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Mobility evaluation in Parkinson's disease: from disease study to therapeutic application



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Mobility evaluation in Parkinson's disease: from disease study to therapeutic application

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Mobility evaluation in Parkinson's disease: from disease study to therapeutic application

Valutazione della mobilità nella malattia di
Parkinson: dallo studio della malattia alle
applicazioni terapeutiche

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To Martina, keeper of my time.

To my family, for being my home, wherever I am.

*To Nicolas, and to my mentors, for their guidance;
to my colleagues, for the shared journey.*

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Abstract

Parkinson’s disease (PD) is the second most common neurodegenerative disease, and the fastest growing. In PD, mobility decline represents a key disabling feature, therefore studying how people with PD (PwPD) move is crucial for disease assessment, monitoring and management. PD symptoms could fluctuate within and between days, therefore, capturing mobility impairment only through laboratory-based tests (capacity) could not be sufficient and requires to integrate monitoring in real-world conditions (performance), across the full 24-hour cycle and for multiple days to collect a full picture of PwPD conditions. The advent of consumer wearables, such as smartwatches, made this assessment viable but most of these devices require validation. Additionally, mobility is not only determined by motor function but influenced by several personal and environmental factors. This is particularly true in PD where non-motor symptoms (NMS) are highly impactful. However, the extent to which motor symptoms (MS) and NMS of PD impact on both capacity and performance is still unclear. This doctoral thesis addressed these challenges in PD through three complementary sections:

- Validation of a commercial smartwatch for step counting. Four studies were included in this section.
- Assessment of the relationship between in-clinic walking capacity and real-world walking performance, and the contribution of MS and NMS to mobility. Three studies were included in this section.
- Assessment of nocturnal mobility, its association with diurnal mobility and response to dopaminergic treatment. Two studies were included in this section.

We built a large multimodal dataset of 121 people with PD including demographic, anthropometric and clinical measures exploring both MS and NMS. We also collected wearable-based measures of supervised (including turning, forward and backward walking) and unsupervised mobility.

In the first section we demonstrated that average daily steps (AvDS) were accurate and reliable in mild-to-moderate PD under ecological conditions, though influenced by disease stage, phenotype, device placement, and pharmacological state. Importantly, we established, for the first time, the minimal clinically important difference (MCID) for AvDS in PD, providing a benchmark to interpret change over time or in response to interventions. Taken together, these findings confirmed the feasibility of smartwatch-based measures as digital mobility outcomes while highlighting disease-specific limitations.

In the second section, we first compared forward walking, backward walking, and turning tasks with AvDS, using Bayesian model averaging. We revealed the limited power of supervised mobility tests in predicting unsupervised mobility. Furthermore, multivariate analyses showed that NMS, particularly executive dysfunction, depression and fatigue, are major determinants of supervised and unsupervised mobility. Their influence was most evident in complex tasks but also in AvDS, sometimes outweighing MS. These results underscore that mobility in PD is multidimensional, shaped by MS, NMS, and environmental factors.

In the third section we reported that patients with impaired nocturnal mobility also exhibited poorer daytime mobility, indicating that motor limitations extend across the full 24-hour cycle. Additionally, in a second pilot study we showed that dopaminergic therapy improved subjective sleep quality but not objective nocturnal mobility, suggesting partially distinct mechanisms. These findings highlight the importance of considering 24-hour mobility patterns in both research and care in PD.

In conclusion, the findings of the present PhD thesis pave the way for more ecologically valid, multidimensional, and patient-centered mobility monitoring strategies. These results can inform clinical decision-making, therapeutic interventions, and the design of meaningful digital mobility outcomes, ultimately improving independence and quality of life in people living with PD.

Chapter 1

State of the art

Mobility: a multifaceted construct

Mobility is one of the fundamental attributes of human life, underlying independence, participation, and social engagement (Mayo & Mate, 2022). It represents the ability to move freely and easily, encompassing both the physical capacity to move and the functional ability to perform daily activities requiring movement (Mikolaizak et al., 2022). In this definition, beyond the mere execution of gait or balance tasks, mobility is recognized as a multidimensional construct, shaped by physical, individual, psychosocial, and contextual factors that together determine a person's ability to move in their environment (Mikolaizak et al., 2022). From a conceptual standpoint, mobility can be divided into capacity and performance. Capacity describes what an individual can do under standardized, controlled conditions typically within the laboratory or clinical setting, whereas performance refers to what the individual actually does in their habitual environment (Maetzler et al., 2021; Mikolaizak et al., 2022). This distinction originates from the International Classification of Functioning, Disability and Health (ICF), which emphasizes that functioning results from the interaction between body structures and contextual factors, including personal and environmental ones (Organization, 2002) (fig. 1.1)

Concerning capacity, this is commonly assessed through standardized tasks designed to isolate specific components of movement. Traditionally, gait capacity has been represented by metrics such as walking speed, stride length, cadence, among others, often recorded over straight, unobstructed walking paths. However, in real life, mobility is rarely linear. People move forward, backward, sideways, turn, stop, start again, and frequently adapt to the surrounding environment. They negotiate obstacles, change directions, and multitask, combining walking with cognitive or manual activities such as talking or carrying objects (Giannouli et al., 2016; Maetzler et al., 2021). To reflect this ecological complexity, modern laboratory assessments incorporate tasks that capture multidirectional and adaptive aspects of movement, such as the Timed Up and Go (TUG) test (Christopher et al., 2021), turning assessments (Mancini et al., 2016), dual-task paradigms (Leone et al., 2017), and obstacle negotiation protocols (Chien et al., 2018). These tasks probe the integration of sensorimotor and executive control processes and offer a more ecological representation of capacity.

Performance, on the other hand, captures what individuals do in their daily lives. It provides a picture of real-world functioning, beyond laboratory constraints. When considering performance, daily steps have emerged as one of the most accessible and informative indicators, as recently reported in a very recent systematic review (Ding et al., 2025). This metric can be continuously and unobtrusively captured through wearables, offering an objective estimation of habitual ambulatory behavior in everyday life (Bassett et al., 2017). Although step count does not provide specific information about gait quality or context, lower values consistently indicate reduced mobility and poorer overall health. In older adults, a lower number of daily steps has been associated with increased all-cause mortality, as reported in a recent meta-analysis (Ding et al., 2025), and with higher incidence of chronic conditions including cardiovascular disease and cancer (Del Pozo Cruz, Ahmadi, et al., 2022), depression (Bizzozzero-Peroni et al., 2024), and dementia (Del Pozo Cruz, Ahmadi, et al., 2022).

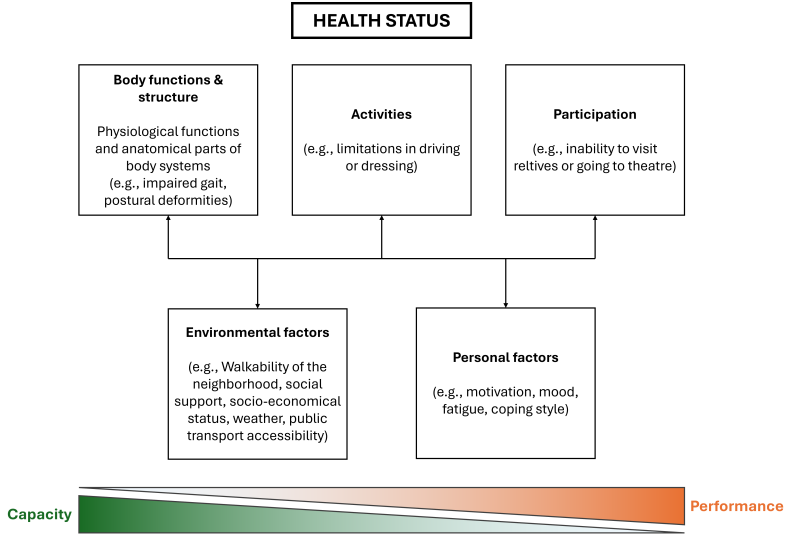


Figure 1.1. The interplay between capacity and performance within the ICF framework (Maetzler et al., 2021; Organization, 2002)

Furthermore, wearables used to capture daily step count can be either research-grade or consumer-grade: the former, such as BTS G-Walk (or Microberts Dynaport) are optimized for high-fidelity data collection under controlled conditions after undergoing rigorous validations (Mazzà et al., 2021; Vítěčková et al., 2020), while the latter, such as FitBit, Apple, or Garmin devices, offer greater scalability, enabling continuous monitoring in real-life settings. Nevertheless, consumer-grade devices require rigorous validation before being used in clinical or research contexts. In addition, step detection accuracy, and thus step count, can be affected by device placement, walking speed, and the presence of abnormal or disease-specific gait patterns, emphasizing the need for standardized validation frameworks to ensure reproducibility and comparability across studies and populations (Chow et al., 2017; Fokkema et al., 2017; Lamont et al., 2018).

However, while step count represents a high-level summary of mobility behavior, it does not provide a detailed understanding of mobility performance. This requires evaluating how movement occurs in daily life in terms of distribution, intensity, variability, and context. In recent years, several studies have demonstrated the feasibility of capturing such aspects using wearable devices, including walking-bout characteristics, turning frequency, gait spatiotemporal parameters, and postural transitions (Maetzler et al., 2021; Micó-Amigo et al., 2023). These real-world mobility measures offer unique insights into behavior outside the clinic and can detect subtle alterations that are not visible during short, supervised assessments. The relevance of performance measures is increasingly recognized by international initiatives such as Mobilise-D (Mikolaizak et al., 2022), and IDEA-FAST (Hinchliffe et al., 2024), which aim to define, validate, and qualify digital mobility outcomes (DMOs) for use as clinical endpoints. These large, multicenter consortia aim to standardize technical and analytical pipelines for wearable data, harmonized definitions of mobility events (e.g., walking bout, lying-to-standing transitions), and explored the relationship between DMOs

and traditional clinical scales. Collectively, they are shaping the future of digital health by establishing frameworks to link real-world mobility behavior with disease mechanisms, therapeutic response, and patient-centered outcomes.

Finally, beyond technical and physiological considerations, it is increasingly evident that mobility is not solely determined by physical ability. Rather, daily movement behavior reflects the interplay between physical, cognitive, psychological, and environmental factors that dynamically shape how individuals engage with their surroundings (Organization, 2002; Roussos et al., 2022). Fear of falling, fatigue, pain, or depressive symptoms may substantially reduce spontaneous activity even in the absence of overt motor limitations, while apathy or reduced motivation can lead to sedentary behavior despite preserved walking capacity. Mobility is also influenced by contextual and environmental affordances. Access to safe walking spaces, transportation options, and supportive social networks can facilitate mobility, whereas architectural barriers, urban density, or adverse weather conditions may discourage outdoor movement (Maetzler et al., 2021; Mikolaizak et al., 2022; Organization, 2002). Socioeconomic disparities further modulate these interactions, affecting not only opportunities for physical activity but also the perception of safety, autonomy, and purpose in daily life.

Altogether, mobility should be viewed as an emergent behavior, the outcome of continuous interactions between body, mind, and environment. It represents not just the ability to move, but the motivation and opportunity to do so. This multidimensional perspective underlines the need to move beyond a purely motor-centric view of mobility, paving the way toward a more holistic framework that captures its biological, psychological, and social determinants.

Mobility issues in Parkinson’s disease

Parkinson’s disease (PD) is a chronic, progressive neurodegenerative disorder and represents the fastest-growing neurological condition worldwide, both in terms of prevalence and associated disability (Dorsey et al., 2018; Su et al., 2025) (fig. 1.2). It affects approximately 1–2% of the population over 65 years of age, but its burden is no longer confined to the elderly. Recent global estimates show that PD prevalence has more than doubled over the past three decades, with a marked increase also observed among younger adults aged 20–50 years (Shen et al., 2025). The drivers of this rise are multifactorial, encompassing population aging, increased life expectancy, environmental exposures, and possibly changes in lifestyle and diagnostic awareness. From a public health and societal perspectives, this expanding burden poses major challenges. PD not only leads to progressive disability but also contributes substantially to caregiver strain, healthcare costs, and loss of independence. As populations age, the number of individuals living with PD is projected to exceed 12 million by 2040, highlighting the urgent need for strategies aimed at early detection, disease modification, and health system adaptation (Dorsey et al., 2018).

Clinically, PD is characterized by a combination of motor and non-motor symptoms resulting from the progressive loss of dopaminergic neurons in the substantia nigra pars compacta and the dysfunction of multiple interconnected neural circuits (Poewe et al., 2017) (table 1.1). Motor features, including bradykinesia, rigidity, resting tremor, and postural instability, are central to the diagnosis, yet their expression is highly heterogeneous and their progression is influenced by both dopaminergic and non-dopaminergic mechanisms (Armstrong & Okun, 2020; Poewe et al., 2017). Among the motor manifestations, mobility impairment represents one of the most disabling aspects of PD and a key determinant of functional decline and loss of independence. Mobility issues in PD encompass a wide range of deficits, including gait disturbances, postural control impairment, balance dysfunction, and freezing of gait (FOG) (Mirelman et al., 2019). These disturbances profoundly affect patients’ quality of life, increase the risk of falls, and limit participation in social and physical activities (Nutt et al., 2014; van Uem et al., 2018).

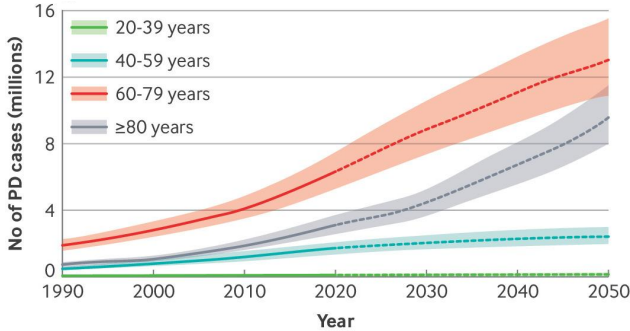


Figure 1.2. Estimated trends of numbers of PD cases by age groups with 95% uncertainty intervals, 1990-2050 worldwide. Solid lines represent values from Global Burden of Disease (1990-2021); dotted lines represent projected values (2022-50). Adapted from (Su et al., 2025) under CC BY-NC 4.0.

