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Exploring the potential of digital mobility outcomes as clinical trial endpoint measures: Protocol for a scoping review

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Exploring the potential of digital mobility outcomes as clinical trial endpoint measures: Protocol for a scoping review

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ABSTRACT

Introduction

Advances in wearable sensor technology now enable frequent, objective monitoring of real-world walking. It has been suggested that walking-related digital mobility outcomes (DMOs) such as real-world gait speed can assess changes in an individual's mobility with greater sensitivity than traditional, in-clinic assessments. However, it is not yet clear which DMOs are most suitable for formal validation. In this scoping review, we will explore the evidence informing construct validity, prognostic value, and responsiveness to intervention of DMOs.

Methods and analysis

The methodological framework for scoping reviews developed by Arksey and O'Malley will guide study conduct. We will search seven databases (Medline, CINAHL, Scopus, Web of Science, EMBASE, IEEE Digital Library, Cochrane Library) and grey literature for studies which (1) measure differences in gait parameters between healthy and pathological walking, (2) assess relationships between DMOs and traditional clinical measurements, (3) assess the prognostic value of DMOs, and (4) use DMOs as endpoints in interventional clinical trials. We will take a multi-diagnostic approach, including studies on Parkinson's disease, multiple sclerosis, chronic obstructive pulmonary disease, and proximal femoral fracture. Two reviewers will independently screen each study according to pre-determined eligibility criteria and chart data according to a pre-defined form. We will then map the literature, perform a narrative synthesis, and identify research gaps.

Ethics and dissemination

As this review is limited to publicly available materials, it does not require ethical approval. This work is part of Mobilise-D, an Innovative Medicines Initiative Joint Undertaking which aims to deliver, validate, and obtain regulatory approval for novel DMOs. Results will be shared with the scientific community and general public in cooperation with the Mobilise-D communication team.

Registration

To ensure transparency, study materials and updates will be made available through the Center for Open Science's OSFRegistry (https://osf.io/k7395).

Keywords

Mobility, real-world walking speed, gait speed, gait variability, digital mobility outcome, wearable, digital biomarker, digital health, scoping review

BACKGROUND

For people living with chronic health conditions, walking impairment is often associated with reduced quality of life,[1–4] disability progression,[1,5,6] fall risk,[7–9] hospitalisation,[10,11] and even mortality.[10,11] Research on novel therapies that can mitigate the high human and economic costs associated with walking impairment is booming. However, before these therapies can be adopted in clinical practice, their efficacy must be established through controlled clinical trials. The endpoint measures used to assess these interventions' efficacy should be valid, sensitive, easy to administer, and representative of real-world function or behaviour.[12]

Box 1: Strengths and limitations of this study

- This is the first scoping review to explore existing evidence on the construct validity, prognostic value, and responsiveness of digital mobility outcomes across four long-term conditions.
- A broad, multi-diagnostic review strategy enables identification of trends across gait parameters, technologies, measurement settings, and disease areas.
- A multidisciplinary team of clinicians, technologists, movement specialists, and epidemiologists from academia and industry will conduct this review.
- Terminology and methodology associated with mobility assessments are fragmented, posing a challenge to study identification and synthesis.
- Following scoping review guidelines, neither critical appraisal nor meta-analysis will be conducted, limiting our ability to assess the strength of existing evidence.

Unfortunately, current assessments of walking ability pose critical limitations. Clinical trials traditionally employ two types of walking assessments: patient reported outcome instruments (PROs) and clinical gait assessments. PROs enable patients to report perceptions of their own mobility in a standardised manner,[13] though results may be subject to recall bias.[14–16] While some clinical assessments are objective measures, others require clinical interpretation and are subject to high inter-rater variability.[17,18] Additionally, clinical assessments are infrequently acquired and may not be representative of real-world behaviour.[14,19,20] Following the recent failure of several high-profile pharmaceutical trials, the sensitivity of current measures to subtle, yet meaningful, changes in early-stage neurological disease has been called into question.[20–22]

Advances in wearable sensor technology now enable frequent, objective monitoring of real-world walking. Digital mobility outcomes (DMOs) such as gait speed, variability, and symmetry have been used to quantify walking under free-living conditions,[23–27] and emerging evidence suggests that their sensitivity may be higher than traditional instruments.[14,20,28–30] While a growing number of studies support this theory,[12,29,31,32] the validity of DMOs as clinical endpoints is not yet established.[12,14,28] The field's fragmentation by disease area, technology, taxonomy, and methodology[14,25,33–37] currently limits our understanding of their potential. To date, no overarching view of the evidence on the clinical utility of DMOs exists.[14] Thus, this study will map existing evidence on DMOs to assess their suitability for formal validation.

STUDY RATIONALE AND OBJECTIVES

This work is part of Mobilise-D, a research program sponsored by the European Union's Innovative Medicines Initiative Joint Undertaking, which aims to deliver, validate, and obtain regulatory approval for a suite of real-world DMOs.[38,39] This study will hone our understanding of the contexts and purposes for which DMOs might be most effectively used as research instruments. Specifically, we aim to compile an initial body of evidence from which their construct validity, prognostic value, responsiveness, and investigational utility can be explored in four disease areas: Parkinson's disease, multiple sclerosis, chronic obstructive pulmonary disease, and proximal femoral fracture (subsequently referred to as 'target populations'). By mapping the literature and providing a

narrative synthesis of our findings, we will identify which DMOs pose the greatest potential as clinical endpoints. The Mobilise-D consortium selected these disease areas as exemplars for DMO development due to their diverse aetiologies of mobility impairment, high public health burden, and existing evidence base. [24,40–42]

Box 2: Scoping Review Research Questions

- Research Question (RQ) 1: What differences in digital mobility outcomes (DMOs) have been identified between target populations and healthy controls?
- RQ2: What is the evidence on the associations between DMOs and clinically-relevant measurements of physical function, health-related quality of life, symptoms, and disease severity in each of the target populations?
- RQ3: What is the evidence on the prognostic value of DMOs in each of the target populations?
- RQ4: In which contexts and for what purposes have DMOs been used as endpoints in interventional studies in each of the target populations?

METHODS AND ANALYSIS

Protocol Structure

This study employs the methodology for scoping reviews developed by Arksey and O'Malley[43] and advanced by Levac et al.[44] Arksey and O'Malley's framework describes six stages of scoping review conduct: 1) identifying the research question, 2) identifying relevant studies, 3) selecting studies, 4) charting the data, 5) collating, summarizing and reporting results, and 6) consulting with relevant stakeholders. In contrast to systematic reviews, which assess the literature to answer narrow research questions, scoping reviews explore a research topic from a broader perspective. They aim to map the state of evidence in a structured yet reflexive manner to identify research gaps or assess the feasibility of future systematic reviews.[43–45] Given the emergent nature of this research field, a scoping review is an appropriate method to explore and chart current literature on DMOs.

Here we present a harmonised review strategy stratified by research question (RQ) and target population. This approach will allow us to explore the nuances of DMO research in individual disease areas while identifying overarching trends.

Stage 1: Identifying the Research Question

Research Questions

The study will address four RQs, described in Box 2. First, we will map the evidence describing differences in DMOs between healthy and pathological gait. We hypothesise that differences in some, but not all, gait parameters will emerge between healthy individuals and target populations.

We will then gather evidence informing the construct validity of DMOs by mapping associations between DMOs and clinically-relevant measurements of health status. We hypothesise that DMOs will exhibit moderate to strong correlations with traditional clinical measures that assess physical function, such as PROs and functional tests of exercise capacity, and weaker correlations with those assessing disease severity or symptoms not directly related to physical function. To test this hypothesis, we will synthesise the results of cross-sectional studies examining the relationship between DMOs and clinically-relevant measures of physical function, health-related quality of life, symptoms, and disease severity in each of the target populations.

Next, we will map the evidence that informs the prognostic value of DMOs with respect to clinically-relevant outcomes. We hypothesise that DMOs will exhibit prognostic value similar to that

established for traditional measures of mobility.[10,46–48] To test this hypothesis, we will synthesise results of prediction models developed with DMOs.

Finally, we will gather evidence that informs the responsiveness of DMOs to intervention. We expect that the use of DMOs as endpoints in interventional studies will be rare.[32] However, we hypothesise that, when they are used, DMOs will be responsive to effective interventions designed to improve physical function or reduce mobility-limiting symptoms.

Wearable systems that provide DMOs under free-living conditions have the potential to characterise subtle differences in gait pathology associated with specific conditions.[14,15,49–51] We hypothesise that some DMOs, such as walking speed, may be universally informative while others may only be sensitive to gait pathology in specific conditions. Therefore we will also compare the evidence collected for each research question across the target populations.

Table 1: Digital mobility outcomes of gait and walking included in this review

Spatial Parameters
Step length (mean, variability, asymmetry)
Stride length (mean, variability)
Step width (mean, variability)
Temporal Parameters
Cadence (mean, variability)
Step time (mean, variability, asymmetry)
Stride time (mean, variability)
Stance time (mean, variability, asymmetry)
Swing time (mean, variability, asymmetry)
Single support time (mean, variability, asymmetry)
Double support time (mean, variability)
Spatiotemporal Parameters
Gait speed (mean, variability)
Stride speed (mean, variability)
Volume of Walking
Walking time
Step count
Number/Duration of walking bouts

Definitions and Study Scope

According to the International Classification of Functioning, Disability, and Health (ICF), "mobility" is defined as *"moving by (a) changing body position or location or by transferring from one place to another, (b) by carrying, moving or manipulating objects, (c) by walking, running or climbing, and (d) by using various forms of transportation."*[52] This definition portrays a complex picture of mobility, inclusive of both functional ability and social participation. In this definition, walking represents a distinct construct encompassed by the broader concept of mobility. In this review, we adhere to the definition of "walking" adopted by the Mobilise-D consortium:

> *"Human walking is a method of locomotion and is defined as initiating and maintaining a forward displacement of the centre of mass in an intended direction involving the use of the two legs which provide both support and propulsion. The feet are repetitively and reciprocally lifted and set down whereby at least one foot is in contact with the ground at all times.*[53,54] *Walking with walking aids is included in this definition. Walking is made up of walking bouts and is equivalent to taking steps/stepping forward (thus stepping in place does not constitute walking) and is defined as starting from initial contact for the initial step until ending with full floor contact of the foot making the last step.*[55]*"*

We define DMOs as *digitally-measured mobility parameters used to assess an individual's health status*, including spatiotemporal parameters, walking bout characteristics, and physical activity. Theoretically, DMOs could include any digital mobility measures encompassed by the ICF definition. However, the scope of this review will be limited to DMOs associated with walking, as walking is the focus of the Mobilise-D project (Table 1). We will include spatiotemporal parameters studied in three widely-accepted factor analyses of gait[56–59] and macrostructural parameters associated with volume of walking. Nonlinear gait and dynamic balance measures, such as Lyapunov

exponents[60,61] and detrended fluctuation analyses,[62] are outside the scope of this review due to the emergent nature of their evidence base. Though we consider digital measurements of physical activity to be DMOs, metrics of physical activity other than those describing walking volume, such as daily energy expenditure or activity intensity, will be excluded from this review since physical activity represents a related, yet broader construct than walking.[63–65] Until recently, studies on gait parameters were largely confined to clinical settings. While methodologically different, laboratory or clinic-based measurements may still provide insight into DMOs' potential as real-world measures. Thus, we will include all valid digital gait assessment methods in the scope of this review, regardless of setting.

For the purposes of RQ2 and RQ3, "measurements" refer to instruments or tests that assess an aspect of a patient's health at a single point in time, while "outcomes" refer to identified changes in health status that result from the handling of a health problem.[66] We will define "clinically-relevant" measurements and outcomes as those that are routinely and broadly used either in clinical practice or in major pharmaceutical or epidemiological studies. A list of included measurements and outcomes was defined a-priori in consultation with technical and clinical subject matter experts on the Mobilise-D research team. In alignment with the reflexive approach outlined by Arksey and O'Malley,[43] we have defined a structured approach to amending this list if required during study conduct.

Stage 2: Identifying Relevant Studies

This study will be conducted between November 2019 and December 2020. We will include published scientific and grey literature, including journal articles, reports, conference papers, and theses. MEDLINE, CINAHL, Scopus, Web of Science, EMBASE, IEEE Digital Library, and the Cochrane Library will be searched for eligible studies, while ACM Digital Library, ProQuest Dissertations, Open Grey, and the National Information Center's Health Services Research Projects in Progress Database will be searched to identify relevant grey literature. Though we will limit studies based on availability of English-language abstracts, we will include full-text articles written in any language spoken by members of the Mobilise-D consortium. To ensure that all relevant studies are identified, the review team will also screen the first 100 search results on Google Scholar twice, with results first sorted by relevance and then by time. Additional sources will include manual searches of reference lists from relevant studies as well as publications from the review team's private libraries. Based on subject matter expert recommendations, the search will be limited to studies published during or after 1999. This time frame reflects advances in gait monitoring technology in the early 2000s and is supported by the findings of previous systematic reviews that included literature from database inception.[67–69]

The search strategy was developed through collaboration between the research team and an experienced information specialist to ensure that it was comprehensive. Each search includes terms related to walking and the target populations according to the structure (walking terms) AND (population terms). The proposed search strategy for EMBASE is provided in Online Supplement 1.

Study design, review conduct, records of de-duplication, reference exclusion, and individual author contributions will be managed in DistillerSR (Evidence Partners, Ottawa, Canada), a web-based software designed for systematic and scoping reviews. Initial reference compilation and de-duplication will be conducted by the information specialist in Endnote (Clarivate Analytics, Boston, USA), while the review libraries will be compiled in Mendeley (Elsevier B.V., Amsterdam, The Netherlands), an open-access reference management software.

Stage 3: Study Selection

Study Selection Process

The study selection process will include three steps: piloting, title and abstract screening, and full-text review. All reviewers will receive training on scoping review conduct prior to abstract screening. Study eligibility criteria will be piloted on a random set of 50 abstracts to ensure sensitivity and mutual understanding between the reviewers. Clarifications will be made on eligibility criteria as necessary. Agreement with the lead reviewer (AP) will then be monitored on an additional 100 abstracts per reviewer at the onset of the screening process. At the full-text review stage, a similar process will be repeated on 15 randomly-selected full-text articles. Prior to screening, duplicate studies will be identified by comparing titles, authors, publication years, and abstracts. If additional duplicates are identified during full text review or data extraction, they will be excluded. Multiple sources reporting on the same study will be linked and analysed as one study during synthesis.

Up to three reviewers will independently screen each abstract for inclusion according to pre-defined eligibility criteria. To ensure a uniform approach to screening, reviewers will use detailed forms and reference sheets describing relevant eligibility criteria at each stage (Online Supplement 2). Abstracts will be included in full-text review if any single reviewer determines that it meets eligibility criteria. If the first reviewer includes the abstract, it will proceed automatically to full text review and will not undergo a second screening. Agreement of two reviewers will be required to exclude an abstract. In cases of high uncertainty, reviewers will be able to request a third screening by the lead reviewer (AP). This highly inclusive approach will be managed automatically by logic built into the DistillerSR software. Due to the anticipated scale of the project, we will involve approximately 15 reviewers at each stage of the review process. Agreement will be assessed between each reviewer and the primary reviewer via Cohen's Kappa and as a group via Fleiss' Kappa. In contrast to Cohen's Kappa, which calculates agreement of two independent raters, Fleiss' Kappa statistic assesses reliability between any number of raters giving categorical ratings to a fixed number of items.[70] We anticipate that disease-specific knowledge will be necessary for full-text eligibility assessment, data extraction, and synthesis. Thus, included studies will be segmented by disease area during the abstract screening process. Consistent with the reflexive nature of scoping reviews, a second round of abstract screening may be conducted if additional eligibility criteria are identified during the study process or if disease-specific knowledge is required to assess abstract eligibility. This round will follow the same procedure as the original screening stage.

Two reviewers will then independently assess each full-text article for inclusion according to pre-defined eligibility criteria. Reason(s) for exclusion will be documented and reviewer agreement will be calculated. The DistillerSR software will then combine lists of eligible studies. Agreement will be calculated as a group via Fleiss' Kappa and via Cohen's Kappa for reviewer pairs. Reviewers will resolve disagreements through discussion. If no consensus can be reached, a senior team member from the respective disease area will review the article and make the final determination.

Eligibility Criteria

Population-specific, general, and RQ-specific eligibility criteria will be applied during abstract and full-text screening. A detailed list of criteria is provided in Online Supplement 3. In short, studies will be included if they address one of our research questions on an included DMO in a population with a confirmed diagnosis of one of our target diseases. In this context, a "confirmed diagnosis" is one made by a clinician based on the relevant diagnostic criteria at the time of the study's publication. Population-specific eligibility criteria regarding age range, disease severity level or sub-type are described in full in Online Supplement 4.

General Eligibility Criteria

Included DMOs are summarised in Table 1 and further defined in Online Supplement 5. We will include literature on supervised, semi-supervised, or unsupervised measurements of included DMOs conducted under laboratory, clinical (inpatient or outpatient), or free-living conditions. Clinical tests of gait speed, such as the 10-meter walk test, will be included as assessments of gait speed if they are measured with a stopwatch, sensor, instrumented walkway, or other digital technology. Longer clinical walk tests such as the 6-Minute Walk Test will not be included as measurements of gait speed, since they measure constructs such as exercise capacity and endurance rather than walking speed[71–76] and are not representative of typical real-world walking bout duration.[49,77,78] We will also exclude studies on gait kinematics of single steps and testing conditions that artificially alter gait. Additional detail on included and excluded measurement conditions are provided in Online Supplement 3.

Research-Question-Specific Eligibility Criteria

RQ-specific eligibility criteria are summarised in Table 2. Studies will be included in the analysis for RQ1 if they assess the differences in at least one included DMO between healthy controls and one of the target populations.

Studies will be included in the analysis for RQ2 if they assess the relationship between at least one included DMO and one clinically-relevant measurement in a target population. A list of included measurements that assess disease severity, health-related quality of life, physical function, cognition, mental health, and other relevant factors, defined a-priori, is included in Online Supplement 6. Studies not reporting the instrument or test used to make a clinical assessment will be excluded.

