The use of digital devices to monitor physical behaviour in motor neuron disease: a systematic review

Lucy Samantha Musson, Nina Mitic, Victoria Leigh-Valero, Gladys Onambele-Pearson, Liam Knox, Frederik J Steyn, Cory J Holdom, Taylor JM Dick, Ruben PA van Eijk, Jordi WJ van Unnik, Lianne CM Botman, Emily Beswick, Deirdre Murray, Alys Griffiths, Christopher McDermott, Esther Hobson, Amina Chaouch, Emma Hodson-Tole

Submitted to: Journal of Medical Internet Research
on: November 06, 2024

Table of Contents

The use of digital devices to monitor physical behaviour in motor neuron disease: a systematic review

Lucy Samantha Musson[1*]; Nina Mitic[2*]; Victoria Leigh-Valero[3]; Gladys Onambele-Pearson[4]; Liam Knox[1]; Frederik J Steyn[5, 6]; Cory J Holdom[7]; Taylor JM Dick[6]; Ruben PA van Eijk[8, 9]; Jordi WJ van Unnik[8]; Lianne CM Botman[8]; Emily Beswick[10]; Deirdre Murray[10]; Alys Griffiths[1]; Christopher McDermott[1, 11]; Esther Hobson[1, 11]; Amina Chaouch[12]; Emma Hodson-Tole[2]

[1]Sheffield Institute for Translational Neuroscience Division of Neuroscience University of Sheffield Sheffield GB
[2]Department of Life Sciences Manchester Metropolitan University Manchester GB
[3]University of Manchester Manchester GB
[4]Department of Sport and Exercise Sciences Manchester Metropolitan University Manchester GB
[5]Department of Neurology Royal Brisbane and Women's Hospital Herston, Queensland AU
[6]School of Biomedical Sciences University of Queensland St Lucia, Queensland AU
[7]Australian Institute for Bioengineering and Nanotechnology University of Queensland St Lucia, Queensland AU
[8]Department of Neurology UMC Utrecht Brain Center University Medical Center Utrecht Utrecht NL
[9]Biostatistics & Research Support Julius Center for Health Sciences and Primary Care University Medical Center Utrecht Utrecht NL
[10]Academic Unit of Neurology School of Medicine Trinity College Dublin Dublin IE
[11]Sheffield Teaching Hospitals NHS Foundation Trust Sheffield GB
[12]Manchester Centre of Clinical Neurosciences Salford Royal NHS Foundation Trust Salford GB
[*]these authors contributed equally

Corresponding Author:
Lucy Samantha Musson
Sheffield Institute for Translational Neuroscience
Division of Neuroscience
University of Sheffield
385a Glossop Road
Sheffield
GB

Abstract

Background: Motor neuron disease (MND) is a progressive and incurable neurodegenerative disease. There is an urgent need for sensitive measures of disease progression that can be used to robustly evaluate new treatments. Measures of physical function, derived from digital devices, are beginning to be used to assess disease progression. Given that MND is relatively rare, there is value in establishing a consensus approach to standardizing use of such devices.

Objective: This systematic review explored how digital devices are being used to quantify free-living physical behaviour in people living with MND (plwMND). We evaluated the feasibility of using the devices and assessed the implications for monitoring physical behaviour for future design of clinical trials.

Methods: Systematic searches of four databases were performed in October 2023 and June 2024. Peer-reviewed articles (including pre-prints) written in English language with plwMND using digital devices to assess free-living physical behaviour were included.

Results: Twelve articles met inclusion criteria for data extraction. Studies used traditional endpoints focusing on duration, intensity, and frequency of physical activity or non-traditional endpoints focusing on features of an individual's movement patterns. Greater monitoring frequencies and improved endpoint sensitivity was shown to provide smaller sample size requirements and shorter durations for hypothetical clinical trials. PlwMND found using devices acceptable and reported low burden. The perspectives of other end-users and implications on clinical practice were not explored.

Conclusions: Remote monitoring of free-living physical behaviour in plwMND is in its infancy but has exciting potential to quantify physical function in MND. It is essential to develop a consensus statement within the MND community, working towards agreed and standardised methods for data collection, analysis and reporting.

(JMIR Preprints 06/11/2024:68479)
DOI: https://doi.org/10.2196/preprints.68479

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

The use of digital devices to monitor physical behaviour in motor neuron disease: a systematic review

Lucy S Musson*
- Sheffield Institute for Translational Neuroscience, Division of Neuroscience, University of Sheffield, Sheffield, United Kingdom

Nina Mitic *
- Department of Life Sciences, Manchester Metropolitan University, Manchester, United Kingdom

***Joint first authors**

Victoria Leigh-Valero
- University of Manchester, Manchester, United Kingdom

Gladys Onambele-Pearson
- Department of Sport and Exercise Sciences, Manchester Metropolitan University, Manchester, United Kingdom

Liam Knox
- Sheffield Institute for Translational Neuroscience, Division of Neuroscience, University of Sheffield, Sheffield, United Kingdom

Frederik J Steyn
- School of Biomedical Sciences, University of Queensland, St Lucia, Queensland, Australia
- Department of Neurology, Royal Brisbane and Women's Hospital, Herston, Queensland, Australia

Cory J Holdom
- Australian Institute for Bioengineering and Nanotechnology, University of Queensland, St Lucia, Queensland, Australia

Taylor JM Dick
- School of Biomedical Sciences, University of Queensland, St Lucia, Queensland, Australia

Ruben P.A. van Eijk
- Department of Neurology, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht, The Netherlands.
- Biostatistics & Research Support, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands.

Jordi W.J. van Unnik
- Department of Neurology, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht, The Netherlands

Lianne C.M. Botman
- Department of Neurology, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht, The Netherlands

Emily Beswick
- Academic Unit of Neurology, School of Medicine, Trinity College Dublin, Ireland

Deirdre Murray
- Academic Unit of Neurology, School of Medicine, Trinity College Dublin, Ireland

Alys Griffiths
- Sheffield Institute for Translational Neuroscience, Division of Neuroscience, University of Sheffield, Sheffield, United Kingdom

Christopher McDermott
- Sheffield Institute for Translational Neuroscience, Division of Neuroscience, University of Sheffield,

Sheffield, United Kingdom
- Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Esther Hobson
- Sheffield Institute for Translational Neuroscience, Division of Neuroscience, University of Sheffield, Sheffield, United Kingdom
- Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Amina Chaouch
- Manchester Centre of Clinical Neurosciences, Salford Royal NHS Foundation Trust, Salford, United Kingdom

Emma Hodson-Tole
- Department of Life Sciences, Manchester Metropolitan University, Manchester, United Kingdom

Corresponding author: Lucy Musson, email: l.s.musson@sheffield.ac.uk

The use of digital devices to monitor physical behaviour in motor neuron disease: a systematic review

Abstract

Background: Motor neuron disease (MND) is a progressive and incurable neurodegenerative disease. There is an urgent need for sensitive measures of disease progression that can be used to robustly evaluate new treatments. Measures of physical function, derived from digital devices, are beginning to be used to assess disease progression. Given that MND is relatively rare, there is value in establishing a consensus approach to standardizing use of such devices. **Objective:** This systematic review explored how digital devices are being used to quantify free-living physical behaviour in people living with MND (plwMND). We evaluated the feasibility of using the devices and assessed the implications for monitoring physical behaviour for future design of clinical trials. **Methods:** Systematic searches of four databases were performed in October 2023 and June 2024. Peer-reviewed articles (including pre-prints) written in English language with plwMND using digital devices to assess free-living physical behaviour were included. **Results:** Twelve articles met inclusion criteria for data extraction. Studies used traditional endpoints focusing on duration, intensity, and frequency of physical activity or non-traditional endpoints focusing on features of an individual's movement patterns. Greater monitoring frequencies and improved endpoint sensitivity was shown to provide smaller sample size requirements and shorter durations for hypothetical clinical trials. PlwMND found using devices acceptable and reported low burden. The perspectives of other end-users and implications on clinical practice were not explored. **Conclusions:** Remote monitoring of free-living physical behaviour in plwMND is in its infancy but has exciting potential to quantify physical function in MND. It is essential to develop a consensus statement within the MND community, working towards agreed and standardised methods for data collection, analysis and reporting.

Introduction

Motor neuron disease (MND), a group of progressive neurodegenerative disorders that includes Amyotrophic Lateral Sclerosis (ALS), is characterised by a loss of motor neurons in the brain, brainstem and/or the spinal cord [1]. Most people living with MND (plwMND) experience progressive weakness and wasting of their

muscles with a life expectancy of only 2-3 years following symptom onset [2] There is no cure for MND, and care is based on providing symptomatic support through multidisciplinary teams. These teams must carefully monitor physical function, nutritional status, respiratory function, cognition, and wellbeing to inform clinical decision-making and provide timely and effective support. PlwMND are usually reviewed every three months [3] however, disease progression is variable, with some plwMND requiring more frequent monitoring, while others need less frequent input due to slower disease progression.

The most used functional measure of disease severity and progression in MND is the Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised (ALSFRS-R) [4]. This questionnaire measures changes in function across four-domains (bulbar, fine motor, gross motor and respiratory) in the context of completing activities of daily living [4]. The ALSFRS-R is predictive of survival and is commonly used as a primary endpoint in clinical trials [5-6]. However, it has limitations. It has been shown that the total score of the ALSFRS-R is multidimensional and does not accurately capture the heterogeneity of plwMND. This means that two individuals can have the same total ALSFRS-R score but have different disease severity, be experiencing different symptoms and have different prognoses [7-9], which can result in under or overestimating treatment effects in clinical trials [10]. Moreover, the ALSFRS-R is not particularly sensitive to disease progression over durations less than 12 months [9]. Thus, there is a need for more objective and sensitive ways of characterising disease progression in MND. To do this it is likely that bespoke tools that provide sensitive assessment across the four disease domains, must be developed. In this review, we focus on the currently available tools to assess physical function in plwMND.

