

Gait Phenotyping in Multiple Sclerosis using Smart Insole Technology

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INTRODUCTION

Gait Patterns in MS

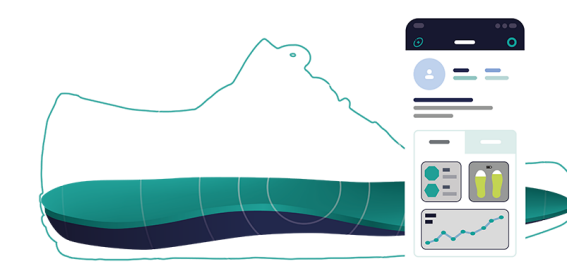
- Gait patterns vary widely among people with MS (PwMS) [1, 2].
- Differences in lesion location and severity can contribute to distinct walking patterns which can be difficult to distinguish through observational gait analysis.

Data-Driven Phenotyping

- Instrumented gait analysis can objectively measure gait features.
- Unsupervised clustering algorithms** group individuals with similar gait features to identify gait phenotypes [3].
- **These phenotypes may help identify groups of individuals with similar underlying impairments to support treatment planning.**

Smart Insoles

- Pressure and inertial measurement unit (IMU) sensors capture gait features outside of specialized gait labs.
- Enable clinic- and home-based gait monitoring.
- Potential for frequent, repeated assessment.
- Accessible platform for data-driven gait phenotyping.**



Objective:

Identify exploratory gait phenotypes from smart insole data via unsupervised clustering, and characterize them using spatiotemporal, IMU, and clinical measures (EDSS, MSWS-12).

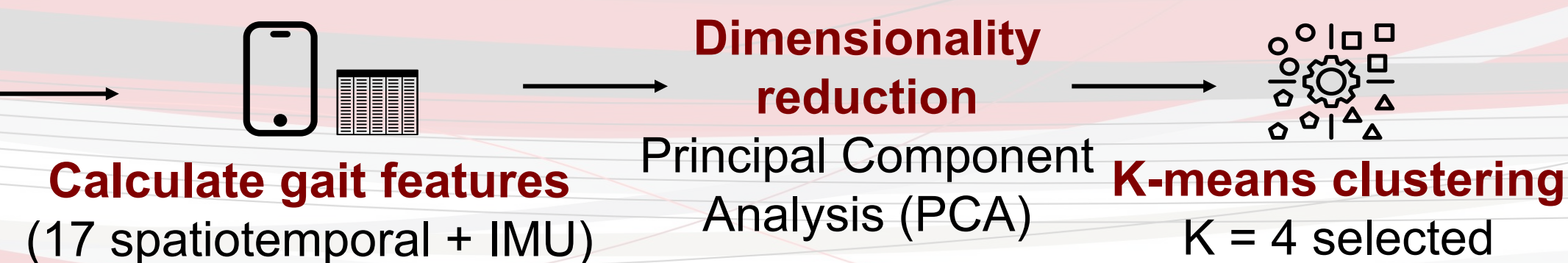
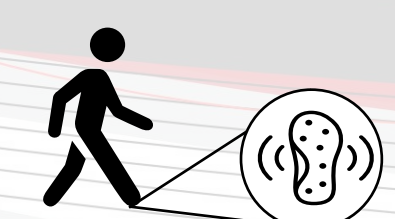
METHODS

Participants

- PwMS (n=108):** 22 male | Age 50 [40, 58] | EDSS 3.5 [2.0, 4.5] | MSWS-12 42.5 [23.7, 69.6].
- 5 sites:** University of Ottawa, The Ottawa Hospital, Technical University of Dresden, Brigham and Women's Hospital, Royal London Hospital.
- Healthy controls (HC) (n=49):** 36 male | Age 30 [27, 42].
- Data presented as median [IQR].**

Protocol

- Smart insoles (Moticon, Germany; 50 Hz) worn during straight-line indoor walks. Data streamed to a gait measurement platform (Celestra Health Systems, Canada) where gait metrics were computed.



Analysis

- Principal components (PCs):** Summarize dimensions of variation in selected gait features. Loadings identify contributing gait features to each PC; correlations with EDSS/MSWS-12 relate PCs to clinical disability.
- Cluster comparisons:** Compare EDSS, MSWS-12, PCs, age, and sex across clusters (Kruskal-Wallis and Dunn's post hoc).
- Gait profiles:** Compare gait features across clusters using generalized linear models adjusted for age and sex.
- Healthy reference:** Compute deviation from healthy controls for each gait feature using age- and sex-adjusted z-scores for each cluster (Figure 2).

