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## Does gait bout definition influence the ability to discriminate gait quality between people with and without multiple sclerosis during daily life?

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### Abstract

**Background:** There is currently no consensus about standardized gait bout definitions when passively monitoring walking during normal daily life activities. It is also not known how different definitions of a gait bout in daily life monitoring affects the ability to distinguish pathological gait quality. Specifically, how many seconds of a pause with no walking indicates an end to one gait bout and the start of another bout? In this study, we investigated the effect of 3 gait bout definitions on the discriminative ability to distinguish quality of walking in people with multiple sclerosis (MS) from healthy control subjects (HC) during a week of daily living.

**Methods:** 15 subjects with MS and 16 HC wore instrumented socks on each foot and one Opal sensor over the lower lumbar area for a week of daily activities for at least 8 h/day. Three gait bout definitions were based on the length of the pause between the end of one gait bout and start of another bout (1.25 s, 2.50 s, and 5.0 s pause). Area under the curve (AUC) was used to compare gait quality measures in MS versus HC.

**Results:** Total number of gait bouts over the week were statistically significantly different across bout definitions, as expected. However, AUCs of gait quality measures (such as gait speed, stride

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#### Declaration of Competing Interest

Drs. McNames, El-Gohary and Horak have significant financial interests in APDM Wearable Technologies, a company that may have a commercial interest in the results of this research. Dr. Horak has also received honoraria from: British Columbia PT Association, Neuropore, Sanofi, Takeda, Adamas, Penn State University, University of Michigan, Johns Hopkins University. This potential conflict of interest has been reviewed and managed by OHSU. Dr. Spain receives honoraria from TG therapeutics.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.gaitpost.2020.11.024>.

length, stride time) discriminating people with MS from HC were not different despite the 3 bout definitions.

**Significance:** Quality of gait measures that discriminate MS from HC during daily life are not influenced by the length of a gait bout, despite large differences in quantity of gait across bout definitions. Thus, gait quality measures in people with MS versus controls can be compared across studies using different gait bout definitions with pause lengths  $\leq 5$  s.

## Keywords

Gait; Free-living; Multiple sclerosis; Bout; Wearable sensors

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## 1. Introduction

Gait impairments are very common in patients with multiple sclerosis (MS), leading to an elevated risk of falls and reduced quality of life [1,2]. Although the contributing factors for gait disability are complex in MS [3]; sensory deficits, imbalance, weakness, spasticity, and/or ataxia impairments are thought to contribute to most of the gait impairments in MS [3]. Gait analysis can often determine the problem(s) underlying the gait disability and then can be useful to test the efficacy of new interventions. Quantitative analysis of gait may be particularly helpful for clinical trials that investigate the effectiveness of novel pharmacologic and non-pharmacologic interventions to ameliorate gait impairments in MS.

Recently, the use of wearable sensors has made it possible to quantify the quality of gait outside the clinic during real-life situations [4,5, 6–25]. Wearable sensors can augment the standard clinical assessment of gait by active monitoring, such as performing predefined walking tests [1,17–20]. Additionally, wearable inertial sensors can be used for passive monitoring to increase the ecological validity of gait assessment by measuring walking quality during daily life in the community (for details, see [6,7,14]).

However, a key challenge in using wearable sensors to passively monitor walking in daily life is no agreement on how to define the start and end of each walking bout to investigate potential digital biomarkers of gait quality [6,26]. Specifically, it is not clear how long a subject can pause walking within a gait bout before identifying it as a separate bout. Allowing variable pause lengths of 1–5 s within walking bouts is likely to alter the number and duration of bouts included in analyses. Since recent studies have shown that bout duration may affect gait quality measures such as naturally faster walking velocity for longer than shorter walking bouts [9,27], it is important to define what constitutes a single walking bout. Daily and weekly average gait quality measures are derived after each walking bout is identified, and the gait quality measures are then used to determine the most discriminative gait measures to use as a digital endpoints for clinical trials [11,24].

In this study, we investigated the effects of different walking bout definitions based on 3 different pause lengths bouts on the discriminative ability of gait quantity and quality measures to distinguish MS from age-matched healthy control subjects (HC). All gait measures (e.g., gait speed, stride length), except activity measures, were referred to as “quality” whereas gait measures reflecting the activity (e.g., number of bouts/hour) were

referred to as “quantity” of gait. We hypothesized that quantity and quality of gait will differ across the 3 bout definitions and hence, will affect the ability to discriminate gait quality between MS and HC groups.