Recently, there has been growing interest in how digital technologies can be used to monitor symptoms in plwMND [11-12]. One technology that seems particularly promising is wearable tri-axial accelerometer devices. These small devices can be worn unobtrusively (e.g., on the wrist like a watch, or on the waist on a belt) and detect accelerations of the body in three orthogonal planes. They enable non-invasive monitoring of people undertaking their free-living, habitual daily activities outside a clinical or research environment. This includes being active, sedentary, and sleeping, which when taken together, can be considered the person's physical behaviour pattern [13].

Accelerometer-derived measures have already been identified as potential markers of disease onset, progression, and response to treatment in neurodegenerative diseases. A recent systematic review of the literature revealed 17 reports of activity monitoring in people living with Parkinson's disease and highlighted their value and application in well-designed clinical trials [14]. In contrast, only one report of physical behaviour monitoring in MND was identified [14]. Changes in physical behaviour will differ between diseases, therefore specific understanding of the potential of activity monitoring to support MND research is required. This need has been recognised by the MND community, with several different devices having been used in research to evaluate motor symptoms in plwMND [15].

Therefore, building on the review by Beswick et al. [15] it is timely to investigate current knowledge of physical

behaviour patterns in MND and the methods by which this knowledge is being accrued so that standards for best practice can be identified and shared. This will not only highlight the potential value of remote monitoring of physical behaviour in plwMND but it may also offer a steppingstone for applying the knowledge to other progressive diseases. Therefore, this systematic review aims to: 1) explore how accelerometer devices are being used to quantify free-living physical behaviour in plwMND; 2) evaluate the feasibility of using these devices for objectively delineating the physical effects of MND; and 3) assess the implications of physical behaviour monitoring for clinical trials design and clinical practice.

Methods

Search strategy

A systematic review of scientific literature (written in English) was conducted in October 2023 using four databases: Europe PMC (11/10/2023), SCOPUS (11/10/2023), Web of Science (11/10/2023) and IEEE Xplore (12/10/2023). The included articles were not restricted by the date of publication. The search was performed in line with the current Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement [16]. To ensure the work published here was as current as possible, an updated search of each database was conducted: Europe PMC (20/06/2024), SCOPUS (20/06/2024), Web of Science (20/06/2024) and IEEE Xplore (20/06/2024). Here the review period was limited to the years 2023-2024, with the aim of identifying and including any study published between the date of the initial search and final manuscript preparation.

The following search strategy was used in each database: (MND or ALS or motor neurone disease or motor neuron disease or amyotrophic lateral sclerosis) AND (Physical activity or exercise or physical behaviour or sedentary behaviour or mobility) AND (Remote monitoring or sensors or digital technology or accelerometer* or actigraphy or GPS or wearable technology or objective monitoring or wearable devices).

Screening for eligibility

Full inclusion and exclusion criteria are presented in Table 1. All references were imported to Rayyan web tool [17] for initial screening. A total of 336 records were identified during the initial search of the databases. Following the removal of duplicates (n = 63), the articles were screened to assess eligibility. Screening was completed by NM. Forward and backwards reference chaining was completed in eligible articles to identify other potential studies not captured by the search. The full screening process is outlined in Figure 1, including the initial and the updated search. A total of 12 articles met criteria for data extraction.

Data extraction

A data extraction tool was created by NM with a focus on extracting information relevant to the study aims (See Supplementary Material 1). Two researchers (NM, LM) independently extracted information from the identified studies. Once extracted, these authors compared results for agreement, with disputes resolved by a third reviewer (EHT).

Table 1: Study inclusion and exclusion criteria

	Inclusion Criteria	Exclusion Criteria
Participants	Study population includes plwMND	Participant with other neurological conditions
Design	Any other design not specified in exclusion criteria	Animal studies Ongoing trials Systematic reviews Meta-analysis
Intervention of interest	Use of remote monitoring devices to assess physical behaviour	Devices used for rehabilitation purposes (such as orthoses) Devices measuring any other parameters which are not physical behaviour
Outcome of interest	Remote monitoring of physical behaviour in free-living conditions	Gait analysis - Gait specific parameters focused on identifying pathological gait pattern in clinical environment Monitoring of prescribed exercises or set movement tasks
Setting	Free-living environment Home/domiciliary monitoring Remote monitoring	Face to face monitoring in clinical environment
Type of publication	Peer-review journal articles Pre-print articles subject to secondary review	Any other publication type e.g., conference abstract, book chapters Pre-prints that are now published
Date of publication	No restriction	No restriction
Language of publication	English	Non-English

Quality assessment

Despite the overarching observational nature of the studies, there was significant heterogeneity in study design between them. Consequently, a decision was made to assess the reporting quality of the studies to inform future research in this area, and in doing so, support evaluation of good practice in use and reporting of free-living physical behaviour in MND. An *a priori* decision was made to include all eligible studies in the review regardless of their quality, due to the infancy of the research area.

The reporting quality of studies was assessed using *Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies* [18]. STROBE guidelines provide researchers with a checklist of 22 items required for good reporting of observational studies [18] (See Supplementary Material 2). In the present study an article was awarded two points for each item that was addressed, one point for each item deemed to be partially reported but required further information, and zero points when no information was provided. LSM and NM independently assessed each article using an Excel spreadsheet. LSM and NM then met to confirm and resolve discrepancies.

Data collation

Two pairs of articles had identical methods, effectively reporting different aspects of the same study. In both cases the first article of the pair [19-20] focused on description of method, while the second [21-22] summarized methods and focused on the main research findings. Therefore, when assessing the methods of data collection the pairs were considered as one study (i.e., the total number of studies for data collection was ten). When assessing study findings, each study in the pair was considered separately, so that 12 articles were included in analysis of findings. If several studies used the same MND population the participant data

was taken from the study publishing findings (rather than articles focusing on methodology or feasibility) or the study which was published first. Several studies used data collected on the same participants population of which details are indicated in Table 3. Due to heterogeneity between the physical behaviour endpoints used in current studies we deemed it inappropriate to complete statistical analysis of findings therefore we focused on narrative review of evidence, descriptive statistics of participant characteristics and outcome measures used in the studies.

Results

Following the removal of duplicates and the full screening process, 12 articles published between 2019-2024 were included in the review [19-30]. Figure 1 provides a flowchart of the complete search process. Studies were conducted in five countries: Australia, Netherlands, Scotland, United Kingdom, and United States of America. We noted three overarching aims of investigation: i) validating remote monitoring of physical behaviour in MND and finding markers of disease progression; ii) investigating feasibility of remote monitoring; and iii) investigating sample size effects of physical behaviour endpoints to inform clinical trial design.

[INSERT FIGURE 1]

Reporting quality

Overall, the scores from reporting quality assessment ranged between 19-40 (maximum available points = 44) (Table 2). The only item which was fully addressed by every article (100%) was the limitations of the study. Whilst all articles attempted to discuss generalisability to all plwMND (e.g., limb *versus* bulbar onset), the reviewers agreed that all the articles would have benefited from providing more detail about this. The most frequently missed item was a description of any efforts to address potential sources of bias with all 12 articles (100%) failing to address this. Eight articles (66.7%) did not explain how the study size was determined and three articles (25%) failed to give the eligibility criteria of participants and/or the methods of participant selection. Two articles (16.7%) failed to describe their statistical methods and two articles (16.7%) failed to define all outcomes, exposures, predictors, potential confounders, and effect modifiers.

Table 2: Scores from the reporting quality assessment for each item of STROBE statement for all studies included in the systematic review.

	Study – by author											
STROBE Statement	**van Eijk et al. [23]**	**Garcia-Gancedo et al. [19]**	**Karas et al. [24]**	**Kelly et al. [21]**	**Rutkove et al. [20]**	**Rutkove et al. [22]**	**Holdom et al. [25]**	**Johnson et al. [26]**	**Gupta et al. [27]**	**van Unik et al. [28]**	**Beswick et al. [29]**	**Straczkiewicz et al. [30]**
Title and abstract												
Introduction												
Background/rationale												
Objectives												
Methods												
Study design												
Setting												
Participants												
Variables												
Data sources/ measurement												
Bias												
Study size												
Quantitative variables												
Statistical methods												
Results												
Participants												
Descriptive data												
Outcome data												
Main results												
Other analyses												
Discussion												
Key results												
Limitations												
Interpretation												
Generalisability												
Funding												
Total points:	**38**	**31**	**36**	**35**	**19**	**25**	**36**	**36**	**27**	**40**	**37**	**37**

Note. Dark grey colour = two points; Medium grey colour = one point; Light grey = zero points

Data Collection

All ten studies employed a longitudinal observational study design; however, methods were very heterogeneous. There were four elements identified as important to data collection methods: i) Participant characteristics, ii) Follow-up, iii) Device set-up, and iv) Other outcome measures, described below.

Participant characteristics

A summary of participant characteristics is presented in Table 3. The participant sample size varied across studies (*n* = 10 – 376 people) and decreased over longitudinal measurement time points, due to loss to follow-up and progression of the disease. However, it was often unclear (or not described) how many participants were included at each measurement point. Overall, there were more male participants (68.6%) in the MND population compared to female (31.4%). The studies reported age as either mean (*n* = 7) or median (*n* = 2). The overall mean age of participants in the studies reporting mean was 59.7 years while the median was 58.8 years. Three studies [20,25,27] included healthy controls, but the sample size was much smaller (*n* = 25 – 58) and was not age or sex matched to the clinical population with median age of 51 years and more female participants compared to male (54% female *versus* 46% male). The reported means and medians of the baseline ALSFRS-R scores ranged from 31.4 to 41.6 points. MND subtype or ALS phenotype at onset were reported in seven studies. The most common subtype of MND was ALS which represented between 50% - 97% of baseline population [23,25,28,29] while the most common ALS phenotype at onset was upper limb which represented 60% of baseline population [19]. Of the seven studies that reported symptom duration at baseline, two predominantly included those who had symptoms for 18 months or less, although it should be noted these two reports use the same data set [19,21]. In the other five studies, participants had predominantly experienced symptoms for over 20 months [23-25,27-28].

