to change as early as month 3**. **SV95C** adds **granularity** by detecting **ambulatory decline** in patients with **stable Q8 < 4**. **More data** is being collected for **validation**

BASELINE RESULTS

RELIABILITY

Test-retest reliability, comparing the first and second 15-day period of the baseline recording

SV95C
0.99
Intraclass correlation coefficient
95% CI 0.996–0.998

0.029
Standard error of measurement
m/s

Nb strides/h
0.90
Intraclass correlation coefficient
95% CI 0.82–0.95

31.14
Standard error of measurement
strides/h

CONVERGENT VALIDITY

SV95C and **Nb strides/h** correlated moderately to strongly with the **MRC**, **6MWT** and **ALSFRS-R gross motor subdomain (GMS)**

Spearman correlation with clinical measures at Baseline; GMS = ALSFRS-R sum of questions 7 to 9; *p < 0.05; **p < 0.01; ***p < 0.001.

	ALSFRS-R	ALSFRS-R GMS	6MWT	MRC
SV95C	0.23	0.72***	0.86***	0.63***
Nb strides/h	0.08	0.61***	0.63***	0.47*

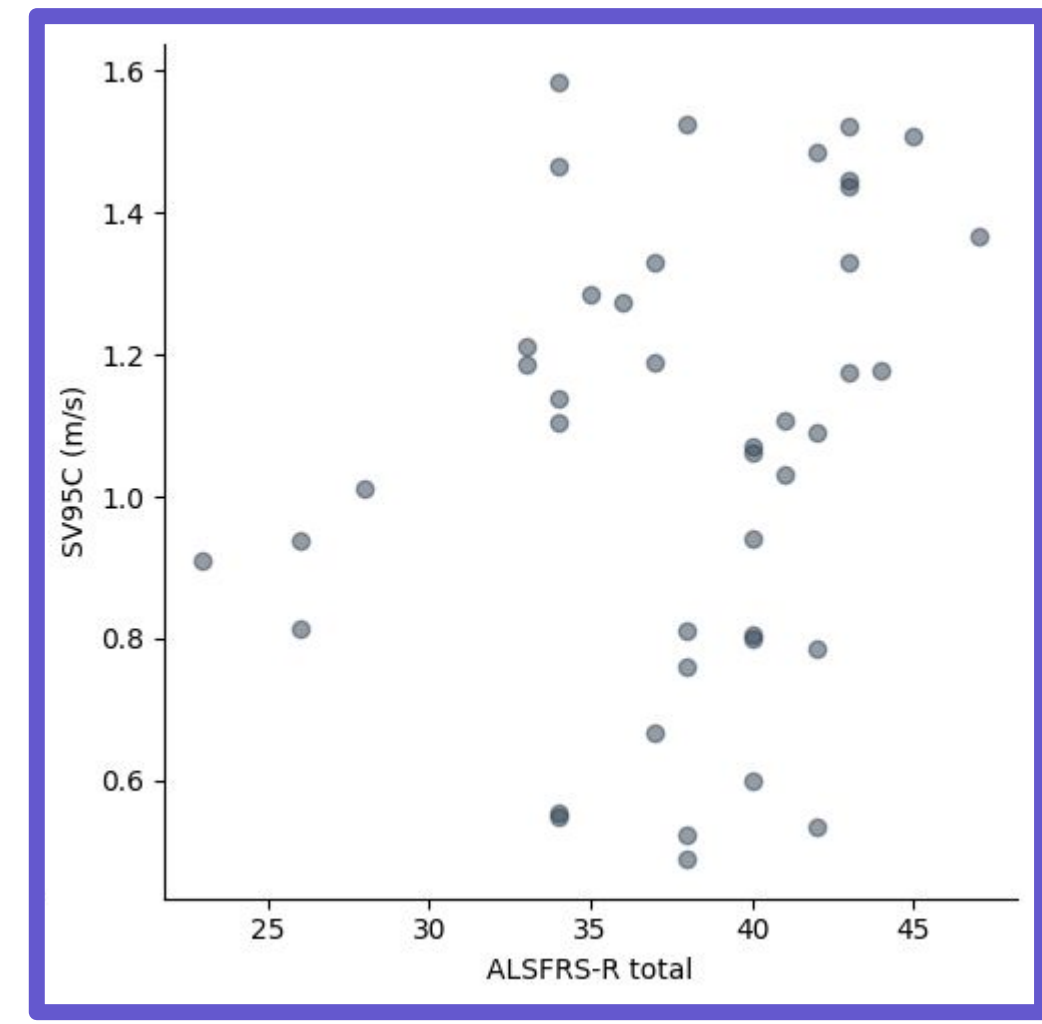


Figure 1. SV95C versus ALSFRS-R total

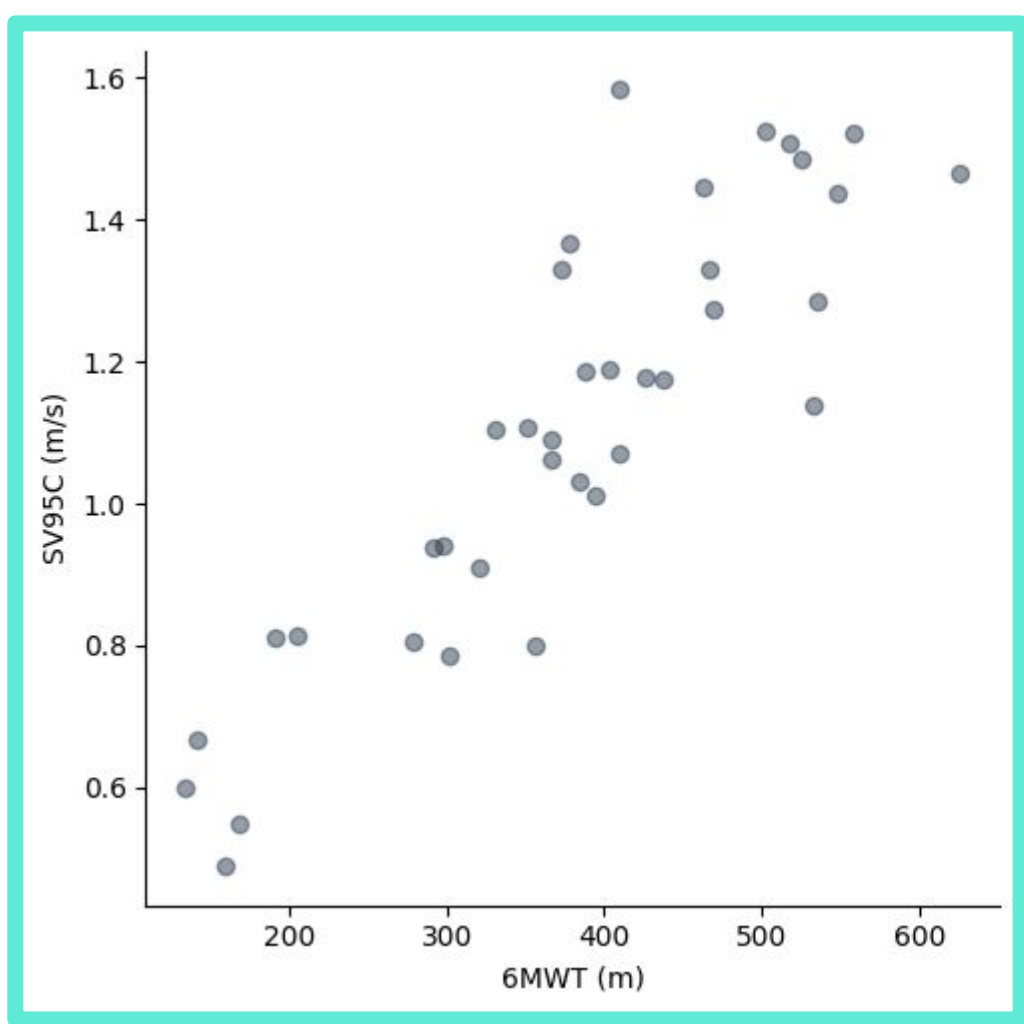


Figure 2. SV95C versus 6MWT

KNOWN-GROUP VALIDITY

Both measures discriminated between **participants** with an **ALSFRS-R Q8 of 2** (walks with assistance) and **Q8 of 3-4** (normal or early ambulation difficulties)

Baseline values compared between ALSFRS-R Q8 = 2 and Q8 = 3-4 (Mann-Whitney U test)