Table 2: Summary of Research-Question-Specific Eligibility Criteria

RQ	Aim	Included Study Designs	Minimum Data Set
RQ1	Identify differences in DMOs between pathological and healthy gait	- Case-control studies - Cross-sectional studies - Cross-sectional analyses in longitudinal studies - Exclude: Case studies or case series	At least 10 patients per study arm included in the final analysis
RQ2	Study the relationship between a DMO and a clinical measurement	- Cross-sectional studies - Cross-sectional analyses in longitudinal studies - Exclude: Case studies or case series	At least 10 patients included in the final analysis
RQ3	Assess the prognostic value of a DMO with respect to a clinical outcome measure	- Cohort studies - Longitudinal studies - Control arms of randomized controlled trials (RCTs)	- Age, sex, and disease severity are included as covariates - At least 20 recorded events of an outcome of interest
RQ4	Use a DMO as an exploratory, secondary, or primary outcome in an interventional study	- RCTs - Non-randomized controlled interventional studies - Published protocols of controlled trials - Exclude: Uncontrolled interventional studies	At least 10 patients per study arm included in final analysis

DMO: Digital Mobility Outcome, RQ: Research Question, RCT: Randomized Controlled Trial

Studies will be included in the analysis for RQ3 if the relationship between at least one DMO and at least one clinically-relevant outcome is studied through multivariate analyses, prediction models, or machine learning in a target population. Included outcomes are described in Online Supplement 7. Models should include at least age, sex, and disease severity as covariates. This will allow us to assess whether DMOs provide additional prognostic value above that provided by other easily-available information. Included models should be based on at least 20 recorded events of an outcome of interest (e.g., 20 falls). A typical rule of thumb suggests that models should be built on at least 10 events per covariate. Thus, a minimum of 20 recorded events (four covariates times five events) represents a low threshold for inclusion. Finally, studies should report at least two measurements: a DMO at baseline and a clinically-relevant outcome measure at follow-up. Studies will not be excluded on the basis of duration, follow-up frequency, explicit references to prediction, specific modelling methods, or level of model validation.

Studies will be included in the analysis for RQ4 if an included DMO is used as a primary, secondary, or exploratory outcome in a controlled interventional study in a target population. Published protocols of controlled trials will be indexed for future analysis. Any type of drug or non-drug intervention will be included. Studies will be excluded if they do not at least report the DMO at baseline and at the end of the study, with the exception of randomised controlled trials, which may be included even if DMOs are only measured at follow-up. Studies will not be excluded on the basis of duration or follow-up frequency.

Addressing Unforeseen Eligibility Criteria

Arksey and O'Malley's framework specifically allows for flexibility in the review process,[43] as appropriate scope and eligibility criteria may not be initially clear when reviewing a previously unmapped research area. As research on gait is rapidly evolving, we expect that it may be necessary to adjust our eligibility criteria and lists of included walking conditions, measurements, and outcomes. If initial findings warrant adjustments, a proposal will be submitted to a team of project leads who will make the final determination on how to adjust eligibility criteria. Adjustments to eligibility criteria will be applied to all identified studies and reported accordingly.

Stage 4: Charting the Data

Data Extraction

Data collection forms will be developed through iterative review with the research team and further refined through expert feedback. Forms will capture all relevant study data and contextual information while ensuring adequate flexibility to capture emerging themes. Prior to initiating data extraction, the form will be tested by reviewers on a random sample of at least five studies. Additional modifications to the form identified through this pilot will be reviewed and approved by the research team.

Data extraction will be conducted independently by two reviewers in DistillerSR. A preliminary set of data items is included in Table 3, which will be further specified following feedback from the disease-specific review groups. Studies' corresponding authors will be contacted if clarification is required. Following the completion of data extraction, the reviewers' data sets will be compared and disagreements will be resolved through discussion. If no consensus can be reached, a third, senior member of the research team will make the final determination.

Adding or Adapting Data Items

If additional relevant data items are identified during the review process, they will be submitted to the team of project leads to decide whether and how to adjust the data extraction form. If included, the new data items will be extracted from all included studies.

Table 3: Preliminary data items to extract

Data Items	Associated Questions
Publication Details (All research questions)	
Authors & Affiliations	Who conducted the research?
Type	In what type of literature was the study published? (Journal, grey literature, conference abstract, etc.)
Year	When was the study published?
Country/Region	In which geographic region(s) did the study take place?
General Details (All research questions)	
Study Design	What was the study's design?
Study Aims	What were the study's aims?
Population	What population was studied? Were there any specific inclusion/exclusion criteria such as disease severity, subtype, or age?
Study Size	How many people participated in the study?
Included DMOs	Which DMOs were measured? How and in what setting were the DMOs measured?
Research Question 1	
Study Design	Were patients and controls matched or are the groups comparable with respect to appropriate criteria (height, age, sex, etc.)? Was gait analysis controlled for gait speed? Did the study focus on a specific subgroup or population?
Differences in DMOs	What differences in DMOs occurred (or did not occur) between target populations and healthy controls? Did these differences reach statistical significance?
Research Question 2	
Analytical Methods	How did the authors measure the relationship between clinically-relevant measurements and DMOs? What association measure was used?
Clinically-Relevant Measurement	What clinically-relevant measurements were studied?
Relationship Strength	What was the strength of the reported relationship between the measurement and the DMO? Was the association statistically significant?
Research Question 3	
Model Description	Does the study report a multivariate analysis, a prediction model, a model based on machine-learning, etc.? Which co-variates were included in the model? Which analytical methods were used?
Clinically-Relevant Outcomes	What clinically-relevant outcomes were studied to assess the DMO's prognostic value?
Prognostic Value	Did the DMO provide prognostic value with respect to the studied outcome?
Research Question 4	
Intervention type	What intervention was studied?
Study Endpoints	Was the DMO used as a primary, secondary, or exploratory endpoint? What other primary, secondary, and exploratory endpoints were

	measured?
Success	Was there a change in the primary endpoint between groups?
Ability to Detect Change	Was the DMO able to detect a change due to the intervention (if a change occurred)?

Stage 5: Collating, Summarizing, and Reporting the Results

The body of evidence addressing each research question will be mapped and analysed through narrative synthesis. Findings will be compiled in tables and figures where appropriate. Narrative synthesis will also be used to make comparisons between populations, disease subtypes, and measurement conditions. We will also identify gaps in the evidence to inform areas of future research. Reporting will adhere to the PRISMA-ScR reporting guidelines for scoping reviews[45] with the exception of risk of bias and evidence strength assessments, which are not mandatory.[43–45]

Stage 6: Consultation

Levac et al. recommend that research teams involve stakeholders throughout review conduct, as stakeholders can provide nuanced insights beyond those reported in the literature.[44] The long-term goal of Mobilise-D is to validate and qualify DMOs that can be used to assess mobility in clinical trials. While such an undertaking involves a number of diverse stakeholders, the present work could be most influenced by the perspectives of industry, patients, and clinical researchers. To gather these insights, Mobilise-D's pharmaceutical industry partners, patient advisory board, and scientific advisory board will be consulted during review conduct and data analysis.

ETHICS AND DISSEMINATION

Since our review is limited to publicly available materials, this study does not require ethical approval. Results will be used to prioritise research questions that will be addressed in the Mobilise-D consortium's future work. In addition to publishing our findings, we will partner with Mobilise-D's communications team to facilitate knowledge sharing on web-based platforms for both academic and industrial audiences. To increase transparency, review materials will be made publicly available at https://osf.io/k7395 through the Center for Open Science's OSFRegistry.

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SUPPLEMENTARY FILES

- Online Supplement 1: Proposed search strategy
- Online Supplement 2: Screening reference sheets and forms
- Online Supplement 3: General and research-question-specific eligibility criteria
- Online Supplement 4: Population definitions and disease-specific eligibility criteria
- Online Supplement 5: Gait and walking parameters included in this review
- Online Supplement 6: Clinically-relevant measurements included in research question 2
- Online Supplement 7: Clinically-relevant outcomes included in research question 3

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Online Supplement 1: Search Strategy

MEDLINE, CINAHL, Scopus, Web of Science, EMBASE, IEEE Digital Library, and the Cochrane Library will be searched for eligible studies, while ACM Digital Library, ProQuest Dissertations, Open Grey, and the National Information Center's Health Services Research Projects in Progress Database will be searched to identify additional grey literature. Searches to these databases will adhere to the general following structure: (gait terms) AND (disease-area terms).

The following search string was developed for EMBASE by an experienced information specialist in consultation with the research team and will be replicated for other included databases. Results reflect a search on November 14th, 2019.

String No.	Query	Results
#1 (Gait terms)	(((step* OR stride*) NEAR/2 (speed OR velocit* OR time* OR length* OR width* OR frequenc* OR rate* OR rhythm* OR variabilit* OR symmetr* OR asymmetr* OR count* OR number* OR distance* OR cadence*)):ti,ab) OR (((swing* OR stance* OR 'single support' OR 'double support') NEAR/2 (time* OR duration* OR variabilit* OR symmetr* OR asymmetr*)):ti,ab) OR (((spatiotemporal OR 'spatio-temporal') NEAR/2 (parameter* OR feature* OR characteristic*)):ti,ab) OR (((gait OR walk* OR ambulat*) NEAR/2 (speed OR velocit* OR time* OR cadence* OR pace* OR rhythm* OR volume* OR bout* OR duration* OR distance* OR intensit* OR variabilit* OR asymmetr* OR symmetr* OR parameter* OR feature* OR characteristic* OR assess* OR examin* OR analys* OR batter* OR measure* OR test*)):ti,ab)	112073
#2 (Disease-area terms)	'chronic obstructive lung disease'/exp OR 'Parkinson disease'/exp OR 'parkinsonism'/exp OR 'multiple sclerosis'/exp OR 'demyelinating disease'/exp OR 'hip fracture'/exp OR (((chronic OR lung OR pulmonary OR respirat* OR airway* OR airflow*) NEAR/3 obstruct*) OR copd):ti,ab OR (parkinson* OR 'paralysis agitans'):ti,ab OR (((multipl* OR disseminated OR insular) NEAR/3 scleros*) OR 'chariot disease' OR demyelinat*):ti,ab OR ((hip* OR femur* OR femoral OR trochant* OR pertrochant* OR intertrochant* OR subtrochant* OR intracapsular* OR extracapsular*) NEAR/5 fracture*):ti,ab	635311
#3 (Final)	#1 AND #2 AND (1999:py OR 2000:py OR 2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018 :py OR 2019:py OR 2020:py)	12307

Online Supplement 2: Screening reference sheets and forms

The following forms and reference sheets are proposed for abstract screening and full-text review. Reference sheets will be extensively piloted, revised as required, and provided to each reviewer to use during screening. Review forms and their associated logic are programmed into DistillerSR, where reviewers assess abstracts or full texts and provide answers to the required questions. Final versions of these materials will be published alongside the final study results.

Reference sheets and forms:

Mobilise-D Scoping Review: Abstract Screening Worksheet

Overview:

- This review will explore the potential of DMOs as clinical trial endpoint measures by identifying, existing evidence on their construct validity, prognostic value, and responsiveness to intervention
- Our four research questions aim to explore the following:
  - RQ1: The differences in GaWPs between target populations and healthy controls
  - RQ2: The relationship between GaWPs and traditional clinical measurements
  - RQ3: The prognostic value of GaWPs
  - RQ4: The use of GaWPs as endpoints in interventional studies

Question 1: Should this paper be included in full-text review? (YES or NO)

	Questions to ask yourself:	**YES or Unsure**	**NO**
A	Is the study on an **included population**? *(human studies on Parkinson's, Multiple Sclerosis, COPD, hip fracture)*	Proceed	Discard
B	Does the study assess **gait speed, gait analysis or an included GaWP**? - See reference sheet for list of included GaWPs - Note that some clinical walking tests are included as measures of gait speed (4 meter walk, 10 meter walk, timed 25 foot walk, etc.) and others are not. See reference sheet for details	Proceed	Discard
C	Is the study an **included design**? ○ Included Designs: ▪ Observational ▪ Case-control (comparing diseased group vs. healthy group) ▪ Cohort ▪ Cross-sectional ▪ Longitudinal ▪ Interventional ○ Excluded Designs: ▪ Case study ▪ Case series (Series of case studies published together) ▪ Review paper	Proceed	Discard
D	Could the study **address one of our research questions?** *(answer YES if any of the following apply)* - **RQ1:** Could the study explore the *differences in DMOs/GaWPs between healthy controls and a target population*? - **RQ2/RQ3:** Could the study *explore a relationship between DMOs/GaWPs and included measurements (RQ2) or outcomes (RQ3) in a target population?* ○ Relationships could be in the form of a correlation, empirical relationship, odds ratio, risk ratio, hazard ratio, prediction model, multivariate analysis, or other association measure - **RQ4:** Does the study appear to be an *interventional study in a target population with a DMO/GaWP as an endpoint*?	Proceed	Discard
E	Are at least **5 individuals (or 20 events** for RQ3) included in the final analysis?	Proceed	Discard

		YES	**NO**
F	Are there any other **inclusion criteria** that the study **clearly does not meet**?	**Discard**	**Keep**

***If you are unsure, please be conservative and include the study in full-text review.*

Mobilise-D Scoping Review Abstract Screen: Reference Sheet

Eligibility Criteria

Criterion	Keep	Discard
Population	PD, MS, Hip Fracture, COPD, heart failure Mixed populations IF a sub-analysis was conducted	Animal Studies All other human disease areas Mixed populations with no sub-analysis
Study Aim	Studies an included Gait and Walking Parameter according to one of our research questions	Studies with no GaWP and/or which do not address a RQ
Study Design	Case-control, cross sectional, longitudinal, cohort, controlled trials, protocols (RQ4 only)	Case study, case series Systematic review (or any review)
Technology	Basically any (sensors, stopwatch, speed gaits, instrumented walkways, video, optometric systems, etc.) Specific clinical tests regardless of technology use (see below)	Pedometers
Setting	Any (home, clinical, lab-based)	NA

Minimum Dataset			
RQ1	5 patients per study arm included in the final analysis	RQ3	Age, sex, and disease severity are included as covariates At least 20 recorded events of an outcome of interest
RQ2	5 patients included in the final analysis	RQ4	5 patients per study arm included in final analysis

Gait and Walking Parameters

Spatial Parameters
Step length (mean, variability, asym.)
Stride length (mean, variability)
Step width (mean, variability)

Temporal Parameters
Cadence (mean, variability)
Step time (mean, variability, asymmetry)
Stride time (mean, variability)
Stance time (mean, variability, asymmetry)
Swing time (mean, variability, asymmetry)
Single support time (mean, variability, asym.)
Double support time (mean, variability)

Spatiotemporal Parameters
Gait speed (mean, variability)
Stride speed (mean, variability)

Volume of Walking
Walking time
Step count (excluding pedometer)
Number, length, duration of walking bouts

Included Walking Conditions

Keep:
- Gait analysis or measurement of any included gait parameters
- Dual-task walking, if testing scenario is included
- Some clinical tests, even no technology was used:
  - 4, 5, 10, 30, 50, etc. meter walk tests (or other short distance) – INCLUDE as gait speed
  - Timed 25 Foot Walk (T25FW) - INCLUDE as gait speed
  - 2 Minute Walk Test – INCLUDE as gait speed

Conditionally Keep:
- Timed Up & Go: ONLY INCLUDE instrumented TUG w/ GaWPs measured during walk
- Treadmill Walking:
  - Fixed-Speed Treadmill: INCLUDE any GaWP EXCEPT gait speed
  - Self-Adjusting Speed Treadmill: INCLUDE any GaWP
- 6Minute WT, 12Minute WT, 400m WT, (or other long walking tests):
  - Non-Instrumented Test: EXCLUDE
  - Instrumented test: INCLUDE any GaWP EXCEPT gait speed

Keep if normal gait may have been be analyzed at baseline or if walking condition was used as intervention (generally keep to be conservative):
- Tandem walking or other abnormal walking patterns
- Walking in time to cues (e.g., beats, music, beeping, etc.)
- Purposefully altering gait (e.g., instructions to concentrate on lifting toes)

Research Questions

RQ1: Comparison of GAWPs between a Mobilise-D population and healthy controls
RQ2: Association between a GaWP and a clinical measurement at a single timepoint
RQ3: Prognostic value: Longitudinal association between a GaWP and a clinical measurement or outcome over time
RQ4: Use of GaWPs as endpoints in controlled interventional studies

Population Terms

	Keep	Discard
PD	Parkinson('s) disease, Parkinsonism, idiopathic Parkinson's disease	Atypical parkinsonian syndromes, drug-induced parkinsonism, vascular parkinsonism, progressive supranuclear palsy, multiple system atrophy, corticobasal syndrome, dementia with lewy bodies
MS	Multiple Sclerosis, relapsing-remitting, primary progressive, secondary progressive MS	
PFF	Hip, femoral, intracapsular (subcapital and transcervical), extracapsular (trochanteric, intertrochanteric, pertrochanteric and subtrochanteric) fractures	Non-fracture-related hip arthroplasty or hip replacement
COPD	Chronic obstructive pulmonary disease Chronic obstructive lung disease Chronic respiratory disease (>age of 65)	Pulmonary hypertension, Studies only including asthma patients

- *If the population is mixed, the study must conduct a sub-analysis of one of our populations to be included. If this is unclear from the abstract, be conservative and include.*
- *If you are unsure about the population and the paper meets all other inclusion criteria, include the paper and the disease-specific team will make the determination.*

FAQs

What do I do when…

I am not sure whether a measurement or outcome is included in RQ2/3 criteria
- Some determinations may require disease-specific knowledge. Be conservative and keep the paper.

A testing scenario or type of study is not covered by our eligibility criteria
- If something is not covered by eligibility criteria, raise a question to Ashley and others in the group. We may need to clarify an unforeseen situation.

The abstract does not indicate the technology or method used to measure a GaWP/DMO?
- Include the paper IF it mentions measuring an included gait parameter, gait analysis, or included clinical test of gait speed AND IF it meets all of our other inclusion criteria

Something is completely unclear, and I can't tell whether to include?
- Think about the item that is unclear with regard to the other inclusion criteria. How realistic is it that the criterion is met, given the information that you have?
- Be pragmatic, but inclusive. If all else fails, be conservative and keep the paper.