Table 3: Summary of participant characteristics

Author and Year	Sample size (baseline)	Controls (n = x)	Sex	Age (years) (M (SD) or Me (IQR))	Disease phenotype	Symptom duration at baseline (months) [M (SD) *or* Mdn (IQR)]	ALSFRS-R total score at baseline [M (SD) *or* Mdn (IQR)]
van Eijk et al. [23]	MND = 42	No	Male = 31 / Female = 11	M = 60 (12)	MND subtypes ALS = 39 PMA = 3 PLS = 0	Mdn = 25 Range = 7-218	M = 36 (8)
Garcia-Gancedo et al. [19]	ALS = 25	No	Male = 21 / Female = 4	M = 53.1 (9.93)	Phenotype at onset UL = 15 LL = 6 UL and LL = 2 Bulbar = 2	Reported in 22 participants as <18 months	M = 41.6 (4.98)
Kelly et al [21]	ALS = 25	No	Male = 21 / Female = 4	M = 53.1 (9.93)	Phenotype at onset UL = 15 LL = 6 UL and LL = 2 Bulbar = 2	<3 months. n = 3 ≥3 <6 months: n = 8 ≥6 <12 months: n = 9 ≥1 year <18 months: n =2 Missing data: n = 3	M = 41.6 (4.98)
Rutkove et al. [20]	ALS = 75 (111 consented, and 75 began contributing data)	Yes (n = 25; 30 consented, 25 began contributing data)	Baseline characteristics* MND - Male = 65 / Female = 42 Controls - Male = 9 / Female = 20	MND - Mdn = 60 (Range = 30-80) Controls - Mdn = 51 (Range = 27-79)	Not disclosed	Not disclosed	Mdn = 34 Range = 9-43
Rutkove et al. [22]	ALS = 72 (113 enrolled, and 72 collected data at least once)	No	Male = 50 / Female = 22	M = 60.1 (9.9)	Not disclosed	Not disclosed	M = 36.1 (no SD reported)
Karas et al. [24]	ALS = 45	No	Male = 29 / Female = 16	M = 60.1 (10.7)	Symptom onset site Nonbulbar = 31 Bulbar = 8 Unknown/not reported = 6	M= 62.3 (60.8) Mdn = 50 Unknown/not reported *n* = 6	M = 36.0 (6.2)
Holdom et al. [25]	MND Wrist = 97 Hip = As van Eijk et al.[23]	Yes (n = 58)	MND wrist: - Male = 75 / Female = 22 MND hip: - As van Eijk et al.[23] Controls wrist - Male = 29 / Female = 29	MND wrist: - Mdn = 60.69 (12.55) MND hip: - As van Eijk et al.[23] Controls wrist: - Mdn = 55.33 (16.11)	MND subtype Wrist: ALS = 87 PMA = 1 PLS = 6 Hip: As van Eijk et al.[23]	MND Wrist: Mdn = 21.31 +/- 13.27 MND Hip: As van Eijk et al.[23]	Wrist: Mdn = 38 (9) Hip: Mdn = As van Eijk et al.[23]
Johnson et al. [26]	ALS = 46 enrolled, 40 met the analysis sample criteria	No	Total - Male = 25 / Female = 15 Wrist Cohort: - Male = 12 / Female = 8 Ankle Cohort : - Male = 13/ Female = 7	Total: - M = 61.8 (12.0) Wrist Cohort: - M = 62.9 (13.4) Ankle Cohort: - M = 60.6 (10.7)	Not disclosed	Not disclosed	Total: - M = 31.4 (8.1) Wrist cohort: - M = 31.4 (8.6) Ankle cohort: - M = 31.4 (7.9)

Gupta et al. [27]	ALS = 376	Yes (n = 26)	ALS - Male = 247 / Female = 129 Controls - Male = 14 / Female = 12	ALS - Mdn = 57 (21-79) Controls - Mdn = 33 (Range = 20-67)	First symptoms include: UL = 159 LL = 164 Bulbar symptoms = 75 Respiratory symptoms = 9	Mdn = 22.8	Mdn = 41 Range = 14-48
Van Unnik et al. [28]	ALS = 97 (two cohorts) 1st cohort = 42 (As van Eijk et al.[23]) 2nd cohort = 55	No	Both Cohorts - Male = 68 / Female = 29 1st cohort: - As van Eijk et al.[23] 2nd cohort: - Male = 37 / Female = 18	Both cohorts - M = 60.5 (11.1) 1st cohort: - As van Eijk et al.[23] 2nd cohort: - M = 61 (10.7)	Both Cohorts ALS = 94 PMA = 3 1st cohort: - As van Eijk et al.[23] 2nd cohort - ALS = 55	Both cohorts - Mdn = 22.1 (17.6) 1st cohort: - As van Eijk et al.[23] 2nd cohort: - Mdn = 18.5 (14.7)	Both cohorts - M = 37.9 (6.8) 1st cohort: - As van Eijk et al.[23] 2nd cohort: - M = 39.1 (5.3)
Beswick et al. [29]	MND=10	No	Male = 8 / Female = 2	M = 62 (12)	ALS = 5 PLS= 2 Not Disclosed = 3	Survival length: Long survivor (>8 years) n = 2	M = 40 (6)
Straczkiewicz et al. [30]	ALS = 20 As Johnson et al.[26] wrist cohort	No	As Johnson et al.[26] wrist cohort	As Johnson et al.[26] wrist cohort M = 61.4 (10.6)	Not disclosed	Not disclosed	No baseline reported - estimated baseline total score = 34.4 (95% CI: [30.4, 38.3])

Note. M = Mean; SD = Standard deviation; Mdn= Median; IQR = Interquartile Range Index; MND = Motor Neuron Disease; ALS = Amyotrophic Lateral Sclerosis, PMA progressive muscular atrophy, PLS = Primary lateral sclerosis, UL = Upper limb, LL = Lower limb **; ****Data provided in Table 1 of Rutkove et al.[20] for the entire group of individuals enrolled*

Follow-up

Follow-up refers to the overall duration of monitoring completed in a study. Measurement frequency refers to how often participants were invited to wear/use a device (e.g., every three months), and the measurement duration refers to the period over which measures were recorded on each device deployment (See **Table 4** for examples). The participant follow-up ranged between 12 weeks – 24 months and the measurement frequency was mostly every 1–4 months (Table 4). The type of measurement was either periodic (*n* = 7) or continuous for the duration of the follow-up (*n* = 3). When the type of measurement was periodic the duration of each measurement ranged from 1-8 consecutive days, with the most common choice of seven days *(n* = 3).

Device set up

Most studies (*n* = 8) used commercially available triaxial accelerometers (Table 4). One study also used a biaxial accelerometer and one study used participant's personal smartphone (GPS and triaxial accelerometer). Most studies (*n* = 8) reported sampling frequency (Hz) of the device which ranged from 10-128 Hz, however, there was little justification for the choice. The most used frequency was 30 Hz (*n* = 4). Device wear location varied and included wrist, chest, hip, and ankle. Most studies mounted the device in one place (*n* = 6), while some studies (*n* = 2) used two cohorts with different wear locations. Two studies mounted the devices to several locations, with Gupta et al. [27] simultaneously comparing four devices (one on each ankle and wrist) per participant and Beswick et al. [29] comparing two devices (right wrist and right ankle) per participant. (See Table 4).

Other outcome measures

All studies used clinician or self-administered ALSFRS-R to track disease progression and used it as a correlation point when assessing validity of the physical behaviour endpoints. Either a total score of ALSFRS-R was used for comparison, or subdomains of ALSFRS-R were used (gross motor, fine motor, bulbar, respiratory). Six studies included other outcome measures, such as additional questionnaires (Hospital Anxiety and Depression Scale, Rasch-built Overall ALS Disability Scale and study specific questionnaires) (*n* = 4), respiratory data (*n* = 2), cardiac data (n=1), speech data (*n* = 2), muscle strength (*n* = 1), mobility tests (*n* = 1) and survival status (*n* = 1) (Table 4). Additional outcome measures were predominantly used as stand-alone measures. Their relationship with physical behaviour endpoints was assessed in two studies. Van Unnik et al. [28] found that participants with lower vertical movement index (VMI) also experienced a significantly lower probability of survival compared participants who had higher VMI during follow-up. Beswick et al. [29] assessed the relationship between a mobility test and physical behaviour endpoints from the devices. They found a significant correlation between the distance walked during 6-min walking test (6MWT) and the total vector magnitude (VM) counts from ankle mounted devices during the 6MWT.

Table 4: Summary of data collection and data analysis approaches

	Type and set up of device			Follow-up		Other outcome measures	Data analysis
Author and Year	**Body location**	**Device (type and name)**	**Sampling frequency (Hz)**	**Duration of follow-up**	**Duration and frequency of measurements**	**Outcome measures**	**Epochs used in analysis**
van Eijk et al. [23]	Right hip (anteroaxillary line)	Triaxial accelerometer ActiGraph GT9XLink	30 Hz	18 months	7 consecutive days every 2-3 months	ALSFRS-R, HADS, weight, wear time log	10 seconds
Garcia-Gancedo et al. [19]	Chest	Triaxial Accelerometer Mega Faros 180	50 Hz	48 weeks	3 consecutive days every month	ALSFRS-R, FVC, HRV Speech	60 seconds
Kelly et al. [21]	Chest	Triaxial Accelerometer Mega Faros 180	50 Hz	48 weeks	3 consecutive days every month	ALSFRS-R, FVC, HRV Speech	60 seconds [based on info in Garcia-Gancedo et al[19]]
Rutkove et al. [20]	Not stated Device designed for wrist	Mi Band R	Not reported	9 months	Daily for 90 days, then biweekly for 180 days	ALSFRS-R, speech, EIM tool, respiratory data, muscle strength, PREMs	Not relevant
Rutkove et al. [22]	Not stated Device designed for wrist	Mi Band R	Not reported	9 months	Daily for 90 days, then biweekly for 180 days	ALSFRS-R, speech, EIM tool, respiratory data, muscle strength, PREMs	Not relevant
Karas et al. [24]	Not relevant	Personal phone (triaxial accelerometer and GPS)	10Hz Accelerometer	Up to 1 year	Continuous cyclical • accelerometer 10 sec on /off • GPS 1min on / 10 min off	ALSFRS-RSE	60 seconds
Holdom et al. [25]	Wrist (Non-dominant) Right hip	Triaxial accelerometer ActiGraph GT9XLink	30 Hz	18 Months	Wrist - 8 consecutive days every 3-4 months Hip - 7 consecutive days every 2-3 months	ALSFRS-R	10 seconds
Johnson et al. [26]	Wrist OR Ankle	Wrist: Triaxial accelerometer ActiGraph Insight Watch Ankle: Biaxial	Wrist: 32 Hz Ankle: 128Hz	6 months	As much as possible for duration of the study	ALSFRS – R, ALSFRS-RSE, ROADS	60 seconds

