Long-term unsupervised mobility assessment in movement disorders

Elke Warmerdam, Jeffrey M Hausdorff, Arash Atrsaei, Yuhan Zhou, Anat Mirelman, Kamiar Aminian, Alberto J Espay, Clint Hansen, Luc J W Evers, Andreas Keller, Claudine Lamoth, Andrea Pilotto, Lynn Rochester, Gerhard Schmidt, Bastiaan R Bloem, Walter Maetzler

Lancet Neurol 2020; 462–70

Published Online February 11, 2020 https://doi.org/10.1016/S1474-4422(19)30397-7

See Comment page 378

Department of Neurology (E Warmerdam MSc, C Hansen PhD, Prof W Maetzler MD) **and Faculty of Engineering, Kiel University, Kiel, Germany** (E Warmerdam, Prof G Schmidt PhD)**; Center for the Study of Movement, Cognition, and Mobility, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel** (Prof J M Hausdorff PhD, Prof A Mirelman PhD)**; Department of Physical Therapy, Sackler Faculty of Medicine and Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel** (Prof J M Hausdorff, Prof A Mirelman)**; Rush Alzheimer's Disease Center and Department of Orthopaedic Surgery, Rush University Medical Center, Chicago, IL, USA** (Prof J M Hausdorff)**; Laboratory of Movement Analysis and Measurement, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland** (A Atrsaei MSc, Prof K Aminian PhD)**; University of Groningen, University Medical Center Groningen, Center for Human Movement Sciences, Groningen, Netherlands** (Y Zhou MSc, C Lamoth PhD)**; Radboud University Medical Center, Donders Institute for Brain, Cognition, and Behaviour, Department of Neurology, Center of Expertise for Parkinson & Movement Disorders, Nijmegen, Netherlands** (L J W Evers BSc, Prof B R Bloem PhD)**; Gardner Family Center for Parkinson's Disease and Movement Disorders, University of Cincinnati, Cincinnati, OH, USA** (Prof A J Espay MD)**; Center for Bioinformatics, Saarland University, Saarbrücken, Germany** (Prof A Keller PhD)**; Department of Neurology and**

Mobile health technologies (wearable, portable, body-fixed sensors, or domestic-integrated devices) that quantify mobility in unsupervised, daily living environments are emerging as complementary clinical assessments. Data collected in these ecologically valid, patient-relevant settings can overcome limitations of conventional clinical assessments, as they capture fluctuating and rare events. These data could support clinical decision making and could also serve as outcomes in clinical trials. However, studies that directly compared assessments made in unsupervised and supervised (eg, in the laboratory or hospital) settings point to large disparities, even in the same parameters of mobility. These differences appear to be affected by psychological, physiological, cognitive, environmental, and technical factors, and by the types of mobilities and diagnoses assessed. To facilitate the successful adaptation of the unsupervised assessment of mobility into clinical practice and clinical trials, clinicians and researchers should consider these disparities and the multiple factors that contribute to them.

Introduction

Deficits in mobility are common in patients with neurological disorders and often affect activities of daily living, work, and socialisation.[1] These deficits predict morbidity, cognitive decline, and mortality[2–5] and negatively affect quality of life, especially in patients with movement disorders.[6,7] For example, in patients with Parkinson's disease, health-related quality of life is strongly associated with the activities and participation components of the International Classification Of Functioning, Disability, and Health model.[8] Therefore, it is crucial for health-care professionals to obtain a full and objective evaluation of a patient's mobility as a basis for individually tailored clinical decision making and prognostication. Mobility assessments are mainly done under supervised conditions in a laboratory or hospital using standardised, mostly qualitative or semi-structured evaluations (panel);[9–11] however, many patients do paradoxically well when they know that they are being observed. Various clinically relevant events are also difficult to capture during these snapshot observations, because they take place over long periods of time (eg, the total amount of physical activity), are rare (eg, falls or freezing episodes),[12] occur at night (eg, sleep disturbances), or have complex fluctuating patterns (eg, the response to dopaminergic treatment in Parkinson's disease). To reliably evaluate such events, it is important to measure patients unobtrusively and for longer periods of time, while they move about freely and unsupervised in their daily-living environment.

Several reviews describe the promise of unsupervised assessments of mobility using novel technologies.[13,14] Unsupervised assessments of mobility using novel technology, although very different from other daily living acquired parameters that are already used in clinical routine (such as the Holter electrocardiogram[15,16] and blood glucose monitoring),[17] could soon be essential for the long-term evaluation of mobility and personalised clinical decision making in neurology.[13,14] Unsupervised assessments might save time and cost by capturing health-related data since these assessments would be largely independent of the availability of health-care services. These assessments are particularly important for patients living in rural areas or developing countries, where the number of health-care professionals is small relative to the population size.[14] Finally, unsupervised assessments offer patients an opportunity to become more actively involved by, for example, using their own devices such as smartphones and receiving feedback about their own daily living performance.[18]

Unsupervised assessments of mobility can provide additional and, at least partly, complementary information compared with supervised assessments. However, differences with respect to the conventional evaluation need to be considered. In this Personal View, we summarise the evidence of the weak association between mobility assessed in the two settings and discuss potential reasons for the observed differences. We also present suggestions to facilitate the implementation of unsupervised mobility assessment in clinical care and future research.

Unsupervised mobility assessment

Unsupervised assessments are usually done with mobile health technologies[13] that can measure physical activity,[19–21] evaluate mobility or specific movements such as gait,[22–24] or detect specific symptoms in unsupervised environments.[25–27] The potential added value of unsupervised assessments in patients with mobility deficits has been shown in several studies. For example, both predicting the risk of future falls and discriminating fallers from non-fallers in older adults (>60 years of age)[28–31] and stroke survivors[32] appears to be more accurate when using data collected in the unsupervised environment. Indeed, the relevance of unsupervised mobility parameters was acknowledged by the US Food and Drug Administration[33] and the European Medicines Agency,[34] both of which encourage the inclusion of parameters from unsupervised mobility assessments as exploratory endpoints in clinical trials.

We did a systematic search to compare the same features of mobility (ie, gait, turns, and postural transitions) in supervised and unsupervised assessments. 12 studies done in three different populations—adults older than 60 years, patients with Parkinson's disease, and patients with multiple sclerosis—were identified (appendix pp 1–3). Strikingly, the same mobility parameters obtained in different settings with identical participants differed from –40% (eg, gait speed and cadence in patients with Parkinson's disease) to 180% (end turn angular velocity in healthy older adults, figure 1). These differences are much larger than the effects usually measured after interventions. Thus, small and even moderate treatment effects might be buried under the variations introduced by the measurement techniques themselves if the differences between supervised and unsupervised assessments are not appropriately considered.