Mobilise-D Scoping Review: Abstract Screening Worksheet

Legend:

Green text – Describes logic included in form
Prompt: … – Answer triggers another question or form
E – Answer causes study to be excluded
I – Answer causes study to be included

1. Should this paper be included in full-text review?
   Radio answers:
   a. Yes (I, prompt Q3)
   b. No (E, prompt Q2)
   c. Very Unsure (prompt 3rd review by lead reviewer)
   d. Abstract not available/Not in my language (prompt search for full abstract or reviewer fluent in the language of the abstract)

2. Keep paper as background information? (i.e., a relevant review)
   Radio answers:
   a. Yes (Add label "Background")

3. Which MobiliseD disease area is included in this study? (Select all that apply)
   Checkbox answers:
   a. Parkinson's Disease (Send to Parkinson's Disease full-text review group)
   b. Multiple Sclerosis (Send to Multiple Sclerosis full-text review group)
   c. COPD (Send to COPD full-text review group)
   d. Hip Fracture (Send to Hip Fracture full-text review group)

Mobilise-D Scoping Review: Full Text Review Screening Form

Legend:

Green text – Describes logic included in form
Prompt: … – Answer triggers another question
E – Answer causes study to be excluded
Include Study – End of decision tree. Answer causes study to be included

Initial Questions – All abstracts

Question 1: Screening – General Eligibility Criteria (Select all that apply)

- A. Full text is not available (E)
- B. Full text is not in English or one of my fluent languages (Prompt: Q3-Which language?)
- C. The study design was a case study, case series, review, letter, Master's thesis, or other non-eligible study type (E)
- D. The article was an interventional **protocol that used a GaWP as an outcome** that otherwise meets the criteria for RQ4 (E)
- E. The study did not assess any GaWPs (E)
- F. The study **only** included GaWPs other than those on our list (E)
- G. GaWPs were assessed, but **only** in/with ineligible settings or measurement conditions (E)
- H. GaWPs were assessed, but **only** with ineligible technologies or methods (E)
- I. GaWPs were assessed, but **only** during gait initiation, turns, stair climbing, or other excluded motions/activities (E)
- J. Study population did not meet our inclusion criteria (E)
- K. Part of the study population met our criteria, but a sub-analysis on these participants was not conducted (E)
- L. The text was an interventional protocol **that used GaWPs as an outcome** (E)
- M. Fewer than 10 participants per study arm were included in any relevant analysis (E)
- N. The study did not address one of our research questions (E)
- None of the above – The study meets general inclusion criteria (Prompt: Q2-Which research question?)

Studies will be excluded unless the language option or 'None of the Above' is selected

Question 2: Which research question(s) did the study address? (Select all that apply)

- Research Question 1 (Prompt: RQ1 screening question)
- Research Question 2 (Prompt: RQ2 screening question)
- Research Question 3 (Prompt: RQ3 screening question)
- Research Question 4 (Prompt: RQ4 screening question)
- Study does not address our research question (E)

Question 3: In which language is the full text available?

- German
- Spanish
- Italian
- French
- ** Screeners will be able to add and select options as needed

A request to find a reviewer fluent in the language will be triggered

RQ-specific Screening Questions

Research Question 1 Screening Questions

RQ1 Eligibility criteria - Was the difference in GaWP measurements assessed between healthy controls and a target population?

A. Yes, but fewer than 10 participants per study arm were included a relevant RQ1 analysis (E)
B. The patient population was mixed and a sub-analysis on an included population was not conducted for RQ1 (E)
C. Yes, and all criteria for RQ1 are met – this paper/analysis should be included (Include Study)

Research Question 2 Screening Questions

RQ2 Eligibility Criteria: Was the relationship between a DMO and a clinical measurement assessed in a target population?

A. Yes, but no included/important measurements were studied (E)
B. Yes, but fewer than 10 patients were included in this analysis (E)
C. Population was mixed and a sub-analysis on an included population was not conducted (E)
D. Yes and all eligibility criteria are met – The study should be included (Include Study)

Research Question 3 Screening Questions

RQ3 Eligibility Criteria: Was the relationship between a DMO and a clinical outcome assessed in a target population through a multivariate analysis, prediction model, or machine learning technique?

A. Yes, but no included/important outcomes were studied (E)
B. The model was not a multivariate analysis, prediction model, or machine learning technique using a GaWP as a variable (E)
C. Study design was not longitudinal or a longitudinal analysis of a control group in an RCT (E)
D. The study looked at GaWPs as outcomes rather than variables (E)
E. Age, sex, and disease severity were not adjusted/controlled for or included as covariates (E)
F. Patient population was mixed and a sub-analysis on an included population was not conducted for RQ3 (E)
G. Fewer than 20 events of an outcome of interest were included in the final analysis (E)
H. Yes and all eligibility criteria are met – The study should be included (Include Study)

Research Question 4 Screening Questions

RQ4 Eligibility Criteria: Was the DMO used as a primary, secondary, or exploratory endpoint in an interventional study?

A. The clinical trial was uncontrolled or did not have a comparator (E)
B. The reference is only a protocol or study registration, and does not report original results (E)
C. The DMO was not assessed at a minimum of two time points (baseline and follow-up) for non-RCTs or one time point (follow-up) for RCTs (E)
D. Patient population was mixed and a sub-analysis on an included population was not conducted for RQ4 (E)
E. Fewer than 10 patients per arm were included in the final analysis (E)
F. Yes and all eligibility criteria are met – The study should be included (Include Study)

Online Supplement 3: General and research-question-specific eligibility criteria

Overview

Eligibility criteria are divided into three categories:

- General eligibility criteria applying to all studies and research questions
- Research-question-specific eligibility criteria
- Disease-specific eligibility criteria (described in Online Supplement 4)

'General' eligibility criteria will be applied to all studies, while 'research-question-specific' criteria will be applied when determining a study's applicability for the analysis associated with a specific research question. Disease-specific criteria will be applied to assess eligibility based on the study's target populations.

Eligibility Criteria

General Eligibility Criteria (All research questions)	
Populations & Patient Characteristics	People having a confirmed diagnosis of one of the following conditions: • Parkinson's Disease (PD) • Multiple Sclerosis (MS) • Proximal Femoral Fracture (PFF) • Chronic Obstructive Pulmonary Disease (COPD) A "confirmed diagnosis" is defined as a diagnosis made by a professional physician based on the relevant diagnostic criteria at the time of the study's publication. Eligibility criteria regarding age range, disease severity level or disease sub-type are disease-specific and are described in Online Supplement 4.
Included DMOs	A list of DMOs adapted from three well-known factor analyses of gait (Verghese et al., 2007 (1); Hollman et al., 2011 (2); Lord et al., 2013 (3)) and measures associated with volume of walking will be included in this study. These lists are summarized below and their definitions are available in Online Supplement 5. *Spatial Parameters* • Step length (mean, variability, asymmetry) • Stride length (mean, variability) • Step width (mean, variability) *Temporal Parameters* • Cadence (mean, variability) • Step time (mean, variability, asymmetry) • Stride time (mean, variability) • Stance time (mean, variability, asymmetry) • Swing time (mean, variability, asymmetry) • Single support time (mean, variability, asymmetry) • Double support time (mean, variability)

	Spatiotemporal parameters • Gait speed (mean, variability) • Stride speed (mean, variability) *Daily Volume of Walking* • Walking time • Step Count • Number, length, and/or duration of walking bouts
Technology Type	DMOs should be measured by at least one of the following technologies: Stopwatch (gait speed only), speed gates, Accelerometer, gyroscope, magnetometer, inertial measurement units (IMU), instrumented/electronic walkways or mats, force plates, optometric gait assessment systems, video-based gait assessment system, radio signal-based gait assessment system, pressure sensors or insoles, mobile phone-based accelerometers, gyroscopes, or magnetometers GPS and barometer will be included if it supplements the measurement of a technology above. Any number, placement (wrist, lower back, ankle, etc.), or configuration of sensors will be included. Step count measured by pedometers will be excluded due to their limited validity in the target populations.
Setting	Supervised, semi-supervised, or unsupervised measurements of DMOs made during research studies in laboratory settings, in-clinic (inpatient or outpatient), or under free-living conditions will be included.
Walking Activity & Conditions	DMOs can be measured during continuous walking, straight walking, curvilinear walking, or a mix of these. Measurements during select clinical gait speed tests will be included: Include: • 4m, 5m, 10m, 30m walk test, timed 25 foot walk, or other short fixed-distance walking test • 2 Minute walk test Conditionally Include: - Timed Up and Go: Include if walking speed is measured via an accelerometer or other digital measure during the walking phase, exclude otherwise Exclude: • 6 or 12 Minute Walk Test • Maximum distance walked • Incremental shuttle walk test • Endurance shuttle walk test • Tandem walk test • Self-reported walking parameters

	• Other walk tests that artificially alter step time or gait parameters, such as stepping in time to a beat or music or consciously altering gait mechanics Any testing speed (e.g., self-selected vs. maximum speed) and start conditions (e.g., static start or rolling start) will be included. Analysis on any bout length or walking distance (other than the exclusions on clinical gait speed tests, above) will be included.
Geographic Region/Location	Any
Language of Publication	To be eligible, literature must have an English-language abstract. Full texts available in English, German, Spanish, French, Italian, Dutch, Norwegian, Hebrew, Catalan, and other languages spoken within the Mobilise-D consortium will be included.
Publication status/type	• Published, peer-reviewed studies • Gray literature (reports, policy documents, theses) • Conference abstracts (if sufficient information to address a research question is reported) • Interventional study protocols (indexed for Research Question 4)
Publication time frame	20 years (1999-2019) Based on recommendations from subject matter experts, reflecting advances in technology in the early 2000s.

Research Question 1: Eligibility Criteria	
DMO Usage	The differences between at least one target population and healthy controls are studied using DMOs
Study Types & Analyses to Include	- Case-control studies - Cross-sectional studies - Cross-sectional analyses in longitudinal studies - Exclude: single case studies or case series (i.e., multiple case studies presented together)
Minimum data set/sample size	At least 10 patients or participants per arm included in the final analysis

Research Question 2: Eligibility Criteria	
DMO Usage	The relationship between at least one DMO and at least one included clinically-relevant measurement (defined below) is studied in a target population. Studies exploring the relationship between two in-clinic walking distance/speed tests (e.g., between 10 meter walk test and the 6 minute walk test) will be excluded.

	Correlations between walking speed measured during clinical tests and other types of tests (e.g., UPDRS, HR-QoL assessments) will be included.

Clinically-relevant measurements	A list of included clinically-relevant measurements was defined a-priori through discussion between the research team and clinical experts. This list is included in Online Supplement 6. This list is comprised of clinically-relevant, validated instruments or tests that assess at least one of the following:
	- Disease Severity & Symptoms
	- Relevant physiological measurements
	- Functional Status (e.g., Ability to perform activities of daily living)
	- Health-Related Quality of Life
	- Mental Health (e.g., Depression and Anxiety)
	- Cognition
	- Physical Function, including:
	  ○ Walking or other functional assessments
	  ○ Motor Function (e.g., Balance, fine and gross motor function, tremor, fall risk, etc.)
	  ○ Functional & Maximal Exercise Capacity
	  ○ Strength
	  ○ Fatigue
	- Other relevant disease-specific factors (e.g., lung function-COPD, ejection fraction-CHF)
	
	Through at least one of the following assessment types:
	- Patient reported outcome measures (e.g., EQ5D or VAS for health-related quality of life)
	- Subjective clinical assessments (scored or assessed by a trained observer – e.g., UPDRS, EDSS, etc.),
	- Objectively-measured clinical assessments (e.g., assessed via technology, timed test, etc.)
	- Home-based assessments
	- Physiological measurements that assess function or disease severity (e.g., number and size of lesions in MS, ejection fraction in CHF, FEV1 in COPD)
	
	Measurements other than those included on this list will be excluded from the review. If the instrument or test used to make assessments is not reported, the study will be excluded. Correlations to symptoms/reports of symptoms without reporting a validated instrument for measuring those symptoms will also be excluded.

Study Types & Analyses to Include	- Cross-sectional studies - Cross-sectional analyses in longitudinal studies - Exclude: single case studies, case series, and other non-included study types
Duration/Follow-up	Data is collected and analysis is conducted based on a single time point (i.e., cross-sectional analysis). If studies are longitudinal, only analyses conducted at a single point are included (for example, correlation between gait speed and the Berg Balance Scale at baseline)
Minimum data set/sample size	To be eligible for inclusion, studies must include a minimum of 10 patients in the final analysis

Research Question 3: Eligibility Criteria

DMO usage	The relationship between at least one DMO and at least one included clinically-relevant outcome is studied in a target population.
Clinically-relevant outcomes	Studies will be included if they assess the relationship between an included DMO and an included outcome. A list of included outcome measurements was defined a-priori by the research team and clinical experts. This list is provided in greater detail in Online Supplement 7. Included outcomes are related to: - Disease/Disability Status or Progression - Health-Related Quality of Life - Mortality - Healthcare Utilization (e.g., hospitalizations, readmissions, home care, costs, invasive procedures, etc.) - Physical Function (e.g., exercise capacity, motor function, balance, strength) - Functional Status (e.g., activities of daily living) - Fatigue - Cognition - Mental Health (e.g., depression, anxiety, apathy) - Falls - Life Space - Residential Status - Use of Mobility Aids - Disease-specific outcomes such as exacerbations (COPD), relapses (MS) or decompensation (CHF) Any relevant method of assessing the outcomes of interest will be included in the review. (e.g., for mortality, both 1-year mortality and 5-year mortality will be included in the review). Outcomes other than those included on this list will be excluded from the review.
Study Types	- Cohort studies - Longitudinal studies - Control arms of RCTs - Exclude: Other non-included study types
Analyses	Study reports multivariate analyses, prediction models, or machine learning analyses with the following minimum criteria: - At least age, sex, and disease severity are included as covariates in the model - At least 20 recorded events of an outcome of interest. Reports of models at any level of maturity will be included (e.g., model development, validation, etc.) If a study meets these criteria for any single outcome of interest, the outcome will be included in the review. Other outcomes reported in the same paper that do not meet these criteria (e.g., too few events) will not be included in the review. Models based on machine learning will be included even if the minimum number of co-variates and events are not reported, as this information is not always provided for such models.

	Exclude: Univariate analyses, models excluding age, sex, or disease severity, models based on less than 20 recorded events of the outcome of interest
Duration/Follow-up	Study reports at least two measurements: the DMO at baseline and a clinically-relevant outcome measure at the end of the study. Studies will not be excluded on the basis of duration or follow-up frequency.

Research Question 4: Eligibility Criteria	
DMO usage	A DMO is used as a primary, secondary, or exploratory outcome in an interventional study in a target population
Study Aims	- To test efficacy/effectiveness of an intervention via DMOs in target populations - To test safety of an intervention via DMOs in target populations
Study Types	- Randomized Controlled Trials - Non-randomized controlled interventional studies - Published protocols of Controlled Trials - Exclude: Uncontrolled interventional studies and other non-included study types
Intervention type	Any type of drug and non-drug intervention
Duration/Follow-up	Study reports at least two measurements: the DMO at baseline at the end of the study (or at least one follow-up in the case of RCTs). Studies will not be excluded on the basis of duration or follow-up time.
Minimum data set/sample size	At least 10 patients per study arm included in final analysis

1. Verghese J, Wang C, Lipton RB, Holtzer R, Xue X. Quantitative gait dysfunction and risk of cognitive decline and dementia. *J Neurol Neurosurg Psychiatry.* 2007; 78(9):929-35. https://www.ncbi.nlm.nih.gov/pubmed/17237140?dopt=Abstract

2. Hollman JH, McDade EM, Petersen RC. Normative spatiotemporal gait parameters in older adults. *Gait Posture*. 2011;34(1):111–118. doi:10.1016/j.gaitpost.2011.03.024

3. Lord S, Galna B, Verghese J, Coleman S, Burn D, Rochester L .Independent domains of gait in older adults and associated motor and nonmotor attributes: validation of a factor analysis approach. *J Gerontol A Biol Sci Med Sci.* 2013; 68(7):820-7 https://www.ncbi.nlm.nih.gov/pubmed/23250001

Online Supplement 4: Population Definitions & Eligibility Criteria

Included Populations:

- Parkinson's Disease
- Multiple Sclerosis
- Hip Fracture
- Chronic Obstructive Pulmonary Disease

Parkinson's Disease

Proposed definition

People who have received a confirmed diagnosis of Parkinson's Disease by a professional physician based on the relevant diagnostic criteria at the time of the study's publication. Studies including participants with any age range and disease severity level will be included in this review.

Relevant Diagnostic Criteria may include, but are not limited to:

- New International Parkinson Disease and Movement Disorder Society Diagnostic Criteria (Postuma, Mov Dis 2015)
- Gelb's Criteria (National Institute of Neurological Disorders and Stroke) (Gelb, JAMA Neurology, 1999)
- Queen's Square Brain Bank/UK Parkinson's Disease Society Brain Bank Diagnostic Criteria (Hughes, J Neurol Neurosurg Psychiatry, 1992)

Population Exclusion Criteria

Studies of persons with atypical parkinsonian syndromes, drug-induced parkinsonism, or vascular parkinsonism will be excluded from this review.

Multiple Sclerosis

Proposed definition

People who have received a confirmed diagnosis of Multiple Sclerosis (MS) by a professional physician based on the relevant diagnostic criteria at the time of the study's publication. Studies including participants with any age range, severity level or sub-type of Multiple Sclerosis will be included in this review.

Relevant Diagnostic criteria may include, but are not limited to:

- McDonald diagnostic criteria (McDonald, Ann Neurol, 2001), including the 2005, 2010, and 2017 revisions
- Poser diagnostic criteria (Poser, Ann Neurol, 1983)

- MAGNIMS consensus guidelines: MRI criteria for the diagnosis of MS (Filippi, Lancet Neurology, 2016)
- Defining the clinical course of multiple sclerosis; The 2013 revisions (Lubin et al, 2014)

Population Exclusion Criteria

Studies of persons experiencing or exhibiting clinically isolated syndrome (CIS), Neuromyelitis Optica Spectrum Disorder (NMOSD), Myelin oligodendrocyte glycoprotein (MOG), or Acute disseminated encephalomyelitis (ADEM) will be excluded. No additional exclusion criteria will be applied.

Proximal Femoral Fracture

Proposed definition

We will include older people (≥ 65 years of age) who have received surgical treatment (fixation or arthroplasty) for a low-energy fracture of the proximal femur. Both (intracapsular (also termed subcapital and transcervical) fractures or extracapsular (also termed trochanteric, intertrochanteric, pertrochanteric and subtrochanteric) fractures will be included.

Relevant diagnostic criteria may include, but are not limited to:

- ICD-10 diagnosis S72.0, S72.1, S72.2 as diagnosed on X-rays of the hip and pelvis

Population Exclusion Criteria

Studies of persons that do not meet the proposed definition of the target population will be excluded. No additional exclusion criteria will be applied.