		accelerometer Modus StepWatch 4					
Gupta et al. [27]	All 4 limbs (wrists and ankles)	Triaxial Accelerometer ActiGraph GT3X	30 Hz	Minimum of 0.75 years stated	7 days every month	ALSFRS-R	1 second
van Unnik et al. [28]	Right hip (anteroaxillary line)	Triaxial accelerometer ActiGraph GT9XLink	30Hz	18-24 months	3-7 days every 2-3 monthly	Survival status, ALSFRS-R (self-administered or physician administered)	10 seconds
Beswick et al. [29]	Right wrist and Right ankle	Triaxial accelerometer ActiGraph GT9X	Not disclosed	12 weeks	24 hours every 2 weeks	ALSFRS-R, 6MWT, questionnaires to provide feedback on their experience of wearing devices, standardized series of movements	Not disclosed
Straczkiewicz et al. [30]	Wrist of choice	Triaxial accelerometer ActiGraph Insight Watch	32Hz	6 months	continuously, except for recharging (required every few weeks)	ALSFRS-RSE	60 seconds for total activity counts

Note. ALSFRS-R = Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised; ALSFRS-RSE = Amyotrophic Lateral Sclerosis Functional Rating Scale self-administered; FVC = Forced vital capacity, HADS = Hospital Anxiety and Depression Scale, HRV = Heart rate variability; EIM = Electrical Impedance myography; ROADS = Rasch-Built Overall ALS Disability Scale, PREMs = Patient-reported experience measures; 6MWT = 6-min walking test

Data analysis

Missing accelerometer data can occur for several reasons, and how this is managed seemed closely related to the device use/wear protocols (e.g., charging, overnight wear, etc.) and the sampling frequency. Since devices can be removed by the participant, non-wear time must be detected (and distinguished from sedentary time) and a minimal wear threshold for sample inclusion in analysis must be decided. For instance, Straczkiewicz et al. [30] excluded days with <21 hours of cumulative wear time, van Eijk et al. [23] van Unnik et al. [28] and Johnson et al. [26] excluded samples with <8 hours recording per day from analysis, while Gupta et al. [27] excluded samples with <3 hours recording per day. In relation to sampling, Karas et al. [24] adopted a smartphone-based acquisition method whereby data collection for accelerometer and GPS cycled between data acquisition periods and periods where no data was acquired (see Table 4 for more details), to avoid excessive battery drain. Therefore, the sample had missing data *a priori* and imputation was performed prior to analysis. The raw acceleration signals were commonly processed into epochs (time periods) prior to analysis. Most studies used 10 second (n = 3) or 60 second (n = 3) epochs for analysis, while other studies adopted 1 second epochs (n = 1) (Table 4). Data were preprocessed and analysed either via algorithms developed by the research team [19,30] or previously developed and reported algorithms, such as activity index [31] or sub-movement analysis [32-33]. Additionally, some studies [23,25-26,28-29] used proprietary algorithms for data preprocessing provided by device vendors.

Even though researcher-developed algorithms or proprietary software were used for data preprocessing, most physical behaviour endpoints were researcher-derived in line with the specific objectives of the study. Table 5 shows all the physical behaviour endpoints used. Many endpoints focused on quantifying traditional physical behavior variables such as duration, intensity, and frequency of physical activity. The majority focused on daytime behaviours, with only Kelly et al. [21] and Johnson et al. [26] including any night-time or sleep based endpoints. Due to different sampling frequencies and data preprocessing steps, the endpoints differed between all studies except two [23,25]. Here, variation of vertical axis, daily VM, and proportion of time spent active were the defined endpoints, and were assessed using the same device, sampling frequency and data-preprocessing although at two different wear locations (hip/wrist) [23,25]. These variables also represent emerging non-traditional physical behaviour measures which may provide a better indication regarding what participants can do, rather than what they choose to do [23]. Five studies explored non-traditional physical behaviour endpoints. Of those, three focused on the endpoint based on variation in vertical axis developed by van Eijk et al. [23] which is based on movement against gravity. Straczkiewicz et al. [30] focused on total daily count and average daily duration of upper limb movements such as flexion, extension, pronation, supination etc. Lastly, Gupta et al. [27] utilised sub-movement analysis based on their previously developed algorithms that identified small segments, termed sub-movements, within the movement patterns of the wrist, recorded during reaching tasks that had been associated with movement impairments in participants with ataxia [32-33]. Additionally, Gupta et al. [27] explored the use of artificial intelligence, such as machine learning approaches, for data analysis rather than traditional statistical analysis (e.g., linear-mixed effects models) which were employed by all studies.

Table 5: Physical behaviour endpoints used in the studies included in the systematic review

Author and Year	Endpoints	
van Eijk et al. [23]	- %active – Vector Magnitude (VM) counts > 100 counts/min - MET score – average daily Metabolic Equivalent of Task estimates (MET) score - Daily VM – (VM average x standard deviation (SD) of VM) - Daily A1 – variation in vertical axis (y)	
Garcia-Gancedo et al. [19]	- "Activity score" algorithms to evaluate "how much" activity is performed - "Activity classification" algorithms to evaluate "what" activities are performed	
Kelly et al. [21]	**Daytime, night-time and 24-hour values for:** - duration of wear time - total activity score **Daytime and night-time values for:** - time and % time spent active - time and % time spent sedentary (not lying), - time and % time spent lying, - time and % time sedentary, - maximum activity score, - mean maximum activity score, - number and average duration of active periods (>1 minute) which were also categorised into 5 categories of activity period duration: o >1 to ≤2 minutes, o >2 to ≤5 minutes, o >5 to ≤15 minutes, o >15 to ≤30 minutes o ≤30 minutes active. **Night-time rest endpoints:** - % time lying down (at night), - number of night-time movement episodes, - number of night-time movement episodes per hour, - % time night-time rest efficiency, - rest fragmentation index (movement time divided by the number of movement episodes), - average duration of movement episodes	
Rutkove et al. [20]	Steps	
Rutkove et al. [22]	Steps	
Karas et al. [24]	Smartphone accelerometer data: - log(Activity Index sum from all day minutes), - log(Activity Index from top 1 minute), - walking cadence from all day minutes (step count-weighted average), - walking cadence from top 1 minute, - log(step count from all day minutes), and - log(step count from top 1 minute) Smartphone GPS data - log(distance travelled) (in kilometers) - time spent at home (in hours)	
Holdom et al. [25]	- Proportion of time active - Vector magnitude - Variation in Axis 1	- Variation in Axis 2 - Variation in Axis 3
Johnson et al. [26]	**Wrist – ActiGraph** **Vendor derived measures** - Light activity [minutes] - Moderate activity [minutes] - Vigorous activity [minutes] - MVPA (moderate-vigorous physical activity) [minutes] - Sedentary [minutes] - Non-sedentary [minutes] - Locomotion [minutes] - Non-locomotion [minutes] - Steps - Calories - METs - Total activity counts	**Ankle – Modus** **Vendor derived measures** - second-level step count data - minute-level step sums - daily level step counts - %time in low activity (1-15 steps/minute) - %time medium activity (16-40 steps/minute) - %time high activity (41+ steps/minute) activity - mean, median, 95th percentile, peak performance index, and max consecutive (60, 20, 5, and 1 minute) cadences.

	- Sleep [minutes] **Investigator derived measures (using Actigraphy minute-level activity count (AC)** - total AC (24-hour AC sum), - log total AC (logarithmic transformation of total activity counts + 1) - total log AC (24-hour sum of logarithmic transformation of AC + 1), - minutes spent active (minutes with AC > 1853) - minutes spent inactive - active to sedentary transition probability - sedentary to active transition probability	
Gupta et al. [27]	**The number in the bracket refers to the number of endpoints per each measure** **Activity index (AI)** - AI mean (1) - AI median (1) - AI mode (1) - AI Entropy (1) - % daytime with low AI (1) - % daytime with moderate AI (1) - % daytime with high AI (1) - % acceleration in single direction (3) **Spectral** - Total power (1) **Activity Bout** - Bout acceleration (2) - Bout jerk (2) **Sub-movement (SM**) - SM Distance (8) The distance in meters traveled during a sub-movement (SM). - SM Velocity (8) - SM Acceleration (8) - SM Jerk (8) - SM Duration (8) - SM PC1 Score (6) - The principal component 1 (PC1) score for a sub-movement. PC1 captures low-frequency characteristics of the SM velocity-time curve (e.g., the SM “shape”). - SM PC2 (Principal component 2) Score (6) - SM PC3 (Principal component 3-5) Score (18)	
van Unnik et al. [28]	Vertical Movement Index (VMI) - based on movements against gravity	
Beswick et al. [29]	Total VM counts VM counts from ankle mounted devices during motor assessments	
Straczkiewicz et al. [30]	- Total daily count of flexions by at least 45, 90, and 135 degrees - Total daily count of extensions by at least 45, 90, and 135 degrees - Total daily count of supinations by at least 45, 90, and 135 degrees - Total daily count of pronations by at least 45, 90, and 135 degrees - Total daily count of flexions and extensions by at least 45, 90, and 135 degrees - Total daily count of supinations and pronations by at least 45, 90, and 135 degrees - Average daily duration of 10 fastest flexions by at least 45, 90, and 135 degrees - Average daily duration of 10 fastest extensions by at least 45, 90, and 135 degrees - Average daily duration of 10 fastest supinations by at least 45, 90, and 135 degrees - Average daily duration of 10 fastest pronations by at least 45, 90, and 135 degrees - Average daily duration of 10 fastest flexions and extensions by at least 45, 90, and 135 degrees - Average daily duration of 10 fastest supinations and pronations by at least 45, 90, and 135 degrees - Total activity counts - a daily (24 h) sum of minute–level activity counts	

Note. For more details around how these physical behaviour endpoints were derived please refer to the original publication

Reported Research Findings

Validating remote monitoring of physical behaviour

The reported research findings consistently demonstrated that physical activity levels decreased longitudinally with MND progression. Moreover, physical behaviour endpoints were associated with total ALSFRS-R score with correlation coefficients ranging from r = 0.31 – 0.78. This was also true for correlation with the gross motor and fine motor domains of ALSFRS-R. Additionally, van Unnik et al. [28] demonstrated high correlation coefficients of changes in the fine motor domain (Pearson's r = 0.86, 95% CI: 0.80–0.90) and gross motor sub-domain (Pearson's r = 0.79, 95% CI: 0.70–0.85). However, while certain endpoints (daily vector magnitude and variation in vertical axis [see Table 5]) resulted in reduced between patient variability (measured as coefficient of variation) [23] some (e.g., average daytime active [min], percentage daytime active [%]) showed greater variability compared to ALSFRS-R [21].