Differences between supervised and unsupervised assessments

Several reasons could explain the substantial differences in mobility parameters when comparing supervised with unsupervised assessments (table 1). Unsupervised movements are typically self-initiated, embedded in a rich behavioural context, and goal directed. By contrast, movements in a supervised setting are usually triggered by a command and done in an isolated, standardised setting with limited ecological validity.[36] For example, self-initiated finger movements activate different brain structures compared with externally triggered movements, suggesting that the brain generates supervised movements using networks that differ from those that generate unsupervised movements.[47,48] Moreover, with an external focus, attention is directed to the outcome of the action (eg, leaving the room), while with an internal focus, attention is directed to controlling the body parts while executing the movement.[49] An external focus of attention results, at least sometimes, in more fluent movements.[50]

Performance can be affected by several psychological and physiological processes that might differ across settings. These factors include alertness, motivation, the white-coat effect (a change [typically worsening] in a parameter because it is measured in a clinical setting), the reverse white-coat effect (a change [typically an improvement] in a clinical parameter because it is measured in a clinical setting), the Hawthorne effect (the change in behaviour of participants because of the awareness of being studied),[51] fatigue, pain, and stress. These effects might explain why patients rise from a chair with lower peak power in unsupervised assessments than during supervised assessments, even when these movements are done in an identical environment and with the same equipment.[24] Similar disparities have been identified for other gait parameters.[52] Supervised assessments seemingly provide a measure of someone's best, rather than their usual performance; that is, they capture capacity rather than performance.[53,54]

***Panel:* Glossary of terms used in mobility assessment**

Daily living
This term, also referred to as free living, real world, or community living, is used to distinguish testing within the normal environment of a participant from testing in a standardised setting, such as in the clinic or laboratory

Inertial measurement units
Sensors that measure acceleration or angular velocity, which can determine the quality and quantity of movement using specifically developed algorithms

Mobile health technologies
Umbrella term for wearable, portable, or domestic-integrated devices that can provide objective measures and that include digital applications, as well as body-worn (adhered to a body surface, mainly inertial measurement units) or frequently used patient-centred devices (eg, smartphone and keyboard)

We focus on technologies that can measure the frequency and quality of movement, and mobility characteristics

Supervised assessment
Refers to the traditional, conventional mode of assessing mobility in a laboratory or clinical setting

Typically, a qualitative or semi-quantitative one-time snapshot evaluation of mobility by a trained health-care professional

Unsupervised assessment
Refers to the quantitative assessment of mobility in the home and daily living environment that is done continuously with new, mainly mobile, health technologies over relatively long periods of time

Wearables
Mobile devices worn on the body, such as inertial measurement units, smartwatches, or Holter electrocardiogram monitors

The environment is usually standardised in supervised conditions (eg, walking in a clean and sterile environment without distractions), but much more variable in unsupervised conditions (eg, furniture, lighting, patterns, colour of the environment, and obstacles). Unsupervised environments can induce large variability and asymmetry in mobility patterns, as shown by studies that assessed walking through busy corridors and through a city centre.[55,56] Different types of seats and couches (eg, firm chair or armchair) in unsupervised conditions can also partly explain the greater variability observed in postural transitions (ie, sit-to-stand and stand-to-sit movements or turning over in bed) in daily living.[24,30,37,41] Moreover, asymmetry can be introduced through a constrained environment that requires gait adaptation or turning in the same direction.

Furthermore, multitasking situations are common in unsupervised environments (eg, walking and texting), but uncommon in supervised assessments, which could further contribute to the observed differences. Even during supervised dual-task walking, the gait quality was usually better than that during unsupervised walking.[39] The presence of a partner or caregiver can also affect mobility in unsupervised conditions. Social interactions

Neurological Sciences, School of Medicine, Stanford University, Stanford, CA, USA (Prof A Keller); **Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy** (A Pilotto MD); **Parkinson's Disease Rehabilitation Centre, Fondazione Europea Ricerca Biomedica, St Isidoro Hospital, Bergamo, Italy** (A Pilotto); **Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK** (Prof L Rochester PhD); **and Newcastle upon Tyne Hospitals, National Health Service Foundation Trust, Newcastle upon Tyne, UK** (Prof L Rochester)

Correspondence to:
Prof Jeffrey M Hausdorff, Center for the Study of Movement, Cognition, and Mobility, Neurological Institute, Tel Aviv Sourasky Medical Center, Tel Aviv 6423906, Israel
jhausdor@tlvmc.gov.il

See Online for appendix

are common during everyday walking: for example, spouses who act as an external cue to improve walking in patients with Parkinson's disease or to relieve anxiety in people with a cautious gait disorder.[57]

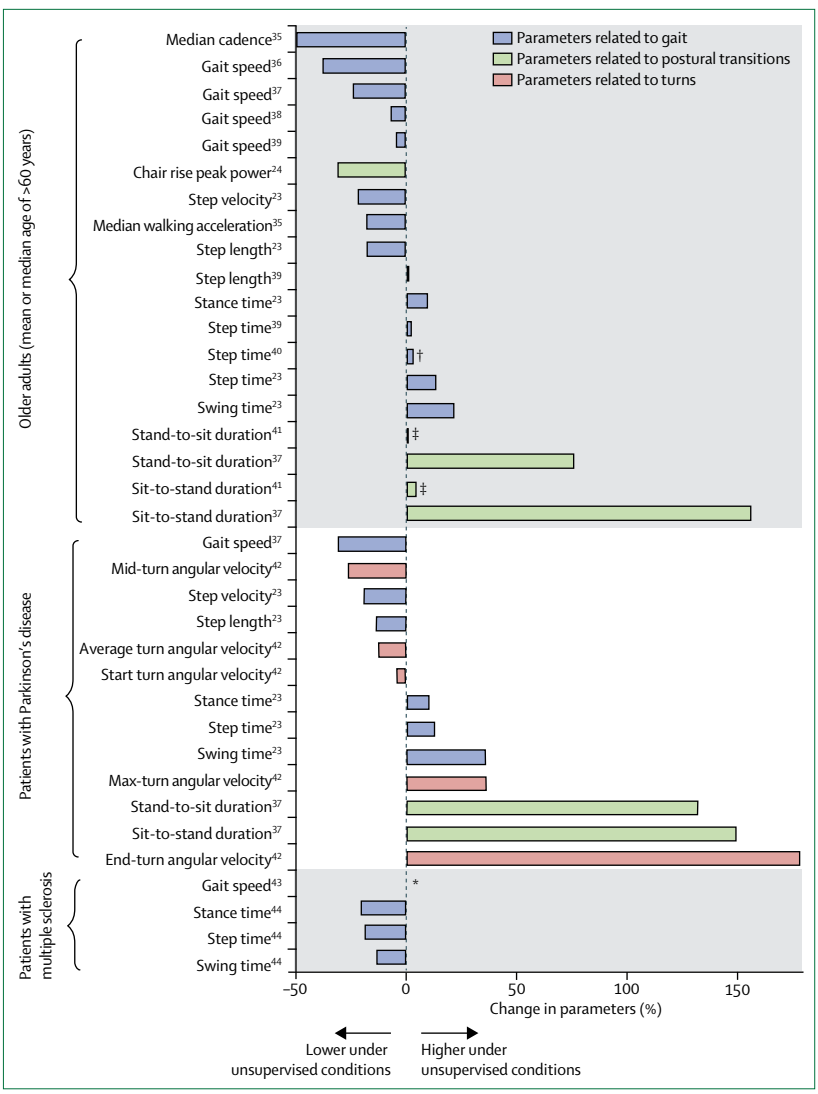

Figure 1: **Percentage change from parameters measured under unsupervised conditions compared with supervised conditions**