RESULTS

Principal Component Analysis

- Three PCs retained (80.3% total variance).
- PC1 (58.4%): pace & signal magnitude.**
 - Correlated with EDSS ($\rho = -0.651$; $p < 0.001$).
 - Correlated with MSWS-12 ($\rho = -0.673$; $p < 0.001$).
- PC2 (13.0%): gait variability.**
- PC3 (8.9%): gait phase timing.**

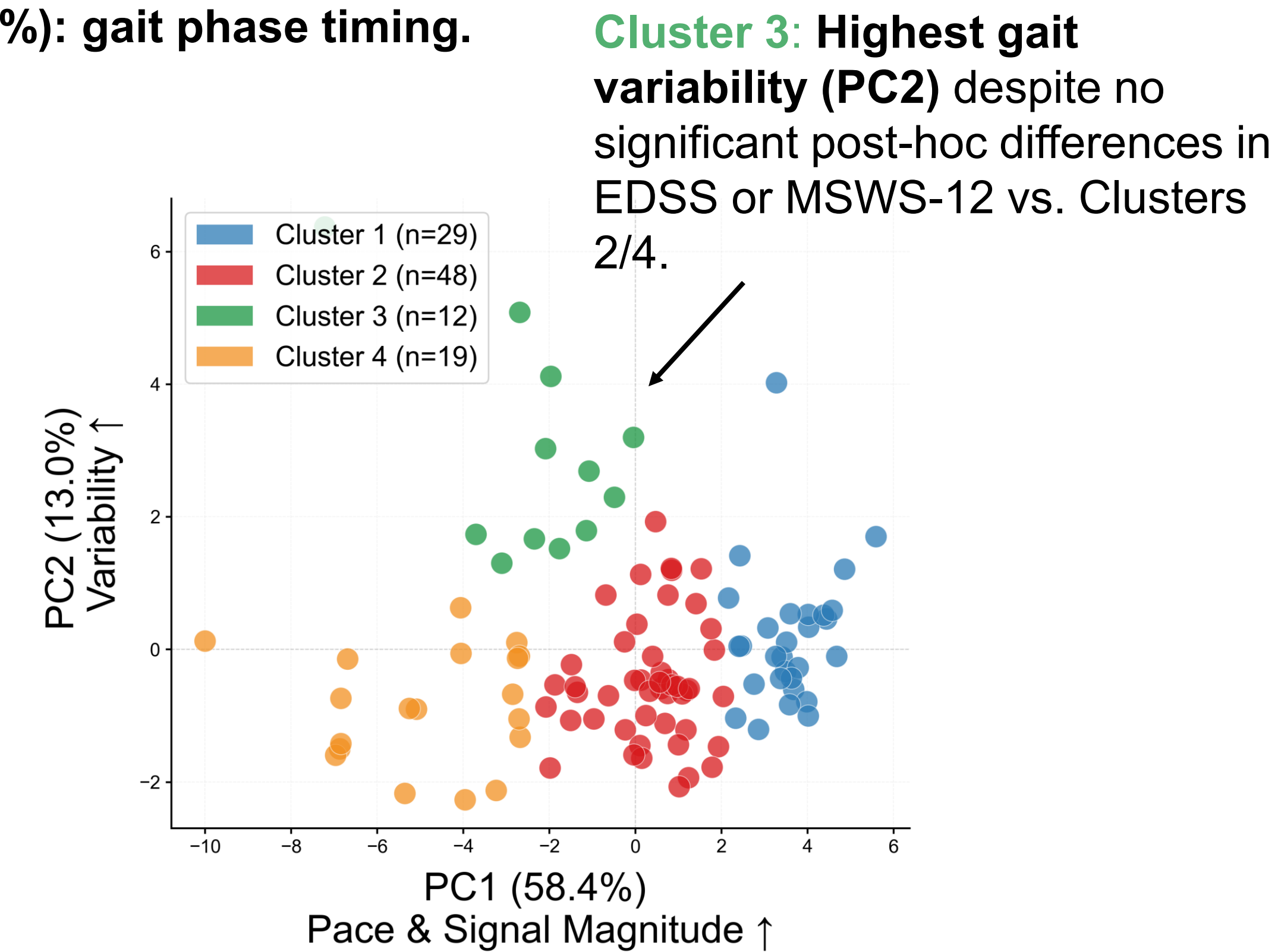


Figure 1. Clusters plotted across principal components 1 and 2 (PC1, PC2). Each point represents a single participant. PC1 was interpreted as representing overall pace and signal magnitude. PC2 was interpreted as representing gait variability.