Device placement influenced reported outcomes. Specifically, wrist-derived outcome measures consistently correlated with functional loss in 'fine-motor' domain in ALSFRS-R; while measures from hip or ankle mounted devices were strongly associated with a change in gross motor function [23,25,27], and most recently shown to also correlate with fine motor domain [28]. Additionally, Gupta et al. [27] demonstrated that when monitoring all four limbs, there is good agreement between right and left limbs for physical behaviour sub-movement outcome measures, with agreement between the left and right ankle stronger (r = 0.81–0.97) than between the left and right wrists (r = 0.65–0.82). Moreover, taking the score of a limb with the maximum progression rate produces a motor outcome measure consistent with, but more sensitive than, ALSFRS-R [27]. None of the studies investigated effects of disease phenotype on physical behaviour endpoints nor most optimal wear location for each phenotype.

Effect of accelerometer-derived outcome measures on sample size requirements

Five studies investigated the effects of using physical behaviour endpoints, including increased measurement frequency, on sample size requirements of hypothetical clinical trials. Four studies found a reduction in sample size would be related to the increased sensitivity of their proposed outcome measures [22-23,27-28]. This was determined either through increasing measurement frequency (daily monitoring) [22], taking the score of a limb with maximum progression rate in a study monitoring all four limbs [27] or, reduced between patient variability (and thus increase sensitivity) of endpoints based on the variation of daily activities [23]. For example, van Eijk et al. [23] demonstrated that, when recording 7-days of data every 2-3 months, endpoints such as daily vector magnitude and variation in vertical axis outperform ALSFRS-R at nine months, and lead to 30% reduction in required sample size at 12 months. Similarly, van Unnik et al. [28] demonstrated that for a study with 7-day recordings, at monthly intervals, with 6-month follow-up 50 participants would be required (80% power) to detect differential progression rates of VMI. Additionally, van Unnik et al. [28] found that if the follow-up duration is increased to 12-months, the sample size can be reduced by 50%. In contrast, Kelly et al. [21] found that their physical behaviour endpoints (average daytime active (min), percentage daytime active (%) etc.) resulted in increased sample size requirement for a hypothetical

clinical trial compared to ALSFRS-R total score (500-700 participant for physical activity endpoints vs. 290 participants for ALSFRS-R). This was explained by greater endpoint variability towards the end of the study compared to ALSFRS-R, possibly due to the relatively small sample size in the reviewed study (*n* = 18) [21].

Feasibility of using accelerometer devices in MND

Nine studies (75%) assessed at least one or more aspects of feasibility in implementing accelerometer-derived measures of physical behavior in plwMND. Feasibility was typically assessed via Likert-type, dichotomous or numerical rating scale questionnaires. The assessment of feasibility report focused on perceptions of participants and did not include input from other individuals such as clinicians, carers or family members. The overall impression was positive, participants found procedures acceptable [19,29] and reported it improved their sense of control of the disease [22].

Device cost was reported by Gupta et al. [27] as US$234-433 over the course of the study and by van Unnik et al. [28]at $315 (as of 2021). Garcia-Gancedo et al. [19] reported adverse events that occurred during the study, all of which related to skin sensitivity to the adhesive used to secure the device to the participant. In terms of technical challenges, Garcia-Gancedo et al. [19] reported one electrical failure of a device whilst it was being charged. Rutkove et al. [20] reported challenges regarding manufacturers stopping production of devices used during their study. In Beswick et al.'s [29] study no participants reported side effects, nor did they have any concerns about remembering to charge the devices or the devices interfering with daily activities. They also found that 90% of participants would be happy to wear the devices for a longer period than the 12 weeks and 70% were supportive that using the devices may result in needing to attend fewer clinic appointments.

Two studies invited participants to visit the study site, where devices were introduced to participants at set-up [19,21]. Six studies were mostly conducted remotely, with varying levels of details reported regarding whether devices and their instructions were posted to participants and the level of support provided over telephone or video conference calls [20,22-24,26,30]. Van Unnik et al. [28] had in-person visits but for some participants the device was sent out via mail. Beswick et al. [29] carried out in-person visits and used video conferencing to do the study assessments. Rutkove et al. [20] was the only study to report issues related to participants being unable to successfully work the device.

Participant adherence to and burden of device wear

Adherence was assessed in eight studies (66.7%), based on the number of valid wear days (days where minimum wear threshold of device was achieved) against the total number of recording days. Overall, adherence was good, ranging from 91.8%-93.0% for hip worn devices [23,28], 92.0% for chest worn devices [19], 86.0%-95.7% for wrist worn devices [25,29] and 87.3% for ankle worn devices [29]. Overall, the number of valid days was higher for wrist worn devices compared to ankle worn devices in studies which assessed multiple devices in one cohort of participants [27,29]. Adherence for chest mounted monitors reduced longitudinally, from 92% at baseline to 56% at the last measurement which was explained by physical inability to meet protocol requirements for attaching

the device, increased reliance on carers to facilitate device use, or decreased willingness to comply with study procedures [19]

Van Eijk et al. [23] assessed the wear burden using a Likert rating scale where 0 indicated no burden and 10 indicated high burden. The mean score was 1.3, indicating a low rate of burden for the hip-worn device. Similarly, Garcia-Gancedo et al. [19] reported that participants found the chest mounted device comfortable to wear, however, 24% (*n* = 6) of participants reported symptoms of local skin irritation (itching and skin reaction potentially due to allergy to the adhesive). Beswick et al. [29] explored patients' expectations of wearing devices. They found that 90% of participants thought wearing the devices would be useful for tracking changes in their symptoms.

Discussion

This systematic review investigated current methods, findings, feasibility, acceptability and implications of remotely monitoring free-living physical behaviour in plwMND. Studies consistently showed decreased physical activity levels occurred over time, as would be expected with MND progression and is currently captured by questionnaire-based assessments and clinical observation. However, heterogenous data collection and analysis procedures were used with little consistency in protocols between studies. Some proposed physical activity endpoints were found to correlate well with the total ALSFRS-R score, and alongside increased monitoring frequency, were shown to provide smaller sample size requirements for hypothetical clinical trials that could be completed within shorter time periods. However, it should be noted that study participants tended to be biased towards slower progressors and those with limb onset phenotypes (Table 3). In addition, device wear location (e.g., upper *versus* lower limb *versus* hip) can influence the results, with outcomes derived from wrist worn devices correlating better with functional loss in the 'fine motor' domain of the ALSFRS-R while hip or lower limb mounted devices were more strongly associated with change in gross motor [25,27]. Nevertheless, van Unnik et al. [28] were able to evidence good correlation between hip worn devices and both gross and fine motor function. This could have implications for recommendations on optimal strategies for monitoring change across different onset presentation groups. Importantly, studies reported positive feedback on the use of accelerometer devices and good adherence by study participants, although this did decrease longitudinally [19].

How are accelerometer devices currently used to study MND?

Currently considerable heterogeneity exists across studies monitoring physical behaviour in MND. This is not surprising given the nascent use of these methods in MND research (~ 5 years), and something that is also seen in other research areas where such methods are much more common [34-37]. Given the rareness of MND (and MND subtypes), and the challenges this presents for accruing large longitudinal data sets, there is value in establishing a consensus approach in MND, and the development of standardising methods of data collection and analysis that would enable harmonization across data sets. This would facilitate data sharing, comparability of findings and support better phenotyping of MND subtypes. From the results presented here it seems particularly

important to consider developing a consensus across aspects of data acquisition, analysis and reporting. Therefore, the following subsections summarise key elements of these factors found in the reviewed studies that require further consideration.

Data acquisition

Across the reviewed studies there were notable differences in total participant follow-up time, frequency, and duration of each measurement period (Table 4). It is important that the total follow-up time should allow observation of clinically relevant changes. The total participant follow-up of 6-24 months in the studies did capture such changes and sits well within the average MND survival of 2-3 years after symptom onset [2] Studies tended to record data either monthly or every 2-3 months, and the latter would coincide with routine—clinical assessment/appointment frequency currently recommended by NICE [3]. Once meaningful changes in physical behaviour are known, remote monitoring could facilitate personalised visit schemes that could reduce travel burden and cost. However, it is important to note studies tended to be biased towards more slowly progressing and predominantly limb onset disease phenotypes (Table 3), and optimal data recording frequency could differ between slower and faster progressors. This concern is not unique to studies on movement, as a bias towards inclusion of slower progressing patients is well-documented in traditional epidemiological studies. This will, in part, be addressed by the release of data from clinical trials (where inclusion is generally biased towards more rapidly progressing patients) that include measures of movement as part of study outcomes.