Data were obtained from the 12 studies identified in our systematic search (appendix pp 1–3). We did not illustrate variability and asymmetry parameters because they are especially sensitive to the environment and are probably higher for unsupervised than for supervised assessments because of the non-instructed performance and more variable physical nature of the environment.[45] Cadence is the rate at which a person steps (about 110–115 steps per min in healthy adults). Chair rise peak power is the maximum power that is exerted to lift the body's centre of mass during a sit-to-stand movement.[46] Median walking acceleration is the median of the magnitude of the acceleration during walking. Stance time is the time one leg is in contact with the surface during a step that is taken during walking. Step time is the time it takes to complete one step (ie, the time between initial contact of one foot and the initial contact of the contralateral foot). Stride time (also known as gait cycle time) is the time to complete two steps (ie, the time between initial contact of one foot and the next initial contact of the same foot). Swing time is the time one leg is not in contact with the surface during a stride that is taken during walking (in healthy young adults, swing time is about 40% of the stride time and with ageing and disease, the time spent in swing time often gets smaller). *Instructions in the supervised setting were to walk as fast as possible. †Supervised assessment was done on a treadmill with fixed speed, the unsupervised parameters used for the comparison were matched to the treadmill speed. ‡Only the best postural transitions reported were used to calculate the duration.

Technical limitations might also add to the differences observed. Most algorithms have been developed and validated in supervised environments. Because the amount and variability of activities and mobility are much larger in unsupervised than in supervised environments, these algorithms might have difficulties differentiating similar movements (such as picking something up from the floor and sit-to-stand movements) that were not evaluated in the supervised assessment.[58,59] Notably, only one study found in our systematic search used algorithms that were explicitly validated in both standardised and non-standardised settings.[44] A further bias might be introduced by the use of different device locations on the body (eg, waist or ankle). The use of distinct mobile health technologies (eg, hardware or algorithms)[37,42] could also play a part, but this aspect is limited as a change in hardware will not have a large influence on the results of a validated algorithm, because the data collected are the same (appendix p 4). The validation of algorithms for unsupervised daily living assessments brings new challenges as gold-standard references are currently absent, and urgently needed.[60,61]

Finally, the statistical approaches for the analysis of supervised assessments (eg, means and SDs), might not be optimal for characterisation of complex data obtained from unsupervised settings. The supervised assessment typically involves one test, whereas the unsupervised evaluation might include thousands of walking bouts, turns, and transitions. It is yet to be determined how to best compare a single value with values obtained from a distribution (or histogram; figure 2; appendix pp 1–3). Several studies showed that the tails of an individual's distribution correspond better to supervised assessments and therefore to clinical endpoints, such as risk of falls, limitation in activities, frailty, and supervised gait speed, compared with mean and median values.[24,36,40]

Effect of movement type and disease on mobility assessment

Some types of mobility (eg, postural transitions) show seemingly larger differences than others (eg, walking) when comparing supervised with unsupervised conditions (figure 1). This difference might even depend on specific parameters. In a study of patients with Parkinson's disease, the velocity at the beginning of the turn was similar in unsupervised and supervised conditions but was lower at the middle and substantially higher at the end of turns under the unsupervised condition.[42]

Notably, the type and severity of a disease might also have an effect on the differences between supervised and unsupervised assessments (figure 1).[23,62] For example, the differences in stand-to-sit duration between both settings were smaller in older adults than in patients with Parkinson's disease.[37] Patients with multiple sclerosis showed an even more surprising pattern. Different to patients with Parkinson's disease and older adults, their performance was comparable under supervised and

unsupervised assessments (gait speed),[43] while showing the opposite behaviour of what was seen in patients with Parkinson's disease and older adults (ie, for stance, step, and swing time, which were all lower in unsupervised conditions).[44] The reasons for these observations are not yet clear, but differences in physical, attentional, and cognitive capabilities might contribute.[63] These differences between supervised and unsupervised performance might even be relevant at the subgroup level. The reported changes in turning parameters in patients with Parkinson's disease[42] differed substantially between fallers and non-fallers, with or without fear of falling. Remarkably, fallers with fear of falling showed slower turns in the supervised assessment, but faster turns in the unsupervised assessment, than did patients in other Parkinson's disease subgroups.[42]

Implementation of unsupervised assessments in clinical practice and future research

As we anticipate that unsupervised assessments will become a prerequisite for future clinical decision making and clinical trials, in this section we provide directions to help move this emerging field forward (table 2). Although there is still insufficient understanding of the association between supervised and unsupervised mobility when interpreting data obtained from unsupervised environments, studies suggest that any extrapolation of unsupervised mobility based on findings from supervised mobility might be substantially influenced by the type, subtype and stage of the disease, as well as type of mobility extracted from the data.[37,40,42,44]

Technical limitations should be also addressed, for example, by using the same mobile health technologies, located in the same place, for both supervised and unsupervised measurements. The algorithms used to calculate mobility parameters should be validated, to the highest degree possible, in both settings. Moreover, algorithms for mobility assessments should be validated separately for each type of neurological movement disorder as they might be associated with distinct movement patterns.[23,64] Notably, even healthy people move differently at different ages[65,66] and fitness levels.[66] Another requirement to increase the usefulness of unsupervised measures is harmonised reporting of parameters (eg, as a core dataset across studies), and should include the reporting of metadata (ie, data that accompany and describe the primary data).[67] The duration of the unsupervised assessments should be standardised and the type of movement assessed should be reported in detail.[67,68]

Special emphasis should also be placed on more sophisticated analyses of unsupervised data. A promising approach is to consider and leverage specific episodes of mobility (eg, turning, sit-to-stand, and stand-to-sit movements, and other movements used regularly during the day) and novel parameters, such as the distribution and extreme values of mobility parameters (figure 2).[24,36,35,40] So far, these analyses have been done only for healthy