## 2. Methods

### 2.1. Participants

Fifteen MS ( $49 \pm 10.25$  years), and 16 age-matched HC ( $44.75 \pm 10.77$  years) participated in this study. Inclusion criteria for MS were a confirmed diagnosis of relapsing-remitting MS [28], a mild-to-moderate MS-associated disability (EDSS score  $\leq 6.0$ ) confirmed by a neurology specialist, and complaints about mobility. Exclusion criteria for all subjects included the inability to follow protocol instructions, other factors affecting gait such as hip replacement, musculoskeletal disorder, uncorrected vision or vestibular problem. All participants provided informed consent approved by the Oregon Health & Science University Institutional Review Board.

### 2.2. Daily life gait data collection

Subjects were asked to wear instrumented socks (prototype developed by APDM Wearable Technologies, Portland, Oregon, USA) on each foot, and one Opal sensor over the lower lumbar area with an elastic belt for a week of daily activities for at least 8 h/day, details in Shah et al. [29]. Briefly, the inertial sensor within the sock is located on the dorsum of the foot like the Opal sensors worn in the laboratory. The main unit containing the battery is located in a second pocket just above the lateral malleolus. To maximize fit, the socks come in different sizes, and the Velcro attachment around the foot and ankle is adjustable to ensure that a snug fit and that the sensor does not move on the foot while being worn. The instrumented socks are synchronized with the Opal (sampling rate =128 Hz) worn on the lumbar area. The subjects removed the socks and the belt at night to recharge the batteries. Data were stored in the internal memory (8 GB) of the Opals. Subjects mailed back the sensors using a pre-paid box after completion of a week of data collection. Data were uploaded to a secure cloud-based database upon return of the devices and downloaded to a local computer for further processing.

### 2.3. Gait measures

The algorithms used for extracting spatial and temporal measures of gait during daily life gait have been detailed previously [30,31]. The algorithm begins by using a fast step detection algorithm that searches for periods when one foot is stationary while the other foot is moving. The algorithm then groups the detected steps into potential bouts, that are periods of continuous walking with sequences of at least 3 steps detected. A sequence of steps only qualifies as a potential bout if the duration between steps is no more than some threshold (depending upon a bout definition), the duration of the sequence of steps is at least 3 s, and the potential bout includes at least 3 steps. When possible, the start of the potential bout is defined as 5 s prior to the first detected step and the end of the potential bout is defined as 5 s after the last detected steps (referred to as potential bouts). This allows the next stage of processing to detect other steps that may not have been detected by the fast step detection algorithm.

Each potential bout is then processed with the commercial gait analysis algorithms included in Mobility Lab (APDM Wearable Technologies, Portland, Oregon, USA) [32] which have been validated previously [33,34]. These algorithms use the Unscented Kalman Filter (UKF) and zero-velocity updates to estimate the orientation of the sensors on the feet from the accelerometers and gyroscopes [35,36]. These algorithms also estimate the orientation and position trajectory of each foot between stance periods. These algorithms also perform another, independent step-detection algorithm with many validation criteria to ensure the final detection is very accurate. After this stage of processing, only bouts that contained validated steps with at least two complete strides during normal forward-progression walking are retained as the final bouts for further processing (referred to as valid bouts). The data processing flow is summarized in Fig. 1.

A set of gait quality measures are calculated for each of the valid bouts. We calculated the average value of each gait quality measure for each bout. Finally, we calculated the mean and coefficient of variation (CV) across all of the measures' bout averages. The list of all gait quality measures that we extracted from the data is given in Table 1.

The thresholds for defining 3 bout definitions for potential bouts were as follows:

- *Bout Definition 1 (1.25 s pause)*: Individual steps are combined into potential bouts of walking, as long as the duration from one step to the next step is no longer than **1.25** seconds.
- *Bout Definition 2 (2.50 s pause)*: Individual steps are combined into potential bouts of walking, as long as the duration from one step to the next step is no longer than **2.50** seconds [8].
- *Bout Definition 3 (5.00 s pause)*: Individual steps are combined into potential bouts of walking, as long as the duration from one step to the next step is no longer than **5.00** seconds.