Chronic Obstructive Pulmonary Disease

Proposed definition:

People who have received a confirmed diagnosis of Chronic Obstructive Pulmonary Disease (COPD). In this context a “confirmed diagnosis” is defined as a diagnosis made by a professional physician based on the relevant diagnostic criteria at the time of the study’s publication. Studies including participants with any age range, severity level or sub-type of COPD will be included in this review.

Relevant diagnostic criteria may include, but are not limited to:

Patients with a diagnosis of chronic obstructive pulmonary disease (COPD), defined by spirometry. Any definition of COPD will be accepted as long as it is based on spirometry. For example, current guidelines recommend FEV1/FVC <0.7 and FEV1 in % predicted <80%.

Population Exclusion Criteria

Studies of persons that do not meet the proposed definition of the target population will be excluded. No additional exclusion criteria will be applied.

Online Supplement 5: Digital mobility outcomes included in this review

The following set of gait and walking parameters will be included in the map and subsequent analysis produced in this scoping review. This list was adapted from three well-known factor analyses of gait [1–3] (Table 1) and from a list of secondary DMOs associated with walking which were prioritized by clinical and technical subject matter experts involved in the Mobilize-D project (Table 2). In keeping with the reflexive nature of scoping reviews, this list may be amended based on initial search findings as described in the study protocol.

Definitions adopted by the Mobilise-D Consoritium:

- Human ***walking*** is a method of locomotion and is defined as initiating and maintaining a forward displacement of the centre of mass in an intended direction involving the use of the two legs which provide both support and propulsion. The feet are repetitively and reciprocally lifted and set down whereby at least one foot is in contact with the ground at all times.[4,5] ***Walking*** with walking aids is included in this definition. ***Walking*** is made up of ***walking bouts*** and is equivalent to taking steps/stepping forward (thus stepping in place does not constitute walking) and is defined as starting from initial contact for the initial step until ending with full floor contact of the foot making the last step.[6]
- A ***step*** is the interval between the initial contacts of the ipsi- and contralateral foot[4] and corresponds to the forward displacement of the foot together with a forward displacement of the trunk.[6]
- A ***stride*** is the interval between two successive initial contacts of the same foot. As such, a ***stride*** is equivalent to the gait cycle and every stride contains two ***steps.***[4]

Table 1: Gait parameters included in the review

Gait Parameter (Unit)	Narrative Definition	Dimension
Spatial Parameters		
Step length (cm)	Typically defined as the anterior-posterior distance from the heel of one footprint to the heel of the opposite footprint.[3] For the purposes of this review, step length may also be measured between the toes or other identifiable markers on opposite footfalls.	Mean, variability, asymmetry
Stride length (cm)	Typically defined as the anterior-posterior distance between heels of two consecutive footprints of the same foot (left to left, right to right); two steps (e.g., a right step followed by a left step) comprise one	Mean, variability

	stride or one gait cycle.[3] For the purposes of this review, stride length may also be measured between the toes or other identifiable markers on consecutive footfalls.	
Step width (cm)	The lateral distance from heel center of one footprint to the line of progression formed by two consecutive footprints of the opposite foot.[3] For the purposes of this review, step width may also be measured between the toes or other identifiable markers on opposite footfalls.	Mean, variability
Temporal Parameters		
Cadence (steps/min)	Cadence is the number of steps per minute, sometimes referred to as step rate or frequency[3]	Mean, variability
Step time (s)	Time elapsed from initial contact of one foot to initial contact of the opposite foot [3]	Mean, variability, asymmetry
Stride time (s)	Time elapsed between the initial contacts of two consecutive footfalls of the same foot [3]	Mean, variability
Stance time (s, % of gait cycle)	The stance phase is the weight bearing portion of each gait cycle initiated at heel contact and ending at toe off of the same foot; stance time is the time elapsed between the initial contact and the last contact of a single footfall [3]	Mean, variability, asymmetry
Swing time (s)	The swing phase is initiated with toe off and ends with initial contact of the same foot; swing time is the time elapsed between the last contact of the current footfall to the initial contact of the next footfall of the same foot [3]	Mean, variability, asymmetry
Single support time (s, % of gait cycle)	Single support occurs when only one foot is in contact with the ground; single support time is the time elapsed between the last contact of the opposite footfall to the initial contact of the next footfall of the same foot [3]	Mean, variability, asymmetry
Double support time (s, % of gait cycle)	Double support occurs when both feet are in contact with the ground simultaneously; double support time is the sum of the time elapsed during two periods of double support in the gait cycle [3]	Mean, variability
Spatiotemporal Parameters		
Gait/Walking Speed (cm/s)	Walking speed is the distance covered by the whole body within a certain time interval / per unit time of walking. It is measured in meters per second and is the magnitude of the velocity vector (velocity includes direction and magnitude of walking). [5]	Mean, variability

Stride Speed (cm/s)	Stride speed is the distance covered by the whole body within a single stride per unit time of walking.	Mean, variability

Table 2: Secondary mobility parameters included in the in-depth map

Secondary Mobility Parameter	Definition
Daily Volume of Walking	
Walking time	The amount of time spent walking during a set period of time. Walking is made up of walking bouts and is equivalent to taking steps/stepping forward and is defined as starting from initial contact for the initial step until ending with full floor contact of the foot making the last step [6]
Step Count	The number of steps made during a set period of time, such as a day or walking bout. A *step* is the interval between the initial contacts of the ipsi- and contralateral foot.[4]
Number, duration, or distance of walking bouts	A ***walking bout*** (WB) is a walking sequence containing at least two consecutive strides of both feet (e.g. *R-L-R-L-R-L* or *L-R-L-R-L-R*). Start and end of a walking bout are determined by a resting period or any other activity (non-walking period). The initial step of a WB follows a non-walking period and the final step precedes the next non-walking period.

References

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Online Supplement 6: Clinically-relevant measurements included in Research Question 2

The following set of "clinically-relevant" measurements, summarized in Table 1, will be included in the map and analysis associated with Research Question 1 in the Mobilise-D scoping review. The general measurements will be included in all disease-area sub-analyses, while disease-specific measurements will be included only in disease-specific analyses. In keeping with the reflexive nature of scoping reviews, this list may be amended based on initial search findings as described in the study protocol.

Definitions

For the purposes of our review, "measurements" will refer to instruments or tests that assess an aspect of a patient's health at a single point in time, while "outcomes" refer to identified changes in health status that result from the handling of a health problem. We will define "clinically-relevant" measurements as those that are routinely and broadly used in either clinical practice or in major pharmaceutical or epidemiological studies.

Excluded Measurement Categories

We will exclude additional categories that are unlikely to provide additional information on the construct validity of gait and walking parameters, even if they are relevant to our included disease areas. However, some of these categories will be included in Research Question 3, allowing us to explore the relationship between these constructs and gait and walking parameters. These categories are:

- Sleep
- Life space
- Comorbidities
- Pain
- Frailty (Lack of common definition or method of testing frailty will limit any assessment of the DMOs' construct validity)
- Hospital re-admissions and longitudinal outcome measures not assessible through cross-sectional study designs

Included Measurements

Included measurements are summarized as acronyms in Table 1 and listed in the order which they appear with full titles in Table 2.

Table 1: Summary of included clinically-relevant measurements by category and disease area. Note that some instruments appear in more than one category. Disease areas include Parkinson's disease (PD), multiple sclerosis (MS), chronic obstructive pulmonary disease (COPD), and proximal femoral fracture (PFF).

Category		All disease areas	PD	MS	COPD	PFF
Disease Severity & Symptoms		CGI, PGI	(MDS)-UPDRS – I, II, III, IV H&Y, RDRS, UDysRS, FoGQ, nFoGQ	EDSS, FSS, MSFC, FAMS Number of relapses PDDS, GNDS, SNRS	GOLD A-D, MMRC, Dyspnea (VAS, Borg) # Exacerbations, CAT, CRQ, SGRQ, CCQ	Harris Hip Score Oxford Hip Score
Physiological Measurements				Number/volume of lesions Brain volume BWCS, BLCS, IVIS	FEV1, FVC FEV1/FVC Ratio	
Functional Status/ADL		Barthel Index Nottingham EADL IADL, LLFDI	Schwab & England MDS-UPDRS – II, SPDDS, SPES, PROMIS, Neuro-QoL	Schwab & England MSIS-29		
HRQoL		EQ-5D (5L or 3L) EQ-VAS, SF-36, SF-12 HUI3, LSQ	PDQ-39, 8	MSIS-29, MSQoL-54 MSQLI, FAMS	CRQ, SGRQ, CCQ Feeling Thermometer	
Depression & Anxiety		HADS, Beck, CES-D, GDS, SDS/Zung, PHQ, MHI	LARS			
Cognition		MMSE, MoCA, SDMT PASAT, CANTAB, CAMCOG-R,	RBANS, ACE-R, PD-CRS, Trail Making Test, Digit Span Stroop Color and Word Test	ACE-R, PDQ, BICAMS, MSFC (PASAT)	*Not relevant*	
Physical Function	Walking or Functional Assessments	4-10 meter walk 2MWT, 6MWT T25FW, TUG, STS		MSWS-12 MSFC (T25FW)	ISWT, ESWT	CAS
	Motor Function & Balance	ABC, Berg Balance, FAB, SPPB BESTest, mini-BESTest FES-I, Incidence of falls Ambulation Index (AI)	360 degree (fast) turn test	MSFC (9-HPT) Disease Step (DS)		
	Physical Activity	IPAQ, PASE			PROactive	
	Strength	Quadriceps, Leg press, Grip				Hip abduction Knee extension

	Fatigue	FIS, mFIS, FSS, FACIT	PFS-16	MFIS		

Table 2: Clinically-relevant measurements included in the review

			Measurement Category										
Acronym	**Instrument/Measurement Name**	**Disease Area**	Disease Severity & Symptoms	Physiological Assessments	Functional Status/ADL	Health-Related Quality of Life	Depression & Anxiety	Cognition	Walking & Mobility Assessments	Motor Function & Balance	Physical Activity	Strength	Fatigue
CGI	Clinical Global Impression Score	All	X										
PGI	Patient Global Impression Score	All	X										
(MDS) UPDRS - I	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, subscores I, II, III, and IV	PD	X										
(MDS) UPDRS - II	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, subscore II	PD	X		X								
(MDS) UPDRS - III	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, subscore III	PD	X										
(MDS) UPDRS - IV	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, subscore IV	PD	X										
H&Y	Hoehn & Yahr Score	PD	X										
RDRS	Rush Dyskinesia Rating Scale	PD	X										
UDysRS	Unified Dyskinesia Rating Scale	PD	X										
FOGQ	Freezing of Gait Questionnaire	PD	X										

nFOGQ	New Freezing of Gait Questionnaire	PD	X										
EDSS	Kurtzke Expanded Disability Status Scale	MS	X										
FSS	Kurtzke Functional Systems Scores	MS	X										
MSFC	Multiple Sclerosis Functional Composite	MS	X					X	X	X			
	Number of Relapses	MS	X										
PDSS	Patient Determined Disease Steps	MS	X										
GNDS	Guy's Neurological Rating Scale	MS	X										
SNRS	Scripps Neurological Rating Scale	MS	X										
GOLD A-D	Global Initiative for Chronic Obstructive Lung Disease, Categories A-D	COPD	X										
MMRC	modified Medical Research Council Dyspnea Scale	COPD	X										
VAS	Dyspnea Visual Analog Scale	COPD	X										
Borg	Dyspnea Borg CR10 Score	COPD	X										
	Number of Exacerbations	COPD	X										
CAT	COPD Assessment Test	COPD	X										
HHS	Harris Hip Score	PFF	X										
OHS	Oxford Hip Score	PFF	X										
	Number/Volume of Lesions	MS		X									
	Brain volume	MS		X									
BWCS	Bowel Control Scale	MS		X									
BLCS	Bladder Control Scale	MS		X									
IVIS	Impact of Visual Impairment Scale	MS		X									
FEV1	Forced Expiratory Volume, 1 second	COPD		X									
FVC	Forced Vital Capacity	COPD		X									
FEV1/FVC	Forced Expiratory Volume/Forced Vital Capacity Ratio	COPD		X									

Barthel	Barthel Index	All			X								
IADL	Lawton Instrumental Activities of Daily Living Scale	All			X								
EADL	Nottingham (Extended) Activities of Daily Living Scale	All			X								
LLDI	Late Life Disability Instrument	All			X								
SE-ADL	Schwab & England Activities of Daily Living Scale	PD, MS			X								
SPDDS	Self-Assessment Parkinson's Disease Disability Scale	PD			X								
SPES	Short Parkinson's Evaluation Scale	PD			X								
PROMIS	Patient-Reported Outcome Measurement Information System (ADL test)	PD			X								
NeuroQoL	Neuro QoL Physical Function	PD			X								
MSIS-29	Miultiple Sclerosis Impact Scale - 29	MS			X	X							
EQ-5D (5L or 3L)	EuroQoL 5 Dimensions	All				X							
EQ-VAS	EuroQoL Visual Analog Scale	All				X							
SF-36	Short Form 36 Health Survey	All				X							
SF-36 MCS	Short Form 36 Mental Component Scale	All				X							
SF-36 PCS	Short Form 36 Physical Component Scale	All				X							
SF-12, RAND	Short Form 12 Health Survey	All				X							
HUI3	Health Utilities Index Mark 3	All				X							
LISAT-9, LSQ	Life Satisfaction Questionnaire	All			X	X							
PDQ-39, PDQ-8	Parkinson's Disease Questionnaire - 39 or 8	PD				X							
MSQOL-54	MS Quality of Life - 54	MS				X							
MSQLI	MS Quality of Life Inventory	MS				X							
FAMS	Functional Assessment of Multiple Sclerosis	MS	X			X							
CRQ	Chronic Respiratory Disease Questionnaire	COPD	X			X							
SGRQ	Saint George's Respiratory Disease Questionnaire	COPD	X			X							

CCQ	Clinical COPD Questionnaire	COPD	X			X							
FT	Feeling Thermometer	COPD				X							
HADS	Hospital Anxiety and Depression Scale	All					X						
BDI, Beck	Beck Depression Inventory	All					X						
CES-D	Center for Epidemiologic Studies Depression Scale	All					X						
GDS	Geriatric Depression Scale	All					X						
SDS, Zung	Zung Self-Rating Depression Scale	All					X						
PHQ	Patient Health Questionnaire 8 or 9	All					X						
MHI	Mental Health Inventory	All					X						
LARS	Lillie Apathy Rating Scale	PD					X						
MMSE	Mini-Mental State Examination	All						X					
MoCA	Montreal Cognitive Assessment	All						X					
SDMT	Symbol Digit Modalities Test	All						X					
PASAT	Paced Auditory Serial Addition Test	All						X					
CANTAB	Cambridge Neuropsychological Test Automated Battery	All						X					
CAMCOG-R	Cambridge Cognitive Assessment (Revised)	All						X					
RBANS	Repeatable battery for the assessment of neuropsychological status	All						X					
ACE-R	Addenbrooke's Cognitive Examination (Revised)	PD, MS						X					
PD-CRS	Parkinson's Disease Cognitive Rating Scale	PD						X					
TMT	Trail Making Test	PD						X					
	Digit Span	PD						X					
Stroop	Stroop Color and Word Test	PD						X					
PDQ	Perceived Deficits Questionnaire	MS						X					
BICAMS	Brief International Cognitive Assessment for MS	MS						X					

	4 to 10 meter walk (i.e., any straight walking test between 4-10 meters in length)	All							X				
2MWT	2 Minute Walk Test	All							X				
6MWT	6 Minute Walk Test	All							X				
T25FW	Timed 25 Foot Walk	All							X				
TUG	Timed Up & Go	All							X				
STS	Sit to Stand Test	All							X				
SPPB	Short Physical Performance Battery	All							X				
MSWS-12	Multiple Sclerosis Walking Scale - 12	MS							X				
CAS	Cumulated Ambulation Score	PFF							X				
FES-I	Falls Self-Efficacy Scale - International	All								X			
ABC	Activities-Specific Balance Confidence Scale	All								X			
BBS	Berg Balance Scale	All								X			
BESTest	Balance Evaluation Systems Test	All								X			
mini-BESTest	Mini-Balance Evaluation Systems Test	All								X			
FAB	Fullerton Advanced Balance Scale	All								X			
	360 Degree (Fast) Turn Test	PD								X			
9-HPT	9-Hole Peg Test	MS								X			
DS	Disease Step	MS								X			
	Number/Incidence of falls	All								X			
AI	Ambulation Index	All								X			
IPAQ	International Physical Activity Questionnaire	All									X		
PASE	Physical Activity Scale for the Elderly	All									X		
PROactive	PROactive	COPD									X	X	
	Quadriceps Strength	All										X	

	Leg Press Strength	All										X	
	Grip Strength	All										X	
	Hip Abduction Strength	PFF										X	
	Knee Extension Strength	PFF										X	
FIS, mFIS	(modified) Fatigue Impact Scale for Daily Use	PD, MS											X
MFIS	MS fatigue impact scale	MS											X
FSS	Fatigue severity scale	PD, MS											X
PFS-16	Parkinson's Fatigue Scale	PD											X

Supplement 7: Clinically-relevant outcomes included in Research Question 3

The following set of "clinically-relevant" outcomes will in included in the map and analysis associated with Research Question 3 in the Mobilise-D scoping review. The general outcomes will be included in all population sub-analyses, while population-specific outcomes will be included only in population-specific analyses. In keeping with the reflexive nature of scoping reviews, this list may be amended based on initial findings as described in the protocol.

Definitions

In this review, "outcomes" refer to identified changes in health status that result from the handling of a health problem. "Clinically-relevant" measurements and outcomes as those that are routinely and broadly used in either clinical practice or in major pharmaceutical or epidemiological studies.