	Supervised assessment	Unsupervised assessment
Clinometric properties (norms and test-retest reliability)	Established	In progress
Setting	Artificial	Ecologically valid (represents real-world performance)
Number of assessments	Snapshot, one-time evaluation	Multiple or even continuously performed tests can be obtained over days, weeks, and months
Sensitivity to fatigue, affect, and mood	Minimal	Yes, reflects typical performance and a range across the day and week, including best and worse behaviours
Sensitive to white-coat, Hawthorne, and related effects	Yes	Minimal
Patient centred	Not necessarily	Yes
Captures real-world challenges	Somewhat	Yes
Real-time feedback for treatment	Questionable	Yes
Interpretation of results	Easy	More challenging
Environmental influences	Minimal	Yes

Table 1: **Advantages and disadvantages of supervised and unsupervised mobility assessments**

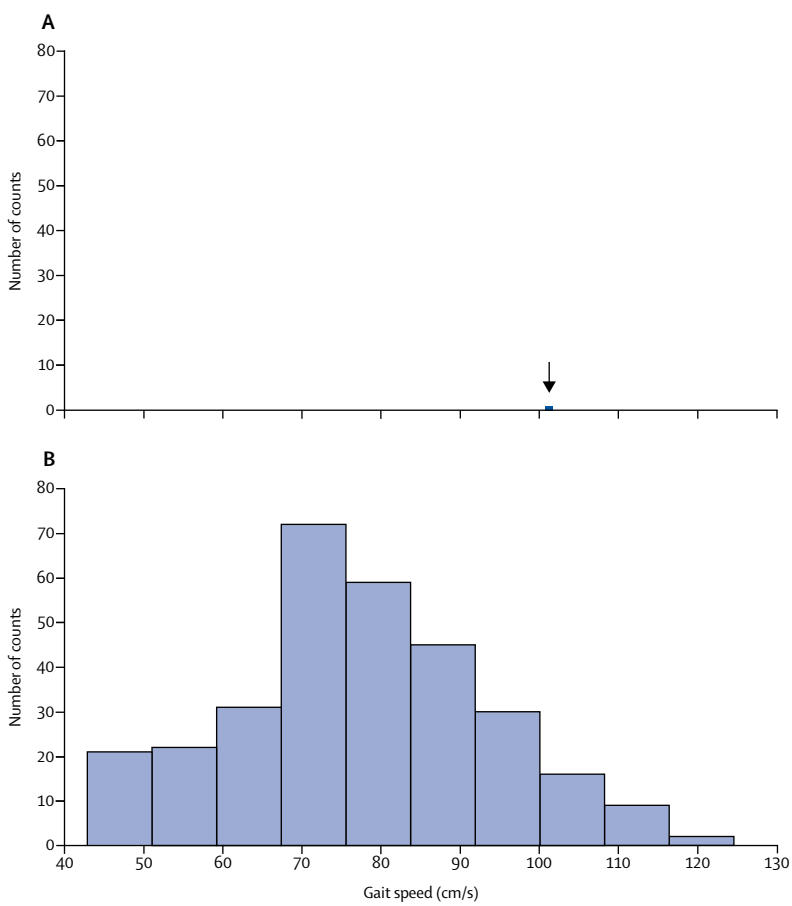

Figure 2: **Gait speed measures based on evaluation in the laboratory and in the daily living environment in a 78-year-old woman with a history of falls**

(A) The supervised testing yields a single value (101 cm/s), as indicated by the arrow. (B) By contrast, the daily living, unsupervised testing yields hundreds of tests of gait speed and a distribution of values. The daily living values are based on 30 s walking bouts from a 1-week recording.[39] Multiple measurements, in contrast to a single, one-time snapshot, might be highly valuable for the improvement of assessment protocols. In many of these unsupervised tests, gait speed is lower than that seen during supervised testing.

	Gaps and challenges	Potential resolution
Supervised versus unsupervised mobility assessment	Weak associations might exist between the measures of these two assessments	Acknowledge the limited understanding when comparing supervised with unsupervised data and conduct more research to gain a better understanding of the interactions between these types of assessments
Algorithms	Algorithms for the assessment of unsupervised mobility are difficult to validate	Work on new approaches that can be used to validate algorithms for unsupervised mobility assessment against, or at least correlated with, clinically established parameters
Age and type of disease	Different age phases and diseases have different mobility performances, and a one-size-fits-all mobility-assessing algorithm might deliver low accuracy values in at least some cohorts	Develop and validate algorithms for the evaluation of unsupervised mobility separately per age groups and diseases
Harmonisation	Description of metadata, assessment protocol, and validation method have not yet been harmonised in the field, hindering the comparison across studies	Use standardised protocols to report, particularly concerning the description of the primary data, duration of assessments, description of the data analysis process, or reference to the algorithm and its validation
Data analysis	Statistical analysis and selection of summary measures of unsupervised data might be very different from usual statistical approaches	Explore new options for data analysis, such as the extremes of mobility performance during the day
Patient-reported outcome measures	Associations between unsupervised assessment and patient-reported outcome measures are scarcely investigated	Studies investigating either unsupervised mobility or patient-reported outcome measures should consider including the other evaluation tool and compare outcomes on an exploratory level
Behaviour	The effect of unsupervised mobility assessment on the behaviour of the user has not been investigated	Studies investigating this aspect are urgently needed; focus should be on assessment systems that provide feedback to the users
Upper body movements	Studies investigating upper body movements under supervised and unsupervised conditions are rare	More studies are necessary to see whether similar results in mobility are seen for upper body movements

Table 2: **Gaps, challenges, and steps toward a more informed use of supervised and unsupervised mobility assessments**

older adults and not for patients with neurological disorders. An example could be the evaluation of the effects of an experimental therapy. The effects might be measured best in the optimum state (improvement in supervised assessment and the best 10% of an individual's distribution of the unsupervised assessment), while the median and lower range of an individual's distribution might be informative of changes throughout the day (figure 2). Future trials could use this information as outcomes.

Variability measures can serve as a useful example of how important it is for clinicians and researchers to have a deep understanding of how their treatment and compounds influence mobility in daily life. Some variability measures (eg, stride length variability) are highly affected by the environment and should be measured in a supervised setting, which better reflects the patient's capacity.[45] In the home environment, decreased variability with similar mean values might be a positive outcome if the goal of an intervention is to reduce motor response fluctuations in patients with Parkinson's disease. In a trial investigating patients with suboptimal treatment, a decrease in variability associated with an improvement of mean values can indicate more consistent good performance during the day. In trials focusing on behavioural symptoms, increased variability might indicate better adaptability, more variable and enriched physical activity, and social interactions. Thus, the context is crucial for evaluating the effect of an intervention.