#### 2.4. Statistical analysis

To compare a total number of potential and valid bouts/hour across 3 bout definitions, we used the Kruskal–Wallis rank-sum test, and for the post-hoc pairwise analysis, we used the Wilcoxon rank-sum test. To investigate which specific gait quality measures best discriminated mobility characteristics between the MS from the control group, we calculated ROC curves [37] and computed the AUC [38]. All the statistical analyses were performed using R Software (version 3.6.1). The same procedure was repeated for all 3 bout definitions to investigate the effects of bout definitions on AUC between MS and controls for each gait quality measures.

### 3. Results

Total wear time was similar in both MS and HC groups with a minimum of 5 days of recordings. Specifically, the grouped average of total wear time was  $60.20 \pm 11.41$  (mean  $\pm$  SD) hours (range: [44–78] h) for MS and  $64.15 \pm 9.91$  h (range: [44–76] h) for HC ( $p = 0.319$ ).

Both the total number of weekly average potential bouts/hour ( $p < 0.001$ ) and valid bouts/hour ( $p = 0.001$ ) (combining both groups) were statistically significantly different among 3 bout definitions (see Fig. 2). Specifically, post-hoc analysis for potential bouts/hour showed that total number of potential bouts/hour were significantly different between bout definition 1 (1.25 s pause) and definition 3 (5.00 s pause) ( $p < 0.001$ ), and between bout definitions 2 (2.50 s pause) and 3 ( $p = 0.007$ ). Similarly, post-hoc analysis for valid bouts/hour showed that total number of valid bouts/hour were significantly different between definitions 1 and 3 ( $p < 0.001$ ), and between bout definitions 2 and 3 ( $p = 0.034$ ). The 3 bout definitions also resulted in different length gait bouts (see Fig. 3). The longest pause between the consecutive steps (5 s pause) resulted in a smaller number of shorter bouts. The detailed group-wise analysis showed that the difference across the 3 bout definitions for weekly average potential and valid bouts/hour was due to the HC group and not from the MS group (see Fig. 4).

AUC for *quantity* of gait (i.e., number of valid bouts/hour) to distinguish MS from HC changed from 0.71 to 0.60 to 0.56, across the 1.25 s, 2.5 s and 5 s pause bout definitions, respectively (see Table 2A).

AUC representing *quality* of gait measures (such as gait speed, stride length, stride duration) were almost unaltered and the most discriminative measures remained the same across the 3 bout definitions (see Table 2A). Table 2B shows the most discriminative gait quality measures for the MS and HC groups, calculated using three bout definitions.

#### 4. Discussion

The ability to discriminate *quantity* of gait (number of valid bouts/hour) between people with MS and healthy control subjects decreased from short to long gait-pause definitions. That is, when pauses of 1.25 s defined the end of one bout and start of another, people with MS showed statistically fewer gait bouts than HC but when pauses of up to 5 s defined the end of one bout and start of another, differences in number of gait bouts per week were no longer significant between groups. The detailed group-wise analysis showed that differences in gait quantity (bouts/hour) across the 3 bout definitions was only observed in the HC group, and not in the MS group suggesting that people with MS might stop for longer periods of time between walking bouts compared to HC and likely longer than our longest bout definition of 5 s pause between steps.

Unlike *quantity* of gait bouts, the ability to discriminate *quality* of gait measures (such as gait speed, stride length, and stride duration) were almost unaltered by the different gait bout definitions contrary to our hypothesis. The lack of effect of bout definitions on AUCs for gait quality measures might be due to the fact that one average gait measure per bout was used to characterize gait quality so long bouts were given just as much weight as short bouts. When a shorter pause duration was used, longer bouts were separated into multiple shorter bouts, giving the quality measures in these shorter bouts more weight statistically. However, this also occurred with shorter bouts, so the effect of dividing bouts into shorter bouts was almost insignificant on the weekly average value of the gait quality measures.

Our gait quality measures are slightly lower than the previously published literature. Specifically, Shema-Shiratzky et al. [21] reported the mean gait speed of 1.15 m/s for HC and 0.94 m/s for MS (calculated from only bouts >30 s), whereas we found the mean gait speed of 1.0 m/s for HC and 0.85 m/s for MS. Similarly, Storm et al. [22] reported the mean stride duration of 1.35 s (<50 steps), whereas we found the mean stride duration of 1.22 s. This discrepancy may be explained by the following possibilities: (1) definition of a bout was different, (2) various bouts durations were considered to calculate gait quality measures, (3) different algorithms used to estimate the gait measures.

