

Digital mobility outcome measure in patients with Amyotrophic Lateral Sclerosis (ALS)

Background & Methods

Data collection & Demographics

Feasibility & Reliability

Longitudinal Data

External Validity

Conclusion

Authors & Acknowledgements

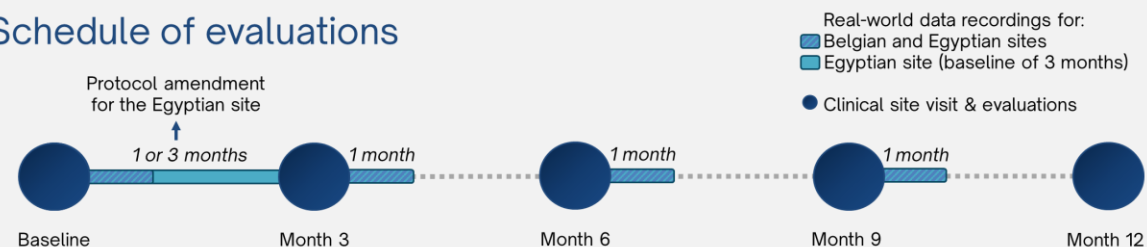
BACKGROUND

- ALS is a progressive neurodegenerative disease that causes motor neuron loss, leading to weakness and eventual death.
- Loss of ambulation contributes to the deterioration of the quality of life of patients.
- Wearable devices provide objective, real-life assessments, offering alternatives to traditional outcomes.
- Newly approved treatments and those under evaluation may slow disease progression, emphasizing the need for precise endpoints.
- Our study assesses digital outcomes' feasibility, reliability and validity in ALS through a longitudinal multisite natural history study.

METHODS

- **Study:** One-Year Multisite Natural History Study
- **Clinical sites:** Belgium and Egypt
- **Clinical outcomes:** ALSFRS-r⁽¹⁾, MRC-SS⁽²⁾, Modified Ashworth Scale, 6MWT⁽³⁾, and Hand Dynamometer tests, every 3 months at clinical site.
- **Real-world function:** Patients are asked to wear Syde[®] sensors, a valid and suitable wearable device qualified by the EMA, on the ankle and wrist for one-month post-visit to capture real-world activity (on the most affected side at baseline).

Schedule of evaluations



⁽¹⁾ Revised Amyotrophic Lateral Sclerosis Functional Rating Scale

⁽²⁾ Medical Research Council Sum Score

⁽³⁾ 6-Minute Walk Test

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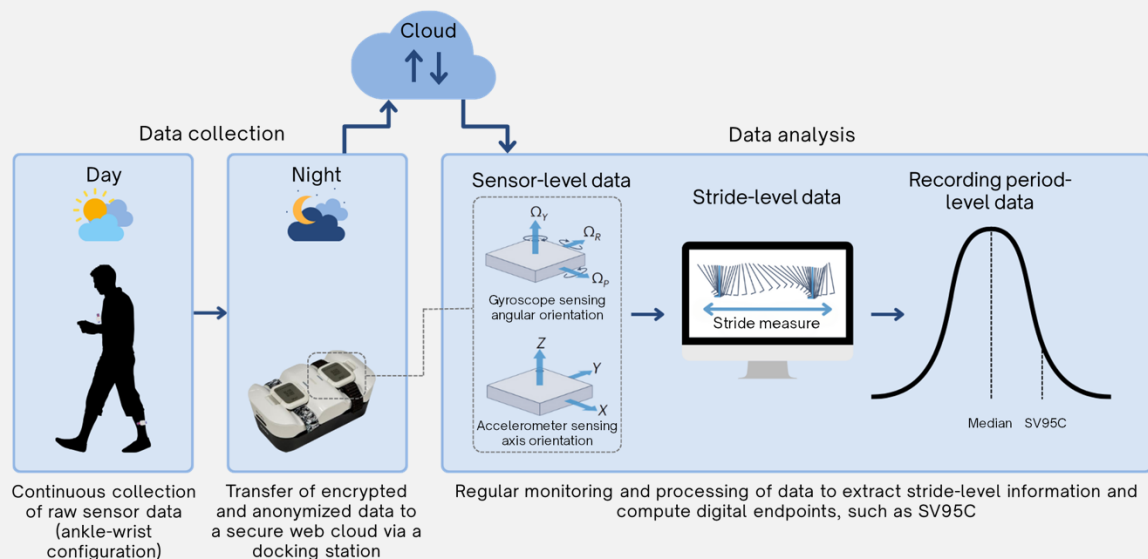
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DATA COLLECTION AND ANALYSIS