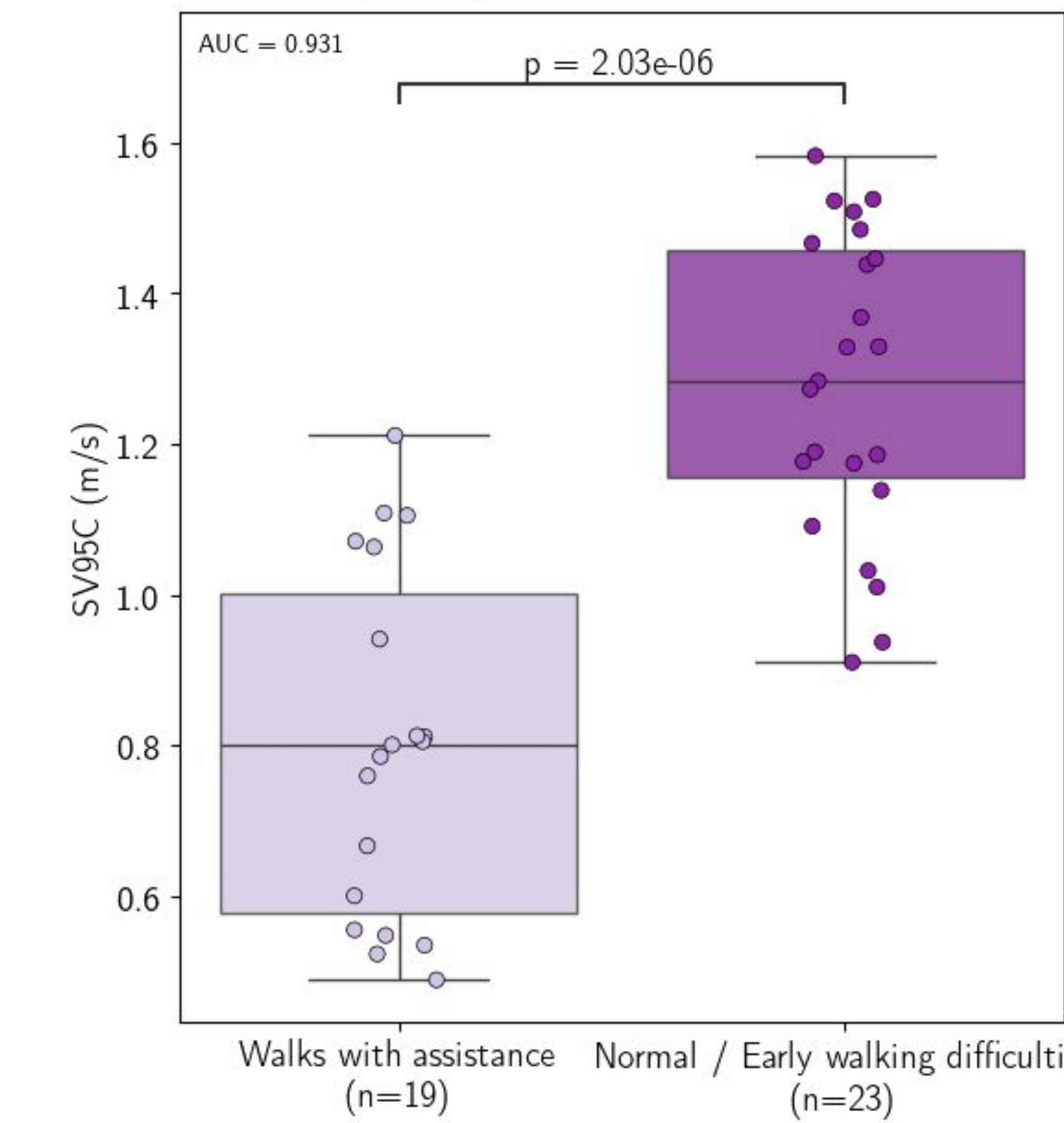


Figure 3. Baseline SV95C by ALSFRS-R Q8 category. One participant with Q8 = 2 is not shown, as no ambulation was captured during the baseline period

LONGITUDINAL RESULTS

SENSITIVITY TO CHANGE

SRM = mean change from baseline divided by SD of that change, per visit, in participants with paired data; within-participant change tested by Wilcoxon signed-rank *p < 0.05; **p < 0.01; ***p < 0.001.