Table 1: Summary of Included Clinically-Relevant Outcomes

General Outcomes: All disease areas			
Disease/Disability Status or Progression Health-Related Quality of Life Mortality Healthcare Utilization (e.g., hospitalizations, readmissions, home care, costs, invasive procedures, etc.) Physical Function (e.g., exercise capacity, motor function, balance, strength) Functional Status (e.g., activities of daily living) Fatigue Cognition Mental Health (e.g., depression, anxiety, apathy) Falls Life Space Residential Status Use of Mobility Aids			
Disease-Specific Outcomes			
Parkinson's Disease	**Multiple Sclerosis**	**COPD**	**Hip Fracture**
Development of Dyskinesia Development of Freezing of Gait Dopaminergic medication use Development of postural instability Dementia	Relapses Lesions & Brain Volume	Exacerbations Lung Function Dyspnea/Breathlessness Cardiovascular Events Medication Usage	Hip score Bone mineral density Incidence of new fracture

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	
Limitations	20	Discuss the limitations of the scoping review process.	
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

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Walking-related digital mobility outcomes as clinical trial endpoint measures: Protocol for a scoping review

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Walking-related digital mobility outcomes as clinical trial endpoint measures: Protocol for a scoping review

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ABSTRACT

Introduction

Advances in wearable sensor technology now enable frequent, objective monitoring of real-world walking. Walking-related digital mobility outcomes (DMOs), such as real-world walking speed, have the potential to be more sensitive to mobility changes than traditional clinical assessments. However, it is not yet clear which DMOs are most suitable for formal validation. In this review, we will explore the evidence on discriminant ability, construct validity, prognostic value, and responsiveness of walking-related DMOs in four disease areas: Parkinson's disease, multiple sclerosis, chronic obstructive pulmonary disease, and proximal femoral fracture.

Methods and analysis

Arksey and O'Malley's methodological framework for scoping reviews will guide study conduct. We will search seven databases (Medline, CINAHL, Scopus, Web of Science, EMBASE, IEEE Digital Library, Cochrane Library) and grey literature for studies which (1) measure differences in DMOs between healthy and pathological walking, (2) assess relationships between DMOs and traditional clinical measures, (3) assess the prognostic value of DMOs, and (4) use DMOs as endpoints in interventional clinical trials. Two reviewers will screen each abstract and full-text manuscript according to predefined eligibility criteria. We will then chart extracted data, map the literature, perform a narrative synthesis, and identify gaps.

Ethics and dissemination

As this review is limited to publicly available materials, it does not require ethical approval. This work is part of Mobilise-D, an Innovative Medicines Initiative Joint Undertaking which aims to deliver, validate, and obtain regulatory approval for DMOs. Results will be shared with the scientific community and general public in cooperation with the Mobilise-D communication team.

Registration

Study materials and updates will be made available through the Center for Open Science's OSFRegistry (https://osf.io/k7395).

Keywords

Mobility, real-world walking speed, gait speed, gait variability, digital mobility outcome, wearable, digital biomarker, digital health, scoping review

BACKGROUND

For people living with chronic health conditions, walking impairment is associated with reduced quality of life,[1–4] disability progression,[1,5,6] fall risk,[7–9] hospitalisation,[10,11] and mortality.[10,11] Research is booming on therapies that can mitigate the high human and economic costs of walking impairment. However, before these therapies can be adopted in clinical practice, their efficacy must be established through controlled clinical trials. The endpoint measures used to assess these interventions' efficacy should be valid, sensitive, easy to administer, and representative of real-world function or behaviour.[12]

Strengths and limitations of this study

- This is the first scoping review to explore existing evidence on the discriminant ability, construct validity, prognostic value, and responsiveness of walking-related digital mobility outcomes.
- A broad review strategy enables identification of trends across methods and settings in four chronic conditions.
- A multidisciplinary team of clinicians, technologists, movement specialists, and epidemiologists from academia and industry will conduct this review.
- Terminology and methodology associated with gait assessments are diverse and fragmented, posing limitations for study identification and synthesis.
- Following scoping review guidelines, neither critical appraisal nor meta-analysis will be conducted, limiting our ability to assess the strength of existing evidence.

Unfortunately, current mobility measures pose critical limitations. Clinical trials traditionally employ two types of mobility assessments: patient reported outcome instruments (PROs) and clinical gait assessments. PROs enable patients to report perceptions of their own mobility in a standardised manner,[13] though results may be subject to recall bias.[14–16] Clinical assessments, such as timed walking tests, are typically more objective. However, many still require clinical interpretation and are subject to high inter-rater variability.[17,18] For example, Zhang et al. conducted a sensitivity analysis to demonstrate the potential impact of inter-rater variability in clinical trials by assessing a trial's primary outcome, the Expanded Disability Status Score (a common measure of function and ambulation in multiple sclerosis) in duplicate. [19] Duplicated ratings differed in over 30% of patients, affecting estimates of treatment effect. Additionally, clinical assessments are often infrequently acquired and may not be representative of real-world behaviour.[14,20,21] Compared to real-world walking, patients consistently walk faster and produce higher-quality gait patterns during "normal" walking in laboratory settings.[20,22,23] These challenges have prompted calls for more sensitive, reliable mobility measures in clinical trials.[21,24]

Advances in wearable sensor technology now enable frequent, objective mobility monitoring. Digital mobility outcomes (DMOs) such as gait speed, variability, and symmetry have been used to quantify real-world walking,[25–29] and emerging evidence suggests that they may be more sensitive to subtle changes than traditional instruments.[14,21,30–32] While a growing body of evidence supports this theory,[12,31,33,34] the validity of DMOs is not well established.[12,14,30] The field's fragmentation by disease area, technology, taxonomy, and methodology[14,27,35–39] currently limits our understanding of their potential. To date, no overarching view of the clinical utility of DMOs exists.[14] Thus, this study will map existing evidence on walking-related DMOs to assess their suitability for formal validation.

STUDY RATIONALE AND OBJECTIVES

This work is part of Mobilise-D, a research program sponsored by the European Union's Innovative Medicines Initiative Joint Undertaking, which aims to deliver, validate, and obtain regulatory approval for a suite of real-world DMOs.[40,41] This study will hone our understanding of the

contexts and purposes for which DMOs might be most effectively used as research instruments. Our primary objective is to map the evidence describing the discriminant ability, construct validity, prognostic value, and responsiveness of walking-related DMOs. We will focus on four disease areas: Parkinson's disease (PD), multiple sclerosis (MS), chronic obstructive pulmonary disease (COPD), and proximal femoral fracture (PFF). By mapping the literature and providing a narrative synthesis of our findings, we will identify which DMOs pose the greatest potential as clinical endpoints.

METHODS AND ANALYSIS

Protocol Structure

This study employs the scoping review methodology developed by Arksey and O'Malley[42] and advanced by Levac et al.[43] Arksey and O'Malley's framework describes six stages of scoping review conduct: 1) identifying the research question, 2) identifying relevant studies, 3) selecting studies, 4) charting the data, 5) collating, summarizing and reporting results, and 6) consulting with relevant stakeholders. In contrast to systematic reviews, which assess the literature to answer narrow research questions, scoping reviews explore a research topic from a broader perspective. They aim to map the state of evidence in a structured yet reflexive manner to identify research gaps or assess the feasibility of future systematic reviews.[42–44]

Here we present a harmonised review strategy stratified by research question (RQ) and population. This approach will allow us to explore the nuances of DMO research in individual disease areas while identifying overarching trends.

Stage 1: Identifying the Research Question

Research Questions

To be used as clinical trial endpoints, measures must be valid, clinically meaningful, and responsive to change. Preliminary searches revealed a highly fragmented body of literature, with no overarching review describing these characteristics. Therefore, this study will map the literature across four research questions (Box 1) in a set of walking-related DMOs (Table 1). Though DMOs have potential to be used in many disease areas, this study will focus on PD, MS, COPD, and PFF, (subsequently referred to as 'included populations'). The Mobilise-D consortium selected these disease areas as exemplars for DMO development due to their diverse aetiologies of mobility impairment, high public health burden, and existing evidence base. [26,45–47]

Box 1: Review Objective and Research Questions (RQs)

Objective: Map existing evidence describing the discriminant ability, construct validity, prognostic value, and responsiveness of walking-related digital mobility outcomes (DMOs)

- RQ1: What differences in DMOs have been identified between the four included populations and healthy controls?
- RQ2: What is the evidence on the associations between DMOs and clinically-relevant measures of physical function, health-related quality of life, symptoms, and disease severity in each of the included populations?
- RQ3: What is the evidence on the prognostic value of DMOs in each of the included populations?
- RQ4: In which contexts and for what purposes have DMOs been used as endpoints in controlled interventional studies in each of the included populations?

RQ1: Discriminant ability

First, we will explore DMOs' discriminant ability by identifying studies which compare healthy and pathological gait (Box 1, RQ1). In this analysis, we will map evidence describing differences in DMOs between people with one of the four target diseases and healthy controls. We hypothesise that differences in some, but not all, DMOs will emerge between healthy individuals and the four included populations.

RQ2: Construct Validity

We will then gather evidence informing the construct validity of DMOs. We hypothesise that DMOs will exhibit moderate to strong associations with measures that assess physical function, such as balance tests, and weaker associations with measures which are not directly related to physical function. To test this, we will map cross-sectional relationships (i.e., assessed across a study population at a single timepoint) between DMOs and clinically-relevant measures of disease severity, physical function, health-related quality of life, and other symptoms in each of the included populations.

RQ3: Prognostic value

Next, we will map the evidence that informs the prognostic value of DMOs (i.e., their ability to predict future health outcomes). We will do this by mapping longitudinal associations between DMOs measured at baseline and clinically-relevant health outcomes assessed at follow-up. We hypothesise that DMOs will exhibit prognostic value similar to that established for traditional measures of mobility.[10,48–50]

Table 1: Walking-related digital mobility outcomes included in this review*

Spatial Parameters
Step length (magnitude, variability, symmetry)
Stride length (magnitude, variability)
Step width (magnitude, variability)
Temporal Parameters
Cadence (magnitude, variability)
Step time (magnitude, variability, symmetry)
Stride time (magnitude, variability)
Stance time (magnitude, variability, symmetry)
Swing time (magnitude, variability, symmetry)
Single support time (magnitude, variability, symmetry)
Double support time (magnitude, variability)
Spatiotemporal Parameters
Gait speed (magnitude, variability)
Stride speed (magnitude, variability)
Volume of Walking
Walking time
Step count
Number/Duration of walking bouts

**A narrative definition of each parameter is provided in Supplement 1.*

RQ4: Responsiveness to intervention

Finally, we will gather evidence that informs the responsiveness of DMOs to intervention. We expect that the use of DMOs as endpoints in interventional studies will be rare.[34] However, we hypothesise that, when they are used, DMOs will be responsive to interventions which improve physical function or reduce mobility-limiting symptoms. To this end, we will map the use and responsiveness of DMOs as endpoints in controlled interventional studies.

Definitions and Study Scope

Preliminary searches revealed that an exhaustive review is infeasible due to inconsistent terminology and reporting practices. Thus, we do not necessarily intend to produce an exhaustive list of all previous studies. Instead, we will adopt a semi-structured approach to map clinically-relevant trends across this large, fragmented body of literature. To do this, we will limit some dimensions of study scope to lengthy lists (i.e., the DMOs, the measures assessed in RQ2, and the outcomes assessed in RQ3) and will apply basic quality thresholds (i.e., a minimum number of participants). This approach allows us to remain inclusive with regard to terminology and

methodology while ensuring feasibility. The decisions used to set this scope are described below. Because understanding of seemingly common terms differs across disciplines, defining the concepts addressed by this review was not trivial. Therefore, our operational definitions of key concepts such as "mobility," "walking," "real-world," and "digital mobility outcomes" are clearly defined in Box 2.

Mobility and Real-World Walking

According to the International Classification of Functioning, Disability, and Health (ICF), "mobility" is a complex concept, inclusive of both functional ability and social participation. "Walking" represents a distinct construct encompassed by this broader concept of mobility. In this review, we adhere to the definition of "walking" adopted by the Mobilise-D consortium (Box 2). Our ultimate aim is to explore the utility of DMOs to characterize "real-world" walking. However, until recently, studies on gait parameters were largely confined to clinical settings. While methodologically different, laboratory or clinic-based measurements may still provide insight into DMOs' potential as real-world

Box 2: Operational definitions of key concepts adopted for this review

► **Mobility**

According to the International Classification of Functioning, Disability, and Health (ICF), "mobility" is defined as *"moving by (a) changing body position or location or by transferring from one place to another, (b) by carrying, moving or manipulating objects, (c) by walking, running or climbing, and (d) by using various forms of transportation."*[66]

► **Walking**

Per the Mobilise-D consortium, *"Human walking is a method of locomotion and is defined as initiating and maintaining a forward displacement of the centre of mass in an intended direction involving the use of the two legs which provide both support and propulsion. The feet are repetitively and reciprocally lifted and set down whereby at least one foot is in contact with the ground at all times.*[67,68] *Walking with walking aids is included in this definition. Walking is made up of walking bouts and is equivalent to taking steps/stepping forward (thus stepping in place does not constitute walking) and is defined as starting from initial contact for the initial step until ending with full floor contact of the foot making the last step.*[69]*"*

► **Real-world walking**

Per the Mobilise-D consortium, *"'Real world' relates to the context in which walking takes place – that is free-living, unsupervised, uncontrolled, and non-standardised. As such, it is unscripted as there are no instructions to the subject. Real-world actions occur in non-simulated everyday situations in unconstrained environments with minimal consciousness of being tested. It is equivalent to actions at home or in the community over continuous periods of time.[23] … Real world walking is distinct from laboratory-based,*[70] *supervised (fully controlled and observed), and semi-controlled (walking 'freely' but with supervision) tests. It also is different from scripted or instructed walking, which can take place in the home or lab."*

► **Digital mobility outcomes**

Digital mobility outcomes are *digitally-measured mobility parameters used to assess an individual's health status*, such as spatiotemporal gait parameters, walking bout characteristics, and physical activity. In this case, "digital" measures refer to those objectively derived from electronic systems, as opposed to qualitative, paper-based, or self-reported measures.

► **Clinically-relevant measures and outcomes**

"Clinically-relevant" measures and outcomes as those that are routinely and broadly used either in clinical practice or in major pharmaceutical or epidemiological studies. "Measures" refer to instruments or tests that assess an aspect of a patient's health at a single point in time, while "outcomes" refer to identified changes in health status that result from the handling of a health problem.[71]

measures. Therefore, we will include walking-related DMOs measured in any setting, real-world or otherwise. This inclusive approach will also enable us to compare DMOs measured during real-world walking, supervised tests, and scripted walking.

Digital Mobility Outcomes

Theoretically, DMOs could include any digital measures encompassed by the ICF definition of "mobility." However, our scope will be limited to a set of 32 DMOs associated with walking, (Table 1) since walking is the primary focus of the Mobilise-D project. This list was compiled in consultation with mobility experts, technologists, and clinicians in the four disease areas. It includes spatiotemporal parameters characterized in three widely-accepted factor analyses of gait[51–54] and parameters associated with daily volume of walking. This list excludes nonlinear gait and dynamic balance measures, such as Lyapunov exponents[55,56] and detrended fluctuation analyses,[57] due to the emergent nature of their evidence base. Though we also consider digital measures of physical activity to be DMOs, physical activity measures indirectly related to walking, such as daily energy expenditure or activity intensity, are also out of scope. This is because physical activity represents a related, yet broader construct.[58–60]

Clinically-Relevant Measures and Outcomes

To ensure study scope remains clear and manageable, lists of included measures (46 general, 67 disease-specific) and outcomes (13 general, 16 disease specific) were defined a-priori in consultation with technical and clinical subject matter experts on the Mobilise-D research team. While these lists are not exhaustive, they contain the most important measures and outcomes used clinically in each of the four populations (Online Supplement 1). In alignment with the reflexive approach outlined by Arksey and O'Malley,[42] we defined a systematic method to amend these lists if additional instruments meeting these criteria are identified during study conduct.

Stage 2: Identifying Relevant Studies

This study will be conducted between November 2019 and December 2020. We will include peer-reviewed and grey literature, including journal articles, reports, research letters, conference papers, doctoral theses, and other publications reporting original results. MEDLINE, CINAHL, Scopus, Web of Science, EMBASE, IEEE Digital Library, and the Cochrane Library will be searched for eligible peer-reviewed literature. ACM Digital Library, ProQuest Dissertations, Open Grey, and the National Information Center's Health Services Research Projects in Progress Database will be searched to identify relevant grey literature. We will supplement these searches with the first 100 results on Google Scholar for each population, with results first sorted by relevance and then by time. Though we will limit studies based on availability of English-language abstracts, we will include full-text articles written in any language spoken by members of the Mobilise-D consortium. Additional sources will include manual searches of reference lists and publications from the review team's private libraries. Based on subject matter expert recommendations, the search will be limited to studies published during or after 1999. This time frame reflects advances in gait monitoring technology in the early 2000s and is supported by the findings of previous systematic reviews.[61–63]

Due to the diverse terminology associated with digital technologies and gait assessment, we opted for a broad search strategy which was agnostic to methodology or technology. This strategy was developed through collaboration between the research team and an experienced information specialist. Each search includes terms related to walking assessments and the four populations according to the structure (walking terms) AND (population terms). The proposed search strategy for EMBASE is provided in Online Supplement 2.

Study design, review conduct, records of de-duplication, reference exclusion, and individual author contributions will be managed in DistillerSR (Evidence Partners, Ottawa, Canada). Initially, references will be compiled in Endnote (Clarivate Analytics, Boston, USA), and the final review libraries will be compiled in Mendeley (Elsevier B.V., Amsterdam, The Netherlands), an open-access reference management software.

Stage 3: Study Selection

Study Selection Process

Study selection will include three steps: piloting, title and abstract screening, and full-text review. All reviewers will receive training on scoping review conduct prior to abstract screening. All reviewers will pilot eligibility criteria on a random set of 50 abstracts to ensure consistency. Clarifications will be made as necessary. Agreement with the lead reviewer (AP) will then be monitored on an additional 100 abstracts per reviewer at the onset of the screening process. In the full-text review stage, a similar process will be repeated on 15 full-text articles. Prior to screening, duplicate studies will be identified by comparing titles, authors, publication years, and abstracts. If additional duplicates are identified during full text review or data extraction, they will be excluded. Multiple sources reporting on the same study will be linked and analysed as one study during synthesis.

Up to three reviewers will independently screen each abstract for inclusion according to pre-defined eligibility criteria. Reviewers will use detailed reference sheets to ensure a uniform approach to screening (Online Supplement 3). Abstracts will proceed to full-text review if any single reviewer determines that it meets eligibility criteria. If the first reviewer includes the abstract, it will proceed automatically to full text review and will not undergo a second screening. Agreement of two reviewers will be required to exclude an abstract. In cases of high uncertainty, reviewers will be able to request a third screening by the lead reviewer (AP). Agreement will be assessed between each reviewer and the primary reviewer via Cohen's Kappa and as a group via Fleiss' Kappa. In contrast to Cohen's Kappa, which calculates agreement of two independent raters, Fleiss' Kappa statistic assesses reliability between any number of raters giving categorical ratings to a fixed number of items.[64] We anticipate that disease-specific knowledge will be necessary for full-text eligibility assessment. Thus, studies will be manually segmented by disease area during abstract screening. Consistent with the reflexive nature of scoping reviews, a second round of abstract screening may be conducted if additional eligibility criteria are identified during the study process or if disease-specific knowledge is required to assess abstract eligibility. This round will follow the same procedure as the original screening stage.