Since the difference between groups by gait quality measures have been shown to influence by the bout length [6,27], and merging the shorter periods of no walking resulting in longer bout length, we expected differences in the ability to discriminate gait quality between groups with different bout definitions. However, our comparison of bout lengths was based on the same data just processed in a different way. Unlike comparing the effects of bout length in daily life on gait quality, comparing the effects of bout length based on definitions of pauses within bouts does not affect subjects' intention to walk short or long distances, which may be responsible for altering gait speed and other gait measures [9].

It is also important to note that during normal daily activities, there is a much broader range of gait speeds than observed in a laboratory. The average value of quality measures should be interpreted with due caution since this is sensitive to the behavior of subjects and their daily habits as well as their ability and impairments due to disease or injury.

There are several limitations to the current study. First, we had a modest sample size of 15–16 subjects in each group and three different thresholds to define a bout with a short to long gait-pauses. Future work is needed to validate these findings with a larger number of subjects and with a broader range of maximum resting pauses between bouts [37]. Second, other gait quantity measures related to the activity such as alpha, mean bout length, and their variability, might be interesting to explore. Last, we performed all the analysis by taking the mean of each gait measure for all the bouts over a week for each subject and thus gave equal weight to each bout. But in reality, gait speed and other measures vary for gait bouts of different lengths [9,27]. Hence, future work will focus on analyzing the effect of bout length on each gait measure and how gait bout length affects the discriminatory power of each gait measure.

## 5. Conclusion

We investigated the effect of different walking bout definitions on the ability to discriminate gait quantity and quality measures between people with multiple sclerosis from healthy control subjects during a week of continuous monitoring of daily living. Results showed that the bout definition did not change the AUC for the most discriminative gait quality measures, although it did affect the difference in quantity of gait bouts between MS and HC.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.