Gait in PD is typically characterized by a slower walking speed, shorter stride length, increased step-to-step variability, and reduced arm swing (Mirelman et al., 2019). Turning, gait initiation, and backward walking are particularly challenging tasks (Hackney & Earhart, 2009; Mancini et al., 2015; Mirelman et al., 2019), reflecting an impaired ability to generate and coordinate sequential motor commands. These abnormalities contribute to an unstable and fragmented gait pattern that worsens with disease progression (Mirelman et al., 2019). Unlike many other aspects of PD motor symptoms, gait and other axial symptoms often respond poorly to dopaminergic treatment (Fabbri et al., 2016), particularly in the later stages of the disease, suggesting that non-dopaminergic mechanisms, involving cholinergic, serotonergic, and noradrenergic systems play a crucial role (Imbalzano et al., 2023; Packer et al., 2025).

In the early stages of PD, mobility impairments may be subtle and episodic, often emerging only under complex or dual-task conditions. Dual-task walking, when a cognitive or motor task is performed concurrently with gait, can reveal underlying deficits in automaticity and the excessive reliance on attentional control mechanisms (Johansson et al., 2021). The basal ganglia normally facilitate automatic execution of learned motor sequences, but in PD, this automaticity breaks down, requiring compensatory activation of prefrontal networks. Among all mobility deficits, freezing of gait (FOG) stands out as one of the most complex and burdensome phenomena (Nutt et al., 2011). It is defined as a brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk (Nutt et al., 2011). FOG typically occurs during gait initiation, turning, or when passing through narrow or crowded spaces, and is frequently triggered by stress or dual tasking. Its episodic and unpredictable nature makes it rather difficult to capture during clinical assessments, yet its consequences are severe, significantly increasing the risk of falls and injuries.

Falls are another major consequence of mobility impairment in PD (Fasano et al., 2017). Around 60% of PwP experience at least one fall per year, and up to one-third fall recurrently (Fasano et al., 2017). Falls result not only from postural instability and FOG, but also from orthostatic hypotension, vision changes, and medication-related fluctuations. Beyond physical injury, the fear of falling can itself exacerbate immobility, reducing outdoor activity and contributing to social isolation (Atrsaiei, Hansen, et al., 2021).

Table 1.1. Motor and non-motor symptoms in PD (Poewe et al., 2017; Schapira et al., 2017).

Motor symptoms	Non-motor symptoms
Bradykinesia	Sleep problems (RBD, EDS, RLS, Insomnia, etc.)
Rigidity	Depression
Tremor	Anxiety
Postural instability	Apathy
Postural abnormalities	Constipation
Gait disturbances	Delayed gastric emptying
Falls	Urinary symptoms
Dysphagia	Sexual dysfunction
Hypophonia	Orthostatic hypotension
Micrographia	Excessive sweating
Hypomimia	Sialorrhea
Nocturnal hypokinesia	Hyposmia
	Fatigue
	Psychotic symptoms
	ICD
	Cognitive impairment (from MCI to dementia)
	Pain
	Blurred vision

EDS: excessive daytime sleepiness; ICD: impulse control disorders; MCI: mild cognitive impairment; PD: Parkinson’s disease; RBD: REM sleep behavior disorder; RLS: restless legs syndrome.

Recent technological advances have revealed that mobility impairment in PD extends well beyond what is observable during in-clinic examinations. This was recently highlighted by a systematic review (Kirk et al., 2025) that provided the first comprehensive synthesis of real-world gait-related DMOs in PD. Across 27 studies, the authors found that real-world DMOs consistently revealed slower walking speed, shorter stride length, and greater gait variability compared to both supervised assessments and healthy controls. Beyond daytime gait and postural control deficits, PwPD frequently experience nocturnal motor impairment, which manifests as difficulty turning in bed, adjusting position, or rising from the supine posture (Sommerauer et al., 2015; Sringean et al., 2020). This phenomenon, referred to as nocturnal hypokinesia (NH), affects a majority of individuals with PD and results from the persistence of bradykinesia, rigidity, and axial stiffness during the night, when dopaminergic medication levels decline controls (Bhidayasiri, Sringean, & Thanawattano, 2016; Bhidayasiri & Trenkwalder, 2018; Sringean et al., 2017). Additionally, nocturnal mobility impairment could be considered as part of a 24-hour continuum of motor dysfunction in PD, extending the concept of mobility beyond the waking day. However, this hypothesis lacks evidence and very few studies investigated mobility as a 24-hour concept in PwPD. Accordingly, addressing NH as an integral component of the 24-hour motor phenotype represents a necessary step toward a more comprehensive understanding of mobility in PD, and this issue will be specifically explored in the present work. Mobility in PD could therefore be best understood as a multidimensional phenomenon resulting from the dynamic interaction of personal (motor and non-motor), and contextual determinants (Maetzler et al., 2021). In this framework, its assessment and management hence require an integrative approach that captures both capacity and real-world performance, thus bridging the gap between laboratory measures and patients’ lived experiences.

Wearable devices for mobility assessment in Parkinson's disease

The objective evaluation of mobility in Parkinson's disease (PD) has evolved considerably over the past two decades, driven by the growing availability of wearable sensing technologies. These devices, which typically incorporate inertial measurement units (IMUs) composed of accelerometers and gyroscopes, have enabled quantitative analysis of gait and postural control both in controlled laboratory settings and during real-world daily activities (Bianchini & Maetzler, 2023) (fig. 1.3).

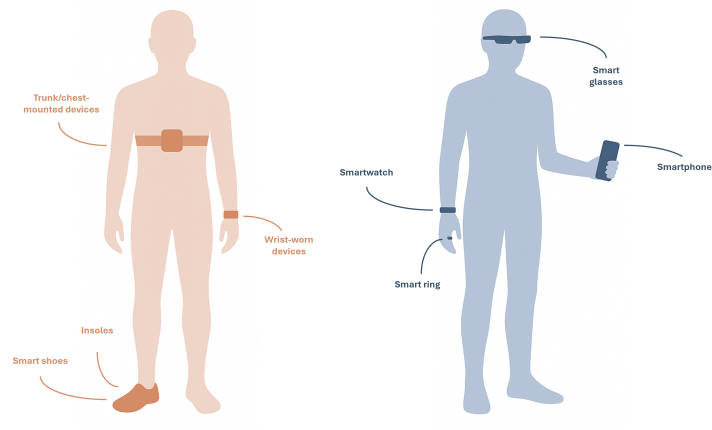


Figure 1.3. Examples of research-grade (left, orange) and commercial (right, blue) wearable devices.

For a decade now, wearable-based assessments have become central to clinical and research efforts aimed at characterizing motor impairment, quantifying disease progression, and identifying digital biomarkers of functional mobility (Espay et al., 2016; Kirk et al., 2025; Moreau et al., 2023; Packer et al., 2025). In laboratory or supervised settings, wearable sensors are used to capture quantitative gait parameters during standardized motor tasks, providing an accurate and repeatable measure of mobility capacity. The use of body-worn sensors in such contexts allows for detailed kinematic analysis with reduced technical constraints compared to traditional optical motion capture systems (Moreau et al., 2023). Wearables can be placed on the lower back, upper and limbs, wrist, ankle or feet, and record three-dimensional acceleration and angular velocity signals from which spatial and temporal gait variables are derived (Moreau et al., 2023).

Laboratory-based wearable assessments have been applied in PD to investigate disease-related alterations in gait and postural control across the disease continuum. Studies have consistently reported reduced walking speed, shorter steps, increased variability, and prolonged double-support phases compared to healthy controls (Mirelman et al., 2019). These parameters worsen with advancing disease severity and are sensitive to medication state: improvements in speed and step length are typically observed after levodopa intake, whereas gait variability and postural instability show limited responsiveness (Imbalzano et al., 2023; Kirk et al., 2025; Packer et al., 2025).

Wearable sensors have also facilitated the evaluation of complex mobility tasks, such as

turning (Mancini et al., 2015), FOG (Mancini et al., 2025), and dual-task walking (Kelly et al., 2012), which are difficult to quantify using visual observation alone. Several wearables have also been validated in PD against optical motion capture systems like demonstrating high accuracy (mean error $<1-2\%$) and strong test-retest reliability across PD and control populations (Moreau et al., 2023). These validations have established wearables as reliable tools for standardized mobility assessments under controlled conditions. While laboratory-based evaluations capture mobility capacity, wearable devices have also been used extensively to measure mobility performance. This approach, often referred to as free-living or real-world monitoring, enables continuous, ecologically valid assessment of gait and physical activity. Real-world monitoring typically involves single- or multi-sensor configurations worn for several days to quantify DMOs such as walking speed, step count, bout duration, and turning frequency (Kirk et al., 2025).

Studies using real-world monitoring have shown that people with PD exhibit marked reductions in daily walking activity compared with healthy peers, characterized by fewer steps, shorter walking bouts, and lower variability in gait speed (Kirk et al., 2025). These parameters correlate with disease severity, functional independence, and patient-reported quality of life. Importantly, continuous monitoring could highlight how mobility variations over the day reflect medication cycles and disease fluctuation, offering a more comprehensive picture of disease burden than isolated laboratory assessments. The possibility of monitoring both in supervised and unsupervised conditions has also made it possible to assess the potential capacity-performance gap. This is the discrepancy between mobility capacity measured in the laboratory and performance in daily life. This gap underscores the contribution of personal and environmental factors that constrain real-world mobility, even when motor capacity is relatively intact (Giannouli et al., 2016). Wearable-based studies have begun to quantify this gap (Atrsaei, Corrà, et al., 2021; Corrà et al., 2021; Del Din et al., 2016; Toosizadeh et al., 2015; Zajac et al., 2022), however this area of research in PD is still understudied.

Beyond research-grade systems, recent years have seen a growing interest in the use of commercial wearables, particularly smartwatches, bracelets and fitness trackers, to monitor mobility in PD (Adams et al., 2023; Powers et al., 2021; Wendel et al., 2018). These devices offer the advantage of being lightweight, non-intrusive, and already integrated into patients' daily routines, thus allowing for high adherence and large-scale data collection under fully ecological conditions (Bianchini & Maetzler, 2023; Moreau et al., 2023). Commercial wearables are typically equipped with triaxial accelerometers and gyroscopes capable of capturing step counts, walking speed, and activity levels continuously. Studies have demonstrated that daily step counts obtained from commercial smartwatches correlate with disease severity and functional independence in PD, suggesting their potential as scalable mobility markers (Christiansen et al., 2017; Mantri et al., 2019; Skidmore et al., 2008).

However, the accuracy and interpretability of commercial devices in PD populations depend on several factors. Tremor, bradykinesia, and reduced arm swing may lead to miscounted steps when wrist-worn devices are used (Kim et al., 2019; Wendel et al., 2018). Furthermore, algorithms implemented by manufacturers are typically optimized for healthy populations and remain proprietary, limiting transparency and reproducibility. Validation studies comparing consumer devices against research-grade sensors have reported variable accuracy (Kim et al., 2019; Lamont et al., 2018; Wendel et al., 2018). Moreover, there is currently no universal consensus on the minimal number of days required for reliable real-world mobility estimation differently from what was reported in other neurological conditions such as multiple sclerosis (Norris et al., 2017) and stroke (Fini et al., 2019). Studies in PD suggest that two days of continuous monitoring are sufficient to achieve stable estimates of step count using an ankle-mounted device (Paul et al., 2016), though no data regarding wrist-worn wearables are available.

Another limitation lies in the interpretation of wearables-derived data. While gait speed

and step count are intuitive metrics, more complex parameters—such as turning angle, gait variability, or bout length distribution—require careful contextualization to ensure clinical interpretability. Moreover, real-world mobility could be influenced by non-motor symptoms such as cognitive impairments, mood disturbances, fatigue, and sleep disturbances, which can confound purely motor interpretations. Finally, no minimal clinically important difference exists for real-world mobility parameters, such as daily steps. Despite these limitations, both the accessibility and usability of commercial wearables make them valuable tools for large-scale studies and for complementing clinical assessments. The widespread use of smartwatches also opens possibilities for long-term monitoring of digital endpoints, provided that data pipelines adhere to standards of transparency, privacy, and analytical validation.

Regarding nighttime periods, the advent of wearable sensors has made it possible to quantify NH objectively and continuously, providing insight into a domain of Parkinson’s disease that was previously difficult to evaluate (Zampogna et al., 2020). Traditional sleep studies or patient questionnaires offer only indirect or episodic information about nighttime movement. In contrast, inertial sensors placed on the wrist, trunk, or limbs can record acceleration and angular velocity throughout the night, allowing computation of key metrics such as total movement time, number and duration of bed turns, and time spent immobile (Bhidayasiri, Sringean, & Thanawattano, 2016; Mirelman et al., 2020; Zampogna et al., 2020). These measures have previously been used to demonstrate the reduced nocturnal mobility in PwPD (Mirelman et al., 2020) and allowed to correlate fluctuations in nocturnal mobility that parallel medication cycles, reflecting dopaminergic pharmacodynamics and OFF-state phenomena (Sringean et al., 2017). Moreover, studies using wearables demonstrated the positive effect of nighttime dopaminergic therapy to improve NH (Bhidayasiri, Sringean, Anan, et al., 2016; Bhidayasiri et al., 2017). Overall, wearable-based assessment of NH represents a key advancement and opportunity in digital mobility research. By extending monitoring beyond the laboratory and across the sleep–wake cycle, these tools provide a comprehensive and ecologically valid picture of motor function, informing both clinical management and the design of 24-hour digital mobility outcomes in Parkinson’s disease.