Two reviewers will then independently assess each full-text article for inclusion according to pre-defined eligibility criteria. Reason(s) for exclusion will be documented and agreement will be calculated. Reviewers will resolve disagreements through discussion. If no consensus can be reached, a senior team member will review the article and make the final determination.

Eligibility Criteria

To be included, studies must address one of our RQs with respect to an included DMO in one of our four populations. Detailed criteria and considerations regarding study design, included DMOs, and patient populations are provided below. We also provide operational definitions of "addressing a research question."

Study Design and Setting

Studies must present original data to be eligible for inclusion. To prevent crowding of results, we will also require that a minimum of 10 individuals per study arm are included in a relevant analysis. Though these two criteria naturally exclude reviews, case studies, and case series, any other design is theoretically eligible. However, not all study designs are capable of addressing all four RQs. Therefore, RQ-specific study design considerations are also provided as appropriate below. We will include studies and walking assessments conducted in any setting (laboratory, in-clinic, real-world, etc.).

DMOs, Technologies, and Methods

For reasons described above, this review will be limited to the DMOs summarised in Table 1. We will include DMOs produced through any digital or electronic measurement method, including wearable sensors, instrumented walkways or treadmills, optometric systems, force plates, mobile phones, stopwatches, and pedometers, among others. We will include DMOs measured during any test or walking condition that includes or simulates normal, over-ground walking. This includes walking at any speed (i.e., top-speed, self-selected, etc.), any start conditions (e.g., static start or rolling start), single-task or dual-task walking, straight or curvilinear walking, etc. Walking may be free or scripted, measured indoors or outdoors, supervised or unsupervised, on a treadmill, walkway, or over-ground on any course regardless of shape or length. Because traditional timed gait speed tests use stopwatches (an included technology) to measure gait speed (an included DMO), they will also be included. However, we will exclude testing conditions that purposefully alter participants' normal gait patterns, such as stepping in time to music. We will also exclude analyses limited to climbing, turning, and analyses of single steps, such as the recovery step after a push.

During pilots, these criteria were consistently interpreted in most cases. However, specific challenges arose regarding the eligibility of timed clinical assessments that include periods of walking. For example, some authors refer to the Timed Up and Go (TUG) test as a measure of gait speed. However, the TUG measures the time required to rise from a seated position, walk around a course, and return to a seated position.[65] In populations with mobility impairment, time spent standing and sitting may not be trivial. Thus, the TUG encompasses multiple constructs. To ensure consistency, it was necessary to define explicit eligibility criteria for common tests such as the TUG. These criteria were developed based on literature searches and in consultation with mobility experts (authors LR, JG, TT, MP, AY, LL, BS), and are described with rationale in Online Supplement 1. Generally, we will include timed gait speed tests, such as the 10-meter walk, but will exclude timed tests that aggregate or assess constructs other than gait speed. However, studies may still be included if DMOs were specifically assessed during the walking portions of excluded tests. For example, if the TUG was instrumented and gait speed or other DMOs were measured during the walking portion of the test, this analysis is included though the total time to complete the TUG is not.

Patient Populations

To be eligible, studies must include patients with a confirmed diagnosis of one of the four included conditions: PD, MS, COPD, and PFF. In this context, a "confirmed diagnosis" is one made by a clinician based on the relevant diagnostic criteria at the time of the study's publication. Further detail is provided in Online Supplement 1. No eligibility criteria on age range, disease severity level, or sub-type will be applied except for PFF populations, which will be limited to adults 65 years of age or older. Studies with mixed populations will also be included if a sub-analysis is conducted on an included population.

Addressing a Research Question

Though we do not pose specific methodological requirements for inclusion, not all statistical methods and study designs are capable of addressing each RQ. For example, case-control designs cannot assess responsiveness to intervention (RQ4), though they can be used to compare pathological and healthy gait (RQ1) and assess relationships between DMOs and clinically-relevant measures (RQ2). In light of these methodological distinctions, each of our RQs could be viewed as separate – though highly inter-related – reviews, harmonized under a common strategy. With this in mind, we will map the literature separately for each RQ and must therefore set specific criteria to determine whether studies address a RQ.

Studies will be eligible to address RQ1 if they compare an included DMO between healthy controls and one of the included populations. No other RQ-specific eligibility criteria will be applied.

Studies will be eligible to address RQ2 if they assess the relationship between an included DMO and an included measure in one of the four populations at a single timepoint (i.e., a cross-sectional analysis). The list of included measures, defined a-priori, is comprised of widely-used measures of disease severity, health-related quality of life, physical function, cognition, mental health, and other factors (Online Supplement 1). We will include any type of statistical or qualitative analysis and set no specific study design requirements, since such an analysis could be conducted within any study design.

Studies will be eligible to address RQ3 if they assess a relationship between an included DMO measured at baseline and an included outcome assessed at follow-up (i.e., a longitudinal analysis). Included outcomes are described in Online Supplement 1. Studies must be longitudinal to address this RQ, though we set no further criteria on the basis of methodology or study duration.

Studies will be eligible to address RQ4 if they use an included DMO as an endpoint in a controlled interventional study in an included population. Published protocols of controlled trials will be indexed for future analysis. Studies will not be excluded on the basis of intervention type, duration or follow-up frequency. We will exclude uncontrolled studies from this RQ, since they are particularly susceptible to placebo effect and other biases. However, uncontrolled interventional studies may still be included in the review if they conduct an analysis which addresses any of the other RQs. We pose no other methodological criteria for RQ4.

At the abstract stage, studies will be included in full-text review if they *could possibly* have conducted an included analysis, since relevant analyses are not consistently reported at the abstract level. Analyses addressing each RQ will be identified during full-text screening.

Addressing Unforeseen Eligibility Criteria

Arksey and O'Malley's framework specifically allows for flexibility in the review process,[42] as appropriate scope and eligibility criteria may not be initially clear when reviewing a previously unmapped research area. As research on gait is rapidly evolving, it may be necessary to adjust our eligibility criteria and lists of included walking conditions, measures, and outcomes. If initial findings warrant adjustments, a proposal will be submitted to a team of project leads who will make the final determination on how to adjust eligibility criteria. Adjustments will be applied to all identified studies and reported accordingly.

Stage 4: Charting the Data

Data Extraction

Data collection forms will be developed through iterative review with the research team and further refined through expert feedback. Forms will capture all relevant study data and contextual information while ensuring adequate flexibility to capture emerging themes. Prior to initiating data extraction, the form will be tested by reviewers on a random sample of at least five studies. Additional modifications to the form identified through this pilot will be reviewed and approved by the research team.

Data extraction will be conducted independently by two reviewers in DistillerSR. A preliminary set of data items is included in Table 2, which will be further specified following feedback from the disease-specific review groups. Studies' corresponding authors will be contacted if clarification is required. Disagreements will be resolved through discussion. If no consensus can be reached, a third, senior member of the research team will make the final determination.

Revising Data Items

If additional relevant data items are identified during the review process, they will be submitted to the team of project leads to decide whether and how to adjust the data extraction form. If included, the new data items will be extracted from all included studies.

Table 2: Preliminary data items to extract

Data Items	Associated Questions
Publication Details (All research questions)	
Authors & Affiliations	Who conducted the research?
Type	In what type of literature was the study published? (Journal, grey literature, conference abstract, etc.)
Year	When was the study published?
Country/Region	In which geographic region(s) did the study take place?
General Details (All research questions)	
Study Design	What was the study's design?
Study Aims	What were the study's aims?
Population	What population was studied? Were there any specific inclusion/exclusion criteria such as disease severity, subtype, or age?
Study Size	How many people participated in the study?
Included DMOs	Which DMOs were measured? How and in what setting were the DMOs measured?
Research Question 1	
Study Design	Were patients and controls matched or are the groups comparable with respect to appropriate criteria (height, age, sex, etc.)? Was gait analysis controlled for gait speed? Did the study focus on a specific subgroup or population?
Differences in DMOs	What differences in DMOs occurred (or did not occur) between the four included populations and healthy controls? Did these differences reach statistical significance?
Research Question 2	
Analytical Methods	How did the authors measure the relationship between clinically-relevant measures and DMOs? What association measure was used?

Clinically-Relevant Measures	What clinically-relevant measures were studied?
Relationship Strength	What was the strength of the reported relationship between the measure and the DMO? Was the association statistically significant?
Research Question 3	
Model Description	Does the study report a multivariate analysis, a prediction model, a model based on machine-learning, etc.? Which co-variates were included in the model? Which analytical methods were used?
Clinically-Relevant Outcomes	What clinically-relevant outcomes were studied to assess the DMO's prognostic value?
Prognostic Value	Did the DMO provide prognostic value with respect to the studied outcome?
Research Question 4	
Intervention type	What intervention was studied?
Study Endpoints	Was the DMO used as a primary, secondary, or exploratory endpoint? What other primary, secondary, and exploratory endpoints were measured?
Success	Was there a change in the primary endpoint between groups?
Ability to Detect Change	Was the DMO able to detect a change due to the intervention (if a change occurred)?

Stage 5: Collating, Summarizing, and Reporting the Results

The evidence addressing each research question will be mapped and analysed through narrative synthesis. Findings will be compiled in tables and figures where appropriate. Narrative synthesis will also be used to make comparisons between populations, disease subtypes, and measurement conditions. We will also identify gaps in the evidence to inform areas of future research. Reporting will adhere to the PRISMA-ScR reporting guidelines for scoping reviews[44] with the exception of risk of bias and evidence strength assessments, which are not mandatory and will not be conducted in this study.[42–44]

Stage 6: Consultation

Levac et al. recommend that research teams involve stakeholders throughout review conduct, as stakeholders can provide nuanced insights beyond those reported in the literature.[43] The long-term goal of Mobilise-D is to validate and qualify DMOs that can be used to assess mobility in clinical trials. While such an undertaking involves a number of diverse stakeholders, the present work could be most influenced by the perspectives of industry, patients, and clinical researchers.

Patient and Public Involvement

Mobilise-D's pharmaceutical industry partners, patient advisory board, and scientific advisory board will be consulted during review conduct and data analysis. Industry partners reviewed the research questions to ensure relevance for clinical trials and regulatory qualification. Patients were not directly involved in the design of this review. However, the Mobilise-D patient advisory board and scientific advisory board will be engaged during data analysis and reporting to ensure analyses align with the priorities of those groups.

Discussion and Limitations

Current literature on DMOs represents a diverse set of research perspectives, resulting in a rich – though fragmented – body of literature. Therefore, we devised a broad review strategy, attempting to map the literature across clinical and technological divides. However, this strategy raises challenges of feasibility; our searches yielded tens of thousands of references. Though carefully designed, these searches may still be limited due to inconsistent terminology and reporting practices. Due to our broad strategy, we expect a high degree of heterogeneity in our results. Though challenging, this heterogeneity is also a strength, as it enables us to compare DMOs measured with various technologies under diverse walking conditions. Therefore, we pre-defined some of the relationships we intend to map (i.e., the DMOs, measures, and outcomes) while leaving other aspects of our scope open (i.e., methodology, walking condition, setting). We have also applied minimal criteria such as study size, excluding the smallest studies which would crowd results. Where appropriate, we will carefully employ the reflexive strategies afforded by scoping review methodology to ensure that the items defined a-priori do not impart bias. For these reasons, this study should be interpreted as identifying clinically-relevant trends within the existing literature, rather than as an exhaustive review. We will not conduct critical appraisal or meta-analysis, limiting our ability to assess the strength of existing evidence. However, we will identify topics ripe for systematic review, which should be conducted in future work.

ETHICS AND DISSEMINATION

Since our review is limited to publicly available materials, this study does not require ethical approval. Results will be used to prioritise research questions that will be addressed in the Mobilise-D consortium's future work. In addition to publishing our findings, we will partner with Mobilise-D's communications team to facilitate knowledge sharing on web-based platforms for both academic and industrial audiences. To increase transparency, review materials will be made publicly available at https://osf.io/k7395 through the Center for Open Science's OSFRegistry.

Authors' contributions: AP, AF, MAP, CB, JGA, LR, and CM devised study scope and research questions. AP, RB, MBB, GB, SB, NC, GDC, LDO, HD, KE, JGA, HG, CH, NH, JK, FK, SK, LL, WM, MEMA, ASM, PP, FS, CS, LS, KS, BS, KT, TT, BV, IV, AJY, CM, CB, LR, MAP, and AF contributed to study design. AP wrote and edited the manuscript. AF and MAP supervised study conduct. AP, RB, MBB, GB, SB, NC, GDC, LDO, HD, KE, HG, CH, FK, SK, LL, MEMA, ASM, FS, LS, KS, KT, and BV will review references and extract data. All authors approved of the final manuscript.

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SUPPLEMENTARY FILES

- Online Supplement 1: Eligibility criteria - details, definitions, and rationale
- Online Supplement 2: Proposed search strategy
- Online Supplement 3: Screening reference sheets and forms

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Online Supplement 1: Eligibility criteria – details, definitions, and rationale

Table of Contents

Walking-Related Digital Mobility Outcome Definitions

The following set of gait and walking parameters will be included in the map and subsequent analysis produced in this scoping review. This list includes spatiotemporal parameters included in three well-known factor analyses of gait [1–3] (Table 1) and parameters associated with volume of walking which were prioritized by clinical and technical subject matter experts involved in the Mobilize-D project (Table 2). In keeping with the reflexive nature of scoping reviews, this list may be amended based on initial search findings as described in the study protocol.

Definitions adopted by the Mobilise-D Consortium:

- Human ***walking*** is a method of locomotion and is defined as initiating and maintaining a forward displacement of the centre of mass in an intended direction involving the use of the two legs which provide both support and propulsion. The feet are repetitively and reciprocally lifted and set down whereby at least one foot is in contact with the ground at all times.[4,5] ***Walking*** with walking aids is included in this definition. ***Walking*** is made up of ***walking bouts*** and is equivalent to taking steps/stepping forward (thus stepping in place does not constitute walking) and is defined as starting from initial contact for the initial step until ending with full floor contact of the foot making the last step.[6]
- A ***step*** is the interval between the initial contacts of the ipsi- and contralateral foot[4] and corresponds to the forward displacement of the foot together with a forward displacement of the trunk.[6]
- A ***stride*** is the interval between two successive initial contacts of the same foot. As such, a ***stride*** is equivalent to the gait cycle and every stride contains two ***steps.***[4]

Table 1: Gait parameters included in the review

Gait Parameter (Unit)	Narrative Definition	Dimension
Spatial Parameters		
Step length (cm)	Typically defined as the anterior-posterior distance from the heel of one footprint to the heel of the opposite footprint.[3] For the purposes of this review, step length may also be measured between the toes or other identifiable markers on opposite footfalls.	Mean, variability, asymmetry
Stride length (cm)	Typically defined as the anterior-posterior distance between heels of two consecutive footprints of the same foot (left to left, right to right); two steps (e.g., a right step followed by a left step) comprise one stride or one gait cycle.[3] For the purposes of this review, stride length may also be measured between the toes or other identifiable markers on consecutive footfalls.	Mean, variability

Step width (cm)	The lateral distance from heel center of one footprint to the line of progression formed by two consecutive footprints of the opposite foot.[3] For the purposes of this review, step width may also be measured between the toes or other identifiable markers on opposite footfalls.	Mean, variability
Temporal Parameters		
Cadence (steps/min)	Cadence is the number of steps per minute, sometimes referred to as step rate or frequency[3]	Mean, variability
Step time (s)	Time elapsed from initial contact of one foot to initial contact of the opposite foot [3]	Mean, variability, asymmetry
Stride time (s)	Time elapsed between the initial contacts of two consecutive footfalls of the same foot [3]	Mean, variability
Stance time (s, % of gait cycle)	The stance phase is the weight bearing portion of each gait cycle initiated at heel contact and ending at toe off of the same foot; stance time is the time elapsed between the initial contact and the last contact of a single footfall [3]	Mean, variability, asymmetry
Swing time (s)	The swing phase is initiated with toe off and ends with initial contact of the same foot; swing time is the time elapsed between the last contact of the current footfall to the initial contact of the next footfall of the same foot [3]	Mean, variability, asymmetry
Single support time (s, % of gait cycle)	Single support occurs when only one foot is in contact with the ground; single support time is the time elapsed between the last contact of the opposite footfall to the initial contact of the next footfall of the same foot [3]	Mean, variability, asymmetry
Double support time (s, % of gait cycle)	Double support occurs when both feet are in contact with the ground simultaneously; double support time is the sum of the time elapsed during two periods of double support in the gait cycle [3]	Mean, variability
Spatiotemporal Parameters		
Gait/Walking Speed (cm/s)	Walking speed is the distance covered by the whole body within a certain time interval / per unit time of walking. It is measured in meters per second and is the magnitude of the velocity vector (velocity includes direction and magnitude of walking). [5]	Mean, variability
Stride Speed (cm/s)	Stride speed is the distance covered by the whole body within a single stride per unit time of walking.	Mean, variability

Table 2: Parameters Assessing Volume of Walking

Mobility Parameter	Definition
Daily Volume of Walking	
Walking time	The amount of time spent walking during a set period of time. Walking is made up of walking bouts and is equivalent to taking steps/stepping forward and is defined as starting from initial contact for the initial step until ending with full floor contact of the foot making the last step [6]
Step Count	The number of steps made during a set period of time, such as a day or walking bout. A *step* is the interval between the initial contacts of the ipsi- and contralateral foot.[4]
Number, duration, or distance of walking bouts	A ***walking bout*** (WB) is a walking sequence containing at least two consecutive strides of both feet (e.g. *R-L-R-L-R-L* or *L-R-L-R-L-R*). Start and end of a walking bout are determined by a resting period or any other activity (non-walking period). The initial step of a WB follows a non-walking period and the final step precedes the next non-walking period.

Population Definitions

Parkinson's Disease

Proposed definition

People who have received a confirmed diagnosis of Parkinson's Disease by a professional physician based on the relevant diagnostic criteria at the time of the study's publication. Studies including participants with any age range and disease severity level will be included in this review.

