

Addressing Unmet Needs for Clinical Endpoints in Rare Disease Using Digital Health Technology: An Example with Amyotrophic Lateral Sclerosis

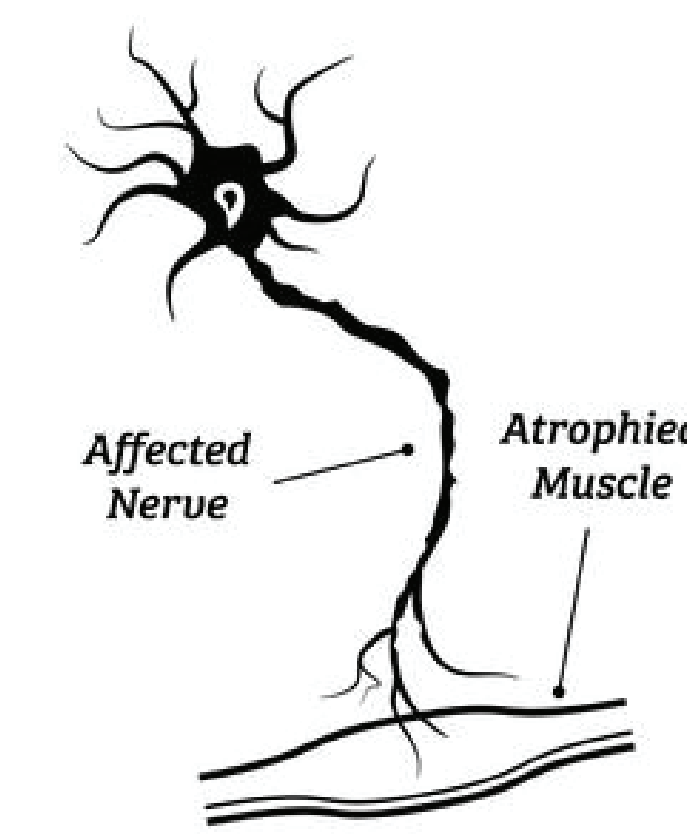
Sylvain Zorman, PhD[1], Rakesh Pilkar, PhD[1], Michael G. Philcock[1], Christine C. Guo, PhD[1], Cory Holdom[2], Frederik Steyn[2]
[1]ActiGraph LLC, Pensacola, FL 32502, USA | [2] University of Queensland, Brisbane, Queensland, Australia

1 Abstract

The development of novel drugs for rare diseases is hampered by the limitations of standard outcome assessment tools such as patient-reported outcomes (PRO) and Clinician Reported Outcomes.

- Sensor-based Digital Health Technologies, such as wearables, provide an opportunity to continuously collect objective data during daily activities, adding a new dimension to clinical evidence of the benefits of investigational therapeutics.
- This project uses amyotrophic lateral sclerosis (ALS) as an example to demonstrate the key steps and specificities of developing a novel assessment using wrist actigraphy.

2 ALS - Symptoms and Disease Progression



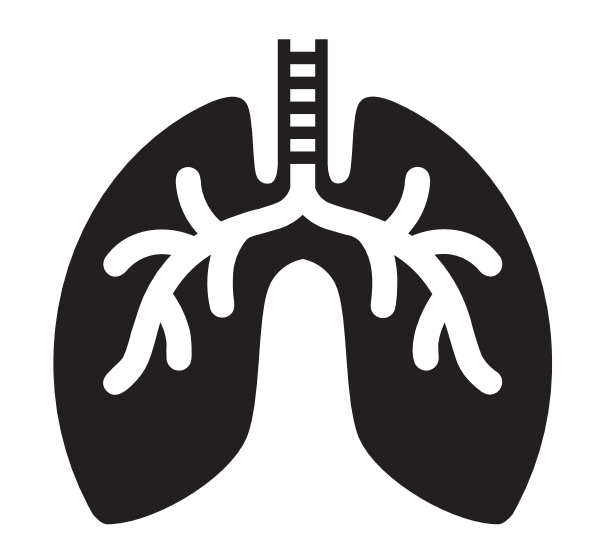
ALS is the most common neuromuscular disease leading to the progressive destruction of motor neurons.