Mobility in Parkinson’s disease: not only a matter of movement

While motor dysfunctions are central to Parkinson’s disease (PD), it has become increasingly evident that NMS, including cognitive, affective, sleep, and autonomic disturbances, play a crucial role in shaping mobility. These symptoms, are now recognized as intrinsic components of PD pathology, reflecting the widespread neurodegeneration that extends well beyond the dopaminergic nigrostriatal system (Schapira et al., 2017). NMS often precede the onset of classical motor manifestations by years and evolve in parallel with disease progression, exerting a cumulative and multifactorial impact on patients’ functional independence, mobility, and quality of life (Ba et al., 2016; Huang et al., 2019; Prakash et al., 2016; Timurtas et al., 2025). The mechanisms linking NMS to mobility alterations in PD arise from diffuse neurochemical and network dysfunctions. Degeneration of dopaminergic projections impairs basal ganglia circuits involved in movement initiation and automaticity, but concomitant loss of cholinergic, noradrenergic, and serotonergic pathways disrupts attention, arousal, and motivation (Bohnen & Albin, 2011; Morris et al., 2019; Politis & Niccolini, 2015; Ray Chaudhuri et al., 2023; Tosslerams et al., 2023). This multisystem involvement compromises both the execution and the regulation of movement, especially in complex or attention-demanding situations. For example, degeneration of the pedunculo-pontine nucleus, a key locomotor hub with cholinergic projections, contributes to postural instability and gait freezing as well as sleep problems (Gallea et al., 2017). Similarly, cortico-striatal disconnection and prefrontal dysfunction underlie deficits in executive control, resulting in reduced gait automaticity and impaired locomotion, particularly under

dual-task (Heremans et al., 2013; Johansson et al., 2021; Yogev-Seligmann et al., 2008). Additionally, mood disorders and fatigue are frequent in PD and contribute significantly to reduced quality of life and disability (Schapira et al., 2017). Depression, anxiety and fear of falling are known negative contributors to mobility by impairing gait (Dragašević-Mišković et al., 2021; Lord et al., 2013) as well as modulating movement initiation and willingness to engage in physical activity (Timblin et al., 2022; van Uem et al., 2018). Similarly, fatigue is known to negatively impact gait in PD (Carvalho et al., 2020; Pilotto et al., 2023) and reduce physical activity (Garber & Friedman, 2003). These factors could interact bidirectionally with mobility. Reduced activity levels reinforce depressive and apathetic states through behavioral deconditioning, while chronic inactivity exacerbates fatigue and physical weakness, perpetuating a vicious cycle. Finally, sleep disturbances represent one of the most pervasive and functionally consequential domains. Up to 90% of people with PD experience some form of sleep problem, including insomnia, fragmented sleep, RBD, and excessive daytime sleepiness (Dodet et al., 2024; Iranzo et al., 2024). RBD, often preceding PD onset by years (Heinzel et al., 2019), reflects dysfunction in brainstem regions also involved in locomotor and postural control, suggesting shared neuroanatomical substrates between sleep and mobility regulation (Gallea et al., 2017). Emerging evidence supports a bidirectional relationship between sleep and mobility. Poor sleep quality and excessive daytime somnolence impair mobility is associated with higher incidence of FOG (Milane et al., 2024a, 2024b). Conversely, decreased physical activity and during the day can disrupt circadian rhythms and worsen sleep quality (Cristini et al., 2021; Yi et al., 2022). In this context, mobility becomes not merely a function of muscle control, but a behavioral output of distributed brain networks integrating motor, cognitive, and affective information. The evidence demonstrates that mobility in PD arises from a complex interplay between motor, nonmotor and environmental factors. This multidimensional construct cannot be fully captured by motor assessments alone, as NMS contribute substantially to functional disability and daily movement behavior. However, it must be underlined that no study to date systematically investigated the contribution of motor and nonmotor determinants of mobility in PD taking into consideration both these domains. Adopting this integrative perspective encourages the development of multidomain interventions targeting both motor and non-motor determinants of mobility. Furthermore, continuous digital monitoring using wearable technologies offers new opportunities to capture the fluctuating interaction between motor and non-motor domains, enabling personalized and dynamic approaches to patient care.

Chapter 2

Thesis aims and rationale

Mobility represents a core aspect of PD. Despite decades of research, the objective and comprehensive assessment of mobility in PD remains challenging. Traditional evaluations rely mainly on short, laboratory-based tests performed under supervision, which provide valuable but limited information about patients' true functional ability. Such clinical tests measure capacity but fail to capture performance. Recent advances in wearable technology, including the widespread availability of commercial devices, have made it possible to measure mobility continuously and unobtrusively in ecological settings. However, several knowledge gaps persist. First, most commercial wearables were designed for healthy users and lack disease-specific validation in PD, where bradykinesia, tremor, and altered gait patterns can affect accuracy and reliability. Moreover, to the best of our knowledge, no threshold has been established to clinically interpret changes in real-world mobility metrics. Second, the relationship between supervised (in-clinic) and unsupervised (real-world) mobility remains poorly understood. It is hence unclear whether laboratory-based measures can reliably predict daily performance or whether they capture distinct facets of mobility. Third, while mobility is often interpreted as a direct expression of motor impairment, converging evidence indicates that it is also shaped by NMS, that profoundly influences daily activity. Yet, the relative contribution of motor and nonmotor symptoms to both capacity and performance remains only partially explored in PD. Finally, mobility in PD has traditionally been studied during daytime. Little is known about how motor impairment extends across the 24-hour cycle, particularly regarding nocturnal mobility and its relation to daytime function and dopaminergic therapy. Along these lines, this doctoral thesis was designed to address these open questions through an integrative, multimodal, and ecologically oriented approach. To answer this, the thesis was articulated into three complementary sections, each targeting a specific dimension of this question:

- Validation of smartwatch-based measures of mobility. The first aim was to determine whether and how a commercial smartwatch could provide accurate and reliable estimates of mobility, specifically average daily steps (AvDS), in people with PD. In addition to accuracy and reliability, it also aimed to establish the Minimal Clinically Important Difference (MCID) for AvDS in PD, defining a benchmark for interpreting meaningful changes over time or following interventions.
- Determinants of supervised and unsupervised mobility. The second aim was to investigate both capacity and performance in PD and their relationship as well as the extent to which MS and NMS influence both these mobility aspects.
- Extension of mobility assessment to the 24-hour cycle. The third aim was to explore mobility beyond the waking day, analyzing nocturnal movement patterns and their association with daytime mobility and dopaminergic nocturnal treatment.

Together, these studies were designed to provide a consistent and progressive exploration of mobility in PD, from measurement validation to multidimensional modeling and clinical insight (fig. 2.1).

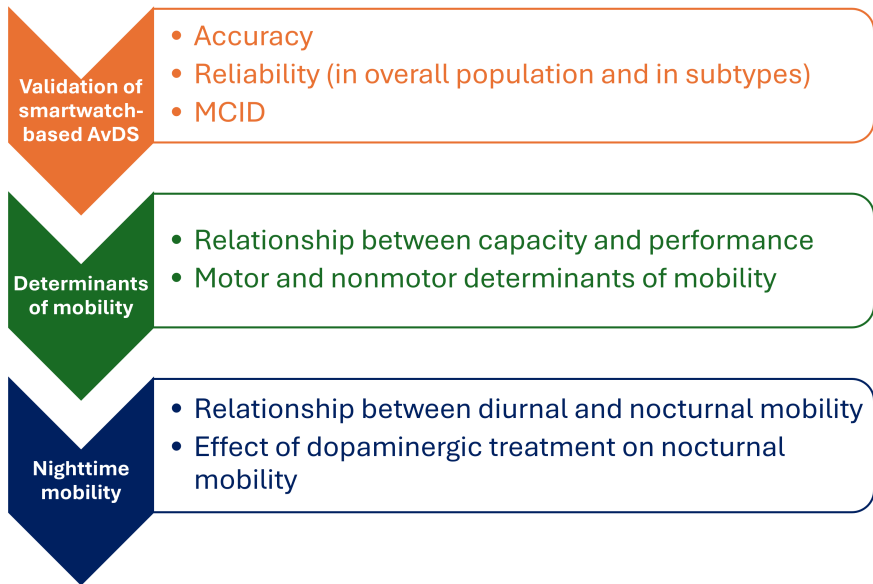


Figure 2.1. Schematic representation of the 3 sections of this doctoral work and their respective aims.

The ultimate rationale of this thesis is to promote a more ecologically valid, multidimensional, and patient-centered understanding of mobility in PD. The findings are intended to inform the development of standardized digital mobility outcomes, guide therapeutic decision-making, and advance personalized monitoring strategies that capture the full spectrum of movement across daily and nocturnal life, ultimately supporting independence and quality of life in people living with PD.

Chapter 3

Project overview and methodology

To achieve the goals previously reported, the overall methodological approach of this doctoral work combined experimental validation, clinical translation, and exploration of physiological and behavioral determinants of mobility across the 24-hour cycle. The details of the methods, instruments and experimental protocol are described in the following section.

Study design and population

All studies were conducted on a shared cross-sectional dataset of mild-to-moderate PwPD, consecutively recruited at the Movement Disorders Centre of Sant'Andrea University Hospital (Sapienza University of Rome, Italy) between 2021 and 2024. Participants provided written informed consent, and all protocols were approved by the local Ethics Committee (Ref. 0372/2022) in accordance with the Declaration of Helsinki.

Inclusion criteria:

- Diagnosis of idiopathic Parkinson's disease according to the Movement Disorder Society (MDS) criteria (Postuma et al., 2015);
- Age 18 years;
- Disease stage < 4 ("severe disability, still able to walk or stand unassisted") according to the modified Hoehn and Yahr (mHY) scale;
- Ability to understand and perform the experimental procedures and to comply with wearable monitoring instructions;

Exclusion criteria:

- Severe cognitive impairment, defined by a Montreal Cognitive Assessment (MoCA) score < 18;
- Orthopedic, rheumatologic, or systemic conditions affecting mobility as judged by the investigator;
- Comorbid neurological diseases or psychiatric conditions interfering with motor assessment;
- Ability to understand and perform the experimental procedures and to comply with wearable monitoring instructions.

Clinical outcome measures

The following demographic, anthropometric and clinical general variables were collected.

- Age (years)
- Sex
- Height (cm)
- Weight (kg)
- Body Mass Index (BMI) (kg/m^2)
- Disease duration (years)
- Modified Hoehn and Yahr (mHY) stage
- Levodopa Equivalent Daily Dose (LEDD) (mg)
- Number of falls in the last 6 months.

The following clinical scales were used:

Movement Disorder Society–Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) parts I– IV. MDS-UPDRS is the most widely used scale to assess PD severity (Goetz et al., 2008). Score ranges from 0 to 260 with higher scores indicating higher disease severity. It is divided into 4 subscales:

- Part I: Non-motor experiences of daily living (range 0-52).
- Part II: Motor experiences of daily living (range 0-52).
- Part III: Motor examination (range 0-132).
- Part IV: Motor complications (range 0-24).

Additionally, from Parts II and III, specific subscores were derived (Adams et al., 2023; Stebbins et al., 2013):

- Tremor Dominant (TD).
- Postural Instability and Gait Disorder (PIGD).
- Akinetic-Rigid (AR).

These subscores were also used to classify participants into TD, PIGD and AR phenotypes.

Montreal Cognitive Assessment (MoCA). MoCA is a widely used screening tool for global cognition. Score ranges from 0 to 30 with lower scores indicating worse performance (Nasreddine et al., 2005). **Word–Color Stroop Test (WCST).** WCST is a standardized neuropsychological assessment widely used to evaluate executive functions, particularly inhibitory control, selective attention, and cognitive flexibility. It is based on the paradigm, in which individuals must suppress an automatic reading response in order to name the color of the ink in which incongruent words are printed (e.g., the word “blue” written in red ink). measure of executive functioning and inhibitory control. Several scoring systems are used to rate WCST performance. In this doctoral work, the time to complete the interference part of the WCST was used as outcome measure (Scarpina & Tagini, 2017), as done in previous work from our group (Assogna et al., 2018).

Parkinson’s Disease Sleep Scale version 2 (PDSS-2). PDSS-2 is a 15-item questionnaire evaluating nocturnal symptoms, including insomnia, restlessness, and nocturnal immobility (score range 0–60) (Trenkwalder et al., 2011). Higher scores indicate worse sleep

quality. A Score 15 indicates the presence of clinically significant sleep problems (Suzuki et al., 2015).

Epworth Sleepiness Scale (ESS). ESS is a 8-item scale assessing daytime sleepiness (score range 0–24). Higher scores indicate worse sleep quality. A Score 10 indicates the presence of clinically significant sleep problems (Johns, 1991).

Fatigue Severity Scale (FSS). FSS is a 9-item questionnaire assessing the impact of fatigue on daily functioning. Individuals must score each item from 1 to 7 and the mean of all the 9 items is computed (range 1–7). A score 4.67 indicates clinically significant fatigue in PD (Siciliano et al., 2019).

Beck Depression Inventory – version II (BDI-II). BDI-II is a 21-item self-administered scale evaluating depressive symptoms- Score ranged 0–63 with higher scores indicating more severe depression (Maggi et al., 2023).

Parkinson’s Disease Questionnaire 39 (PDQ-39). PDQ-39 is a standardized assessment of quality of life across 8 domains (mobility, ADL, emotional well-being, stigma, social support, cognition, communication, bodily discomfort) (Jenkinson et al., 1997). Individuals must rate each of the 38 items from 0 to 4. For each domain, the raw item scores are summed, divided by the maximum possible score for that domain, and multiplied by 100 to obtain a percentage score ranging from 0 to 100. Higher scores indicate worse perceived quality of life. An overall summary measure is then calculated as the mean of the eight domain scores. From the first 16 items of PDQ-39, the **Functional Mobility Composite Score (FMCS)** was computed. The FMCS is a composite metric designed to provide an integrated overview of functional mobility (Hanff et al., 2023).

Wearing-Off Questionnaire 19 (WOQ-19). WOQ-19 is a screening tool to identify motor and non-motor wearing-off fluctuations. For each item, patients are asked to respond “Yes” or “No” to two questions: Whether the symptom is experienced during the day and whether the symptom improves after the next medication dose. Each symptom that improves with medication is scored as present wearing-off. The total WOQ-19 score corresponds to the number of items marked “Yes” for improvement after medication, thus ranging from 0 to 19. A higher score indicates greater frequency or burden of wearing-off phenomena and a score 2 indicates the presence of clinically significant WO (Mantese et al., 2018).

Freezing of Gait Questionnaire (NFOG-Q). NFOG-Q is a validated self-administered instrument designed to assess the presence, frequency, and severity of FOG in PD (Nieuwboer et al., 2009). The scale consists of nine items, covering different aspects of FOG episodes, including their occurrence in daily life, duration, frequency, and the impact on mobility. In this thesis, only item 1 of the questionnaire was used as a screening tool to determine the presence of FOG. A score of 1 was used to define the presence of FOG.

Falls Efficacy Scale International (FES-I). FES-I is a self-administered questionnaire designed to assess fear of falling and the level of concern about falling during a range of common daily activities (Mehdizadeh et al., 2019). It includes 16 items covering both basic and more demanding physical and social activities (e.g., dressing, bathing, walking on uneven surfaces, visiting friends or relatives). Total scores ranging from 16 to 64. Higher scores indicate greater fear of falling and reduced confidence in performing daily activities. The FES-I has been validated in older adults and in people with Parkinson’s disease as a reliable measure of fall-related self-efficacy and perceived mobility limitations.

Short Physical Performance Battery (SPPB). The SPPB is a standardized and validated test battery used to evaluate lower extremity function and global mobility capacity in older adults and individuals with neurological disorders (Guralnik et al., 1994). It consists of three components: balance tests, gait speed, and a five-time sit-to-stand test. Total score ranges from 0 to 12. Higher scores indicate better physical function.