Relevant Diagnostic Criteria may include, but are not limited to:

- New International Parkinson Disease and Movement Disorder Society Diagnostic Criteria (Postuma, Mov Dis 2015)
- Gelb's Criteria (National Institute of Neurological Disorders and Stroke) (Gelb, JAMA Neurology, 1999)
- Queen's Square Brain Bank/UK Parkinson's Disease Society Brain Bank Diagnostic Criteria (Hughes, J Neurol Neurosurg Psychiatry, 1992)

Population Exclusion Criteria

Studies of persons with atypical parkinsonian syndromes, drug-induced parkinsonism, or vascular parkinsonism are not included under these diagnostic criteria.

Multiple Sclerosis

Proposed definition

People who have received a confirmed diagnosis of Multiple Sclerosis (MS) by a professional physician based on the relevant diagnostic criteria at the time of the study's publication. Studies including participants with any age range, severity level or sub-type of Multiple Sclerosis will be included in this review.

Relevant Diagnostic criteria may include, but are not limited to:

- McDonald diagnostic criteria (McDonald, Ann Neurol, 2001), including the 2005, 2010, and 2017 revisions
- Poser diagnostic criteria (Poser, Ann Neurol, 1983)
- MAGNIMS consensus guidelines: MRI criteria for the diagnosis of MS (Filippi, Lancet Neurology, 2016)
- Defining the clinical course of multiple sclerosis; The 2013 revisions (Lubin et al, 2014)

Population Exclusion Criteria

Studies of persons experiencing or exhibiting clinically isolated syndrome (CIS), Neuromyelitis Optica Spectrum Disorder (NMOSD), Myelin oligodendrocyte glycoprotein (MOG), or Acute disseminated encephalomyelitis (ADEM) will be excluded. No additional exclusion criteria will be applied.

Proximal Femoral Fracture

Proposed definition

We will include older people (≥ 65 years of age) who have received surgical treatment (fixation or arthroplasty) for a low-energy fracture of the proximal femur. Both (intracapsular (also termed subcapital and transcervical) fractures or extracapsular (also termed trochanteric, intertrochanteric, pertrochanteric and subtrochanteric) fractures will be included.

Relevant diagnostic criteria may include, but are not limited to:

- ICD-10 diagnosis S72.0, S72.1, S72.2 as diagnosed on X-rays of the hip and pelvis

Population Exclusion Criteria

Studies of persons that do not meet the proposed definition of the target population will be excluded. No additional exclusion criteria will be applied.

Chronic Obstructive Pulmonary Disease

Proposed definition:

People who have received a confirmed diagnosis of Chronic Obstructive Pulmonary Disease (COPD). In this context a "confirmed diagnosis" is defined as a diagnosis made by a professional physician based on the relevant diagnostic criteria at the time of the study's publication. Studies including participants with any age range, severity level or sub-type of COPD will be included in this review.

Relevant diagnostic criteria may include, but are not limited to:

Patients with a diagnosis of chronic obstructive pulmonary disease (COPD), defined by spirometry. Any definition of COPD will be accepted as long as it is based on spirometry. For example, current guidelines recommend FEV1/FVC <0.7 and FEV1 in % predicted <80%.

Population Exclusion Criteria

Studies of persons that do not meet the proposed definition of the target population will be excluded. No additional exclusion criteria will be applied.

Clinically-Relevant Measures included in Research Question 2

The following set of "clinically-relevant" measurements, summarized in Table 1, will be included in the map and analysis associated with Research Question 1 in the Mobilise-D scoping review. The general measurements will be included in all disease-area sub-analyses, while disease-specific measurements will be included only in disease-specific analyses. In keeping with the reflexive nature of scoping reviews, this list may be amended based on initial search findings as described in the study protocol.

Definitions

For the purposes of our review, "measurements" will refer to instruments or tests that assess an aspect of a patient's health at a single point in time, while "outcomes" refer to identified changes in health status that result from the handling of a health problem. We will define "clinically-relevant" measurements as those that are routinely and broadly used in either clinical practice or in major pharmaceutical or epidemiological studies.

Excluded Measurement Categories

We will exclude additional categories that are unlikely to provide additional information on the construct validity of gait and walking parameters, even if they are relevant to our included disease areas. However, some of these categories will be included in Research Question 3, allowing us to explore the relationship between these constructs and gait and walking parameters. These categories are:

- Sleep
- Life space
- Comorbidities
- Pain
- Frailty (Lack of common definition or method of testing frailty will limit any assessment of the DMOs' construct validity)
- Hospital re-admissions and longitudinal outcome measures not assessible through cross-sectional study designs

Included Measurements

Included measurements are summarized as acronyms in Table 3 and listed in the order which they appear with full titles in Table 4.

Table 3: Summary of included clinically-relevant measurements by category and disease area. Disease areas include Parkinson's disease (PD), multiple sclerosis (MS), chronic obstructive pulmonary disease (COPD), and proximal femoral fracture (PFF). Instrument names are provided in full in Table 4.

Category		All disease areas	PD	MS	COPD	PFF
Disease Severity & Symptoms		CGI, PGI	(MDS)-UPDRS – total, I, II, III, IV H&Y, RDRS, UDysRS, FoGQ, nFoGQ	EDSS, FSS, MSFC, Number of relapses PDDS, GNDS, SNRS	GOLD A-D, MMRC, Dyspnea (VAS, Borg) # Exacerbations	Harris Hip Score Oxford Hip Score
Physiological Measurements				Number/volume of lesions Brain volume BWCS, BLCS, IVIS	FEV1, FVC FEV1/FVC Ratio	
Functional Status/ADL		Barthel Index Nottingham EADL IADL, LLFDI	Schwab & England MDS-UPDRS – II, SPDDS, SPES, PROMIS, Neuro-QoL	Schwab & England MSIS-29		
HRQoL		EQ-5D (5L or 3L), EQ-VAS, SF-36 (RAND), SF-12, HUI3, LSQ	PDQ-8, 10 or 39	MSQoL-54 MSQLI, FAMS	CAT, CRQ, SGRQ, CCQ Feeling Thermometer	
Depression & Anxiety		HADS, Beck, CES-D, GDS, SDS/Zung, PHQ (2, 8, or 9), MHI	LARS			
Cognition		MMSE, MoCA, SDMT PASAT, CANTAB, CAMCOG-R,	RBANS, ACE-R, PD-CRS, Trail Making Test, Digit Span Stroop Color and Word Test	ACE-R, PDQ, BICAMS	*Not relevant*	
Falls		FES-I, Incidence of falls				
Physical Function	Walking or Functional Assessments	6MWT, TUG, STS, SPPB		MSWS-12	ISWT, ESWT	CAS
	Motor Function & Balance	ABC, Berg Balance, FAB, BESTest, mini-BESTest Ambulation Index (AI)	360 degree (fast) turn test	9-HPT (MSFC) Disease Step		
	Physical Activity	IPAQ, PASE			PROactive	
	Strength	Quadriceps, Leg press, Grip				Hip abduction Knee extension
	Fatigue	FIS, mFIS, FSS, FACIT	PFS-16			

Table 4: Summary of included clinically-relevant measurements by category and disease area.

Disease area	Category	Acronym	Full Name(s)
A - All	01 - Disease Severity	CGI	Clinical Global Impression Score
A - All	01 - Disease Severity	PGI	Patient Global Impression Score
A - All	02 - Functional Status/ADL	Barthel	Barthel Index
A - All	02 - Functional Status/ADL	LLFDI	Late Life Function & Disability Instrument
A - All	02 - Functional Status/ADL	IADL	Lawton Instrumental Activities of Daily Living Scale
A - All	02 - Functional Status/ADL	EADL	Nottingham (Extended) Activities of Daily Living Scale
A - All	03 - HRQoL	EQ-5D (5L or 3L)	EuroQoL 5 Dimensions
A - All	03 - HRQoL	EQ-VAS	EuroQoL Visual Analog Scale
A - All	03 - HRQoL	HUI3	Health Utilities Index Mark 3
A - All	03 - HRQoL	LISAT-9, LSQ	Life Satisfaction Questionnaire
A - All	03 - HRQoL	SF-12, RAND	Short Form 12 Health Survey
A - All	03 - HRQoL	SF-36	Short Form 36 Health Survey
A - All	03 - HRQoL	SF-36 MCS	Short Form 36 Mental Component Scale
A - All	03 - HRQoL	SF-36 PCS	Short Form 36 Physical Component Scale
A - All	04 - Mental Health	BDI, Beck	Beck Depression Inventory
A - All	04 - Mental Health	CES-D	Center for Epidemiologic Studies Depression Scale
A - All	04 - Mental Health	GDS	Geriatric Depression Scale
A - All	04 - Mental Health	HADS	Hospital Anxiety and Depression Scale
A - All	04 - Mental Health	MHI	Mental Health Inventory
A - All	04 - Mental Health	PHQ	Patient Health Questionnaire 8 or 9
A - All	04 - Mental Health	SDS, Zung	Zung Self-Rating Depression Scale
A - All	05 - Cognition	CAMCOG-R	Cambridge Cognitive Assessment (Revised)
A - All	05 - Cognition	CANTAB	Cambridge Neuropsychological Test Automated Battery
A - All	05 - Cognition	MMSE	Mini-Mental State Examination
A - All	05 - Cognition	MoCA	Montreal Cognitive Assessment

A - All	05 - Cognition	PASAT	Paced Auditory Serial Addition Test
A - All	05 - Cognition	SDMT	Symbol Digit Modalities Test
A - All	06 - Falls	FES-I	Falls Self-Efficacy Scale - International
A - All	06 - Falls		Incidence of falls
A - All	07 - Walking or Functional Assessments	2MWT	2 Minute Walk Test
A - All	07 - Walking or Functional Assessments		4 to 10 meter walk (i.e., any straight walking test between 4-10 meters in length)
A - All	07 - Walking or Functional Assessments	6MWT	6 Minute Walk Test
A - All	07 - Walking or Functional Assessments	SPPB	Short Physical Performance Battery
A - All	07 - Walking or Functional Assessments	STS	Sit to Stand Test
A - All	07 - Walking or Functional Assessments	T25FW	Timed 25 Foot Walk
A - All	07 - Walking or Functional Assessments	TUG	Timed Up & Go
A - All	08 - Motor Function & Balance	ABC	Activities-Specific Balance Confidence Scale
A - All	08 - Motor Function & Balance	AI	Ambulation Index
A - All	08 - Motor Function & Balance	BESTest	Balance Evaluation Systems Test
A - All	08 - Motor Function & Balance	BBS	Berg Balance Scale
A - All	08 - Motor Function & Balance	FAB	Fullerton Advanced Balance Scale
A - All	08 - Motor Function & Balance	mini-BESTest	Mini-Balance Evaluation Systems Test
A - All	09 - Physical Activity	IPAQ	International Physical Activity Questionnaire
A - All	09 - Physical Activity	PASE	Physical Activity Scale for the Elderly
A - All	10 - Strength		Grip Strength
A - All	10 - Strength		Leg Press Strength

A - All	10 - Strength		Quadriceps Strength
A - All	11 - Fatigue	FIS, mFIS	(modified) Fatigue Impact Scale for Daily Use
A - All	11 - Fatigue	FSS	Fatigue severity scale
A - All	11 - Fatigue	MFIS	MS fatigue impact scale
B - Parkinson's	01 - Disease Severity	(MDS)-UPDRS - I	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, subscore I
B - Parkinson's	01 - Disease Severity	(MDS)-UPDRS - III	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, subscore III
B - Parkinson's	01 - Disease Severity	(MDS)-UPDRS - IV	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, subscore IV
B - Parkinson's	01 - Disease Severity	(MDS)-UPDRS Total	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, sum of all subscores (I, II, III, and IV)
B - Parkinson's	01 - Disease Severity	FOGQ	Freezing of Gait Questionnaire
B - Parkinson's	01 - Disease Severity	H&Y	Hoehn & Yahr Score
B - Parkinson's	01 - Disease Severity	nFOGQ	New Freezing of Gait Questionnaire
B - Parkinson's	01 - Disease Severity	RDRS	Rush Dyskinesia Rating Scale
B - Parkinson's	01 - Disease Severity	UDysRS	Unified Dyskinesia Rating Scale
B - Parkinson's	02 - Functional Status/ADL	(MDS)-UPDRS - II	(Movement Disorder Society) Unified Parkinson's Disease Rating Scale, subscore II
B - Parkinson's	02 - Functional Status/ADL	NeuroQoL	Neuro QoL Physical Function
B - Parkinson's	02 - Functional Status/ADL	PROMIS	Patient-Reported Outcome Measurement Information System (ADL test)
B - Parkinson's	02 - Functional Status/ADL	SE-ADL	Schwab & England Activities of Daily Living Scale
B - Parkinson's	02 - Functional Status/ADL	SPDDS	Self-Assessment Parkinson's Disease Disability Scale
B - Parkinson's	02 - Functional Status/ADL	SPES	Short Parkinson's Evaluation Scale
B - Parkinson's	03 - HRQoL	PDQ-39, PDQ-8, PDQ-10	Parkinson's Disease Questionnaire - 39 or 8 or 10
B - Parkinson's	04 - Mental Health	LARS	Lillie Apathy Rating Scale
B - Parkinson's	05 - Cognition	ACE-R	Addenbrooke's Cognitive Examination (Revised)

B - Parkinson's	05 - Cognition		Digit Span
B - Parkinson's	05 - Cognition	PD-CRS	Parkinson's Disease Cognitive Rating Scale
B - Parkinson's	05 - Cognition	RBANS	Repeatable battery for the assessment of neuropsychological status
B - Parkinson's	05 - Cognition	Stroop	Stroop Color and Word Test
B - Parkinson's	05 - Cognition	TMT	Trail Making Test
B - Parkinson's	08 - Motor Function & Balance		360 Degree (Fast) Turn Test
B - Parkinson's	11 - Fatigue	PFS-16	Parkinson's Fatigue Scale
C - Multiple Sclerosis	01 - Disease Severity	EDSS	Kurtzke Expanded Disability Status Scale
C - Multiple Sclerosis	01 - Disease Severity	FSS	Kurtzke Functional Systems Scores
C - Multiple Sclerosis	01 - Disease Severity	MSFC	Multiple Sclerosis Functional Composite
C - Multiple Sclerosis	01 - Disease Severity		Number of Relapses
C - Multiple Sclerosis	01 - Disease Severity	PDSS	Patient Determined Disease Steps
C - Multiple Sclerosis	01 - Disease Severity	GNDS	Guy's Neurological Rating Scale
C - Multiple Sclerosis	01 - Disease Severity	SNRS	Scripps Neurological Rating Scale
C - Multiple Sclerosis	02 - Functional Status/ADL	SE-ADL	Schwab & England Activities of Daily Living Scale
C - Multiple Sclerosis	02 - Functional Status/ADL	MSIS-29	Miultiple Sclerosis Impact Scale - 29
C - Multiple Sclerosis	02 - Functional Status/ADL	MSQOL-54	MS Quality of Life - 54
C - Multiple Sclerosis	03 - HRQoL	MSQLI	MS Quality of Life Inventory
C - Multiple Sclerosis	03 - HRQoL	FAMS	Functional Assessment of Multiple Sclerosis
C - Multiple Sclerosis	03 - HRQoL	ACE-R	Addenbrooke's Cognitive Examination (Revised)
C - Multiple Sclerosis	05 - Cognition	PDQ	Perceived Deficits Questionnaire
C - Multiple Sclerosis	05 - Cognition	BICAMS	Brief International Cognitive Assessment for MS
C - Multiple Sclerosis	07 - Walking or Functional Assessments	MSWS-12	Multiple Sclerosis Walking Scale - 12
C - Multiple Sclerosis	08 - Motor Function & Balance	9-HPT	9-Hole Peg Test
C - Multiple Sclerosis	08 - Motor Function & Balance	DS	Disease Step

C - Multiple Sclerosis	12 - Physiological Measurements		Number of lesions
C - Multiple Sclerosis	12 - Physiological Measurements		Volume of lesions
C - Multiple Sclerosis	12 - Physiological Measurements		Brain volume
C - Multiple Sclerosis	12 - Physiological Measurements	BWCS	Bowel Control Scale
C - Multiple Sclerosis	12 - Physiological Measurements	BLCS	Bladder Control Scale
C - Multiple Sclerosis	12 - Physiological Measurements	IVIS	Impact of Visual Impairment Scale
D - COPD	1 - Disease Severity	GOLD A-D	Global Initiative for Chronic Obstructive Lung Disease Stages A-D
D - COPD	1 - Disease Severity	MMRC	Modified Medical Research Council Dyspnea Scale
D - COPD	1 - Disease Severity	Dyspnea VAS	Dyspnea Visual Analog Scale
D - COPD	1 - Disease Severity	Dyspnea Borg	Dyspnea Borg Scale
D - COPD	1 - Disease Severity		Number of Exacerbations
D - COPD	12 - Physiological Measurements	FEV1	Forced Expiratory Volume 1%
D - COPD	12 - Physiological Measurements	FVC	Functional Vital Capacity
D - COPD	12 - Physiological Measurements	FEV1/FVC	Forced Expiratory Volume to Functional Vital Capacity Ratio
D - COPD	03 - HRQoL	CAT	COPD Assessment Test
D - COPD	03 - HRQoL	CRQ	Chronic Respiratory Disease Questionnaire
D - COPD	03 - HRQoL	SGRQ	St. George's Respiratory Questionnaire
D - COPD	03 - HRQoL	CCQ	Clinical COPD Questionnaire
D - COPD	03 - HRQoL	FT	Feeling Thermometer
D - COPD	07 - Walking or Functional Assessments	ISWT	Incremental Shuttle Walk Test

D - COPD	07 - Walking or Functional Assessments	ESWT	Endurance Shuttle Walk Test
D - COPD	09 - Physical Activity	PROactive	PROactive instruments to measure physical activity
E - PFF	1 - Disease Severity	HHS	Harris Hip Score
E - PFF	1 - Disease Severity	OHS	Oxford Hip Score
E - PFF	7 - Walking or Functional Assessments	CAS	Cumulated Ambulation Score
E - PFF	10 - Strength		Hip abduction strength
E - PFF	10 - Strength		Knee Extension strength

Clinically-Relevant Outcomes Included in Research Question 3

The following set of "clinically-relevant" outcomes will in included in the map and analysis associated with Research Question 3 in the Mobilise-D scoping review. The general outcomes will be included in all population sub-analyses, while population-specific outcomes will be included only in population-specific analyses. In keeping with the reflexive nature of scoping reviews, this list may be amended based on initial findings as described in the protocol.

Definitions

In this review, "outcomes" refer to identified changes in health status that result from the handling of a health problem. "Clinically-relevant" measurements and outcomes as those that are routinely and broadly used in either clinical practice or in major pharmaceutical or epidemiological studies.