	SV95C	Nb strides/h	ALSFRS-R GMS
M3	-0.43* n = 32	-0.59** n = 33	-0.18 n = 31
M6	-0.81*** n = 30	-0.28* n = 33	-0.64** n = 31
M9	-0.80*** n = 21	-0.87*** n = 22	-0.61** n = 22

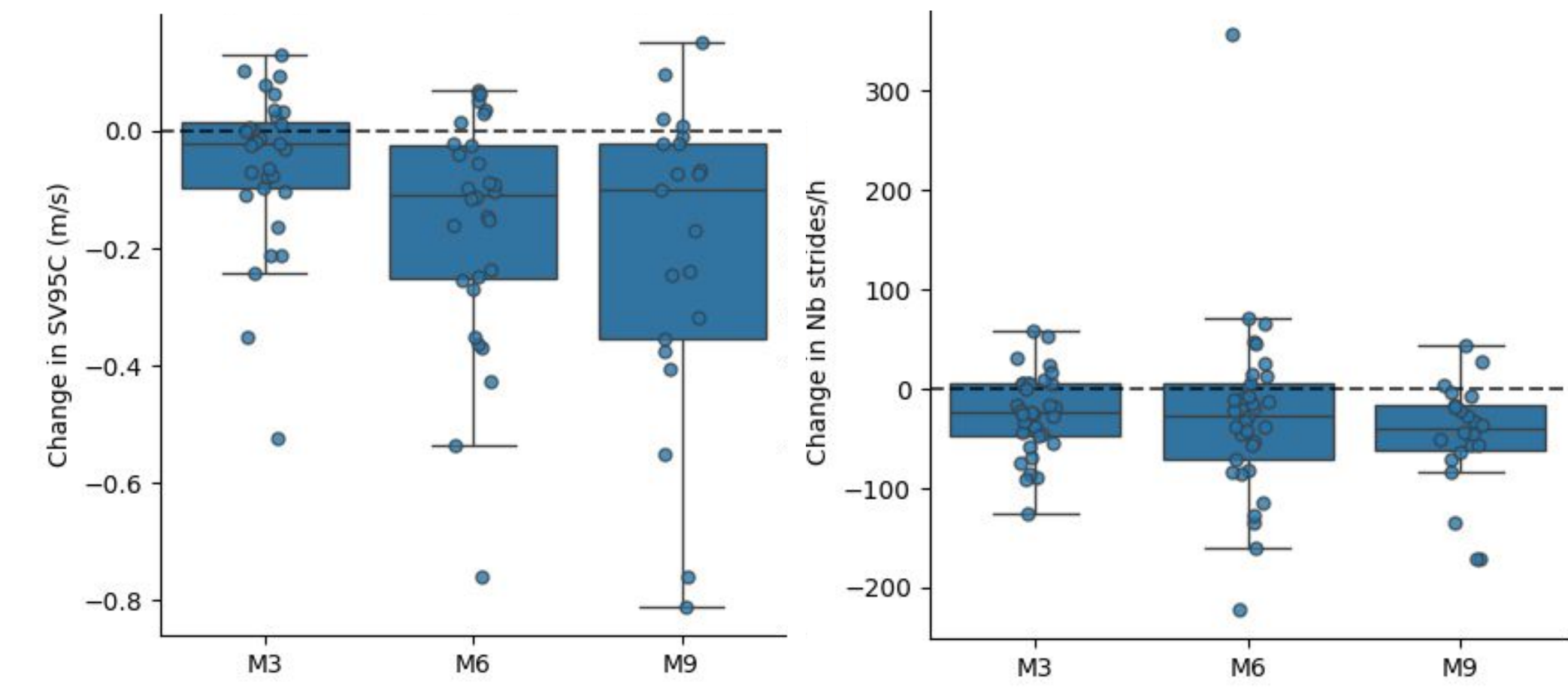


Figure 4. Change from baseline at each visit for SV95C (left) and Nb strides/h (right)

Over 9 months, the **SRM** showed **progressive declines** in **SV95C** and **Nb strides/h**, changes **less evident** in the **ALSFRS-R GMS**. This suggests these digital outcomes are more sensitive to gait changes (Figure 4)