To capture accurate information on participant's current functional ability, the duration of each measurement period should capture day-to-day variations in behaviour [38]. Larger day-to-day variations in physical behaviour necessitate longer monitoring periods to be robustly captured, however day-to-day variations were not reported in any of the reviewed studies. This makes it difficult to identify the optimal duration of recording. Most included studies recorded over seven consecutive days (Table 4). This duration is considered adequate to capture most physical behaviour variables [38-39] and accounts for variations in social/work activities that occur over a week yet does not exceed the battery life for most commercially available accelerometers [40-42]. However, if future MND specific research establishes that there is little day-to-day variability for MND specific endpoints, the duration of each measurement could be reduced, which could provide several benefits including reduced wear burden for participants.

While accelerometers were the most used device, the method of their attachment and the wear location varied (Table 4). The studies suggest that wear location has the potential to influence the outcomes [25]. However, the most appropriate location is yet to be determined and will likely depend on the aspect of physical function of main interest (i.e., fine vs. gross motor skill). Moreover, optimal wear location and the endpoint most sensitively reflecting physical function may differ across MND presentation and phenotype. Participants living with different MND subtypes were reported to be

included in four studies, and ALS site of symptom onset was reported in three studies (Table 3). It is not clear whether people living with different MND subtypes participated in the other studies, and these details were not reported or whether all participants had the same subtype. Either way, this means the influence of disease-specific factors on the suitability of different physical behaviour endpoint measures has not yet been assessed in detail and represents a gap in current knowledge.

An additional parameter of importance in data acquisition is the device sampling frequency. This varied greatly between the studies (10-128 Hz, Table 4) with limited justification for the frequency used. Research suggests the major frequency components of human movement are low, occurring up to 20 Hz [43-45]. In gait most of the energy is contained below 15 Hz, therefore, to conserve 99% of the signal power, the sampling frequency must be a minimum of 30 Hz [43,46] and this was the most used sampling frequency within the reviewed studies (Table 3). However, Khan et al. [47] eloquently demonstrated that data sets of different activities (e.g. Parkinson's disease, walking and physical monitoring etc.) each have different optimal sampling frequency ranges (26-63 Hz). Therefore, the optimal sampling frequency for sensitively detecting changes in physical function in MND, while avoiding battery drain and large storage requirements, may warrant further assessment.

Data analysis

Reviewing the data analysis approaches employed across studies revealed large differences in data preprocessing undertaken to derive physical behaviour metrics, which has implications for endpoint comparison across studies. For example, ActiGraph devices were the most used in reviewed studies, and five studies used the manufacturer's proprietary software (ActiLife) to derive activity counts from the raw data that were used for construction of physical behaviour endpoints. However, activity counts can be calculated in different ways (not universal) with a complex relationship between raw data and counts that differs between device models [48]. This will influence the generalizability of results and could also pose challenges when comparing studies that have used different versions of the same software. It therefore seems important for researchers to consider the implications of data preprocessing via proprietary algorithms, a point that must be balanced against the availability of technical expertise in the research team. There is likely value in the MND research community working towards provision of transparent and accessible processing tools (e.g., through an Open Science framework, as used to share Activity Index analysis code) to facilitate replication of findings and standardization across study sites.

A further feature of data analysis that warrants consideration is the reduction of measured signals into epochs. This approach of reducing data sizes was routinely used across studies, with 10- or 60-sec epochs commonly used. However, this can result in loss of information. For example, tri-axial accelerometer data (100 Hz) recorded while an individual completed 10 sit-to-stand movement cycles were compressed into 1-, 10- and 60-seconds epochs. The daily vector magnitude was calculated for each epoch length (as per van Eijk et al. [23]) and Table 6 shows the differences in this measure that

occur. Future research should consider and justify the choices of data compression to balance the difference in information against the feasibility and demands of processing large quantities of uncompressed data.

Table 6: Differences for a physical behaviour endpoint (daily VM as per van Eijk et al. [23]) calculated from a sample data (10 sit to stands) using a right thigh mounted triaxial accelerometer at 100Hz and 10 Hz sampling frequency compressed to 1, 10 and 60 second epochs.

	Daily VM at 100Hz	Daily in VM at 10Hz
Raw data	0.053	0.048
1 second epoch	0.035	0.040
10 second epoch	0.078	0.081
60 second epoch	0.082	0.084

Once data are preprocessed many studies focused on traditional physical behaviour endpoints such as frequency, intensity, and duration of physical activity. However, it seems inevitable these measures will decline with MND progression so the additional insight to disease progression is unclear. Some (e.g., average daytime active (min), percentage daytime active (%)) even led to greater data variability compared to ALSFRS-R [21], a feature of any new endpoint metric that could be undesirable. In contrast, there seems significant potential in considering non-traditional measures such as ones related to movement quality. For example, the daily vector magnitude measures proposed by van Eijk et al. [23] and sub-movement analysis used by Gupta et al. [27] both show significant potential value for sensitive detection of change in physical function. Additionally, Straczkiewicz et al. [30] demonstrated that physical behaviour endpoints specific to total daily counts and duration of upper limb movement (see Table 5 for details) also have an association with total ALSFRS-R score.

Reporting of physical behaviour studies in MND

The growing interest in studying accelerometer-derived free living physical behaviour endpoints in MND means there is value to ensuring transparent and clear reporting. This would facilitate identification of problems arising from conducting studies, the clarity and quality of reporting and hence accelerate consensus around optimal study design(s). For example, a clear representation of participants at each stage of the study, potentially in the form of a flowchart, would allow clear reflection of longitudinal attrition rates and their causes. In addition, there should be justification for design choice, including clear description of the type of follow-up, accelerometer location, method of attachment and sampling frequency. Consideration should also be made of the requirements for reporting data preprocessing, as this is something that differed significantly between studies. As such, work to develop standard reporting criteria would be particularly timely and valuable to the MND community.

To support development of a consensus approach for quantification of physical function from

accelerometer devices in MND and enhance opportunity for data harmonisation, we present currently unanswered questions and recommendations for future research in this area (Table 7). None of the reviewed studies evaluated the use of devices for clinical care, and research has not explored the implications of remotely monitoring physical behaviour on clinical care. Further research is warranted, and it is likely further considerations will need to be made to mature and translate the technology for clinical practice.

Table 7: Current unanswered question in MND actigraphy research and future recommendations, ranked in terms of perceived importance

Question	What is known so far?	Recommendation
User-related: Are these devices and procedures feasible for use by plwMND?	Adherence is good and participants largely thought the devices were acceptable and reported low burden of use.	Research to explore people's lived experience of using the devices. Qualitative research methods will enable in-depth exploration of feasibility and allow identification of barriers and facilitators to using digital technologies.
User-related: Are the devices and procedures feasible for family members, carers, and healthcare professionals?	Research has not comprehensively explored the experiences of individuals using the devices/procedures.	Research to explore the experiences and perceptions of these individuals. Qualitative research methods will be helpful in identifying barriers and facilitators.
Clinical practice-related: Is PB related to other symptoms of MND?	PB is only a small part of MND, and no research has investigated relationships to other relevant disease domains.	Research to explore whether PB is related to other objective measure areas e.g., respiratory function, muscle strength.
Clinical practice-related: Are PB endpoints more sensitive measures of disease related change in physical function than the ALSFRS-R?	The evidence is inconclusive. Some studies have found that accelerometry data have greater variability than the ALSFRS-R whilst others found less variability than the ALSFRS-R.	Research to quantify variability in PB endpoints relative to that in ALSFRS-R. Consideration of effects of different MND phenotypes on measurement variability will be required here; as well estimation of clinically meaningful effect size.
Methods-related: What is the optimum follow up design to capture changes in PB?	There is no consensus on the duration of follow-up, frequency of measurement or duration of measurement. A measurement period of 7 days can account for potential day-to-day variation in PB.	Research to identify the optimum durations of follow-up, frequency of measurement and length of measurement. Using qualitative methods to explore people's experiences of this will also contribute to our knowledge of what is feasible for patients and healthcare professionals.
Methods-related: What is/are the most optimal wear location(s) to capture and predict changes in PB with MND progression?	The wrist location correlated better with the ALSFRS-R fine motor domain; lower limb placement (hip or ankle) correlated better with the gross-motor domain. PB endpoints may need to vary based on device wear location.	Research to identify optimal wear location(s); including consideration of impacts on use of other devices or collection of additional data (e.g., pulse oximetry). Studies should consider ease of use and participant burden and impacts of their evolution with disease progression.
Methods-related: Is there an optimum device location and outcome measure for each MND phenotype?	Research has not investigated if there are differences in outcome measures between MND phenotypes.	Research to explore IMU performance, optimum wear location, and PB endpoints across MND phenotypes.
Clinical practice-related: Does monitoring PB offer a cost-effective means of assessing change in physical function?	Research has not explored the cost implications or economics associated with using PB endpoints.	Research evaluating the cost effectiveness of using PB end points in both clinical trials and in care is required.
Clinical practice-related: Do PB endpoints provide information that is clinically relevant or related to clinical milestones?	Research has not explored the impact of PB endpoints on clinical decision-making, nor relationships to milestones e.g., loss of ambulation or care dependency.	Research to explore how using devices will impact clinical decision-making. Qualitative research methods will be helpful for exploring this in depth.

Note. ALSFRS-R = ALS functional rating scale revised; IMU = inertial measurement unit; MND = Motor neurone disease; PB = physical behaviour; plwMND = people living with MND.

Perspectives on the feasibility of monitoring physical behaviour in MND

When recorded, reviewed studies consistently found that participants had positive attitudes towards remote monitoring of physical behaviour, excellent adherence, and reported a low rate of burden. Despite limited evidence specific to accelerometry, other studies of telehealth tools in MND also found that plwMND are accepting towards using remote monitoring approaches [11,49]. It is clear however, that participants face challenges using accelerometer devices over the course of a study. For example, the physical challenge of removing and reattaching a device may, coupled with the progression of MND, influence adherence [19] Research by Gupta et al. [27] and Beswick et al. [29] have also shown that adherence differs between wear locations. However, there was very limited information on factors that reduced adherence (including consideration of family member or carer burden). This restricts the evidence base on which future study protocols can be optimised to maintain participant involvement and further research is needed to expand our knowledge of the influencing factors.