Table 5: Summary of Included Clinically-Relevant Outcomes

General Outcomes: All disease areas			
Disease/Disability Status or Progression Health-Related Quality of Life Mortality Healthcare Utilization (e.g., hospitalizations, readmissions, home care, costs, invasive procedures, etc.) Physical Function (e.g., exercise capacity, motor function, balance, strength) Functional Status (e.g., activities of daily living) Fatigue Cognition Mental Health (e.g., depression, anxiety, apathy) Falls Life Space Residential Status Use of Mobility Aids			
Disease-Specific Outcomes			
Parkinson's Disease	**Multiple Sclerosis**	**COPD**	**Hip Fracture**
Development of Dyskinesia Development of Freezing of Gait Dopaminergic medication use Development of postural instability Dementia	Relapses Lesions & Brain Volume	Exacerbations Lung Function Dyspnea/Breathlessness Cardiovascular Events Medication Usage	Hip score Bone mineral density Incidence of new fracture

Timed Walking Tests: Explicit Eligibility Criteria & Rationale

During pilots, these criteria were easily and consistently interpreted in most cases. However, specific challenges arose regarding the eligibility of timed clinical assessments that include periods of walking. Generally, we will include timed gait speed tests, such as the 10-meter walk, but will exclude tests that aggregate or assess constructs other than gait speed. However, studies may still be included if DMOs were specifically assessed during the walking portions of excluded tests. Detailed instructions related to questions that arose during pilots are provided in Table 6.

Table 6: Instructions to reviewers for categorizing and interpreting traditional timed walking tests in this review

Test	How should the test be categorized/managed?
4 meter, 7 meter, 10 meter walk test Timed 25 foot walk 2 Minute Walk test Walk tests of any distance up to 100m	Timed tests should be categorized as gait speed and captured in our review. Studies reporting these measures within the context of our research questions are included. Though the 2MWT is also referred to as a measure of exercise capacity, we include it to be conservative because it is not necessarily a different length or time than other traditional gait speed tests in mobility-impaired populations. 100m is an arbitrary threshold for distance-based walking tests such that they are roughly the same as the 2MWT.
6 Minute Walk Test, Walk tests of any distance over 100m	The total walk time should not be interpreted as walking speed. However, if the test is instrumented, any DMO captured during these tests should be included. This is because long clinical walk tests such as the 6-Minute Walk Test measure constructs such as exercise capacity and endurance rather than walking speed[7–12] and are not representative of typical real-world walking bout duration.[13–15]
Timed Up and Go test	Any DMO measured during the walking portion of the test should be captured and included. The total time required to complete the Timed Up and Go should not be interpreted as walking speed. This is because the test also includes the time required to stand from seated position and return to a seated position.[16]
Incremental Shuttle Walk Test Endurance Shuttle Walk Test	Neither the ISWT nor the ESWT should be included as tests of gait speed in this review. Similar to the 6MWT, they are measures of exercise endurance rather than walking speed.[17,18] Further, they require that patients walk in time to audible cues, artificially altering cadence and gait speed. Therefore, no DMOs measured during these tests should be included in this review.
Tests conducted on a set-speed treadmill	Speeds set by the researcher should not be interpreted as a patient's self-selected or top gait speed. However, other DMOs collected during treadmill walking should be included.

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Online Supplement 2: Search Strategy

MEDLINE, CINAHL, Scopus, Web of Science, EMBASE, IEEE Digital Library, and the Cochrane Library will be searched for eligible studies, while ACM Digital Library, ProQuest Dissertations, Open Grey, and the National Information Center's Health Services Research Projects in Progress Database will be searched to identify additional grey literature. Searches to these databases will adhere to the general following structure: (gait terms) AND (disease-area terms).

The following search string was developed for EMBASE by an experienced information specialist in consultation with the research team and will be replicated for other included databases. Results reflect a search on November 14th, 2019.

String No.	Query	Results
#1 (Gait terms)	(((step* OR stride*) NEAR/2 (speed OR velocit* OR time* OR length* OR width* OR frequenc* OR rate* OR rhythm* OR variabilit* OR symmetr* OR asymmetr* OR count* OR number* OR distance* OR cadence*)):ti,ab) OR (((swing* OR stance* OR 'single support' OR 'double support') NEAR/2 (time* OR duration* OR variabilit* OR symmetr* OR asymmetr*)):ti,ab) OR (((spatiotemporal OR 'spatio-temporal') NEAR/2 (parameter* OR feature* OR characteristic*)):ti,ab) OR (((gait OR walk* OR ambulat*) NEAR/2 (speed OR velocit* OR time* OR cadence* OR pace* OR rhythm* OR volume* OR bout* OR duration* OR distance* OR intensit* OR variabilit* OR asymmetr* OR symmetr* OR parameter* OR feature* OR characteristic* OR assess* OR examin* OR analys* OR batter* OR measure* OR test*)):ti,ab)	112073
#2 (Disease-area terms)	'chronic obstructive lung disease'/exp OR 'Parkinson disease'/exp OR 'parkinsonism'/exp OR 'multiple sclerosis'/exp OR 'demyelinating disease'/exp OR 'hip fracture'/exp OR (((chronic OR lung OR pulmonary OR respirat* OR airway* OR airflow*) NEAR/3 obstruct*) OR copd):ti,ab OR (parkinson* OR 'paralysis agitans'):ti,ab OR (((multipl* OR disseminated OR insular) NEAR/3 scleros*) OR 'chariot disease' OR demyelinat*):ti,ab OR ((hip* OR femur* OR femoral OR trochant* OR pertrochant* OR intertrochant* OR subtrochant* OR intracapsular* OR extracapsular*) NEAR/5 fracture*):ti,ab	635311
#3 (Final)	#1 AND #2 AND (1999:py OR 2000:py OR 2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018 :py OR 2019:py OR 2020:py)	12307

Online Supplement 3: Screening reference sheets and forms

The following forms and reference sheets are proposed for abstract screening and full-text review. Reference sheets will be extensively piloted, revised as required, and provided to each reviewer to use during screening. Review forms and their associated logic are programmed into DistillerSR, where reviewers assess abstracts or full texts and provide answers to the required questions. Final versions of these materials will be published alongside the final study results.

Acrynyms:
DMO - Digital Mobility Outcome
GaWP - Gait and Walking Parameter
PD – Parkinson's Disease
MS – Multiple Sclerosis
COPD – Chronic Obstructive Pulmonary Disease
PFF – Proximal Femoral Fracture

Reference sheets and forms:

1. Abstract Screening Checklist (p. 2)
2. Abstract Screening Reference Sheet (p.3)
3. Abstract Screening Review Form (p. 4)
4. Proposed Full Text Review Form (p. 5)

Mobilise-D Scoping Review: Abstract Screening Worksheet

Overview:

- This review will explore the potential of DMOs as clinical trial endpoint measures by identifying, existing evidence on their construct validity, prognostic value, and responsiveness to intervention
- Our four research questions aim to explore the following:
  - RQ1: The differences in GaWPs between target populations and healthy controls
  - RQ2: The relationship between GaWPs and traditional clinical measurements
  - RQ3: The prognostic value of GaWPs
  - RQ4: The use of GaWPs as endpoints in interventional studies

Question 1: Should this paper be included in full-text review? (YES or NO)

Questions to ask yourself:		YES or Unsure	NO
A	Is the study on an **included population**? *(human studies on Parkinson's, Multiple Sclerosis, COPD, hip fracture)*	Proceed	Discard
B	Does the study assess **gait speed, gait analysis or an included GaWP**? - See reference sheet for list of included GaWPs - Note that some clinical walking tests are included as measures of gait speed (4 meter walk, 10 meter walk, timed 25 foot walk, etc.) and others are not. See reference sheet for details	Proceed	Discard
C	Is the study an **included design**? ○ Examples of Included Designs: ▪ Observational ▪ Case-control (comparing diseased group vs. healthy group) ▪ Cohort ▪ Cross-sectional ▪ Longitudinal ▪ Interventional ○ Excluded Designs: ▪ Case study ▪ Case series (Series of case studies published together) ▪ Review paper	Proceed	Discard
D	Could the study **address one of our research questions?** *(answer YES if any of the following apply)* - **RQ1:** Could the study explore the *differences in DMOs/GaWPs between healthy controls and a target population*? - **RQ2/RQ3:** Could the study *explore a relationship between DMOs/GaWPs and included measurements (RQ2) or outcomes (RQ3) in a target population?* ○ Relationships could be in the form of a correlation, empirical relationship, odds ratio, risk ratio, hazard ratio, prediction model, multivariate analysis, or other association measure - **RQ4:** Does the study appear to be an *interventional study in a target population with a DMO/GaWP as an endpoint*?	Proceed	Discard
E	Are at least **10 individuals** included in the final analysis?	Proceed	Discard

		YES	NO
F	Are there any other **inclusion criteria** that the study **clearly does not meet**?	Discard	Keep

***If you are unsure, please be conservative and include the study in full-text review.*

Mobilise-D Scoping Review Abstract Screen: Reference Sheet

Eligibility Criteria

Criterion	Keep	Discard
Population	PD, MS, Hip Fracture, COPD Mixed populations IF a sub-analysis was conducted	Animal Studies All other human disease areas Mixed populations with no sub-analysis
Study Aim	Studies an included Gait and Walking Parameter according to one of our research questions	Studies with no GaWP and/or which do not address a RQ
Study Design	Any (Case-control, cross sectional, longitudinal, cohort, controlled or uncontrolled trials, protocols (RQ4 only))	Case study, case series Systematic review (or any review)
Technology	Any (sensors, pedometers, stopwatch, speed gaits, instrumented walkways, video, optometric systems, etc.) Specific clinical tests regardless of technology use (see below)	Self-report measures
Setting	Any (home, clinical, lab-based)	NA
Minimum Dataset	10 patients per study arm included in the final analysis	

Gait and Walking Parameters

Spatial Parameters
Step length (mean, variability, asym.)
Stride length (mean, variability)
Step width (mean, variability)

Temporal Parameters
Cadence (mean, variability)
Step time (mean, variability, asymmetry)
Stride time (mean, variability)
Stance time (mean, variability, asymmetry)
Swing time (mean, variability, asymmetry)
Single support time (mean, variability, asym.)
Double support time (mean, variability)

Spatiotemporal Parameters
Gait speed (mean, variability)
Stride speed (mean, variability)

Volume of Walking
Walking time
Step count (excluding pedometer)
Number, length, duration of walking bouts

Included Walking Conditions

Keep:
- Gait analysis or measurement of any included gait parameters
- Dual-task walking, if testing scenario is included
- Some clinical tests, even no technology was used:
  - 4, 5, 10, 30, 50, etc. meter walk tests (or other short distance) – INCLUDE as gait speed
  - Timed 25 Foot Walk (T25FW) - INCLUDE as gait speed
  - 2 Minute Walk Test – INCLUDE as gait speed

Conditionally Keep:
- Timed Up & Go: ONLY INCLUDE instrumented TUG w/ GaWPs measured during walk
- Treadmill Walking:
  - Fixed-Speed Treadmill: INCLUDE any GaWP EXCEPT gait speed
  - Self-Adjusting Speed Treadmill: INCLUDE any GaWP
- 6Minute WT, 12Minute WT, 400m WT, (or other long walking tests):
  - Non-Instrumented Test: EXCLUDE
  - Instrumented test: INCLUDE any GaWP EXCEPT gait speed

Keep if normal gait may have been be analyzed at baseline or if walking condition was used as intervention (generally keep to be conservative):
- Tandem walking or other abnormal walking patterns
- Walking in time to cues (e.g., beats, music, beeping, etc.)
- Purposefully altering gait (e.g., instructions to concentrate on lifting toes)

Research Questions

RQ1: Comparison of GAWPs between a Mobilise-D population and healthy controls
RQ2: Association between a GaWP and a clinical measurement at a single timepoint
RQ3: Prognostic value: Longitudinal association between a GaWP and a clinical measurement or outcome over time
RQ4: Use of GaWPs as endpoints in controlled interventional studies

Population Terms

	Keep	Discard
PD	Parkinson('s) disease, Parkinsonism, idiopathic Parkinson's disease	Atypical parkinsonian syndromes, drug-induced parkinsonism, vascular parkinsonism, progressive supranuclear palsy, multiple system atrophy, corticobasal syndrome, dementia with lewy bodies
MS	Multiple Sclerosis, relapsing-remitting, primary progressive, secondary progressive, progressing-relapsing MS	
PFF	Hip, femoral, intracapsular (subcapital and transcervical), extracapsular (trochanteric, intertrochanteric, pertrochanteric and subtrochanteric) fractures	Non-fracture-related hip arthroplasty or hip replacement
COPD	Chronic obstructive pulmonary disease Chronic obstructive lung disease Chronic respiratory disease (>age of 65)	Pulmonary hypertension, Studies only including asthma patients

- *If the population is mixed, the study must conduct a sub-analysis of one of our populations to be included. If this is unclear from the abstract, be conservative and include.*
- *If you are unsure about the population and the paper meets all other inclusion criteria, include the paper and the disease-specific team will make the determination.*

FAQs

What do I do when…

I am not sure whether a measurement or outcome is included in RQ2/3 criteria
- Some determinations may require disease-specific knowledge. Be conservative and keep the paper.

A testing scenario or type of study is not covered by our eligibility criteria
- If something is not covered by eligibility criteria, raise a question to Ashley and others in the group. We may need to clarify an unforeseen situation.

The abstract does not indicate the technology or method used to measure a GaWP/DMO?
- Include the paper IF it mentions measuring an included gait parameter, gait analysis, or included clinical test of gait speed AND IF it meets all of our other inclusion criteria

Something is completely unclear, and I can't tell whether to include?
- Think about the item that is unclear with regard to the other inclusion criteria. How realistic is it that the criterion is met, given the information that you have?
- Be pragmatic, but inclusive. If all else fails, be conservative and keep the paper.

Mobilise-D Scoping Review: Abstract Screening Worksheet

Legend:

Green text – Describes logic included in form
Prompt: … – Answer triggers another question or form
E – Answer causes study to be excluded
I – Answer causes study to be included

1. Should this paper be included in full-text review?
Radio answers:
   a. Yes (I, prompt Q3)
   b. No (E, prompt Q2)
   c. Very Unsure (prompt 3rd review by lead reviewer)
   d. Abstract not available/Not in my language (prompt search for full abstract or reviewer fluent in the language of the abstract)

2. Keep paper as background information? (i.e., a relevant review)
Radio answers:
   a. Yes (Add label "Background")

3. Which MobiliseD disease area is included in this study? (Select all that apply)
Checkbox answers:
   a. Parkinson's Disease (Send to Parkinson's Disease full-text review group)
   b. Multiple Sclerosis (Send to Multiple Sclerosis full-text review group)
   c. COPD (Send to COPD full-text review group)
   d. Hip Fracture (Send to Hip Fracture full-text review group)

Mobilise-D Scoping Review: Full Text Review Screening Form

Legend:

Green text – Describes logic included in form
Prompt: … – Answer triggers another question
E – Answer causes study to be excluded
Include Study – End of decision tree. Answer causes study to be included

Initial Questions – All abstracts

Question 1: Screening – General Eligibility Criteria (Select all that apply)

- A. Full text is not available (E)
- B. Full text is not in English or one of my fluent languages (Prompt: Q3-Which language?)
- C. The study design was a case study, case series, review, or other non-eligible study type (E)
- D. The article was an interventional **protocol that used a GaWP as an outcome** that otherwise meets the criteria for RQ4 (E)
- E. Only excluded GaWPs were studied (E)
- F. GaWPs were assessed, but **only** during turns, stair climbing, tandem walking, or other excluded walking motions/conditions (E)
- M. Fewer than 10 participants per study arm were included in any relevant analysis (E)
- J. Study population did not meet our inclusion criteria (E)
- K. Part of the study population met our criteria, but a sub-analysis on these participants was not conducted (E)
- N. The study did not address one of our research questions (E)
- None of the above – The study meets general inclusion criteria (Prompt: Q2-Which research question?)

Studies will be excluded unless the language option or 'None of the Above' is selected

Question 2: Which research question(s) did the study address? (Select all that apply)

- Research Question 1 (Prompt: RQ1 screening question)
- Research Question 2 (Prompt: RQ2 screening question)
- Research Question 3 (Prompt: RQ3 screening question)
- Research Question 4 (Prompt: RQ4 screening question)

Question 3: In which language is the full text available?

- German
- Spanish
- Italian
- French
- ** Screeners will be able to add and select options as needed

A request to find a reviewer fluent in the language will be triggered

RQ-specific Screening Questions

Research Question 1 Screening Questions

RQ1 Eligibility criteria - Was the difference in GaWP measurements assessed between healthy controls and a target population?

A. Yes, but fewer than 10 participants per study arm were included a relevant RQ1 analysis (E)

B. The patient population was mixed and a sub-analysis on an included population was not conducted for RQ1 (E)
C. Yes, and all criteria for RQ1 are met – this paper/analysis should be included (Include Study)

Research Question 2 Screening Questions

RQ2 Eligibility Criteria: Was the relationship between a DMO and a clinical measurement assessed in a target population?

A. Yes, but no included/important measurements were studied (E)
B. Yes, but fewer than 10 patients were included in this analysis (E)
C. Population was mixed and a sub-analysis on an included population was not conducted (E)
D. Yes and all eligibility criteria are met – The study should be included (Include Study)

Research Question 3 Screening Questions

RQ3 Eligibility Criteria: Was the relationship between a DMO and a clinical outcome assessed in a target population through a multivariate analysis, prediction model, or machine learning technique?

A. Yes, but no included/important outcomes were studied (E)
B. Study design was not longitudinal (E)
C. The study looked at GaWPs as outcomes rather than variables (E)
D. Patient population was mixed and a sub-analysis on an included population was not conducted for RQ3 (E)
E. Yes and all eligibility criteria are met – The study should be included (Include Study)

Research Question 4 Screening Questions

RQ4 Eligibility Criteria: Was the DMO used as a primary, secondary, or exploratory endpoint in an interventional study?

A. The clinical trial was uncontrolled (E)
B. The reference is only a protocol or study registration, and does not report original results (E)
C. Patient population was mixed and a sub-analysis on an included population was not conducted for RQ4 (E)
D. Fewer than 10 patients per arm were included in the final analysis (E)
E. Yes and all eligibility criteria are met – The study should be included (Include Study)

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	
Limitations	20	Discuss the limitations of the scoping review process.	
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.