PARTICIPANTS

Table 1. Demographics and baseline characteristics of the 21 ALS patients

Age (years) (*)	54 [20-70]
Sex (N)	F: 6, M: 15
ALSFRS-r (*)	38 [23-47]
MRC-SS (*)	52 [38-60]
Time between symptom onset and inclusion (years) (*)	2.4 [1.3-4.9]

(*) Results presented as: median [min-max]

DIGITAL OUTCOMES

All outcomes are calculated over a one-month period:

- Stride Velocity 95th Centile (SV95C): Top 5% of fastest strides.
- Walked Distance 90th Centile (WD90C): Top 10% of distance covered.
- Strides per hour (SH): Number of strides per hour of recording.
- Median Stairs Climb Speed (MSCS): Median speed at which stairs are climbed.

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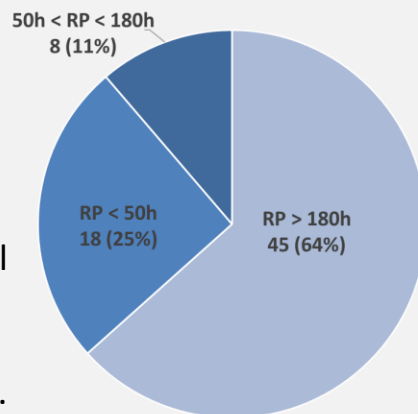
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FEASIBILITY

- **Sufficient-Length Recording Periods (RP):** 53 out of 71 RP (75%) had recordings of sufficient length (> 50 hours), and 64% exceeded the optimum threshold for analysis (180 hours).
- **Factors for Insufficient RP Duration:** Clinical decline, protocol misunderstanding, hospitalization, and being bedridden.
- **Device Tolerance:** No issues were reported.



RELIABILITY

- **Great robustness:** ICC > 0.9 for **MSCS**, **SV95C** and **WD90C** and when computed for recording periods of one month with more than 50 hours.
- **SV95C:** It proves to be more reliable compared to simply counting the number of steps (SH).

Table 2. Digital outcome reliability

Digital outcome	ICC (N=19)
MSCS	0.99
SV95C	0.97
WD90C	0.91
SH	0.86

ICC: Intra Class Correlation (2,k) computed on the aggregated variables across two 2-week periods within a one-month recording period.

§ Two withdrawn patients have not recorded sufficient data (< 50 h).

For Egyptian site, the three-month baseline recordings were divided into three one-month intervals.

Compliance was assessed for each individual month (Figure 2).

ICC was determined based on the first month of recordings with more than 50 hours (Table 2).