Conclusion

Remote monitoring of free-living physical behaviour in people living with MND is in its infancy but has exciting potential to quantify physical function in MND. Most research to date has aimed to describe changes in physical behaviour associated with MND progression or identify physical behaviour endpoints that are more sensitive than the ALSFRS-R and may be used in clinical trials to decrease sample sizes. Exploration of feasibility in all end-users is necessary as this will help to translate the technology into clinical practice and will also help to guide the design of future studies through co-creation with patient and carer involvement.

It is essential to develop a consensus statement within the MND community, working towards agreed and standardised methods for data collection, analysis and reporting. The unanswered questions and recommendations for future research (Table 7) offer a foundation from which such efforts can begin. While aspects relating to study design will take longer to resolve, agreement on standards for reporting should be achievable in the shorter term. This is important in facilitating future data harmonisation across cohorts, study replication and standardising collection and analysis procedures.

Acknowledgments

LSM is supported by a My Name’5 Doddie Foundation Doctoral Fellowship (DOD/14/17) and CMD’S National Institute for Health Research (NIHR) Professorship (NIHR301648). NM is supported by a PhD studentship from the MND Association (Hodson-Tole/Oct22/912-792). CMD is supported by a NIHR Professorship (NIHR301648). CM, LSM, EH and AG are also supported by the NIHR Sheffield Biomedical Research Centre. The authors are part of a working group interested in using digital outcome measures for MND (DIGITALS - Digital Innovation Group for Improving Technologies Addressing Locomotion and Sensorimotor impairments in ALS/MND).

Conflicts of interest

All authors declare no financial or non-financial competing interests.

Abbreviations

6MWT: 6-minute walking test
ALS: Amyotrophic Lateral Sclerosis
ALSFRS-R: Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised
ALSFRS-RSE: Amyotrophic Lateral Sclerosis Functional Rating Scale self-administered
EIM: Electrical Impedance Myography
FVC: Forced vital capacity
HADS: Hospital Anxiety and Depression Scale
HRV: Heart rate variability
IMU: Inertial measurement unit
LL: Lower limb
MET: Metabolic equivalent of task
MND: Motor neuron disease
MVPA: Moderate-vigorous physical activity
PB: Physical behaviour
PC: Principal component
PLS: Primary lateral sclerosis
PlwMND: People living with motor neuron disease
PMA: Progressive muscular atrophy
PREMs: Patient-reported experience measures
ROADS: Rasch-Built Overall ALS Disability Scale
UL: Upper limb
VM: Vector magnitude
VMI: Vertical movement index

Data availability

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study

Author contributions

LM (joint lead author): Methodology. Data Extraction. Analysis and interpretation of the data. Writing original draft and revising based on feedback. NM (joint lead author): Methodology. Literature search and data acquisition. Data Extraction. Analysis and interpretation of the data. Writing original draft and revising based on feedback VL-V: Critical review of the manuscript and revising the work (providing feedback). GO-P: Supervision of lead author NM. Critical review of the manuscript and revising the work (providing feedback). CMD: Supervision of lead author LM. Supervision of lead author NM. Critical review of the manuscript and revising the work (providing feedback). AG: Supervision of lead author LM. Critical review of the manuscript and revising the work (providing feedback). LK: Critical

review of the manuscript and revising the work (providing feedback). FJS: Critical review of the manuscript and revising the work (providing feedback). CJH: Critical review of the manuscript and revising the work (providing feedback). TJMD: Critical review of the manuscript and revising the work (providing feedback). RPAv.: Critical review of the manuscript and revising the work (providing feedback). JWJvU: Critical review of the manuscript and revising the work (providing feedback). LCMB: Critical review of the manuscript and revising the work (providing feedback). EB: Critical review of the manuscript and revising the work (providing feedback). DM: Critical review of the manuscript and revising the work (providing feedback). EH: Supervision of lead author LM. Supervision of lead author NM. Critical review of the manuscript and revising the work (providing feedback). AC: Conception and design of the work. Supervision of lead author NM. Critical review of the manuscript and revising the work (providing feedback). EH-T: Conception and design of the work. Methodology. Supervision of lead author NM. Critical review of the manuscript and revising the work (providing feedback). Working on the original draft. All authors contributed to reviewing and editing the manuscript. All authors approved the final manuscript.

References

1. Feldman EL, Goutman SA, Petri S, et al. Amyotrophic lateral sclerosis. Lancet 2022;400(10360):1363-1380. doi:10.1016/S0140-6736(22)01272-7.
2. Rafiq MK, Proctor AR, McDermott CJ, et al. Respiratory management of motor neurone disease: a review of current practice and new developments. Pract Neurol 2021;12:166–176. doi:10.1136/practneurol-2011-000199.
3. National Institute for Health and Care Excellence. Motor neurone disease: assessment and management. 2019. https://www.nice.org.uk/guidance/ng42/resources/motor-neurone-disease-assessment-and-management-pdf-1837449470149
4. Cedarbaum JM, Stambler N, Malta E, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. J Neurol Sci 1999;169(1-2):13–21. doi:10.1016/s0022-510x(99)00210-5.
5. Tornese P, Lalli S, Cocco A, et al. Review of disease-modifying drug trials in amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 2022;93(5):521–529. doi:10.1136/jnnp-2021-328470.
6. Wong C, Stavrou M, Elliott E, et al. Clinical trials in amyotrophic lateral sclerosis: a systematic review and perspective. Brain Commun 2021;3(4):fcab242. doi:10.1093/braincomms/fcab242.
7. Andres PL, Allred MP, Stephens HE, et al. Fixed dynamometry is more sensitive than vital capacity or ALS rating scale. Muscle Nerve 2017;56(4):710–715. doi:10.1002/mus.25586.
8. Genge A, Cedarbaum JM, Shefner J, et al. The ALSFRS-R Summit: a global call to action on the use of the ALSFRS-R in ALS clinical trials. Amyotroph Lateral Scler Frontotemporal Degener 2024;25(3–4):382–387. doi:10.1080/21678421.2024.2320880
9. Young CA, Chaouch A, Mcdermott CJ, et al. Improving the measurement properties of the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R): deriving a valid measurement total for the calculation of change. Amyotroph Lateral Scler Frontotemporal Degener 2024;25(3-4):400-409. doi:10.1080/21678421.2024.2322539.

10. Van Eijk RPA, de Jongh AD, Nikolakopoulos S, et al. An old friend who has overstayed their welcome: the ALSFRS-R total score as primary endpoint for ALS clinical trials. Amyotroph Lateral Scler Frontotemporal Degener 2021;22(3-4):300-307. doi:10.1080/21678421.2021.1879865.
11. Helleman J, Johnson B, Holdom C, et al. Patient perspectives on digital healthcare technology in care and clinical trials for motor neuron disease: an international survey. J Neurol 2022;269(11):6003-6013. doi:10.1007/s00415-022-11273-x.
12. van Eijk RPA, Beelen A, Kruitwagen ET, et al. A Road Map for Remote Digital Health Technology for Motor Neuron Disease. J Med Internet Res 2021;23(9):e28766. doi:10.2196/28766.
13. Onambele-Pearson G, Wullems J, Doody C, et al. Influence of habitual physical behavior - sleeping, sedentarism, physical activity - on bone health in community-dwelling older people. Front Physiol 2019;10:408. doi:10.3389/fphys.2019.00408.
14. Breasail MÓ, Biswas B, Smith MD, et al. Wearable GPS and accelerometer technologies for monitoring mobility and physical activity in neurodegenerative disorders: A systematic review. Sensors (Basel) 2021;21(24):8261. doi:10.3390/s21248261.
15. Beswick E, Fawcett T, Hassan Z, et al. A systematic review of digital technology to evaluate motor function and disease progression in motor neuron disease. J Neurol 2022;269(12):6254-6268. doi:10.1007/s00415-022-11312-7.
16. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:10.1136/bmj.n71.
17. Ouzzani M, Hammady H, Fedorowicz Z. et al. A. Rayyan—a web and mobile app for systematic reviews. Syst Rev 2016;5:210. doi:10.1186/s13643-016-0384-4.
18. Von Elm E, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. BMJ 2007;335:806–808. doi:10.1136/bmj.39335.541782.AD
19. Garcia-Gancedo L, Kelly ML, Lavrov A, et al. Objectively monitoring amyotrophic lateral sclerosis patient symptoms during clinical trials with sensors: Observational study. JMIR Mhealth Uhealth 2019;7(12):e13433. doi:10.2196/13433.
20. Rutkove SB, Qi K, Shelton K, et al. ALS longitudinal studies with frequent data collection at home: study design and baseline data. Amyotroph Lateral Scler Frontotemporal Degener 2019;20(1-2):61-67. doi:10.1080/21678421.2018.1541095.
21. Kelly M, Lavrov A, Garcia-Gancedo L, et al. The use of biotelemetry to explore disease progression markers in amyotrophic lateral sclerosis. Amyotroph Lateral Scler Frontotemporal Degener 2020;21(7-8):563-573. doi:10.1080/21678421.2020.1773501.
22. Rutkove SB, Narayanaswami P, Berisha V, et al. Improved ALS clinical trials through frequent at-home self-assessment: a proof of concept study. Ann Clin Transl Neurol 2020;7(7):1148-1157. doi:10.1002/acn3.51096.
23. van Eijk RPA, Bakers JNE, Bunte TM, et al. Accelerometry for remote monitoring of physical activity in amyotrophic lateral sclerosis: a longitudinal cohort study. J Neurol 2019;266(10):2387-2395. doi:10.1007/s00415-019-09427-5.
24. Karas M, Olsen J, Straczkiewicz M, et al. Tracking amyotrophic lateral sclerosis disease

progression using passively collected smartphone sensor data. Ann Clin Transl Neurol 2024;11(6):1380-1392. doi:10.1002/acn3.52050.