Limb Weakness
and Spasticity



Slurred
Speech



Dyspnea and
Respiratory Insufficiency

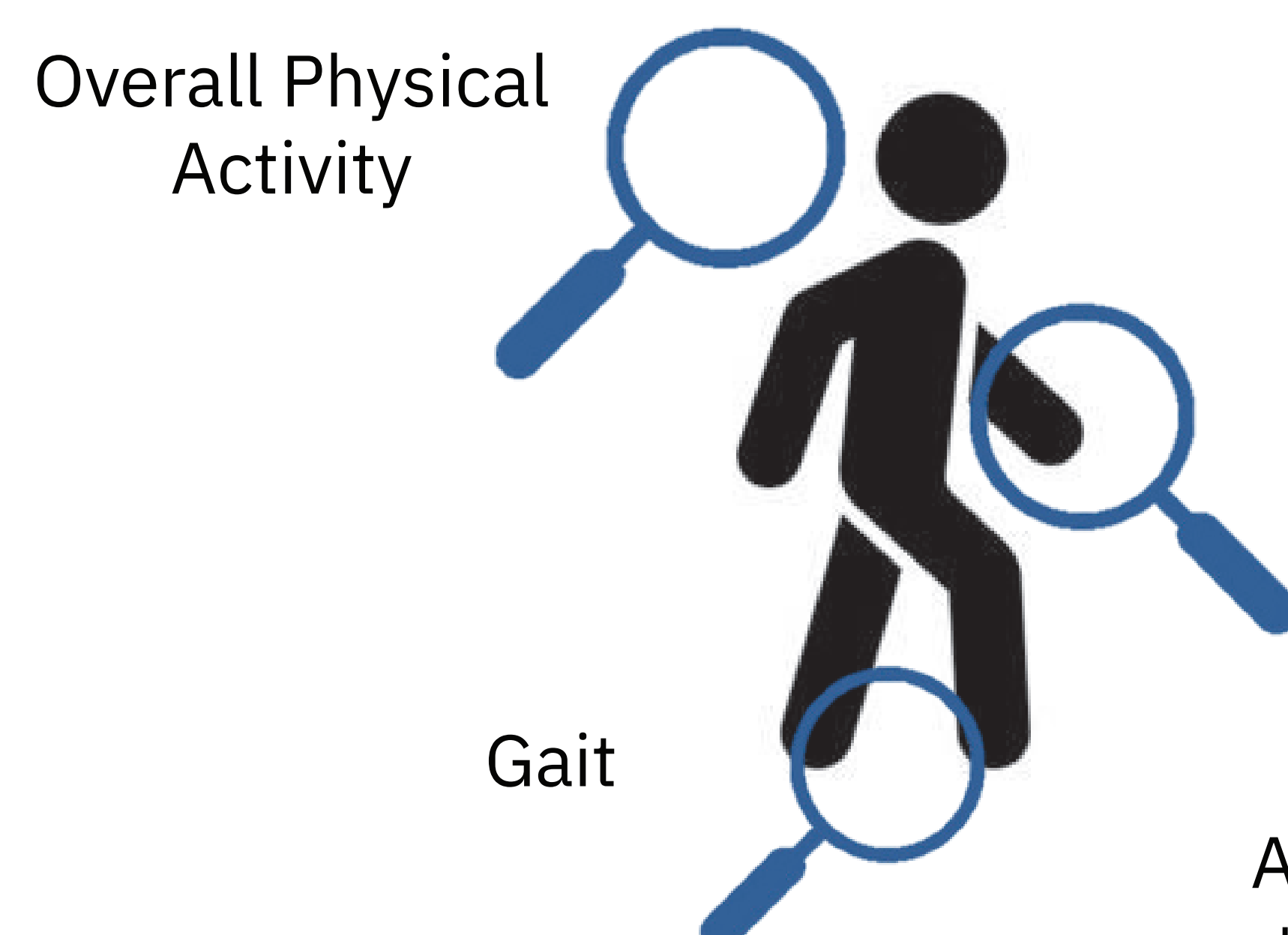
3 Digital Health Technologies

Compared with standard measures, actigraphy enables:

- High-frequency data collection (>30Hz)
- Low burden, longitudinal recording
- Patient-centric measures: capture functions and behaviors in daily living



ActiGraph
LEAP
Next-Generation
Multi-sensor Wearable



Upper Limb
Movement

A single sensor simultaneously captures
three domains relevant to ALS patients

4 Data Collection

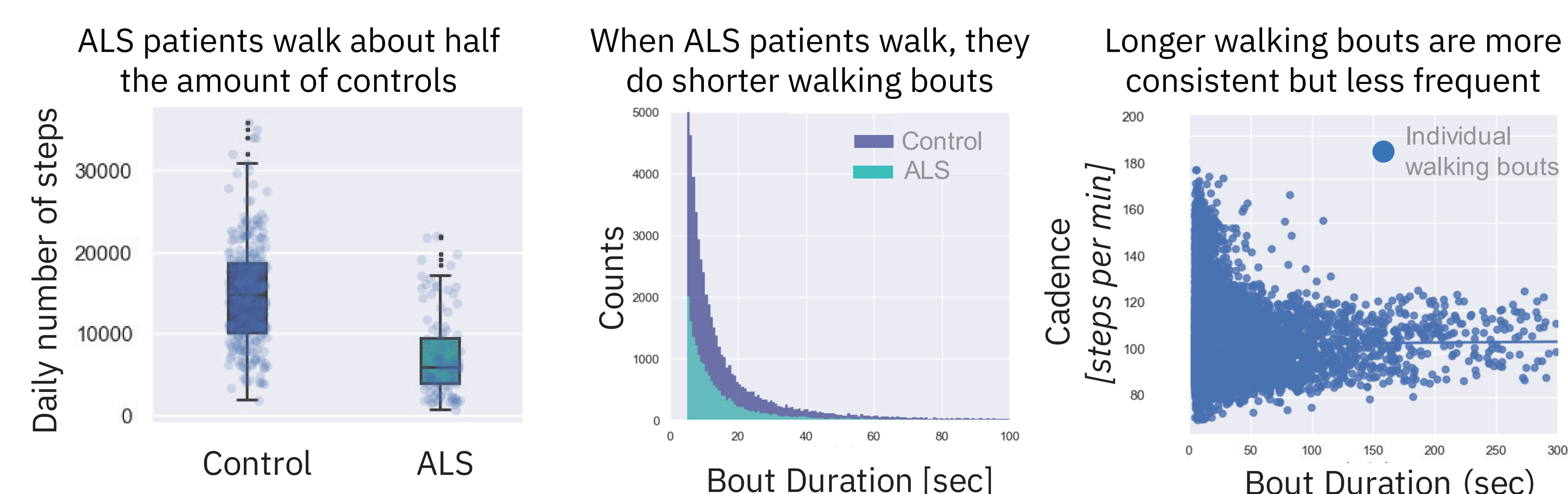
- GT9X activity monitors were placed on non-dominant wrists
- Continuous recording for up to 8 days