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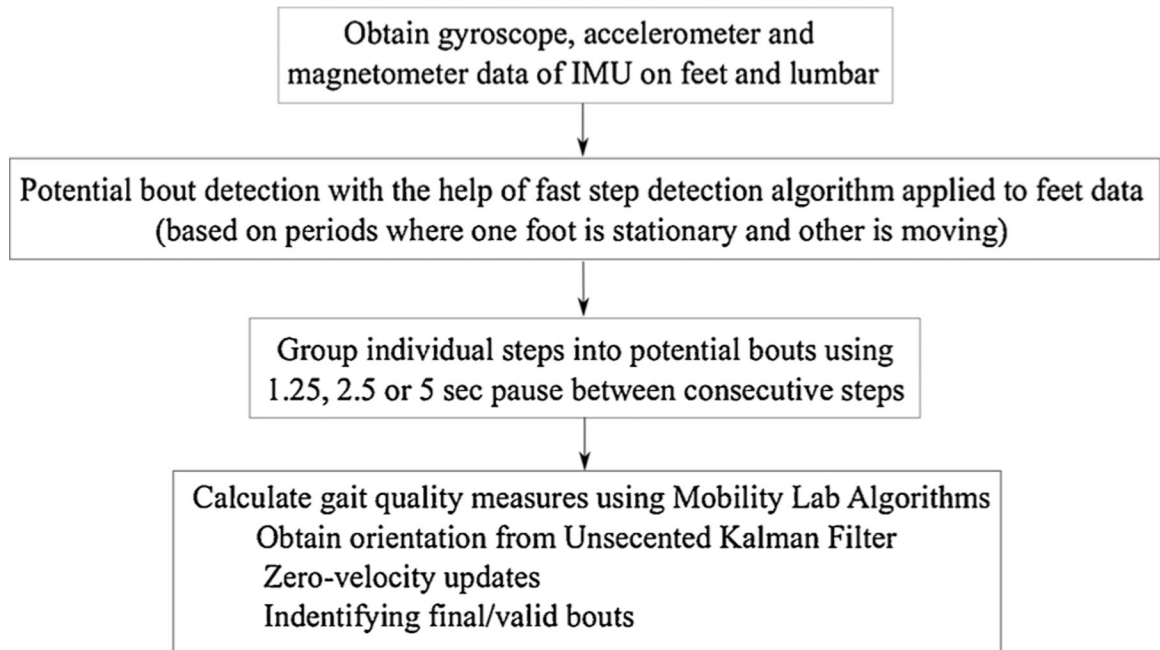
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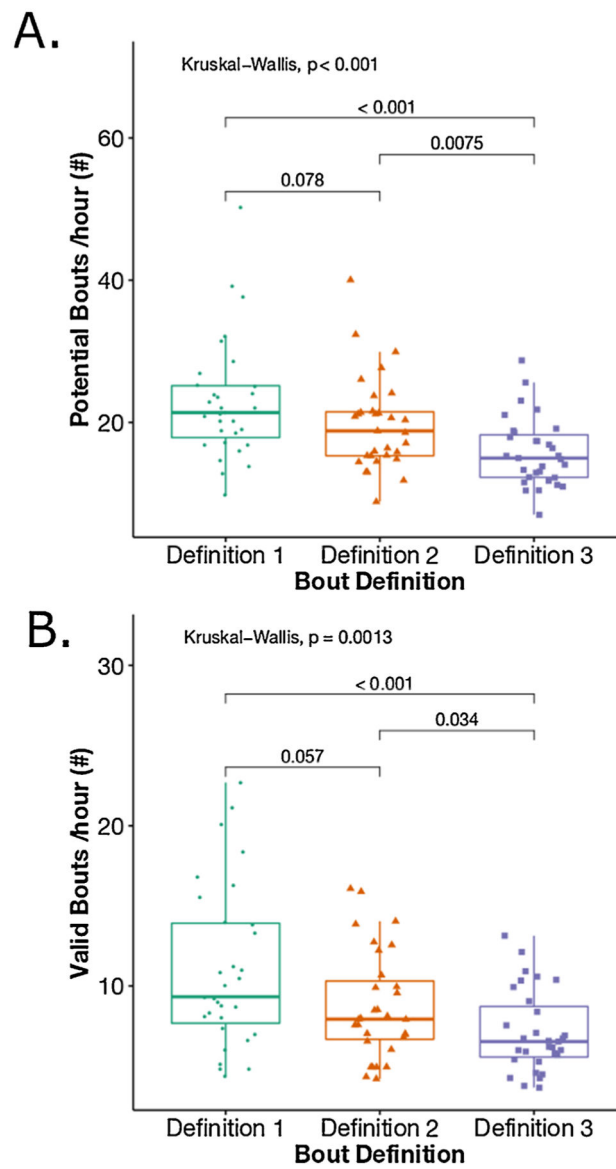
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