Wearable devices and mobility data collection

To comprehensively characterize mobility in people with Parkinson’s disease (PwPD), both supervised (capacity-based) and unsupervised (performance-based) mobility assessments were conducted using a combination of research-grade and consumer-grade wearable sensors. This multimodal approach allowed for the integration of controlled laboratory metrics with real-world mobility data, enabling the evaluation of mobility across ecological contexts and timescales.

Supervised mobility assessment (capacity)

Supervised mobility tasks were performed in a clinical setting under standardized conditions to assess mobility capacity. All participants were equipped with a research-grade inertial measurement unit (IMU) (BTS G-WALK, BTS Bioengineering, Milan, Italy) placed on the lower back at the level of the fifth lumbar vertebra (L5) using an adjustable elastic belt. This device includes a triaxial accelerometer, gyroscope, and magnetometer, connected via Bluetooth to the G-Studio analysis software (BTS Bioengineering, Milan, Italy). The IMU records linear accelerations and angular velocities across three axes, which are automatically processed by the manufacturer’s algorithms to derive validated spatiotemporal gait and turning parameters. The G-WALK system has been extensively validated for gait analysis in both healthy and pathological populations, including PD (Vítečková et al., 2020), demonstrating high concurrent validity compared with optical motion capture systems. Each participant performed a standardized battery of two mobility tasks, designed to explore complementary dimensions of functional mobility: First, participants were instructed to walk 20 meters in a straight line at their self-selected comfortable pace. From this task, the following spatiotemporal parameters were extracted:

- Walking speed (m/s);
- Cadence (steps/min);
- Stride length normalized to height (%);
- Gait cycle duration (s);
- Stance and swing phase durations (% of gait cycle).

These gait metrics were grouped into pace (speed, cadence, stride length) and rhythm (cycle, stance, swing) domains according to the conceptual framework proposed by Lord et al. (Lord et al., 2013). Then, an instrumented Timed Up and Go (iTUG) task was performed to assess functional mobility and postural transitions (Ortega-Bastidas et al., 2023). Participants were asked to rise from a chair, walk three meters, turn 180°, return, and sit down at a self-selected pace. The following parameters were extracted from the IMU data:

- Turn duration (s);
- Mean angular velocity (MAV) (°/s);
- Peak angular velocity (PAV) (°/s).
- Total iTUG duration (s)

Finally, a 3-Meter Backward Walking Test (3MBWT) (Barta et al., 2025; Kocer et al., 2023) was included to evaluate backward walking, a complex locomotor task requiring dynamic balance and proprioceptive control, often impaired early in PD. Participants were instructed to walk backward along a 3-meter walkway as quickly and safely as possible while being supervised by an investigator for safety. Three trials were recorded, and time to complete each trial was recorded. For completion time, the average backward walking speed (m/s) of the three trials was then computed as the test outcome (Barta et al., 2025).

Unsupervised mobility monitoring (performance)

To capture mobility performance participants underwent continuous monitoring of physical activity in free-living conditions using a consumer-grade smartwatch (Garmin Vivosmart 4; Garmin Ltd., Olathe, KS, USA). This wrist-worn device integrates a triaxial accelerometer and optical heart rate sensor to estimate step count, heart rate, sleep duration, and activity levels. Each participant was asked to wear the smartwatch continuously for 5 consecutive days, including both weekdays and weekend days, 24 hours per day (except during bathing, showering, or swimming). The device was configured according to the manufacturer's specifications, including entry of age, sex, height, weight, and wrist dominance. Participants were instructed to perform their usual daily activities without altering their activity level. No reminders or prompts were provided during the monitoring period. During monitoring, participants could access limited information on the smartwatch display (e.g., total steps, heart rate, and sleep time), but the device provided no feedback, cues, or motivational messages, ensuring unbiased recording of habitual behavior. Data was downloaded from the Garmin Connect online dashboard. The total daily number of steps was extracted for each valid recording day. A day was considered "valid" if the device was worn for at least 80% of awake time, which was estimated as 24 hours minus the total sleep duration reported by the device. Days not meeting this threshold were excluded. The average daily steps (AvDS) was computed as the mean number of steps recorded over all valid days. This metric was used as a global indicator of unsupervised mobility performance (fig. 3.1)

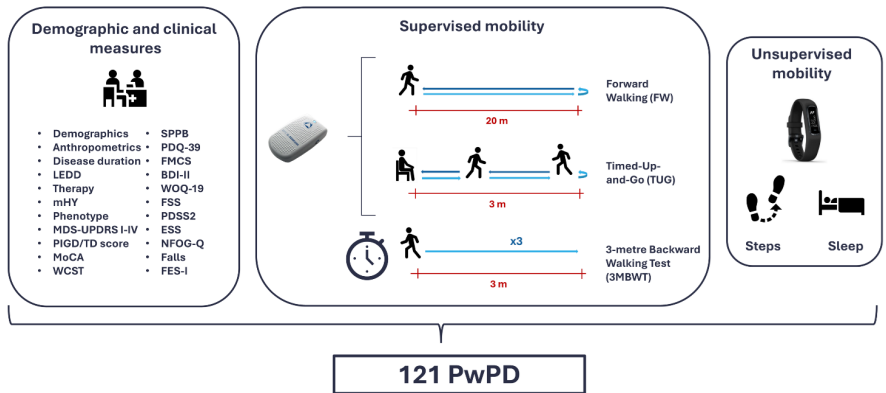


Figure 3.1. Graphical representation of the experimental design of the project.

Population characteristics

A total of 121 PwPD were enrolled, representing a mild-to-moderate population with a median disease stage of 2 (2–2.5; range 1–3). The average disease duration was 6.1 ± 4.3 (range 1–20) years. Participants' mean age was 69.7 ± 9.7 (range 51–87) years. Of the 121 participants, 83 (68%) were males and 38 (32%) were females. Details of the enrolled cohort is shown in table 3.1.

Table 3.1. Demographic, anthropometric and clinical characteristics of the enrolled population.

	PwPD (n=121)
Age (y)	69.7 (9.7)
Height (cm)	171.1 (8.8)
Weight (kg)	75.7 (12.6)
BMI (kg/m ²)	25.7 (3.3)
Sex, n (%)	
Male	83 (68)
Female	38 (32)
Disease duration (y)	6.1 (4.3)
LEDD (mg)	538 (292)
mH&Y	2 (2-2.5)
MDS-UPDRS part I	6 (4-9)
MDS-UPDRS part II	4 (2-8)
MDS-UPDRS part III	27 (21-32)
MDS-UPDRS part IV	0 (0-2)
MDS-UPDRS total	39 (28-49)
PDQ-39	12.4 (9.5)
FMCS	86.8 (14.7)
PDSS-2	10 (7-14)
ESS	6 (4-8)
WOQ-19	0 (0-2)
FSS	3.3 (1.7)
FES-I	21 (18-27)
WCST (s)	41.5 (15.7)
BDI-II	7 (4-10)
MoCA	26 (25-28)
FOG, n (%)	16 (13)
Phenotype, n (%)	
TD	39 (32)
PIGD	69 (57)
IND	13 (11)
WO, n (%)	33 (27)
Sleep problems, n (%)	25 (21)
EDS, n (%)	15 (12)
Fallers, n (%)	19 (16)
SPPB, median (IQR)	10 (9-12)

BDI-II: Beck Depression Inventory-II; EDS: excessive daytime sleepiness; ESS: Epworth Sleepiness Scale; FES-I: Falls Efficacy Scale-International; FMCS: Functional Mobility and Confidence Scale; FOG: freezing of gait; FSS: Fatigue Severity Scale; IND: indeterminate; LEDD: levodopa equivalent daily dose; MDS-UPDRS: Movement Disorder Society Unified Parkinson Disease Rating Scale; mH&Y: modified Hoehn and Yahr scale; MoCA: Montreal Cognitive Assessment; PD: Parkinson disease; PDQ-39: Parkinson Disease Questionnaire-39; PDSS-2: Parkinson Disease Sleep Scale-2; PIGD: postural instability and gait disorder; PwPD: people with Parkinson disease; SPPB: Short Physical Performance Battery; TD: tremor dominant; WCST: Word-color Stroop test; WO: wearing-off; WOQ-19: Wearing-Off Questionnaire-19.

Additional procedures

In a subgroup of participants fulfilling the additional inclusion criterion of having a clinical indication for initiating therapy with Opicapone (OPC) or subcutaneous foslevodopa/foscarbidopa (fLD/fCD), an ancillary exploratory study was conducted to characterize nocturnal mobility and sleep-related symptoms before and after treatment optimization. These two treatments were chosen because both OPC and fLD/fCD showed a favorable profile to improve dopaminergic tone during nighttime (Andrić et al., 2025; Chaudhuri et al., 2024; Ferreira et al., 2025; R. Hauser et al., 2024; R. A. Hauser et al., 2024; Malaty et al., 2025). Participants underwent an extended clinical and instrumental assessment, including the administration of specific questionnaires addressing sleep quality and nocturnal motor impairment, and continuous 24-hour monitoring using a wearable sensor.

Clinical evaluation

The following additional scales were administered:

Insomnia Severity Index (ISI). A self-administered questionnaire designed to assess the nature, severity, and impact of insomnia over the preceding two weeks (Castronovo et al., 2016). It consists of 7 items, with a total score ranging from 0 to 28, where higher values indicate greater insomnia severity.

Nocturnal Hypokinesia Questionnaire (NHQ). A disease-specific patient-reported outcome measure developed to evaluate nocturnal mobility impairment in Parkinson's disease (Bhidayasiri et al., 2019). It investigates the frequency and severity of night-time movement difficulties (e.g., turning in bed, changing position, getting out of bed, adjusting blankets) and their impact on sleep quality and comfort. The instrument includes both patient- and bed-partner-reported sections that could be used separately. Since we were interested in the patient's reported outcome related to NH, only the patient-reported section was used in the present work. The questionnaire includes ten items (five assessing frequency and five assessing severity) with a total score range from 0 to 10.

Instrumental evaluation

Participants were monitored using the MoveMonitor (McRoberts, The Hague, Netherlands), a validated triaxial accelerometer worn at the lumbar level (L5–S1) for at seven consecutive days and nights (Mazzà et al., 2021; Mirelman et al., 2020). This device provides objective parameters of nocturnal mobility, including:

- Number of transitions according to amplitude: small, medium, large, and extra-large turns.
- Number of times getting out of bed;
- Percentage of time spent in each position (supine, prone, left lateral, right lateral);
- Frequency of rotational movements during the night;
- Mean velocity of rotational movements;
- Mean duration of rotational movements.

All evaluations were performed before therapy modification (T0) and repeated at least four weeks after reaching treatment stability (T1). This allowed comparison of nocturnal mobility, sleep-related disturbances, and clinical outcomes before and after the introduction of the new pharmacological regimen (fig. 3.2).

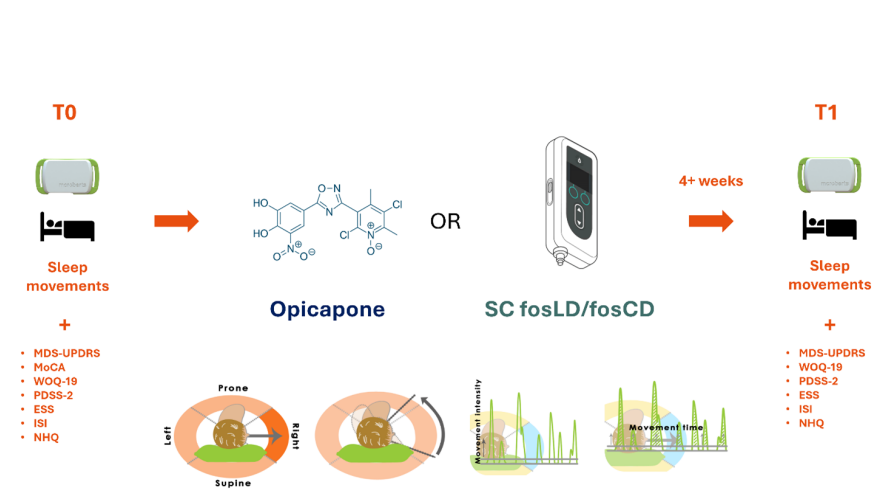


Figure 3.2. Graphical representation of the experimental design of the additional procedure of the project.

VALIDATION OF A
SMARTWATCH FOR
STEP COUNTING IN
PARKINSON'S DISEASE

Chapter 4

Contribution 1: Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables

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Abstract

Commercial smartwatches could be useful for step counting and monitoring ambulatory activity. However, in Parkinson's disease (PD) patients, an altered gait, pharmacological condition, and symptoms lateralization may affect their accuracy and potential usefulness in research and clinical routine. Steps were counted during a 6 min walk in 47 patients with PD and 47 healthy subjects (HS) wearing a Garmin Vivosmart 4 (GV4) on each wrist. Manual step counting was used as a reference. An inertial sensor (BTS G-Walk), placed on the lower back, was used to compute spatial-temporal gait parameters. Intraclass correlation coefficient (ICC) and mean absolute percentage error (MAPE) were used for accuracy evaluation and the Spearman test was used to assess the correlations between variables. The GV4 overestimated steps in PD patients with only a poor-to-moderate agreement. The OFF pharmacological state and wearing the device on the most-affected body side led to an unacceptable accuracy. The GV4 showed an excellent agreement and MAPE in HS at a self-selected speed, but an unacceptable performance at a slow speed. In PD patients, MAPE was not associated with gait parameters and clinical variables. The accuracy of commercial smartwatches for monitoring step counting might be reduced in PD patients and further influenced by the pharmacological condition and placement of the device.

Introduction

Walking is one of the most common motor activities in daily life, is essential for the correct functioning of several physiological systems, affects quality of life, and contributes to personal and social relationships (MacKinnon, 2018). Gait parameters such as a reduced step length and walking speed are useful indexes of morbidity and mortality in older adults (Studenski et al., 2011). In particular, a daily step count is rather easy to collect, and may represent a useful surrogate measure of physical and ambulatory activity that is associated with relevant clinical outcome parameters (Bassett et al., 2017). For example, previous studies associated a reduced number of steps per day with relevant pathological conditions, including cancer and cardiovascular diseases (Del Pozo Cruz, Ahmadi, et al., 2022), obesity, major depressive disorder, diabetes and hypertension (Master et al., 2022), and in general mortality (Paluch et al., 2021, 2022). As to neurodegenerative disorders, a recent report showed the link between the daily number of steps collected through a wrist-worn accelerometer and the incidence of dementia in a large cohort of patients (Del Pozo Cruz, Ahmadi, et al., 2022). The diffusion of wearable devices encompassing step-counting algorithms, in particular consumer-grade wearables such as smartwatches, enabled the easy collection and monitoring of daily steps for prolonged periods. Consequently, research focused on investigating the accuracies of these devices in step counting, with positive results in general (Degroote et al., 2018; Straiton et al., 2018). However, step-detection algorithms are generally trained on healthy, young subjects during continuous physiological walking; therefore, performance may be reduced when applied to patients under real-world conditions and showing altered walking parameters and/or pathological gaits.