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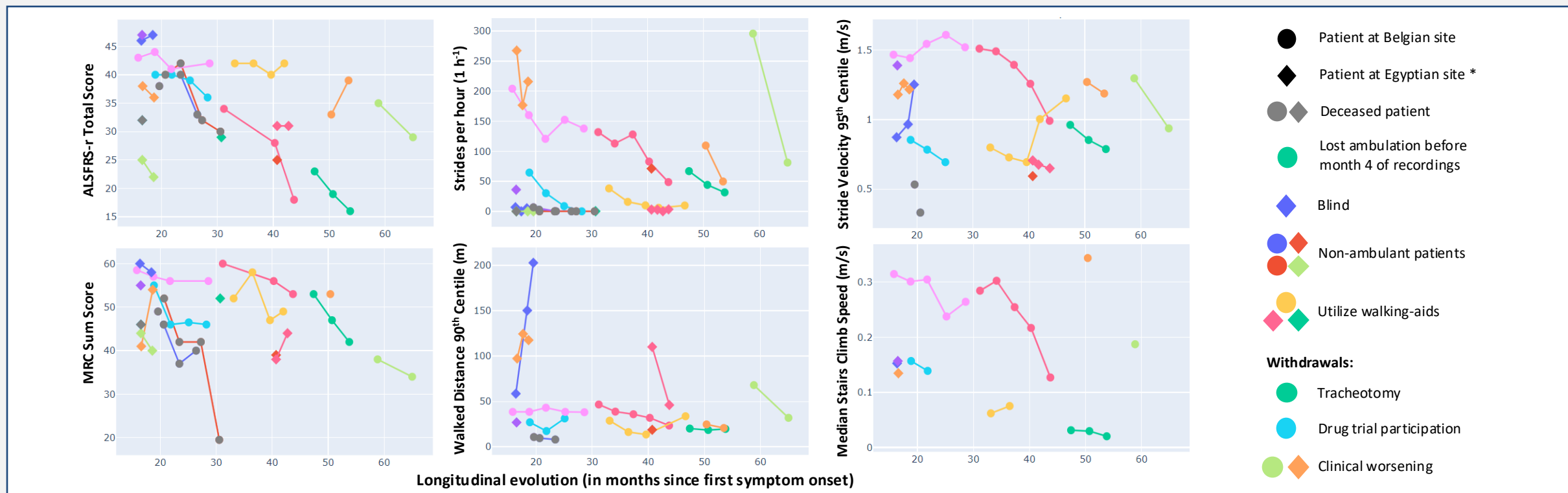
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ASSESSING LOWER LIMB FUNCTION

- Digital Outcomes Reveal a Decline Over Time: SV95C, WD90C, SH, MSCS and clinical scores (ALSFRS-r and MRC-SS) are indicative of lower limb function decline over time.



Only patients with more than 50 hours of recordings per period are included.

* Patients from the Egyptian site are still participating in the study, and the three months of baseline recordings have been split into three periods of one month.

In the case of ◆, although compliance is good, steps were detected during only 3 days of recordings, possibly due to blindness and needing help with sensor placement. His high performance on digital outcomes is understandable given clinical assessments.

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VALIDITY OF DIGITAL OUTCOMES