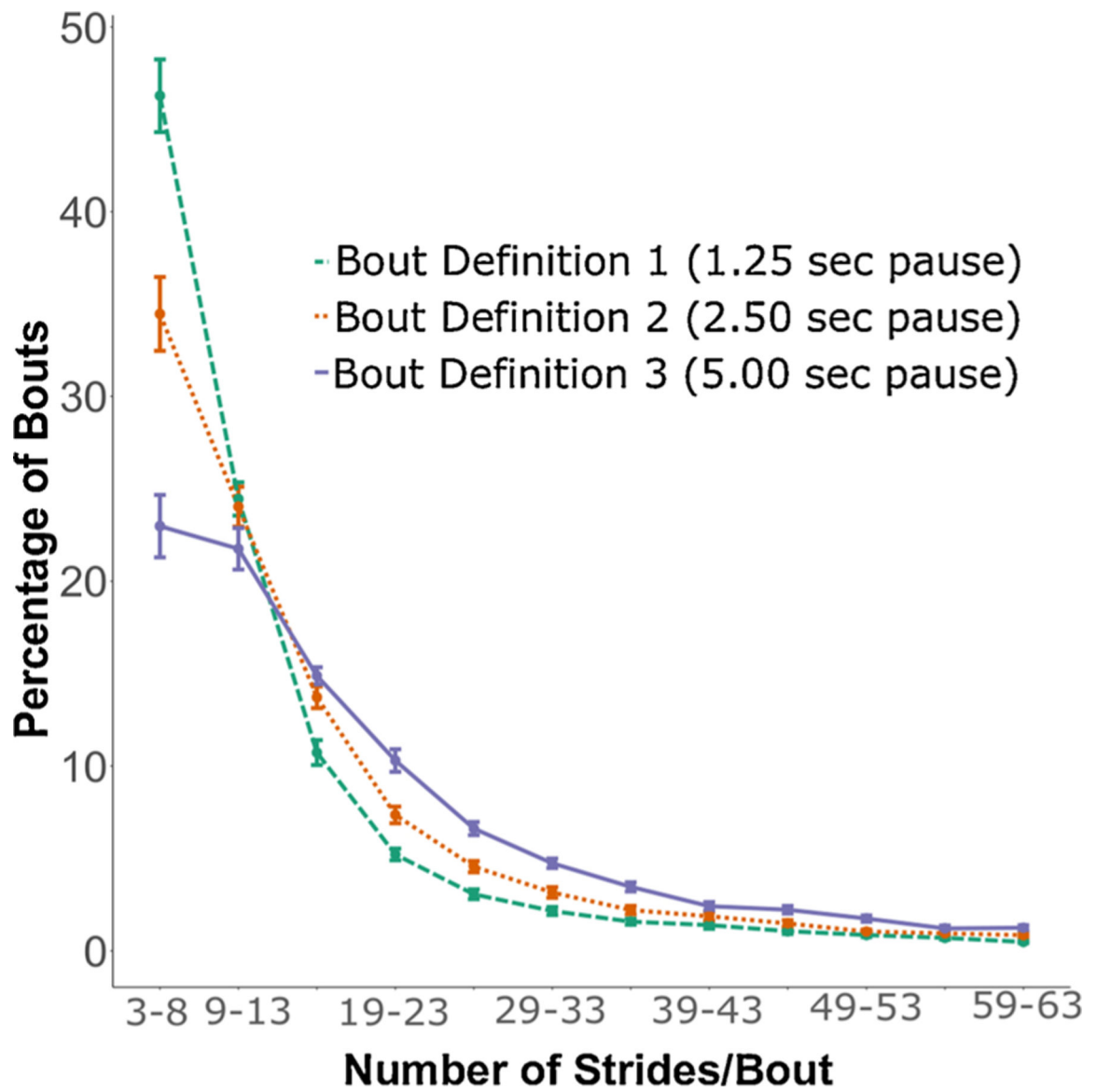
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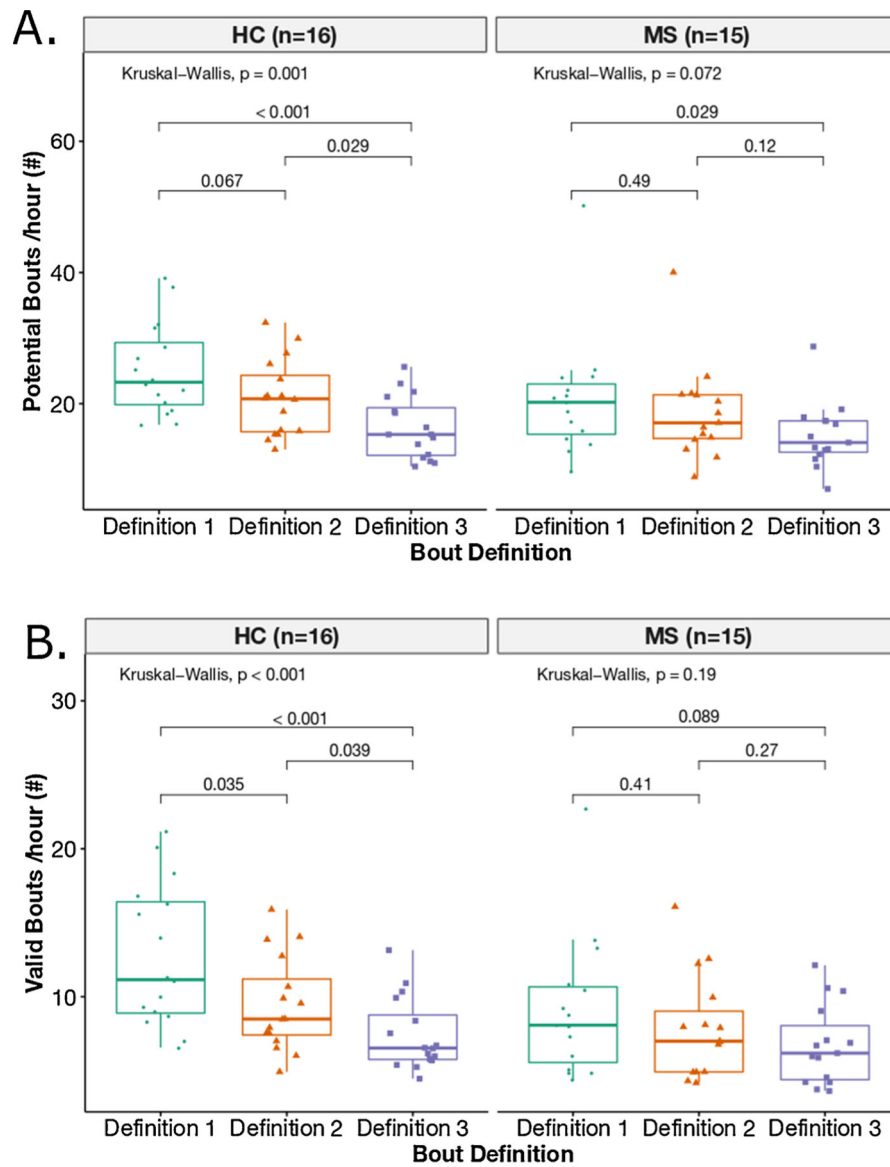
**Fig. 1.** Flowchart of data processing to calculate gait measures.