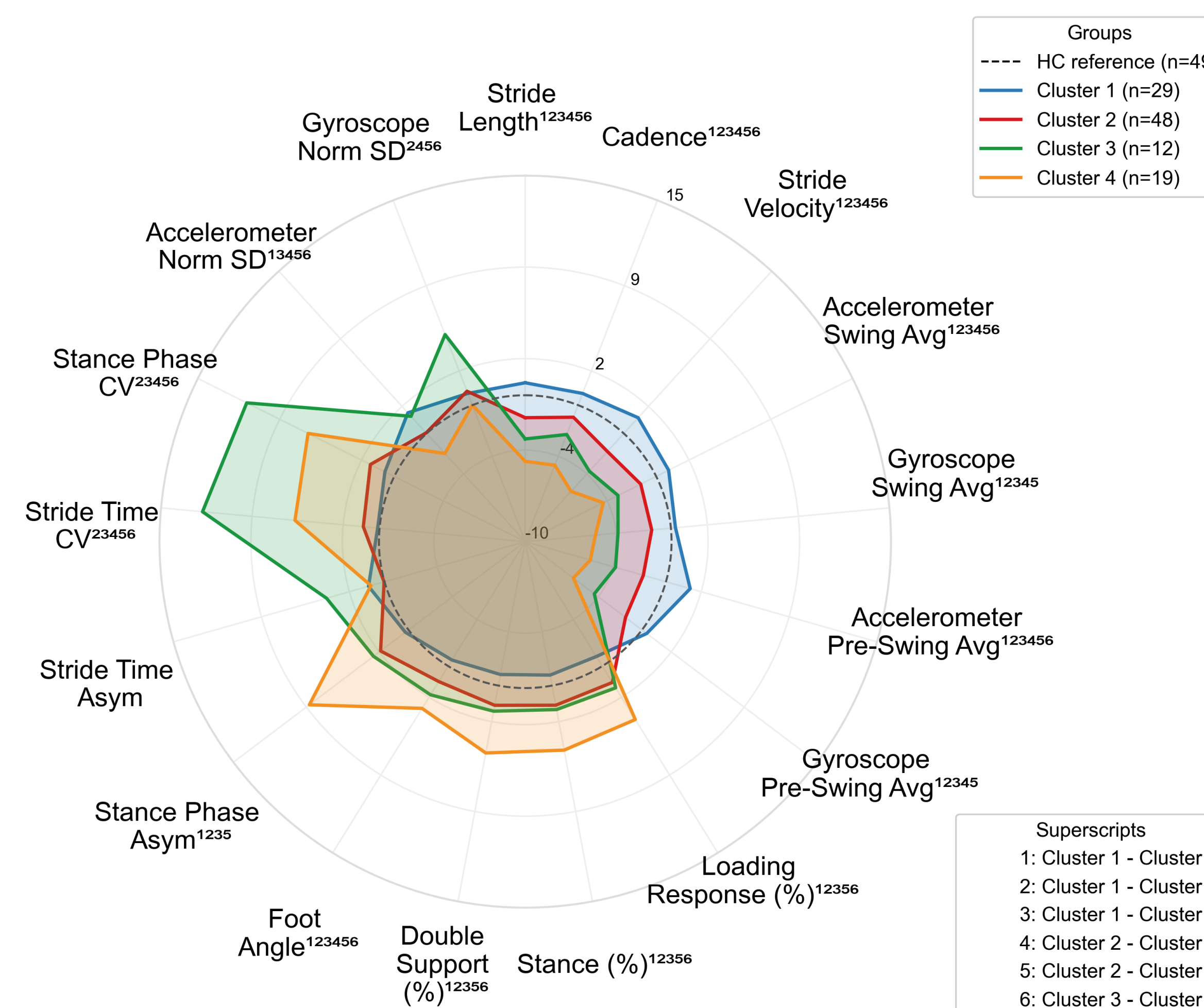


Figure 2. Radar plot with age- and sex-adjusted z-scores relative to healthy controls (HC). Significant differences after post hoc correction denoted by superscripts. Asym = asymmetry; CV = coefficient of variation; SD = standard deviation; Avg = average.

RESULTS (CONT'D)

Cluster	EDSS (median [IQR])	Interpretation
Cluster 1 (n = 29)	2.0 [1.5, 3.5]	Most preserved gait
Cluster 2 (n = 48)	3.5 [2.5, 4.0]	Moderate impairment, low variability
Cluster 3 (n = 12)	3.8 [3.4, 4.8]	Highest gait variability
Cluster 4 (n = 19)	5.5 [4.8, 6.0]	Greatest impairment, slowest gait, high stance asymmetry & foot angle deviation

DISCUSSION

Key Findings

- ✓ Four gait phenotypes identified in PwMS from smart insole features during a standardized walking assessment.
- ✓ Phenotypes generally converge with those using lab-based systems for gait assessment (motion capture, instrumented walkways) [4, 5].
- **Clinical take-home:** Smart insole-derived gait measures revealed differences beyond those captured by EDSS or MSWS-12, with **Cluster 3** showing particularly high gait variability despite similar clinical measures to other clusters.

Implications

- Smart insole-derived gait phenotypes may provide candidate digital biomarkers for longitudinal disease monitoring and future clinical endpoints, pending longitudinal validation.

Future Directions

- Track phenotypes longitudinally to evaluate membership stability.
- Link phenotypes to additional outcome measures.
- Extend to free-living gait collections.
- Strengthen HC comparisons with age- and sex-matched cohorts given differences in demographic distributions in the current sample.

REFERENCES

- [1] Joy JE, Johnston RB Jr. (2001). In: *Multiple Sclerosis: Current Status and Strategies for the Future*. National Academies Press, 115–75., [2] Benedetti MG, et al. (1999). *Mult Scler*. 5(5):363–8., [3] Hummel J, et al. (2024). *Digit Biomark*. 8(1):93–101., [4] Filli L, et al. (2018). *Sci Rep*. 8(1):4984., [5] Inojosa H, et al. (2025). *Brain Commun*. 7(5):fcaf381.

DISCLOSURES

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