Parkinson's disease (PD) is a neurodegenerative disease characterized by bradykinesia, rigidity, and a resting tremor (Armstrong & Okun, 2020). Aside from these symptoms, gait disturbances and balance impairments are frequent and significantly increase the risk of falls (Fasano et al., 2017), carrying heavy impacts on functional independence and quality of life. In addition to motor symptoms, a constellation of non-motor symptoms has been reported in PD patients, including cognitive impairment (Schapira et al., 2017). This is characterized by the involvement of executive functions (Aarsland et al., 2021), and may further predispose to gait impairment. Indeed, previous studies have demonstrated the link between dysexecutive symptoms and reduced performances in walking tasks (Yogev-Seligmann et al., 2008). Gait impairments in PD patients include a shuffling gait, reduced step length and automaticity, diminished arm swing, increased double-support time and cadence, as well as episodic disturbances such as freezing of gait (FOG) (Mirelman et al., 2019). The potential usefulness of gait parameters, particularly step length, to monitor disease progression has been shown recently (Welzel et al., 2021; Wilson et al., 2020), and interest in wearable devices for the evaluation of gait impairments in PD patients has been growing rapidly (Varghese et al., 2021). A patient's total daily step count was associated with disease severity (Skidmore et al., 2008), and has been used to study ambulatory activity in PD patients (Cavanaugh et al., 2012; Christiansen et al., 2017) and also to guide exercise to increase physical activity (Handlery et al., 2021). However, concerns have been raised about the accuracy of consumer-grade wearables for step counting in patients with PD. In particular, two studies showed positive results (Lai et al., 2020; Lamont et al., 2018), whereas a third investigation showed disappointing performances for wrist-worn devices during overground walking (Wendel et al., 2018). It was hypothesized that gait alterations and motor symptoms of PD patients could hamper the performances of step detection algorithms if not adequately validated in such cohorts showing altered mobility performances. In particular, the performances of these devices are lower with a reduced gait speed (Chow et al., 2017; Fokkema et al., 2017; Svarre et al., 2020) and increased cadence (Lamont et al., 2018), which are both features of a parkinsonian gait, and during discontinuous walking (Wendel et al., 2018) that likely occurs in daily living and may be exacerbated in PD patients due to reduced automaticity and episodes of FOG. Moreover, tremors and dyskinesia may lead to the overestimation of the step count (Kim et al., 2019), particularly when using wrist-worn devices, while bradykinesia and reduced arm swing may

cause underestimation (Wendel et al., 2018). The side on which the device is worn might also affect device performance, which may be an issue especially in PD, a disease where the lateralization of symptoms regularly occurs. Eventually, all of these issues may vary during daytime due to fluctuations of symptoms.

To our best knowledge, no study to date investigated the accuracy of commercial smartwatches in counting steps in PD patients taking into account the side on which the watch is worn and the pharmacological state of the patients. Similarly, no research studied the relationships between step-count error and spatiotemporal gait parameters, executive functions, and clinical scores in people with PD.

Materials and Methods

Study design and ethics

This was a cross-sectional study aimed at investigating the accuracy of a consumer-grade smartwatch in counting steps in PD patients in comparison with a reference population of healthy subjects (HS). Moreover, we explored the possible effects of side on which the watch was worn, the pharmacological state, and the association between step-count error and spatiotemporal gait parameters, executive functions, and clinical scores. This study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. Approval was granted by the local Ethical Committee. Data collection and processing followed the current European regulation for data protection. All participants provided written informed consent before the start of measurements.

Population

Participants were longitudinally recruited in the Movement Disorder Outpatient Service of the Sant'Andrea University Hospital, Rome, Italy, in the period between June 2021 and September 2022. The inclusion criteria were: (i) age 18 years or older; (ii) ability to walk independently without walking aids; (iii) ability to perform the experimental procedure. For PD patients, the following adjunctive criteria were applied: (iv) diagnosis of idiopathic PD according to MDS criteria (Postuma et al., 2015); (v) disease stage <4 according to the modified Hoehn & Yahr (H&Y) scale (Hoehn & Yahr, 1967). The exclusion criteria were: (i) cognitive impairment as defined by a Mini Mental State Examination (MMSE) score <24 ; (ii) orthopedic, rheumatologic, or systemic conditions affecting mobility as judged by the assessor. For PD patients, the following adjunctive criterion was applied: (iii) presence of FOG as defined by a score >1 at item 2.13 of the Movement Disorder Society Unified Parkinson's Disease Rating Scale part II (MDS-UPDRS).

Experimental Procedure

Participants were evaluated in the morning, and they were asked to perform a 6 min walking task (6MWT) on a 25 m indoor corridor while wearing two Garmin Vivosmart 4 (GV4) smartwatches, one at each wrist. The smartwatches were configured according to the producer's recommendations by indicating the patient's age, height, weight, and the wrist on which the smartwatch was worn (i.e., left or right). As a reference measure, steps were counted manually by a dedicated and trained operator using a digital click counter. Participants were also asked to wear a research-grade wearable inertial-motion unit sensor (BTS G-walk, BTS Engineering Inc., Milan) at their lower back (L5) through an elastic belt to compute spatial-temporal gait parameters. HS performed the 6MWT at both a self-selected speed and at a gait speed self-perceived as "slow". PD patients performed the test only at

self-selected speed before the usual morning dose of L-DOPA (OFF) and at least 1 h after the dose administration (ON). If the patients were not in treatment with L-DOPA, they were evaluated only in the ON condition. Demographics (age, sex) and anthropometric measures (weight, height, BMI) were collected for all participants. For PD patients, disease duration, disease stage according to the H&Y scale, and the Levodopa equivalent daily dose (LEDD) were also collected. The MDS-UPDRS (Goetz et al., 2008) parts I–II were used to assess the impact of motor and non-motor symptoms on daily life. The Parkinson’s Disease Questionnaire-39 (PDQ-39) was used to evaluate the quality of life of the patients (Peto et al., 1995). The functional independence measure (FIM) was used to assess functional independence in daily life activities (Keith et al., 1987). The MDS-UPDRS part III and the word color Stroop test (WCST) (Stroop, 1935) were administered both in the OFF and ON conditions to evaluate the motor symptoms’ severity and executive cognitive functions of enrolled patients, respectively. Steps were collected from both smartwatches at the end of each walking trial. For PD patients, steps counted by the smartwatch worn on the most-affected side (MA) and on the least-affected side (LA) were recorded. To compare PD patients and HS, the average of steps counted by the smartwatches worn on right and left wrists were calculated. Spatiotemporal gait parameters from G-Walk were extracted using the software G-Studio (BTS Engineering Inc., Milan) (Vítečková et al., 2020). These included the total traveled distance (m), gait speed (m/s), cadence (steps/min), and stride length (m). Gait parameters were the average across the 6 min walking trial. The first and last 25 m walking bouts were excluded from the analysis by the software as the default setting. From the number of steps counted by GV4 and manually, the mean percentage error (MPE) and the mean absolute percentage error (MAPE) were calculated as follows:

$$\text{MPE} = \frac{(\text{steps counted manually}) - (\text{steps counted by smartwatch})}{(\text{steps counted manually})} \times 100$$

$$\text{MAPE} = \frac{|(\text{steps counted manually}) - (\text{steps counted by smartwatch})|}{(\text{steps counted manually})} \times 100$$

The MPE was used to evaluate the direction-of-error of the smartwatch compared with manual counting. A negative value indicated an overestimate of counting and vice-versa. The MAPE was used to assess the magnitude-of-error of GV4 in step counting compared with manual counting. Recently, the Consumer Technology Association Health and Fitness Technology Subcommittee recommended a MAPE threshold within 10% for wearable technology in step counting (CTA/ANSI, 2016). On this basis, in our study, we set the MAPE cut-off for acceptability at 10% considering the upper bound of the 95% confidence interval (CI). In addition to the acceptability threshold, according to previous studies (Evenson & Spade, 2020), we set a cut-off for optimal performance at a MAPE < 5%.

Statistical analyses

Statistical analyses were performed using JASP v0.16.3 (JASP Team, University of Amsterdam, Amsterdam, The Netherlands), R v4.0.3, and RStudio v2022.07.1 + 554 for Windows (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were calculated for the examined variables. To assess the agreement between the number of steps counted by GV4 and manual counting (gold standard), the intraclass correlation coefficient (ICC) [1,2] was used. The following reference cut-off values for the ICC interpretation were used (Koo & Li, 2016): Excellent: >0.90; Good: 0.75–0.90; Moderate: 0.50–0.75; Poor: <0.50. The Mann–Whitney test was used to compare the MPE and MAPE between the general PD population and HS at a self-selected speed (HS-SE). In PD patients, the average of the values collected in ON and OFF was used for the comparison. The Wilcoxon test was performed to assess the difference between the MA and LA and between ON and OFF in the MAPE and MPE of the PD patients. Spearman’s rho correlation coefficient was

used to test the correlation between the MAPE and gait parameters in walking trials from the overall population, as well as from HS and PD patients. Spearman's coefficient was also used to assess the correlation between the MAPE and clinical variables in PD walking trials. To control error from multiple tests, Bonferroni's correction was performed. The significance threshold was set at < 0.05 . All data were reported as the mean $\pm$ SD or median (Q1–Q3) for numerical data and N (%) for categorical variables.

Results

A total of 52 PD patients and 47 healthy participants were enrolled in this study. Five PD patients were excluded from the analysis due to technical problems. Among the PD patients, 36 were evaluated in ON and 34 in OFF (with 23 patients evaluated in both conditions). Relevant demographic and clinical parameters are shown in table 4.1. More details on clinical scores and gait parameters are presented in table S4.1 and table S4.2.

Table 4.1. Demographic and clinical features of the enrolled population.

Variable	PD (N = 47)	HS (N = 47)
Age (years)	66.3 $\pm$ 6.2	42.0 $\pm$ 15.3
Females	14 (33%)	33 (63%)
Weight (kg)	77.6 $\pm$ 12.2	71.0 $\pm$ 13.8
Height (cm)	173.9 $\pm$ 8.7	170.6 $\pm$ 7.6
BMI	25.6 $\pm$ 2.9	24.4 $\pm$ 4.3
H&Y	2 (2–2)	–
Disease duration (years)	6.1 $\pm$ 5.1	–
LEDD (mg)	576 $\pm$ 317	–

BMI: body mass index; H&Y: Hohen and Yahr disease stage; HS: healthy subjects; LEDD: Levodopa equivalent daily dose; PD: Parkinson's disease.

In PD patients, GV4 demonstrated a poor-to-moderate ICC with manual step counting in the overall group and in the ON state, irrespective of the side where the watch was worn. In the OFF state, GV4 demonstrated a poor ICC, particularly when the watch was worn on the most-affected side (table 4.2).

Considering the MAPE, GV4 showed an acceptable but sub-optimal accuracy in PD patients in all conditions but wearing the device on the most-affected body side during the OFF pharmacological state. Under this latter combination of instances, the accuracy range was unacceptable (fig. 4.1 and table 4.3). The MAPE was significantly higher when the smartwatch was worn on the most-affected compared with the least-affected body side, and in the OFF compared with the ON condition. The MPE showed negative values in all conditions, indicating an overestimation of step counting by GV4 (table 4.3). In the HS population, GV4 demonstrated a good-to-excellent ICC with manual step counting while walking at a self-selected speed. On the contrary, during slow walking, GV4 demonstrated only a moderate-to-good ICC (table 4.2). GV4 demonstrated optimal accuracy when walking at a self-selected speed, with a significantly lower MAPE compared with PD patients. Conversely, in slow walking, an unacceptable accuracy was achieved (fig. 4.1).

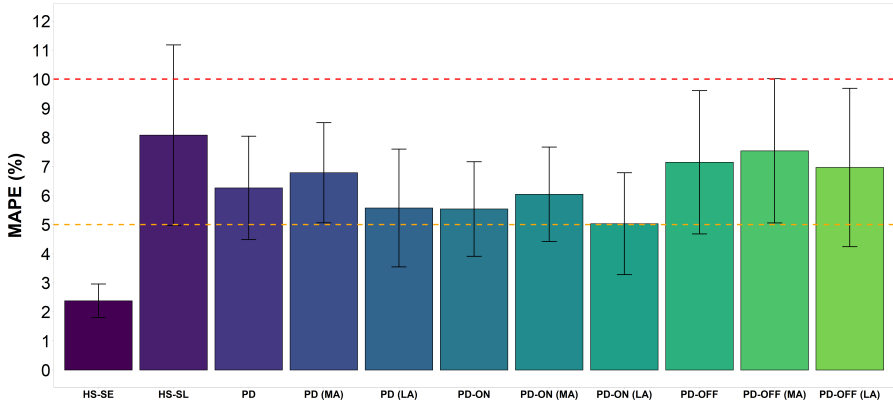
MAPE in the different groups and experimental conditions

Figure 4.1. MAPE between the number of steps recorded by GV4 and manual counting in the two groups and in the different experimental conditions. In HS, data are reported for self-selected speed and slow speed. In PD patients, data are reported for the overall population, in ON, in OFF, and for the most- and least-affected body sides. Columns represent the mean of MAPE and the vertical bars represent the CI 95% upper and lower bounds. Two red and orange horizontal dashed lines were added to mark the cut-offs of 10% and 5%, respectively. HS-SE: Healthy subjects at self-selected speed; HS-SL: Healthy subjects at slow speed; LA: Least-affected side; MA: Most-affected side; MAPE: Mean absolute percentage error; PD: Parkinson’s disease.

MPE showed a positive value in this latter condition, indicating an underestimation of step counting. Details of the MAPE and MPE values are shown in table 4.3. Details of the measured steps by GV4 and manual counting are shown in table S4.3.

The Spearman test showed a weak negative correlation between the MAPE and the walked distance, gait speed, and stride length in the overall population. When considering the HS group, these findings were confirmed, and a weak negative correlation between cadence and the MAPE was also found. However, no correlation was found between the spatiotemporal gait parameters and MAPE in PD patients (fig. 4.2 and table 4.4). Similarly, no correlations were found between other demographic or clinical variables in PD patients.