**Fig. 2.** Boxplot representation of a total number of A) potential bouts/hour, and B) valid bouts/hour across the three definitions combining both MS and HC.



**Fig. 3.** Percentage of bouts (mean and SE) vs bout length (# strides/bout) across 3 bout definitions (combining HC and MS groups).



**Fig. 4.** Boxplot representation of a total number of potential bouts/hour A) and valid bouts/hour B) across the three definitions per each group (HC and MS).

**Table 1**

List of the 24 gait quality measures.

<b>Gait Speed (m/s)</b>	<b>Elevation at Mid Swing (cm)</b>
Stride Duration (s)	Stride Length (m)
Double Support (%)	Cadences (strides/min)
Swing Time (%)	Pitch at Initial Contact (°)
Pitch at Toe Off (°)	Transverse Range of Motion (rad)
Coronal Range of Motion (rad)	Sagittal Range of Motion (rad)
Gait Speed CV (-)	Elevation at Mid Swing CV (-)
Stride Duration CV (-)	Stride Length CV (-)
Double Support CV (-)	Cadence CV (-)
Swing Time CV (-)	Pitch at Initial Contact CV (-)
Pitch at Toe Off CV (-)	Transverse Range of Motion CV (-)
Coronal Range of Motion CV (-)	Sagittal Range of Motion CV (-)

CV = Coefficient of Variation.



**Table 2A**

AUC for gait quantity and quality measures discriminating MS from HC (AUC > 0.8) for different bout definitions.

Gait measures	AUC using bout def. 1 (1.25 s pause)	AUC using bout def. 2 (2.5 s pause)	AUC using bout def. 3 (5 s pause)
<b>Quantity</b>			
Valid bouts/hour (#)	0.71	0.60	0.56
<b>Quality</b>			
Gait Speed (m/s)	0.89	0.89	0.88
Double Support (%)	0.84	0.84	0.83
Stride Length (m)	0.84	0.81	0.80
Swing Time (%)	0.83	0.83	0.83
Cadence (strides/minutes)	0.81	0.80	0.80
Stride Duration (s)	0.80	0.80	0.79

**Table 2B**

Mean and SD of gait quality measures with AUC > 0.8 for different bout definitions.

Gait quality measures	Boutdef. 1 (1.25 s pause)	Bout def. 2 (2.5 s pause)	Bout def. 3 (5 s pause)
Gait Speed (m/s)			
HC	1.1 ± 0.16	1.07 ± 0.16	1.05 ± 0.15
MS	0.85 ± 0.13	0.82 ± 0.12	0.82 ± 0.13
Double Support (%)			
HC	21.49 ± 3.15	21.96 ± 3.19	22.14 ± 3.12
MS	26.04 ± 3.33	26.48 ± 3.4	26.57 ± 3.46
Stride Length (m)			
HC	1.17 ± 0.15	1.15 ± 0.15	1.14 ± 0.15
MS	0.99 ± 0.15	0.97 ± 0.15	0.97 ± 0.15
Swing Time (%)			
HC	39.33 ± 1.62	39.12 ± 1.66	39.05 ± 1.63
MS	36.97 ± 1.73	36.77 ± 1.76	36.71 ± 1.77
Cadence (strides/minutes)			
HC	54.99 ± 3.96	54.48 ± 3.79	54.22 ± 3.75
MS	50.66 ± 3.26	50.24 ± 3.49	50.08 ± 3.58
Stride Duration (s)			
HC	1.13 ± 0.09	1.14 ± 0.08	1.15 ± 0.08
MS	1.22 ± 0.08	1.23 ± 0.09	1.24 ± 0.09