Group	n	age (years)	height (cm)	weight (kg)
control	56	55.09 (11.97)	171.0 (8.44)	78.84 (20.54)
Als	24	61.39 (8.43)	173.59 (11.17)	78.54 (16.4)

Participant Demographics



5 Results

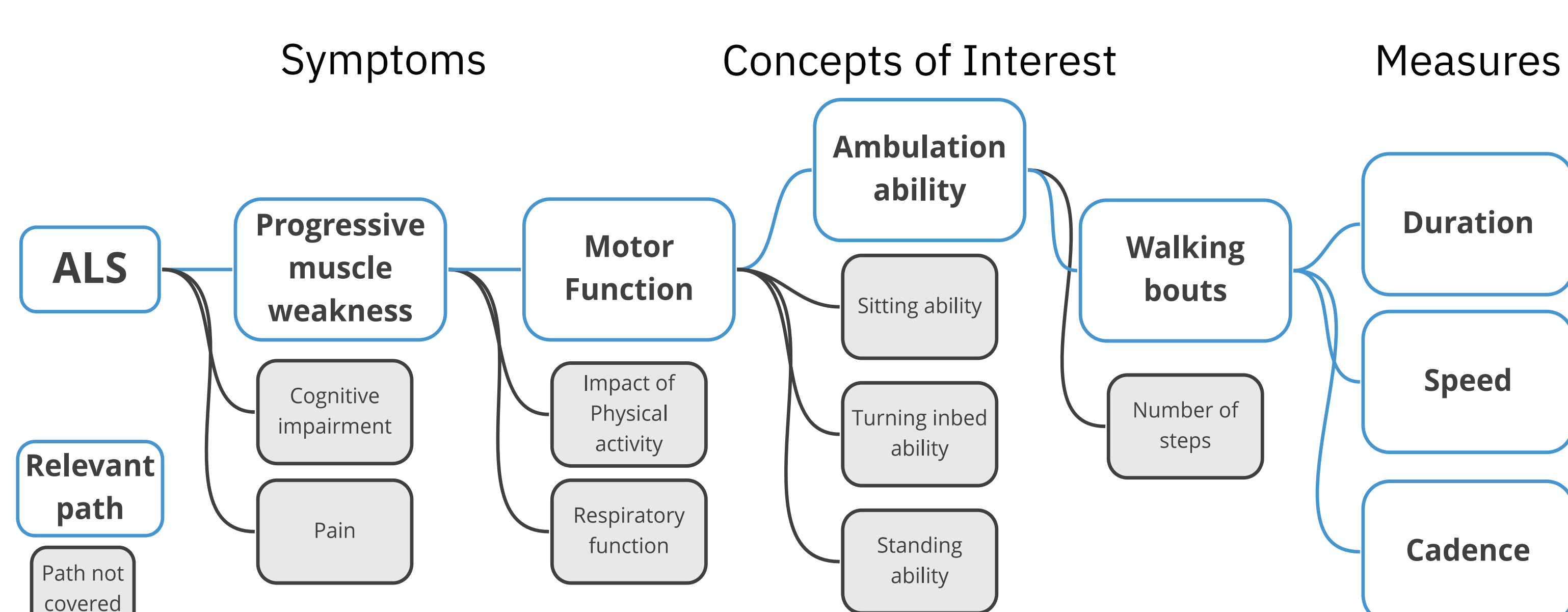


Capturing peak performance metrics (e.g., cadence of the top 30% most extended walking bouts) might lead to higher reliability

6 Conclusion

This project of developing a novel actigraphy-based endpoint for ALS address the three most critical aspect of forming a digital endpoint:

- Address an unmet clinical need
- Finding the statistically best measure
- Eliciting the patient meaningfulness of the measure



A simplified conceptual framework elicits the meaningfulness of walking bout characteristics.