Whether data obtained from unsupervised environments provide relevant progression and treatment response information, rather than acting as markers of routine, fixed behaviours or trait markers, should be evaluated in future studies. Trait markers could still be good measures of progression, but appropriate interpretation is key for practical use. For example, the actions done during daily living are very different per individual, but show a surprisingly similar pattern within an individual.[69]

Future statistical analyses should take advantage of the high number of repeated, specific movements occurring during long-term observation periods in unsupervised environments (figure 2).[24,42] Deep learning, machine learning, and artificial intelligence approaches should be applied. Algorithms that learn from data have shown remarkable success in making accurate predictions for complex problems that previously depended on human skills (eg, referral for eye diseases,[70] detection of Parkinson's disease motor fluctuations).[71]

Future work should further explore the associations between objective digital measures with conventional measures of mobility, and with patient-reported outcome measures (PROMs) and caregiver-reported outcomes. Both PROMs (in this case, subjectively) and mobile health technologies (in this case, objectively) offer remote measurements in the unsupervised setting, and both approaches are potentially more ecologically valid and more meaningful to patients and their caregivers than are data acquired in the traditional clinical setting. Among the studies that we identified, only four assessed correlations with PROMs related to mobility, with contrasting findings (appendix pp 1–3).

We should keep in mind that mobile health technologies might alone cause behavioural changes, even when no feedback is provided (eg, Hawthorne effect), but especially if feedback is provided (eg, to induce compliance). Studies are needed to investigate if and when the performance of the user in the unsupervised setting becomes similar to that in the supervised setting,

and whether the induced behavioural changes themselves might have therapeutic effects that could interfere with the evaluation. For example, patients who know that they are equipped with mobile health technologies might increase their level of physical activity, particularly when feedback about their own performance is provided.

Health-care professionals should also interpret their supervised assessments cautiously, as these findings could have limited ecological value. To improve their value, we suggest to provide natural, everyday life-like situations and instructions during supervised assessments. Explicit goals should be given to the patients, forcing them to focus on the goal instead of on the actual movements that must be performed to reach the goal.[67] For example, instructing a sitting person to walk allows for a more naturalistic observation of the sit-to-stand performance, because the person focuses more on the walking task rather than the necessary transition from sit-to-stand. Other opportunities to observe uninstructed movements occur when patients move in the waiting room or on their way to the clinician's office.[72] It is also essential to gain as much information as possible about the living environment of the person being assessed. If the person has cluttered furniture at home, health-care professionals might focus more on assessing mobility in small, crowded places instead of large, open hospital hallways. Additionally, the type of furniture, lighting, patterns, and other environmental factors might be important.[73]

Mobility differences between the supervised and unsupervised setting can also be relevant for the measurement of other symptoms and deficits. For example, deficits in upper extremity movement occur in many patients with neurological disorders,[74] and several methods have been proposed to continuously assess upper limb bradykinesia in daily life.[75] However, a direct comparison of these various symptoms in supervised and unsupervised settings remains absent. One exception is a study that assessed habitual keyboard typing behaviour in patients with Parkinson's disease.[76] This study showed that various keystroke metrics as measured in the clinic were strongly correlated with those obtained at the patient's home, suggesting that some upper extremity performances (in this case, a measure of bradykinesia) are similar under supervised and unsupervised conditions. This finding underscores the need to assess different aspects of motor functioning on a case-by-case basis.

Conclusions

There is increasing evidence that, depending on whether mobility is assessed under supervised or unsupervised conditions, the results can differ substantially.[24,36,38,39] These striking differences and the importance of measurements obtained in both settings call for expanding our knowledge about unsupervised mobility (table 2). Unsupervised mobility parameters could be implemented to improve clinical care and could act as primary or secondary endpoints in future intervention trials.

Search strategy and selection criteria

We searched PubMed, Web of Science, and Google Scholar for articles published in English, Dutch, or German between Aug 1, 2014, to Aug 1, 2019 with the search terms "environment* OR setting* OR compare", "supervised OR lab OR laboratory OR standard* OR clinic*", "unsupervised OR home OR real life OR real world OR daily life OR daily living OR free living", and "wearable sensor OR inertial sensor OR inertial measurement unit OR acceleromet* OR gyroscope OR pendant sensor", not "intervention [Title/Abstract] OR rehabilitation[Title/Abstract] OR heart rate[Title/Abstract] OR energy expenditure[Title/Abstract] OR classification[Title/Abstract]". Studies were relevant if they measured similar mobility parameters with a wearable device in a supervised and in an unsupervised setting among patients with a neurological disorder or older adults (with mean or median age of at least 60 years). Reference lists of relevant articles were screened for additional references to generate the final reference list, and the authors were asked to provide input. The final reference list was generated on the basis of the relevance of papers to the topics that are discussed in this Personal View.

Contributors

EW, JMH, and WM developed the idea. EW did the literature search. EW, JMH, CH, and WM framed the outline. BRB, JMH, AA, YZ, AM, KA, AJE, CH, AK, CL, AP, LR, GS, and LJWE worked on different aspects of the manuscript. All authors commented on the manuscript and approved the final version.

Declaration of interests

EW, AA, and YZ are supported by Keep Control from the EU's Horizon 2020 (H2020) research and innovation programme under the Marie Skłodowska-Curie grant agreement number 721577. JMH, AM, KA, LR, and WM are supported by Mobilise-D from the Innovative Medicines Initiative 2 Joint Undertaking (grant number 820820); this Joint Undertaking receives support from the EU's H2020 research and innovation programme and the European Federation of Pharmaceutical Industries and Associations. JMH has received grant support from the US National Institutes of Health (NIH), the Michael J Fox Foundation for Parkinson's Research, the EU (H2020), and the US-Israel Binational Science Foundation, and has served or currently serves on the Movement Disorders Society Technology (MDS) Task Force, Michael J Fox Foundation task force on gait, board of the International Society for the Measurement of Physical Behavior, and advisory boards for Sanofi and Biogen. AM has received grant support from the Michael J Fox Foundation for Parkinson's Research, EU (H2020), Israeli Science Foundation, and Ministry of Science and Technology; chairs the Michael J Fox Foundation task force on gait; and is a consultant for Biogen Biotechnologies. AM and JMH have submitted a patent application on the use of body-fixed sensors for assessing Parkinson's disease symptoms, the intellectual property rights for which are held by the Tel Aviv Medical Center (Tel Aviv, Israel). KA has received a grant from the Swiss National Science, CTI, Innosuisse, EU (H2020, FP7, and FP6), Lausanne Orthopedics Research Foundation, Austria Research Promotion Agency, Swiss Multiple Sclerosis Society, Swiss Heart Foundation, Pierre Mercier Foundation, Swiss Federal Office of Sport, EHC-Hospital of Morges (Morges, Switzerland), and Suvaliv, and was co-founder of Gait Up, serving as its board member until 2018. AJE has received grant support from the NIH, Great Lakes NeuroTechnologies, and the Michael J Fox Foundation for Parkinson's Research; personal fees as a consultant and scientific advisory board member for AbbVie, Adamas, Acadia Pharmaceuticals, Acorda Therapeutics, NeuroDerm, Impax, Sunovion, Lundbeck, Osmotica Pharmaceutical, and US