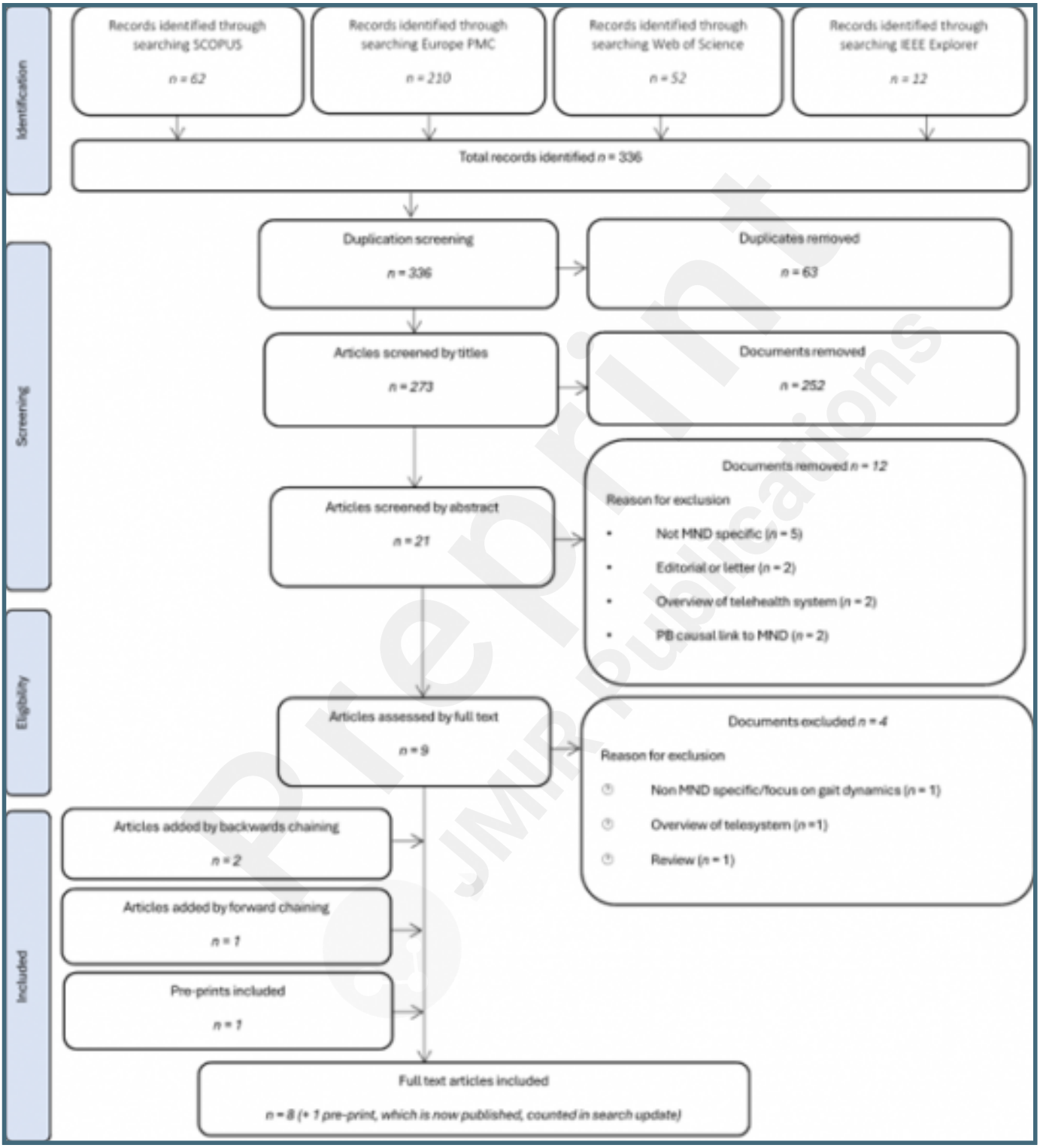
25. Holdom CJ, van Unnik JWJ, van Eijk RPA, et al. Use of hip- versus wrist-based actigraphy for assessing functional decline and disease progression in patients with motor neuron disease. J Neurol 2023;270(5):2597-2605. doi:10.1007/s00415-023-11584-7.
26. Johnson SA, Karas M, Burke KM, et al. Wearable device and smartphone data quantify ALS progression and may provide novel outcome measures. NPJ Digit Med 2023;6(1):34. doi:10.1038/s41746-023-00778-y.
27. Gupta AS, Patel S, Premasiri A, et al. At-home wearables and machine learning sensitively capture disease progression in amyotrophic lateral sclerosis. Nat Commun 2023;14:5080 3). doi:10.1038/s41467-023-40917-3.
28. Van Unnik JWJ, Meyjes M, Janse van Mantgem MR, et al. Remote monitoring of amyotrophic lateral sclerosis using wearable sensors detects differences in disease progression and survival: a prospective cohort study. EBioMedicine 2024;103:105104. doi:10.1016/j.ebiom.2024.105104.
29. Beswick E, Christides A, Symonds A, et al. Exploratory study to evaluate the acceptability of a wearable accelerometer to assess motor progression in motor neuron disease. J Neurol 2024;271(8):5083-5101. doi:10.1007/s00415-024-12449-3.
30. Straczkiewicz M, Karas M, Johnson SA, et al. Upper limb movements as digital biomarkers in people with ALS. EBioMedicine 2024;101:105036. doi:10.1016/j.ebiom.2024.105036.
31. Bai J, Di C, Xiao L, et al. An activity index for raw accelerometry data and its comparison with other activity metrics. PLOS ONE 2016;11(8): e0160644. doi:10.1371/journal.pone.0160644.
32. Gupta AS, Luddy AC, Khan NC, et al. Real-life wrist movement patterns capture motor impairment in individuals with ataxia-telangiectasia. Cerebellum 2023;22(2):261-271. doi:10.1007/s12311-022-01385-5.
33. Eklund NM, Ouillon J, Pandey V, et al. Real-life ankle submovements and computer mouse use reflect patient-reported function in adult ataxias. Brain Commun *2023;5(2):*fcad064. doi:10.1093/braincomms/fcad064
34. Grant D, Tomlinson D, Tsintzas K, et al. Minimizing sedentary behavior (without increasing medium-to-vigorous exercise) associated functional improvement in older women is somewhat dependent on a measurable increase in muscle size. Aging 2020;12(23):24081-24100. doi:10.18632/aging.202265.
35. Grant D, Tomlinson D, Tsintzas K, et al. Displacing sedentary behaviour with light intensity physical activity spontaneously alters habitual macronutrient intake and enhances dietary quality in older females. Nutrients 2020;12(8):2431. doi:10.3390/nu12082431.
36. Wullems JA, Degens H, Verschueren SMP, et al. Sedentary behaviour (especially accumulation pattern) has an independent negative impact on skeletal muscle size and architecture in community-dwelling older adults. PLOS ONE 2024;19(2):e0294555. doi:10.1371/journal.pone.0294555.
37. Wullems JA, Verschueren SMP, Degens H, et al. Concurrent validity of four activity monitors in older adults. Sensors 2024;24(3):895. doi:10.3390/s24030895.

38. Arvidsson D, Fridolfsson J, Börjesson M. Measurement of physical activity in clinical practice using accelerometers. J Intern Med 2019;286(2):137-153. doi:10.1111/joim.12908.
39. Migueles JH, Cadenas-Sanchez C, Ekelund U, et al. Accelerometer data collection and processing criteria to assess physical activity and other outcomes: A systematic review and practical considerations. Sports Med 2017;47(9):1821-1845. doi:10.1007/s40279-017-0716-0.
40. ActiGraph. User Guide ActiGraph GT9X Link + ActiLife. 2020. https://s3.amazonaws.com/actigraphcorp.com/wp-content/uploads/2020/03/05155628/ActiGraph_Link_UserGuide_E.200.6001_Revision6_FINAL.pdf
41. Activinsights. GENEActiv Instructions for Use. 2022. https://activinsights.com/wp-content/uploads/2022/06/GENEActiv-Instructions-for-Use-v1_31Mar2022.pdf
42. Mega Electronics Ltd. eMotion Faros Series Manual. 2017. https://ecgcloud.co.uk/software/800778-2.3.0%20eMotion%20Faros%20Series%20Manual.pdf
43. Antonsson EK, Mann RW. The frequency content of gait. J Biomech 1985;18(1):39-47. doi:10.1016/0021-9290(85)90043-0.
44. Bouten CV, Koekkoek KT, Verduin M, et al. A triaxial accelerometer and portable data processing unit for the assessment of daily physical activity. IEEE Trans Biomed Eng 1997;44(3):136-47. doi:10.1109/10.554760.
45. Karantonis DM, Narayanan MR, Mathie M, et al. Implementation of a real-time human movement classifier using a triaxial accelerometer for ambulatory monitoring. IEEE Trans Inf Technol Biomed 2006;10(1):156-67. doi:10.1109/titb.2005.856864.
46. Shannon CE. Communication in the presence of noise. PROC IRE 1949;37(1):10-21. doi:10.1109/JRPROC.1949.232969.
47. Khan A, Hammerla N, Mellor S, et al. Optimising sampling rates for accelerometer-based human activity recognition. Pattern Recognition Letters 2016;73:33–40. doi:10.1016/j.patrec.2016.01.001.
48. Neishabouri A, Nguyen J, Samuelsson J, et al. Quantification of acceleration as activity counts in ActiGraph wearable. Sci Rep 2022;12(1):11958. doi:10.1038/s41598-022-16003-x.
49. Helleman J, Kruitwagen ET, van den Berg LH, et al. The current use of telehealth in ALS care and the barriers to and facilitators of implementation: a systematic review. Amyotroph Lateral Scler Frontotemporal Degener 2020;21(3-4):167-182. doi:10.1080/21678421.2019.1706581.

Supplementary Files

Figures

PRISMA flowchart of the search process which includes the initial search in October 2023 and search update completed in June 2024 (Date limit: 2023-2024). The number of articles at each stage was reported separately for each search.



CONSORT (or other) checklists

Supplementary material 2: PRISMA Checklist.
URL: http://asset.jmir.pub/assets/1c917f1c19cf0aea32536947af5aefe3.pdf