Table 4.2. Intraclass correlation coefficient between the number of steps recorded by GV4 and manual counting. ICC is reported as point estimate (CI 95%). The values are reported for at-selected speed and slow speed for healthy participants. In gray, values are reported for overall population. In ON, in OFF, and both affected sides.

	HS-SE	HS-SL	PD	PD ON	PD OFF
ICC [1,2]	0.901 (0.856–0.933)	0.686 (0.535–0.789)	0.658 (0.306–0.825)	0.749 (0.407–0.881)	0.305 (0.039–0.535)
ICC [1,2] (MA)	–	–	0.644 (0.247–0.824)	0.719 (0.424–0.856)	0.184 (–0.085–0.434)
ICC [1,2] (LA)	–	–	0.632 (0.344–0.795)	0.755 (0.392–0.887)	0.328 (0.042–0.563)

Blue: Excellent (>0.90); Green: Good (0.75–0.90); Yellow: Moderate (0.50–0.75); Red: Poor (<0.50). HS-SE: Healthy subjects at self-selected speed; HS-SL: Healthy subjects at slow speed; ICC: Intraclass correlation coefficient; LA: Least-affected side; MA: Most-affected side; PD: Parkinson's disease.

Table 4.3. MAPE and MPE between the number of steps recorded by GV4 and manual counting. Variables are reported as mean (CI 95%) for MAPE and mean $\pm$ SD for MPE. In HS, data are reported for self-selected speed and slow speed. In PD patients, data are reported for the overall population, in ON, in OFF, and for the most- and least-affected sides.

	HS-SE	HS-SL	PD	PD ON	PD OFF	HS-SE vs. PD	ON vs. OFF
MAPE	2.38 (1.80–2.9)	8.07 (4.97–11.)	6.26 (4.48–8.0)	5.53 (3.91–7.1)	7.14 (4.66–9.61)	$p < 0.001$	$p = 0.047$
MAPE (MA)	–	–	6.79 (5.06–8.5)	6.04 (4.32–7.6)	7.54 (5.05–10.02)	NS	NS
MAPE (LA)	–	–	5.7 (3.54–7.8)	5.03 (3.26–6.7)	6.96 (4.24–9.69)	–	$p = 0.018$
MA vs. LA	–	–	$p = 0.029$	NS	NS	–	–
MPE	–0.46 ± 2.98	4.38 $\pm$ 11.60	–4.67 ± 7.01	–4.39 ± 6.48	–4.74 ± 9.40	–	–
MPE (MA)	–	–	–5.16 ± 7.27	–4.07 ± 7.02	–5.78 ± 9.78	–	–
MPE (LA)	–	–	–4.32 ± 7.59	–4.48 ± 6.40	–3.93 $\pm$ 10.96	–	–
MA vs. LA	–	–	NS	NS	NS	–	–

Blue: Optimal error (<5%); Yellow: Acceptable error (5–10%); Red: Unacceptable error (>10%).

HS-SE: Healthy subjects at self-selected speed; HS-SL: Healthy subjects at slow speed; LA: Least-affected side; MA: Most-affected side; MAPE: Mean absolute percentage error; MPE: Mean percentage error; PD: Parkinson's disease.

Table 4.4. Spearman rho correlation coefficient between spatiotemporal gait parameters and MAPE in the general population, PD patients, and healthy participants. Significant correlations are reported as follows: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

		Distance (m)	Speed (m/s)	Cadence (Step- s/min)	Stride Length (m)
MAPE	Overall	-0.199 *	-0.213 **	-0.048	-0.224 **
	PD	0.169	0.106	0.256	-0.018
	HS	-0.345 ***	-0.341 ***	-0.357 ***	-0.230 *

HS: Healthy subjects; MAPE: Mean absolute percentage error; PD: Parkinson's disease.

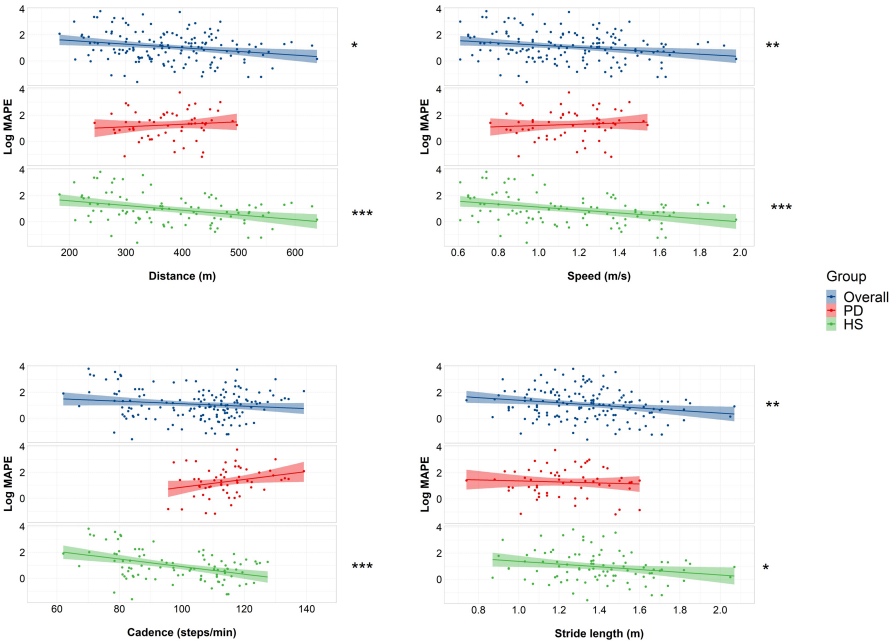


Figure 4.2. Scatterplots showing association between spatiotemporal gait parameters and MAPE. Scatterplots are presented for the overall population (all participants, PD + HS) (upper grid panels, in blue), PD patients (middle grid panels, in red), and healthy participants (bottom grid panels, in green). MAPE is reported as logarithm. A continuous line was drawn to show the linear tendency. The shaded area around the tendency line corresponds to the 95% confidence interval. Significance is reported as follows: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. HS: Healthy subjects; MAPE: Mean absolute percentage error; PD: Parkinson's disease.

Discussion

This was a cross-sectional study investigating the accuracy of GV4 in counting steps during overground walking in PD patients in comparison with a reference population (HS) and exploring the possible effects lateralization of symptoms, pharmacological state, and the association between step-count error, spatiotemporal gait parameters, and clinical variables in PD patients.

We found that: (i) GV4 overestimated steps in PD with only a poor-to-moderate agreement; (ii) in PD patients, the OFF condition and wearing the smartwatch on the most-affected side negatively affected the step-count accuracy with an unacceptable error when combining the two factors; (iii) GV4 showed a good-to-excellent agreement and MAPE in HS at a self-selected speed, but an unacceptable performance at slow speed, and; (iv) the MAPE was associated with gait parameters in HS, but no association with gait and clinical variables was found in PD patients. These results are discussed in detail in the following.

Accuracy of GV4 vs. Manual Step Counting

In PD patients, GV4 showed a poor-to-moderate agreement, with an overall acceptable error range based on the *a priori* criterion. Conversely, in HS, GV4 showed a good-to-excellent agreement and an optimal error at a self-selected speed, but only a moderate-to-good agreement with an unacceptable error at slow speed. The sub-optimal performance of GV4 in PD patients found in our study may be due to altered gait biomechanics and the possible interference by the motor symptoms of the disease. PD gait is characterized by a reduced gait speed and step length, higher cadence, and variability (Mirelman et al., 2019). Previous reports demonstrated that the accuracy of step counting by commercial smartwatches is reduced with a lower gait speed (Chow et al., 2017; Fokkema et al., 2017; Svarre et al., 2020), higher cadence (Lamont et al., 2018), and discontinuous gait (Wendel et al., 2018). The present observation of reduced accuracy during slow-speed walking (0.86 ± 0.15 m/s) as compared with self-selected-speed walking (1.44 ± 0.22 m/s) in HS is in line with this idea. Moreover, the altered gait features of a parkinsonian gait could affect the step-counting performance through a decreased signal-to-noise ratio in the accelerometer signal and a consequently reduced performance of the built-in step-detection algorithm. This is also in line with a previous study showing the low accuracy of wrist-worn smartwatches in step counting in PD patients (Wendel et al., 2018). The present results are in contrast with previous studies, suggesting the good accuracy and agreement between commercial smartwatches and reference measures in PD subjects (Lai et al., 2020; Lamont et al., 2018). In particular, Lai and collaborators (Lai et al., 2020) reported an excellent ICC (0.96–0.99) with a 0.99% error for the Garmin Vivosmart 3 smartwatch in 31 PD patients at a self-selected speed. Despite similar demographic, anthropometric, clinical, and experimental features, the authors used a different device, and no information was given on the pharmacological state or the side on which the smartphones were worn. Moreover, Lamont and colleagues (Lamont et al., 2018) reported a very good ICC (0.88–0.97) and low error (<3%) for a Garmin Vivosmart HR worn on the most-affected side when compared with a research-grade device in 33 mild-to-moderate PD patients walking at a self-selected speed. However, almost half of the cases of the cohort enrolled in that study were classified as H&Y stage one, indicating an early disease stage and (mild) unilateral symptoms, which usually display less pronounced gait disturbances than our cohort, with a median disease stage of two. Moreover, a shorter and more continuous walking paradigm (2 min, 44 m walking) was applied, and a thigh-worn research-grade activity tracker (ActivPAL3) was used as a reference, without manual counting. The usefulness of the ActivePAL3 as a reference, however, might be questioned, as the underestimation of step counting has been reported in a previous study (Godfrey et al., 2016).

Effect of Side and Pharmacological State

In PD patients, step counting by GV4 was less accurate when the smartwatch was worn on the most-affected side. This finding is consistent with our hypothesis that the asymmetry of PD could affect the performance of wrist-worn smartwatches. Indeed, PD is an asymmetric disorder, usually presenting with unilateral symptoms at onset that subsequently spread to the other side, and even when the disease becomes bilateral, a degree of asymmetry is still retained (Miller-Patterson et al., 2018). Thus, bradykinesia and tremors could lead to step counting underestimation or overestimation, respectively, in a different manner according to the laterality of symptoms. With this respect, only two previous reports evaluated this aspect using two commercial smartwatches (Garmin Vivosmart HR and Fitbit Charge HR) (Lamont et al., 2018) or a research-grade actigraph (ActiGraph GT3X+) (Cederberg et al., 2021), and the results are in contrast with ours. The study from Lamont and colleagues (Lamont et al., 2018) reported no significant differences between the steps recorded on the most-affected side and the least-affected one. However, the authors only compared the absolute number of steps, and did not compare the error in step counting between the two sides. Moreover, enrolled PD patients were at an early disease stage, and were evaluated only in the ON condition. This could have masked the difference. Conversely, the study from Cederberg and collaborators (Cederberg et al., 2021) showed that the accuracy of the investigated device was higher when it was worn on the side most-affected by the disease. The authors suggested that the reduced movement on this side in PD patients would be advantageous for a wrist-worn detector because the most-affected side could be considered as a “non-dominant” wrist, and a previous study on healthy participants reported a better accuracy in step counting while performing daily activities when the watch was worn on the non-dominant arm (Cederberg et al., 2021). However, other studies reported no effect of wrist placement on step counting in the general unimpaired population (Chen et al., 2016; Chow et al., 2017). In addition, the explanation only considers the reduction of arm swing, and does not take into account the presence of a tremor during walking in PD patients. Indeed, approximately 70% of PD patients have a tremor, and this is usually more prominent at the upper-limb level and generally worsens during walking (Baumann, 2012). Moreover, in more advanced PD patients, involuntary movements (i.e., dyskinesias) are often observed (Armstrong & Okun, 2020). Our findings support the idea that wearing a smartwatch on the most-affected side could hinder the accuracy of step counting, and the negative values of MPE indicate that the direction of error is toward an overestimation of steps, likely due to the positive motor symptoms observed in PD patients.

We also found that the pharmacological state influenced step-counting accuracy in PD patients, with a lower agreement and increased error in the OFF condition. This aspect was neglected in previous studies (Lai et al., 2020; Lamont et al., 2018; Wendel et al., 2018), and only one pharmacological condition was investigated (Lamont et al., 2018) or it was not reported at all (Lai et al., 2020; Wendel et al., 2018). Dopaminergic treatment could influence the step-counting performance through the improvement of motor symptoms (i.e., reduced tremor and bradykinesia, increased arm swing), as well as the improvement of gait parameters. Previous research, in fact, suggested that arm swing (Warmerdam et al., 2021), as well as gait speed and step length, may improve with L-DOPA (Mirelman et al., 2019), while other gait aspects, such as cadence, do not seem to respond significantly to treatment (Mirelman et al., 2019). Most PD patients develop daily motor fluctuations along the disease course due to the combination of pulsating drug administration and disease progression (Poewe et al., 2017). Therefore, such different accuracies between the ON and OFF conditions may limit the reliability of commercial smartwatches concerning step counting in fluctuating PD patients, particularly when combined with the aforementioned effect of device placement. In our study, indeed, the combination of the OFF pharmacological state with the placement of the device on the most-affected side leads to an unacceptable MAPE based on the a priori criterion of 10%. To this end, it would be important for future investigations to report information about device placement and pharmacological state, and smartwatches should be worn on the side less-affected by the disease to increase the accu-

racy and reliability of step counting. Moreover, it would be relevant for validation studies to evaluate the device in both the ON and OFF conditions. Alternatively, a potential solution to overcome these limitations could be the development of dedicated step-detection algorithms using IMU data from smartwatches. However, this option would greatly reduce real-world applicability and hinder the benefits of using an off-the-shelf device, especially in settings where engineering and software-development expertise are not available.

Association of Step-Count Error, Spatiotemporal Gait Parameters, and Clinical Variables

The MAPE showed a weak correlation in the overall population and in HS with walked distance, gait speed, and stride length, whereas no correlations between the MAPE and gait variables were found in PD patients. The observation that spatial-temporal gait parameters may affect the step-counting accuracy when measured with wrist-worn sensors has already been shown in previous studies (Chow et al., 2017; Fokkema et al., 2017; Lamont et al., 2018; Svarre et al., 2020); however, this was only assessed through discrete speed values on a treadmill (Chow et al., 2017; Fokkema et al., 2017; Svarre et al., 2020) or discrete cadences through the use of a metronome (Lamont et al., 2018), and not on a continuous range of values. The difference we found between PD patients and HS may be explained by the altered gait biomechanics in PD patients. The reduced gait speed coupled with the lower stride length may lead to a decreased signal-to-noise ratio in the accelerometer signal and a possible masking effect of the association between spatiotemporal gait parameters and the MAPE. Finally, the lack of correlation between the MAPE and clinical variables in PD patients is in contrast with our hypothesis of an error increase with a higher motor-symptoms severity and reduced executive functions. Previous studies, indeed, demonstrated that, in PD patients, 24% of variation-in-difference in daily step-counting between waist-worn and wrist-worn devices may be explained by tremor, dyskinesias, and bradykinesia, with 19% explained by tremor and dyskinesias alone (Kim et al., 2019). An effect of executive functions on ambulation has also been reported in the general population (Yogev-Seligmann et al., 2008) and PD patients (Morris et al., 2019), even though a recent study questioned the extent of this influence in these latter patients (Geritz et al., 2022). The results from our study suggest that PD, at least with the disease severity included in our study, is more likely to affect the step-counting performance by its presence or absence in a more dichotomous way than on a continuous range of symptoms severities.