INDIVIDUAL TRAJECTORIES

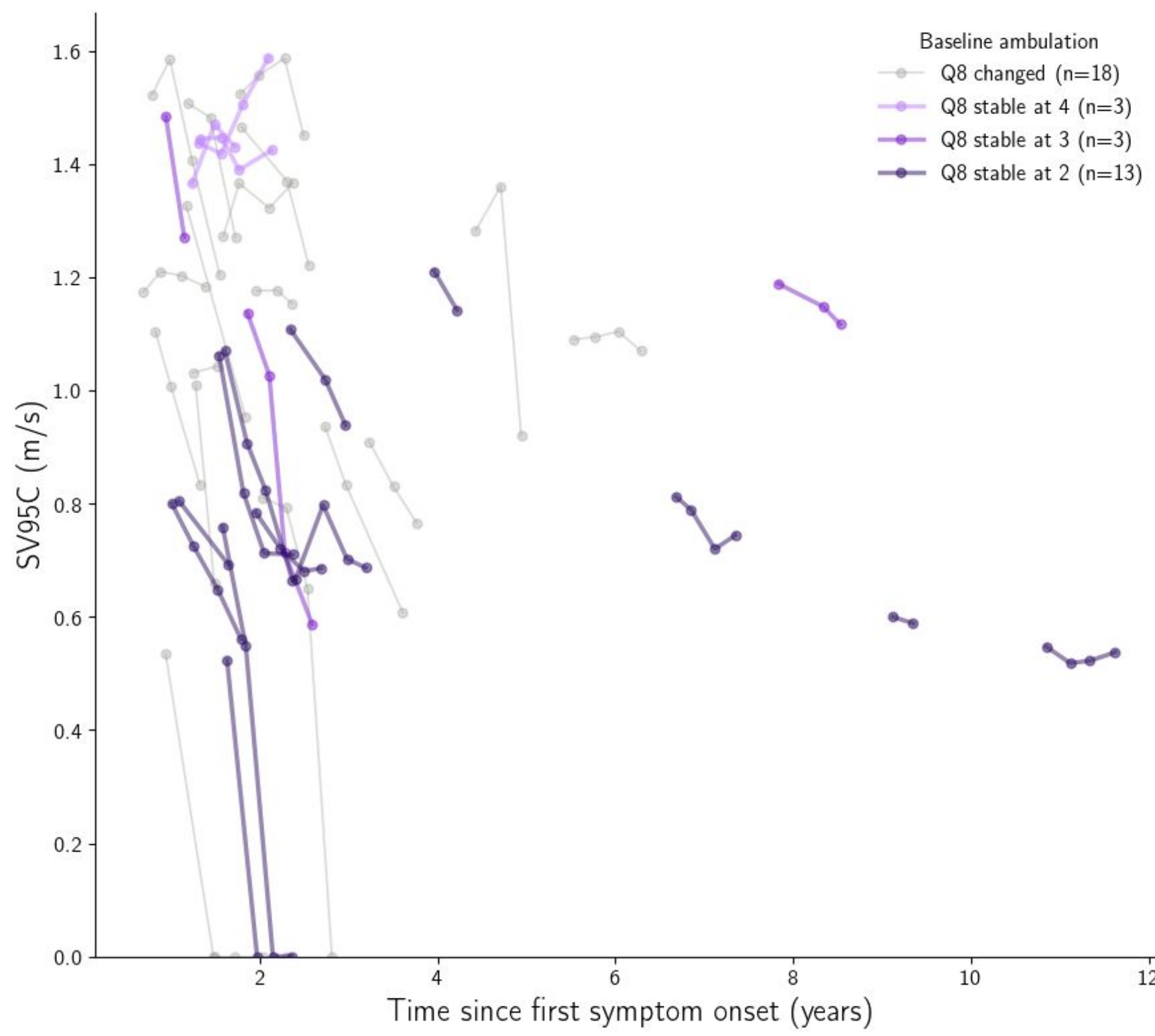


Figure 5. Change in SV95C over time since symptom onset, stratified by ALSFRS-R Q8 stability. Only participants with ≥2 visits where both SV95C and ALSFRS-R were available are shown

In participants with **unchanged Q8 scores below 4**, **SV95C** still declined, adding **granularity** beyond the categorical clinical scale (Figure 5)

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