WorldMeds; publishing royalties from Lippincott Williams & Wilkins, Cambridge University Press, and Springer; honoraria from US WorldMeds, Lundbeck, Acadia, Sunovion, the American Academy of Neurology, and the Movement Disorders Society. AJE serves as the chair of the MDS Technology Task Force. AK receives grants from the Michael J Fox Foundation for Parkinson's Research and Schaller-Nikolich Foundation, and is co-founder of and has shares in Hummingbird Diagnostics. CL has received funding from the EU (Interreg IVC) progamme, Northern Netherlands Alliance innovation grant, and Data Science Support Programme University of Groningen (Groningen, Netherlands), for Cotutelle PhD Programmes with the Université Grenobles Aples (Grenoble, France); is a board member of Hanze University of Applied Science, Master Sensor System Engineering–Institute of Engineering; has received speaker's fees for the conference on geriatric care (Maastricht, Netherlands); and is on the expert review-panel for the European Union ACTIVAGE project. LJWE is funded by Topconsortium voor Kennis en Innovatie Life Sciences and Health, the Michael J Fox Foundation for Parkinson's Research, Philips Research, and the Netherlands Organisation for Health Research and Development (91215076). AP has received speaker honoraria from BioMarin Pharmaceutical, Chiesi Pharmaceuticals, Nutricia Pharmaceuticals, UCB Pharma, and Zambon Pharmaceuticals; personal compensation as consultant or advisory board member for Z-cube (technology division of Zambon Pharmaceuticals); and travel grants from AbbVie Pharmaceuticals, BioMarin Pharmaceutical, Nutricia Pharmaceuticals, Zambon Pharmaceuticals, and the Italian Movement Disorder Society. LR receives grant support from the EU, Parkinson's UK, the UK Stroke Association, the UK Medical Research Council, the UK National Institute of Health Research, and New Zealand Health Research Council, and has served on advisory board for Biogen. GS receives funding from the German Research Foundation. BRB currently serves as an associate editor for the Journal of Parkinson's Disease; serves on the editorial of Practical Neurology and Digital Biomarkers; has received honoraria from serving on the scientific advisory board for AbbVie, Biogen, UCB, and Walk with Path; has received fees for speaking at conferences from AbbVie, Zambon, Roche, GE Healthcare, and Bial; and has received research support from the Netherlands Organisation for Scientific Research, the Michael J Fox Foundation for Parkinson's Research, UCB, AbbVie, the Stichting Parkinson Fonds, the Hersenstichting Nederland, the Parkinson's Foundation, Verily Life Sciences, H2020, the Topsector Life Sciences and Health, and the Parkinson Vereniging. WM receives or received funding from the EU, the German Federal Ministry of Education of Research, the Michael J Fox Foundation, the Robert Bosch Foundation, Neuroalliance, Lundbeck, and Janssen; has received speaker honoraria from AbbVie, Bayer, GlaxoSmithKline, Licher Medical Therapy, Rölke Pharma, and UCB; was invited to advisory boards of AbbVie, Biogen, Lundbeck, and Market Access and Pricing Strategy; serves as the co-chair of the MDS Technology Task Force; and is an advisory board member of Critical Path for Parkinson's. CH declares no competing interests.

References

1 WHO. International Classification of Functioning, Disability and Health. 2001. https://psychiatr.ru/download/1313?view=name=CF_18.pdf (accessed Jan 3, 2019).

2 Tolea MI, Galvin JE. The relationship between mobility dysfunction staging and global cognitive performance. *Alzheimer Dis Assoc Disord* 2016; **30:** 230–36.

3 Bergland A, Jørgensen L, Emaus N, Strand BH. Mobility as a predictor of all-cause mortality in older men and women: 11·8 year follow-up in the Tromsø study. *BMC Health Serv Res* 2017; **17:** 22.

4 Mahmoudi R, Novella JL, Manckoundia P, et al. Is functional mobility an independent mortality risk factor in subjects with dementia? *Maturitas* 2017; **103:** 65–70.

5 Wallace LMK, Theou O, Godin J, Andrew MK, Bennett DA, Rockwood K. Investigation of frailty as a moderator of the relationship between neuropathology and dementia in Alzheimer's disease: a cross-sectional analysis of data from the rush memory and aging project. *Lancet Neurol* 2019; **18:** 177–84.

6 Shafrin J, Sullivan J, Goldman DP, Gill TM. The association between observed mobility and quality of life in the near elderly. *PLoS One* 2017; **12:** e0182920.

7 Davis JC, Bryan S, Li LC, et al. Mobility and cognition are associated with wellbeing and health related quality of life among older adults: a cross-sectional analysis of the Vancouver falls prevention cohort. *BMC Geriatr* 2015; **15:** 75.

8 van Uem JMT, Marinus J, Canning C, et al. Health-related quality of life in patients with Parkinson's disease-a systematic review based on the ICF model. *Neurosci Biobehav Rev* 2016; **61:** 26–34.

9 Goetz CG, Tilley BC, Shaftman SR, et al. Movement disorder society-sponsored revision of the unified Parkinson's disease rating scale (MDS-UPDRS): scale presentation and clinimetric testing results. *Mov Disord* 2008; **23:** 2129–70.

10 Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983; **33:** 1444–52.

11 van Lummel RC, Walgaard S, Hobert MA, et al. Intra-rater, inter-rater and test-retest reliability of an instrumented timed up and go (iTUG) test in patients with Parkinson's disease. *PLoS One* 2016; **11:** e0151881.

12 Mancini M, Curtze C, Stuart S, et al. The impact of freezing of gait on balance perception and mobility in community-living with Parkinson's disease. *Conf Proc IEEE Eng Med Biol Soc* 2018: **2018:** 3040–43.

13 Espay AJ, Hausdorff JM, Sánchez-Ferro Á, et al. A roadmap for implementation of patient-centered digital outcome measures in Parkinson's disease obtained using mobile health technologies. *Mov Disord* 2019; **34:** 657–63.

14 Dorsey ER, Glidden AM, Holloway MR, Birbeck GL, Schwamm LH. Teleneurology and mobile technologies: the future of neurological care. *Nat Rev Neurol* 2018; **14:** 285–97.

15 Holter NJ. Radioelectrocardiography: a new technique for cardiovascular studies. *Ann NY Acad Sci* 1957; **65:** 913–23.

16 Wachter R, Gröschel K, Gelbrich G, et al. Holter-electrocardiogram-monitoring in patients with acute ischaemic stroke (Find-$AF_{RANDOMISED}$): an open-label randomised controlled trial. *Lancet Neurol* 2017; **16:** 282–90.

17 Bally L, Thabit H, Hartnell S, et al. Closed-loop insulin delivery for glycemic control in noncritical care. *N Engl J Med* 2018; **379:** 547–56.

18 van Uem JMT, Isaacs T, Lewin A, et al. A viewpoint on wearable technology-enabled measurement of wellbeing and health-related quality of life in Parkinson's disease. *J Parkinsons Dis* 2016; **6:** 279–87.