Limitations

We acknowledge that this study has limitations. First, the in-lab experimental setting, consisting of a straight walking task on a 25 m walkway, is not highly representative of everyday walking behavior. Indeed, daily walking is characterized by a more discontinuous gait pattern with briefer walking bouts and more frequent turning events (Hillel et al., 2019). However, it must be noted that, under daily life conditions, a deterioration in automatic gait analysis performance likely occurs. Therefore, the results of a suboptimal accuracy in the step counting of GV4 under in-lab conditions are particularly relevant, and could point toward an even-lower performance in a real-world setting. Second, the PD patients included in our studies had, on average, relatively high levels of physical and cognitive abilities, and participants with a more severe disease stage, reporting FOG and using walking aids, were not included. This could limit the generalization of our results, and suggests that further studies enrolling participants with lower functional scores, greater disease severities, and more severe cognitive impairments are necessary. However, this might suggest a potential further deterioration in step-counting performance when applied to patients with more severe impairments. Third, the PD patients and HS were different in terms of age and anthropometric data, and this could hamper the comparison between the two populations. With this respect, however, our HS cohort has not been enrolled to perform a strict matched

comparison, but rather to include a reference population more representative of the subjects on which smartwatches' algorithms are often trained. Finally, a question might arise about the accuracy of the BTS G-Walk in measuring gait parameters in PD patients, due to the fact that a previous study (Vítečková et al., 2020) suggested that variables in the temporal domain (e.g., gait cycle duration, double and single support, etc.) should be used with caution due to the presence of a systematic error. However, in the present study, we did not use temporal gait parameters, and the device demonstrated a good accuracy for the included variables (Vítečková et al., 2020).

Conclusions

In PD patients, GV4 overestimated the number of steps with acceptable but sub-optimal accuracy. The accuracy worsened when the device was worn on the most-affected side and the patients were in the OFF state, and was unacceptable with the two element combined. These findings could be due to the altered gait biomechanics or the worsening of tremor and dyskinesias. In HS, the performance was optimal at a self-selected speed but unacceptable when walking at slow speed. The error in step counting increased with a decreasing gait speed, stride length, cadence, and walked distance in HS, while no association between gait parameters and error was found in PD patients. This could be due to the decreased signal-to-noise ratio in the accelerometer signal. Eventually, no association between the error in step counting and clinical variables was found in PD patients. Commercial smartwatches might be used to monitor steps in mild-to-moderate PD patients, but the overall reduced accuracy in PD patients must be considered together with the negative effect of the OFF pharmacological state and wearing the device on the most-affected side.

Supplementary material

Table S4.1. Clinical scores of PD patients. Data are reported for the overall PD population and in ON and OFF condition.

	PD	PD ON	PD OFF
MDS-UPDRS-I	7 (6–11)	–	–
MDS-UPDRS-II	7 (4–10)	–	–
MDS-UPDRS-III	25 (18–33)	21 (16–29)	30 (21–36)
WCST time (s)	40.3 ± 16.1	39.5 ± 11.7	40.2 ± 19.8
WCST errors	1 (0–3)	1 (0–3)	1 (0–4)
FIM	124 (118–126)	–	–
PDQ-39	17 (8–28)	–	–

MDS-UPDRS: Movement Disorders Society Unified Parkinson’s Disease rating Scale; PD: Parkinson’s Disease; PDQ-39: Parkinson’s Disease Questionnaire 39; WCST: Word color Stroop-test; FIM: Functional Independence Measure.

Table S4.2. Spatiotemporal gait parameters. Data are reported for healthy participants at both self-selected and slow speed and for the PD patients, in the overall population, in ON and OFF condition.

	HS-SE	HS-SL	PD	PD ON	PD OFF
Distance (m)	473 ± 70	287 ± 51	379 ± 73	382 ± 62	382 ± 75
Speed (m/s)	1.44 ± 0.22	0.86 ± 0.15	1.15 ± 0.19	1.18 ± 0.20	1.14 ± 0.18
Cadence (steps/min)	112 ± 9	83 ± 9	114 ± 10	116 ± 11	113 ± 7
Stride length (m)	1.56 ± 0.22	1.24 ± 0.18	1.22 ± 0.20	1.24 ± 0.20	1.23 ± 0.19

HS-SE: Healthy subjects at self-selected pace; HS-SL: Healthy subjects at slow pace; PD: Parkinson’s Disease.

Table S4.3. Number of steps measured manually and by GV4. Data are reported for healthy participants at both self-selected and slow speed and for the PD patients, in the overall population, in ON and OFF condition.

	HS-SE	HS-SL	PD	PD ON	PD OFF
Manual	661 ± 42	493 ± 52	639 ± 56	649 ± 62	637 ± 41
GV4	664 ± 46	473 ± 82	667 ± 58	676 ± 62	666 ± 58
GV4 (MA)	–	–	670 ± 62	675 ± 62	675 ± 68
GV4 (LA)	–	–	664 ± 58	677 ± 63	659 ± 62

GV4: Garmin Vivosmart 4; HS-SE: Healthy subjects at self-selected pace; HS-SL: Healthy subjects at slow pace; LA: Least affected side; MA: Most affected side; PD: Parkinson’s Disease.

References

- Aarsland, D., Batzu, L., Halliday, G. M., Geurtsen, G. J., Ballard, C., Ray Chaudhuri, K., & Weintraub, D. (2021). Parkinson disease-associated cognitive impairment. *Nature Reviews. Disease Primers*, 7(1), 47. <https://doi.org/10.1038/s41572-021-00280-3>
- Armstrong, M. J., & Okun, M. S. (2020). Diagnosis and Treatment of Parkinson Disease: A Review. *JAMA*, 323(6), 548–560. <https://doi.org/10.1001/jama.2019.22360>
- Bassett, D. R., Toth, L. P., LaMunion, S. R., & Crouter, S. E. (2017). Step Counting: A Review of Measurement Considerations and Health-Related Applications. *Sports Medicine (Auckland, N.Z.)*, 47(7), 1303–1315. <https://doi.org/10.1007/s40279-016-0663-1>
- Baumann, C. R. (2012). Epidemiology, diagnosis and differential diagnosis in Parkinson's disease tremor. *Parkinsonism & Related Disorders*, 18 Suppl 1, S90–92. [https://doi.org/10.1016/S1353-8020\(11\)70029-3](https://doi.org/10.1016/S1353-8020(11)70029-3)
- Cavanaugh, J. T., Ellis, T. D., Earhart, G. M., Ford, M. P., Foreman, K. B., & Dibble, L. E. (2012). Capturing ambulatory activity decline in Parkinson's disease. *Journal of neurologic physical therapy: JNPT*, 36(2), 51–57. <https://doi.org/10.1097/NPT.0b013e318254ba7a>
- Cederberg, K. L. J., Jeng, B., Sasaki, J. E., Lai, B., Bamman, M., & Motl, R. W. (2021). Accuracy and precision of wrist-worn actigraphy for measuring steps taken during overground and treadmill walking in adults with Parkinson's disease. *Parkinsonism & Related Disorders*, 88, 102–107. <https://doi.org/10.1016/j.parkreldis.2021.06.009>
- Chen, M.-D., Kuo, C.-C., Pellegrini, C. A., & Hsu, M.-J. (2016). Accuracy of Wristband Activity Monitors during Ambulation and Activities. *Medicine and Science in Sports and Exercise*, 48(10), 1942–1949. <https://doi.org/10.1249/MSS.0000000000000984>
- Chow, J. J., Thom, J. M., Weweg, M. A., Ward, R. E., & Parmenter, B. J. (2017). Accuracy of step count measured by physical activity monitors: The effect of gait speed and anatomical placement site. *Gait & Posture*, 57, 199–203. <https://doi.org/10.1016/j.gaitpost.2017.06.012>
- Christiansen, C., Moore, C., Schenkman, M., Kluger, B., Kohrt, W., Delitto, A., Berman, B., Hall, D., Josbeno, D., Poon, C., Robichaud, J., Wellington, T., Jain, S., Comella, C., Corcos, D., & Melanson, E. (2017). Factors Associated With Ambulatory Activity in De Novo Parkinson Disease. *Journal of neurologic physical therapy: JNPT*, 41(2), 93–100. <https://doi.org/10.1097/NPT.0000000000000169>
- CTA/ANSI. (2016). CTA 2056-2016 (ANSI) - Physical Activity Monitoring for Fitness Wearables: Step Counting. Retrieved October 19, 2022, from <https://webstore.ansi.org/Standards/ANSI/cta20562016ansi>
- Degroote, L., De Bourdeaudhuij, I., Verloigne, M., Poppe, L., & Crombez, G. (2018). The Accuracy of Smart Devices for Measuring Physical Activity in Daily Life: Validation Study. *JMIR mHealth and uHealth*, 6(12), e10972. <https://doi.org/10.2196/10972>
- Del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK. *JAMA neurology*, 79(10), 1059–1063. <https://doi.org/10.1001/jamaneurol.2022.2672>
- Del Pozo Cruz, B., Ahmadi, M. N., Lee, I.-M., & Stamatakis, E. (2022). Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. *JAMA internal medicine*. <https://doi.org/10.1001/jamainternmed.2022.4000>
- Evenson, K. R., & Spade, C. L. (2020). Review of Validity and Reliability of Garmin Activity Trackers. *Journal for the Measurement of Physical Behaviour*, 3(2), 170–185. <https://doi.org/10.1123/jmpb.2019-0035>
- Fasano, A., Canning, C. G., Hausdorff, J. M., Lord, S., & Rochester, L. (2017). Falls in Parkinson's disease: A complex and evolving picture. *Movement Disorders: Official Journal of the Movement Disorder Society*, 32(11), 1524–1536. <https://doi.org/10.1002/mds.27195>

- Fokkema, T., Kooiman, T. J. M., Krijnen, W. P., VAN DER Schans, C. P., & DE Groot, M. (2017). Reliability and Validity of Ten Consumer Activity Trackers Depend on Walking Speed. *Medicine and Science in Sports and Exercise*, 49(4), 793–800. <https://doi.org/10.1249/MSS.0000000000001146>
- Geritz, J., Welzel, J., Hansen, C., Maetzler, C., Hobert, M. A., Elshehabi, M., Sobczak, A., Kudelka, J., Stiel, C., Hieke, J., Alpes, A., Bunzeck, N., & Maetzler, W. (2022). Does Executive Function Influence Walking in Acutely Hospitalized Patients With Advanced Parkinson's Disease: A Quantitative Analysis. [Place: Switzerland]. *Frontiers in neurology*, 13, 852725. <https://doi.org/10.3389/fneur.2022.852725>
- Godfrey, A., Morris, R., Hickey, A., & Del Din, S. (2016). Beyond the front end: Investigating a thigh worn accelerometer device for step count and bout detection in Parkinson's disease. *Medical Engineering and Physics*, 38(12), 1524–1529. <https://doi.org/10.1016/j.medengphy.2016.09.023>
Export Date: 14 April 2025; Cited By: 14.
- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Handlery, R., Stewart, J. C., Pellegrini, C., Monroe, C., Hainline, G., Flach, A., Handlery, K., & Fritz, S. (2021). Physical Activity in De Novo Parkinson Disease: Daily Step Recommendation and Effects of Treadmill Exercise on Physical Activity. *Physical Therapy*, 101(10), pzab174. <https://doi.org/10.1093/ptj/pzab174>
- Hillel, I., Gazit, E., Nieuwboer, A., Avanzino, L., Rochester, L., Cereatti, A., Croce, U. D., Rikkert, M. O., Bloem, B. R., Pelosin, E., Del Din, S., Ginis, P., Giladi, N., Mirelman, A., & Hausdorff, J. M. (2019). 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. *European Review of Aging and Physical Activity: Official Journal of the European Group for Research into Elderly and Physical Activity*, 16, 6. <https://doi.org/10.1186/s11556-019-0214-5>
- Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: Onset, progression and mortality. *Neurology*, 17(5), 427–442. <https://doi.org/10.1212/wnl.17.5.427>
- Keith, R. A., Granger, C. V., Hamilton, B. B., & Sherwin, F. S. (1987). The functional independence measure: A new tool for rehabilitation. *Advances in Clinical Rehabilitation*, 1, 6–18.
- Kim, D. W., Hassett, L. M., Nguy, V., & Allen, N. E. (2019). A Comparison of Activity Monitor Data from Devices Worn on the Wrist and the Waist in People with Parkinson's Disease. [Place: United States]. *Movement disorders clinical practice*, 6(8), 693–699. <https://doi.org/10.1002/mdc3.12850>
- Koo, T. K., & Li, M. Y. (2016). A Guide-line of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *Journal of Chiropractic Medicine*, 15(2), 155–163. <https://doi.org/10.1016/j.jcm.2016.02.012>
- Lai, B., Sasaki, J. E., Jeng, B., Cederberg, K. L., Bamman, M. M., & Motl, R. W. (2020). Accuracy and Precision of Three Consumer-Grade Motion Sensors During Overground and Treadmill Walking in People With Parkinson Disease: Cross-Sectional Comparative Study. *JMIR rehabilitation and assistive technologies*, 7(1), e14059. <https://doi.org/10.2196/14059>
- Lamont, R. M., Daniel, H. L., Payne, C. L., & Brauer, S. G. (2018). Accuracy of wearable physical activity trackers in people with Parkinson's disease. [Place: England]. *Gait & posture*, 63, 104–108. <https://doi.org/10.1016/j.gaitpost.2018.04.034>
- MacKinnon, C. D. (2018). Sensorimotor anatomy of gait, balance, and falls. *Handbook of Clinical Neurology*, 159, 3–26. <https://doi.org/10.1016/B978-0-444-63916-5.00001-X>