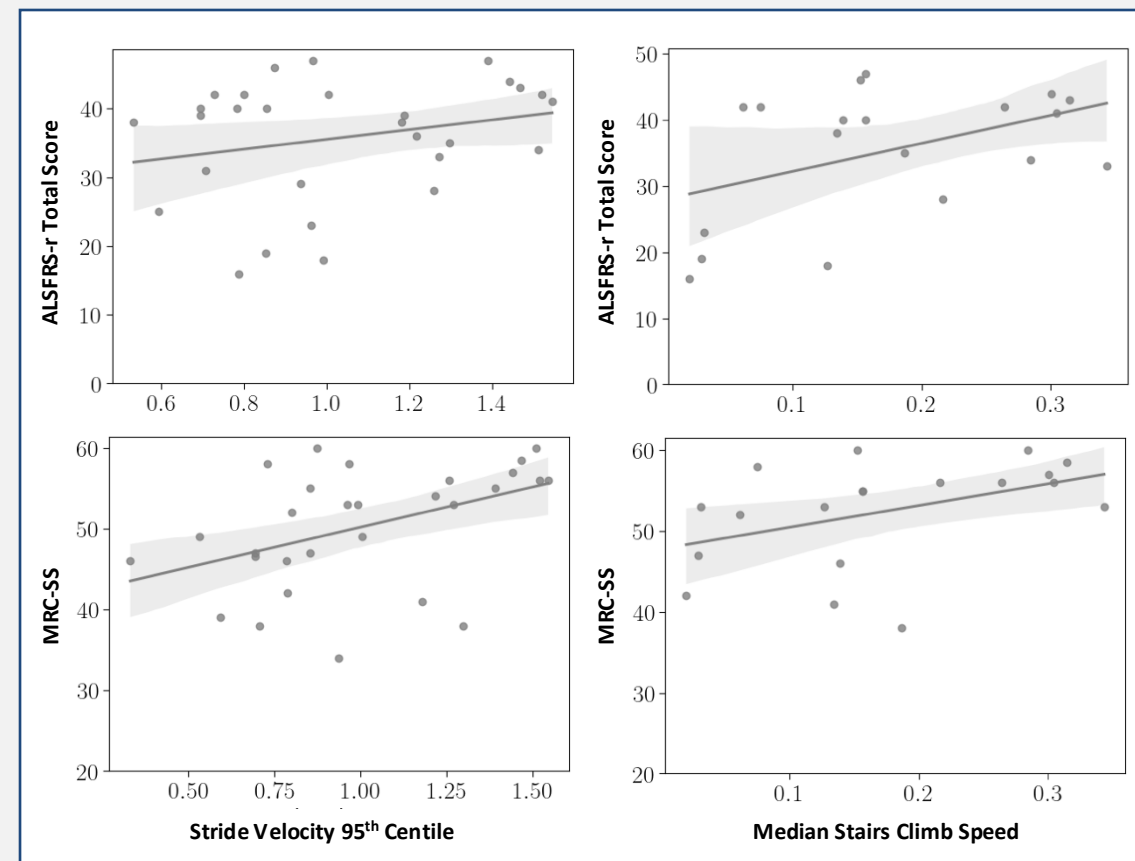
- **Significant Correlation with MRC-SS:** Positive correlation for SV95C, MSCS, and SH.
- **ALSFERS-r Shows Lower Overall Correlation:** Likely due to its comprehensive assessment of various disease aspects (1 in Table 3).
- **Significant Correlation with Gross Motor Subdomain:** SV95C, SH and WD90C show a positive correlation with ALSFRS-r Gross Motor Subdomain (1.1 in Table 3).
- **Measuring Motor Function:** SV95C and MSCS demonstrate superior validity to basic step counting (SH) when compared to clinical assessments.

Table 3. Correlation of gold standards and digital outcomes

Digital outcome	SV95C	MSCS
1 ALSFRS-r Total	0.24	0.37
1.1 ALSFRS-r GMS	0.64*	0.44
2 MRC-SS	0.52*	0.5*
2.2 MRC-SS Lower Limb	0.7*	0.28

Spearman's coefficients of correlation. * $p < 0.05$

GMS: Gross Motor Subdomain, i.e., turning in bed, walking, and climbing stairs.



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DIGITAL OUTCOMES:

-  Promising for monitoring lower limb function decline.
-  Great robustness with ICC > 0.9 for MSCS, SV95C and WD90C.
-  Offer finer granularity and improved representativity (thanks to daily measurements) compared to in-clinic assessments.





PROTOCOL AMENDMENT:

-  Introducing a 3-month baseline.
-  Captures rapid motor changes without in-clinic visits.

ADDRESSING COMPLIANCE & MORTALITY CHALLENGES:

-  Ongoing study in the US.
-  Future studies in Europe.

FUTURE EFFORTS:

-  Enhancing digital outcomes' performance.
-  Reducing operator subjectivity.
-  Predicting decline over time.
-  Exploring upper limb outcomes.

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AUTHORS

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DISCLOSURE

Laurent Servais has given consultancy in the DMD field for Biogen, Novartis, Astellas, Evox, PTC, BioHaven, Zentech, MitoRX, Pfizer, Sarepta, Dyne, Santhera, Italfarmaco, Roche and **SYSNAV**.

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