19 Block VAJ, Pitsch E, Tahir P, Cree BAC, Allen DD, Gelfand JM. Remote physical activity monitoring in neurological disease: a systematic review. *PLoS One* 2016; **11:** e0154335.

20 Ryan JM, Fortune J, Stennett A, et al. Changing physical activity behaviour for people with multiple sclerosis: protocol of a randomised controlled feasibility trial (iStep-MS). *BMJ Open* 2017; **7:** e018875.

21 Barrett TM, Liebert MA, Schrock JM, et al. Physical function and activity among older adults in Jodhpur, India. *Ann Hum Biol* 2016; **43:** 488–91.

22 Pham MH, Elshehabi M, Haertner L, et al. Algorithm for turning detection and analysis validated under home-like conditions in patients with Parkinson's disease and older adults using a 6 degree-of-freedom inertial measurement unit at the lower back. *Front Neurol* 2017; **8:** 135.

23 Del Din S, Godfrey A, Galna B, Lord S, Rochester L. Free-living gait characteristics in ageing and Parkinson's disease: impact of environment and ambulatory bout length. *J Neuroeng Rehabil* 2016; **13:** 46.

24 Zhang W, Regterschot GRH, Geraedts H, Baldus H, Zijlstra W. Chair rise peak power in daily life measured with a pendant sensor associates with mobility, limitation in activities, and frailty in old people. *IEEE J Biomed Health Inform* 2017; **21:** 211–17.

25 Ramsperger R, Meckler S, Heger T, et al. Continuous leg dyskinesia assessment in Parkinson's disease-clinical validity and ecological effect. *Parkinsonism Relat Disord* 2016; **26:** 41–46.

26 Teshuva I, Hillel I, Gazit E, Giladi N, Mirelman A, Hausdorff JM. Using wearables to assess bradykinesia and rigidity in patients with Parkinson's disease: a focused, narrative review of the literature. *J Neural Transm* 2019; **126:** 699–710.

27 Silva de Lima AL, Evers LJW, Hahn T, et al. Freezing of gait and fall detection in Parkinson's disease using wearable sensors: a systematic review. *J Neurol* 2017; **264:** 1642–54.

28 van Schooten KS, Pijnappels M, Rispens SM, et al. Daily-life gait quality as predictor of falls in older people: a 1-year prospective cohort study. *PLoS One* 2016; **11:** e0158623.

29 Weiss A, Brozgol M, Dorfman M, et al. Does the evaluation of gait quality during daily life provide insight into fall risk? A novel approach using 3-day accelerometer recordings. *Neurorehabil Neural Repair* 2013; **27:** 742–52.

30 Iluz T, Weiss A, Gazit E, et al. Can a body-fixed sensor reduce Heisenberg's uncertainty when it comes to the evaluation of mobility? Effects of aging and fall risk on transitions in daily living. *J Gerontol A Biol Sci Med Sci* 2016; **71:** 1459–65.

31 Del Din S, Galna B, Godfrey A, et al. Analysis of free-living gait in older adults with and without Parkinson's disease and with and without a history of falls: identifying generic and disease-specific characteristics. *J Gerontol A Biol Sci Med Sci* 2019; **74:** 500–06.

32 Punt M, Bruijn SM, Wittink H, van de Port IG, van Dieën JH. Do clinical assessments, steady-state or daily-life gait characteristics predict falls in ambulatory chronic stroke survivors? *J Rehabil Med* 2017; **49:** 402–09.

33 Clinical Trials Transformation Initiative. CTTI recommendations: developing novel endpoints generated by mobile technology for use in clinical trials. June, 2017. https://www.ctti-clinicaltrials.org/files/novelendpoints-recs.pdf (accessed March 25, 2019).

34 Cerreta F. EMA experience on mHealth technology. April 17, 2018. https://www.ema.europa.eu/en/documents/presentation/presentation-ema-experience-mhealth-technology-emas-pcwp-hcpwp-joint-meeting-francesca-cerreta_en.pdf (accessed March 25, 2019).

35 Urbanek JK, Zipunnikov V, Harris T, Crainiceanu C, Harezlak J, Glynn NW. Validation of gait characteristics extracted from raw accelerometry during walking against measures of physical function, mobility, fatigability, and fitness. *J Gerontol A Biol Sci Med Sci* 2018; **73:** 676–81.

36 Van Ancum JM, van Schooten KS, Jonkman NH, et al. Gait speed assessed by a 4-m walk test is not representative of daily-life gait speed in community-dwelling adults. *Maturitas* 2019; **121:** 28–34.

37 Toosizadeh N, Mohler J, Lei H, Parvaneh S, Sherman S, Najafi B. Motor performance assessment in Parkinson's disease: association between objective in-clinic, objective in-home, and subjective/semi-objective measures. *PLoS One* 2015; **10:** e0124763.

38 Takayanagi N, Sudo M, Yamashiro Y, et al. Relationship between daily and in-laboratory gait speed among healthy community-dwelling older adults. *Sci Rep* 2019; **9:** 3496.

39 Hillel I, Gazit E, Nieuwboer A, et al. Is every-day walking in older adults more analogous to dual-task walking or to usual walking? Elucidating the gaps between gait performance in the lab and during 24/7 monitoring. *Eur Rev Aging Phys Act* 2019; **16:** 6.

40 Rispens SM, van Schooten KS, Pijnappels M, Daffertshofer A, Beek PJ, van Dieën JH. Do extreme values of daily-life gait characteristics provide more information about fall risk than median values? *JMIR Res Protoc* 2015; **4:** e4.

41 Moufawad El Achkar C, Lenbole-Hoskovec C, Paraschiv-Ionescu A, Major K, Büla C, Aminian K. Classification and characterization of postural transitions using instrumented shoes. *Med Biol Eng Comput* 2018; **56:** 1403–12.

42 Haertner L, Elshehabi M, Zaunbrecher L, et al. Effect of fear of falling on turning performance in Parkinson's disease in the lab and at home. *Front Aging Neurosci* 2018; **10:** 78.

43 Supratak A, Datta G, Gafson AR, Nicholas R, Guo Y, Matthews PM. Remote monitoring in the home validates clinical gait measures for multiple sclerosis. *Front Neurol* 2018; **9:** 561.

44 Storm FA, Nair KPS, Clarke AJ, Van der Meulen JM, Mazzà C. Free-living and laboratory gait characteristics in patients with multiple sclerosis. *PLoS One* 2018; **13:** e0196463.

45 Rispens SM, Van Dieën JH, Van Schooten KS, et al. Fall-related gait characteristics on the treadmill and in daily life. *J Neuroeng Rehabil* 2016; **13:** 12.

46 Zijlstra W, Bisseling RW, Schlumbohm S, Baldus H. A body-fixed-sensor-based analysis of power during sit-to-stand movements. *Gait Posture* 2010; **31:** 272–78.

47 Jenkins IH, Jahanshahi M, Jueptner M, Passingham RE, Brooks DJ. Self-initiated versus externally triggered movements: II. The effect of movement predictability on regional cerebral blood flow. *Brain* 2000; **123:** 1216–28.

48 Wessel K, Zeffiro T, Toro C, Hallett M. Self-paced versus metronome-paced finger movements. A positron emission tomography study. *J Neuroimaging* 1997; **7:** 145–51.

49 Hunt C, Paez A, Folmar E. The impact of attentional focus on the treatment of musculoskeletal and movement disorders. *Int J Sports Phys Ther* 2017; **12:** 901–07.

50 Kal EC, van der Kamp J, Houdijk H. External attentional focus enhances movement automatization: a comprehensive test of the constrained action hypothesis. *Hum Mov Sci* 2013; **32:** 527–39.

51 Paradis E, Sutkin G. Beyond a good story: from Hawthorne Effect to reactivity in health professions education research. *Med Educ* 2017; **51:** 31–39.

52 Robles-García V, Corral-Bergantiños Y, Espinosa N, et al. Spatiotemporal gait patterns during overt and covert evaluation in patients with Parkinson's disease and healthy subjects: is there a Hawthorne effect? *J Appl Biomech* 2015; **31:** 189–94.

53 Brodie MAD, Coppens MJM, Lord SR, et al. Wearable pendant device monitoring using new wavelet-based methods shows daily life and laboratory gaits are different. *Med Biol Eng Comput* 2016; **54:** 663–74.

54 van Lummel RC, Walgaard S, Pijnappels M, et al. Physical performance and physical activity in older adults: associated but separate domains of physical function in old age. *PLoS One* 2015; **10:** e0144048.

55 Storm FA, Buckley CJ, Mazzà C. Gait event detection in laboratory and real life settings: accuracy of ankle and waist sensor based methods. *Gait Posture* 2016; **50:** 42–46.

56 Tamburini P, Storm F, Buckley C, Bisi MC, Stagni R, Mazzà C. Moving from laboratory to real life conditions: influence on the assessment of variability and stability of gait. *Gait Posture* 2018; **59:** 248–52.

57 Jones D, Rochester L, Birleson A, et al. Everyday walking with Parkinson's disease: understanding personal challenges and strategies. *Disabil Rehabil* 2008; **30:** 1213–21.

58 Lee JA, Williams SM, Brown DD, Laurson KR. Concurrent validation of the Actigraph gt3x+, polar active accelerometer, Omron HJ-720 and Yamax Digiwalker SW-701 pedometer step counts in lab-based and free-living settings. *J Sports Sci* 2015; **33:** 991–1000.

59 Pham MH, Warmerdam E, Elshehabi M, et al. Validation of a lower back "wearable"-based sit-to-stand and stand-to-sit algorithm for patients with Parkinson's disease and older adults in a home-like environment. *Front Neurol* 2018; **9:** 652.

60 Bourke AK, Ihlen EAF, Helbostad JL. Development of a gold-standard method for the identification of sedentary, light and moderate physical activities in older adults: definitions for video annotation. *J Sci Med Sport* 2019; **22:** 557–61.

61 Bourke AK, Ihlen EAF, Bergquist R, Wik PB, Vereijken B, Helbostad JL. A physical activity reference data-set recorded from older adults using body-worn inertial sensors and video technology—the ADAPT study data-set. *Sensors* 2017; **17:** e559.

62 Hausdorff JM, Hillel I, Shustak S, et al. Everyday stepping quantity and quality among older adult fallers with and without mild cognitive impairment: initial evidence for new motor markers of cognitive deficits? *J Gerontol A Biol Sci Med Sci* 2018; **73:** 1078–82.

63 Dujmovic I, Radovanovic S, Martinovic V, et al. Gait pattern in patients with different multiple sclerosis phenotypes. *Mult Scler Relat Disord* 2017; **13:** 13–20.

64 Moon Y, Sung J, An R, Hernandez ME, Sosnoff JJ. Gait variability in people with neurological disorders: a systematic review and meta-analysis. *Hum Mov Sci* 2016; **47:** 197–208.

65 Schloemer SA, Thompson JA, Silder A, Thelen DG, Siston RA. Age-related differences in gait kinematics, kinetics, and muscle function: a principal component analysis. *Ann Biomed Eng* 2017; **45:** 695–710.

66 Slater LV, Simpson AS, Blemker SS, et al. Biomechanical adaptations during running differ based on type of exercise and fitness level. *Gait Posture* 2018; **60:** 35–40.

67 Lindemann U, Zijlstra W, Aminian K, et al. Recommendations for standardizing validation procedures assessing physical activity of older persons by monitoring body postures and movements. *Sensors* 2014; **14:** 1267–77.

68 Badawy R, Hameed F, Bataille L, et al. Metadata concepts for advancing the use of digital health technologies in clinical research. *Digit Biomark* 2019; **3:** 116–32.

69 van Schooten KS, Rispens SM, Elders PJM, Lips P, van Dieën JH, Pijnappels M. Assessing physical activity in older adults: required days of trunk accelerometer measurements for reliable estimation. *J Aging Phys Act* 2015; **23:** 9–17.

70 De Fauw J, Ledsam JR, Romera-Paredes B, et al. Clinically applicable deep learning for diagnosis and referral in retinal disease. *Nat Med* 2018; **24:** 1342–50.

71 Zhan A, Mohan S, Tarolli C, et al. Using smartphones and machine learning to quantify Parkinson disease severity: the mobile Parkinson disease score. *JAMA Neurol* 2018; **75:** 876–80.

72 Araújo R, van de Warrenburg B, Lang A, Lees A, Bloem B. The waiting room: neurological observations made outside the movement disorder specialist's consulting office. *Pract Neurol* 2019; **19:** 295–301.

73 Domingos J, Keus SHJ, Dean J, de Vries NM, Ferreira JJ, Bloem BR. The European physiotherapy guideline for Parkinson's disease: implications for neurologists. *J Parkinsons Dis* 2018; **8:** 499–502.

74 Buckley C, Galna B, Rochester L, Mazzà C. Upper body accelerations as a biomarker of gait impairment in the early stages of Parkinson's disease. *Gait Posture* 2019; **71:** 289–95.

75 Del Din S, Godfrey A, Mazzà C, Lord S, Rochester L. Free-living monitoring of Parkinson's disease: lessons from the field. *Mov Disord* 2016; **31:** 1293–313.

76 Arroyo-Gallego T, Ledesma-Carbayo MJ, Butterworth I, et al. Detecting motor impairment in early Parkinson's disease via natural typing interaction with keyboards: validation of the neuroQWERTY approach in an uncontrolled at-home setting. *J Med Internet Res* 2018; **20:** e89.