- Master, H., Annis, J., Huang, S., Beckman, J. A., Ratsimbazafy, F., Marginean, K., Carroll, R., Natarajan, K., Harrell, F. E., Roden, D. M., Harris, P., & Brittain, E. L. (2022). Association of step counts over time with the risk of chronic disease in the All of Us Research Program. *Nature Medicine*, 28(11), 2301–2308. <https://doi.org/10.1038/s41591-022-02012-w>
- Miller-Patterson, C., Buesa, R., McLaughlin, N., Jones, R., Akbar, U., & Friedman, J. H. (2018). Motor asymmetry over time in Parkinson's disease. *Journal of the Neurological Sciences*, 393, 14–17. <https://doi.org/10.1016/j.jns.2018.08.001>
- Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L., Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)
- Morris, R., Martini, D. N., Smulders, K., Kelly, V. E., Zabetian, C. P., Poston, K., Hiller, A., Chung, K. A., Yang, L., Hu, S.-C., Edwards, K. L., Cholerton, B., Grabowski, T. J., Montine, T. J., Quinn, J. F., & Horak, F. (2019). Cognitive associations with comprehensive gait and static balance measures in Parkinson's disease. *Parkinsonism & Related Disorders*, 69, 104–110. <https://doi.org/10.1016/j.parkreldis.2019.06.014>
- Paluch, A. E., Bajpai, S., Bassett, D. R., Carnethon, M. R., Ekelund, U., Evenson, K. R., Galuska, D. A., Jefferis, B. J., Kraus, W. E., Lee, I.-M., Matthews, C. E., Omura, J. D., Patel, A. V., Pieper, C. F., Rees-Punia, E., Dallmeier, D., Klenk, J., Whincup, P. H., Dooley, E. E., ... Fulton, J. E. (2022). Daily steps and all-cause mortality: A meta-analysis of 15 international cohorts [Publisher: Elsevier]. *The Lancet Public Health*, 7(3), e219–e228. [https://doi.org/10.1016/S2468-2667\(21\)00302-9](https://doi.org/10.1016/S2468-2667(21)00302-9)
- Paluch, A. E., Gabriel, K. P., Fulton, J. E., Lewis, C. E., Schreiner, P. J., Sternfeld, B., Sidney, S., Siddique, J., Whitaker, K. M., & Carnethon, M. R. (2021). Steps per Day and All-Cause Mortality in Middle-aged Adults in the Coronary Artery Risk Development in Young Adults Study. *JAMA network open*, 4(9), e2124516. <https://doi.org/10.1001/jamanetworkopen.2021.24516>
- Peto, V., Jenkinson, C., Fitzpatrick, R., & Greenhall, R. (1995). The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, 4(3), 241–248. <https://doi.org/10.1007/BF02260863>
- Poewe, W., Seppi, K., Tanner, C. M., Halliday, G. M., Brundin, P., Volkmann, J., Schrag, A.-E., & Lang, A. E. (2017). Parkinson disease. *Nature Reviews. Disease Primers*, 3, 17013. <https://doi.org/10.1038/nrdp.2017.13>
- Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., Obeso, J., Marek, K., Litvan, I., Lang, A. E., Halliday, G., Goetz, C. G., Gasser, T., Dubois, B., Chan, P., Bloem, B. R., Adler, C. H., & Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 30(12), 1591–1601. <https://doi.org/10.1002/mds.26424>
- Schapira, A. H. V., Chaudhuri, K. R., & Jenner, P. (2017). Non-motor features of Parkinson disease. *Nature Reviews. Neuroscience*, 18(7), 435–450. <https://doi.org/10.1038/nrn.2017.62>
- Skidmore, F. M., Mackman, C. A., Pav, B., Shulman, L. M., Garvan, C., Macko, R. F., & Heilman, K. M. (2008). Daily ambulatory activity levels in idiopathic Parkinson disease. *Journal of Rehabilitation Research and Development*, 45(9), 1343–1348.
- Straiton, N., Alharbi, M., Bauman, A., Neubeck, L., Gullick, J., Bhindi, R., & Gallagher, R. (2018). The validity and reliability of consumer-grade activity trackers in older, community-dwelling adults: A systematic review. *Maturitas*, 112, 85–93. <https://doi.org/10.1016/j.maturitas.2018.03.016>
- Stroop, J. R. (1935). Studies of interference in serial verbal reactions [Place: US Publisher: Psychological Review Company]. *Journal of Experimental Psychology*, 18(6), 643–662. <https://doi.org/10.1037/h0054651>
- Studenski, S., Perera, S., Patel, K., Rosano, C., Faulkner, K., Inzitari, M., Brach, J., Chandler, J., Cawthon, P., Connor, E. B.,

- Nevitt, M., Visser, M., Kritchevsky, S., Badinelli, S., Harris, T., Newman, A. B., Cauley, J., Ferrucci, L., & Guralnik, J. (2011). Gait speed and survival in older adults. *JAMA*, 305(1), 50–58. <https://doi.org/10.1001/jama.2010.1923>
- Svarre, F. R., Jensen, M. M., Nielsen, J., & Villumsen, M. (2020). The validity of activity trackers is affected by walking speed: The criterion validity of Garmin Vivosmart® HR and StepWatch™ 3 for measuring steps at various walking speeds under controlled conditions. *PeerJ*, 8, e9381. <https://doi.org/10.7717/peerj.9381>
- Varghese, J., Alen, C. M. v., Fujarski, M., Schlake, G. S., Sucker, J., Warnecke, T., & Thomas, C. (2021). Sensor Validation and Diagnostic Potential of Smartwatches in Movement Disorders. *Sensors (Basel, Switzerland)*, 21(9), 3139. <https://doi.org/10.3390/s21093139>
- Vítečková, S., Horáková, H., Poláková, K., Krupička, R., Růžicka, E., & Brožová, H. (2020). Agreement between the GAITRite® System and the Wearable Sensor BTS G-Walk® for measurement of gait parameters in healthy adults and Parkinson's disease patients. *PeerJ*, 8, e8835. <https://doi.org/10.7717/peerj.8835>
- Warmerdam, E., Romijnders, R., Hansen, C., Elshehabi, M., Zimmermann, M., Metzger, F. G., von Thaler, A.-K., Berg, D., Schmidt, G., & Maetzler, W. (2021). Arm swing responsiveness to dopaminergic medication in Parkinson's disease depends on task complexity. *NPJ Parkinson's disease*, 7(1), 89. <https://doi.org/10.1038/s41531-021-00235-1>
- Welzel, J., Wendtland, D., Warmerdam, E., Romijnders, R., Elshehabi, M., Geritz, J., Berg, D., Hansen, C., & Maetzler, W. (2021). Step Length Is a Promising Progression Marker in Parkinson's Disease. [Place: Switzerland]. *Sensors (Basel, Switzerland)*, 21(7). <https://doi.org/10.3390/s21072292>
- Wendel, N., Macpherson, C. E., Webber, K., Hendron, K., DeAngelis, T., Colon-Semenza, C., & Ellis, T. (2018). Accuracy of Activity Trackers in Parkinson Disease: Should We Prescribe Them? [Place: United States]. *Physical therapy*, 98(8), 705–714. <https://doi.org/10.1093/ptj/pty054>
- Wilson, J., Alcock, L., Yarnall, A. J., Lord, S., Lawson, R. A., Morris, R., Taylor, J.-P., Burn, D. J., Rochester, L., & Galna, B. (2020). Gait Progression Over 6 Years in Parkinson's Disease: Effects of Age, Medication, and Pathology. *Frontiers in Aging Neuroscience*, 12, 577435. <https://doi.org/10.3389/fnagi.2020.577435>
- Yogev-Seligmann, G., Hausdorff, J. M., & Giladi, N. (2008). The role of executive function and attention in gait. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(3), 329–342, quiz 472. <https://doi.org/10.1002/mds.21720>

Chapter 5

Contribution 2: Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch

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Abstract

Daily steps could be a valuable indicator of real-world ambulation in Parkinson's disease (PD). Nonetheless, no study to date has investigated the minimum number of days required to reliably estimate the average daily steps through commercial smartwatches in people with PD. Fifty-six patients were monitored through a commercial smartwatch for 5 consecutive days. The total daily steps for each day was recorded and the average daily steps was calculated as well as the working and weekend days average steps. The intraclass correlation coefficient (ICC) (3,k), standard error of measurement (SEM), Bland–Altman statistics, and minimum detectable change (MDC) were used to evaluate the reliability of the step count for every combination of 2–5 days. The threshold for acceptability was set at an ICC ≥ 0.8 with a lower bound of CI 95% ≥ 0.75 and a SAM $< 10\%$. ANOVA and Mann–Whitney tests were used to compare steps across the days and between the working and weekend days, respectively. Four days were needed to achieve an acceptable reliability (ICC range: 0.84–0.90; SAM range: 7.8–9.4%). In addition, daily steps did not significantly differ across the days and between the working and weekend days. These findings could support the use of step count as a walking activity index and could be relevant to developing monitoring, preventive, and rehabilitation strategies for people with PD.

Introduction

Parkinson’s disease (PD) is a progressive neurodegenerative disease characterized by motor and non-motor symptoms (Armstrong & Okun, 2020). Bradykinesia (slowness of movement), rigidity (increased muscle stiffness), and rest tremor are the three cardinal motor manifestations in PD, but gait and balance disturbances are rather common, particularly with disease progression (Poewe et al., 2017). Gait is an essential motor activity and its disturbances have a profound impact on functional independence, disability, quality of life, and mortality in older adults (M. Lee et al., 2021; Paluch et al., 2022; Studenski et al., 2011). Gait impairments in PD include continuous alterations such as reduced step length and speed, increased cadence and variability, diminished arm swing, and episodic disturbances such as freezing of gait (FOG) (Mirelman et al., 2019). Alterations in biomechanics and the disorders associated with the disease make walking an energetically unfavorable activity in PD (Maggioni et al., 2012), and can severely affect a patient’s quality of life and functional autonomy (Walton et al., 2015), increasing the risk of falls (Creaby & Cole, 2018).

Daily steps are rather easy to collect and represent a useful measure of ambulatory activity and mobility (Bassett et al., 2017). More importantly, daily step count has been reported to be associated with general mortality (Inoue et al., 2023; I.-M. Lee et al., 2019; Paluch et al., 2021, 2022; Saint-Maurice et al., 2020) as well as with the incidence of several pathological conditions such as cancer (Del Pozo Cruz, Ahmadi, et al., 2022), cardiovascular disease (Del Pozo Cruz, Ahmadi, et al., 2022), and dementia (Del Pozo Cruz, Ahmadi, et al., 2022) in older adults. In PD patients, previous studies have reported an association between the degree of disease severity (Skidmore et al., 2008) and average physical activity (Mantri et al., 2019). The spread of commercial devices, such as smartphones and smartwatches (Bianchini & Maetzler, 2023), has made step counting even more accessible, and high interest is growing in sensor-based mobility assessment in healthy adults (Bate et al., 2023) and several diseases (Soultard et al., 2022), including PD patients (Correno et al., 2022). However, a critical point is whether these commercial devices are sufficiently accurate, reliable, and valid for measuring steps. Step counting algorithms are usually designed to work with people with physiological walking patterns, therefore PD could represent a challenge. Motor symptoms increase the background noise of the recording leading to an inaccurate estimate of the number of steps particularly if the device is worn on the wrist (Bianchini et al., 2022; Kim et al., 2019; Wendel et al., 2018). We have recently demonstrated the accuracy of a commercial smartwatch in measuring steps against manual step counting when the smartwatch was worn on the side least affected by the disease (Bianchini et al., 2022). Furthermore, a recent work from Ginis and colleagues (Ginis et al., 2023) demonstrated criterion validity for average daily steps measured using commercial smartwatches against a research-grade inertial sensor.

When measuring step count in real-world conditions, the number of days required for monitoring daily steps is another crucial aspect to ensure a reliable estimate of the variable of interest that could be representative of habitual walking behavior. Furthermore, it must be considered whether daily steps are collected on consecutive days or random days since the latter has been reported to reduce the reliability of step counting (Kang et al., 2009). Indeed, in previous work from Kang et al. (Kang et al., 2009), 5 consecutive days were sufficient to reliably estimate the daily step count in healthy older adults through a research-grade, wrist-worn, inertial sensor, while 6 days were needed when using non-consecutive days. This aligns with previous studies reporting that a period from 2 to 7 consecutive days can accurately predict walking activity in healthy older adults (Clemes & Griffiths, 2008; Hart et al., 2011; Sigmundová et al., 2013; van Schooten et al., 2015; Yao et al., 2021). Other works also reported that a monitoring window of 2 consecutive days, irrespective of the type of day, could be sufficient in patients with disability from neurologic diseases, such as multiple sclerosis (Norris et al., 2017) and poststroke patients (Finis et al., 2019). In PD, a limited number of studies have investigated the minimum number of days required to

achieve a reliable estimate of the average daily steps in a real-world setting (Paul et al., 2016), using an ankle-mounted, research-grade inertial sensor (step activity monitor Herge-roeder et al., 2018) in 92 mild to moderate PD patients, for 7 consecutive days. The authors concluded that 2 days of monitoring were sufficient to obtain good reliability in estimating daily steps, as indicated by an intraclass correlation coefficient (ICC) (2,1) > 0.9. Notwithstanding, ankle-mounted devices are generally less tolerated by users (Lim et al., 2018; Rousham et al., 2006) compared with wrist-worn sensors (Artese et al., 2023; Germini et al., 2022; Lim et al., 2018) and research-grade devices are usually expensive, less available on the market, and require a higher level of expertise to be used (Bianchini & Maetzler, 2023), thus limiting their application. To this end, the use of commercial, wrist-worn devices, such as smartwatches, could help disseminate this technology and increase the possibility of monitoring walking at home. However, no study has investigated the minimum number of monitoring days required to achieve a reliable estimate of the average daily steps measured in an unsupervised, real-world setting, through a commercial smartwatch in PD patients.

Material and Methods

Study design and ethics

This was a cross-sectional study aimed at investigating the minimum number of days needed to reliably estimate daily step count using a commercial smartwatch, in an unsupervised, real-world setting, in people with mild to moderate PD. The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. Approval was granted by the local Ethics Committee. Data collection and processing followed the current European regulation for data protection. All participants provided written informed consent before the start of measurements.

Population

Participants were longitudinally recruited in the Movement Disorder Outpatient Service of the Sant'Andrea University Hospital, Rome, Italy, in the period between March 2023 and July 2023. The inclusion criteria were as follows: (i) diagnosis of idiopathic PD according to MDS criteria (Postuma et al., 2015); (ii) age 18 years or older; (iii) disease stage < 4 according to the modified Hoehn and Yahr scale (mHY) ("severe disability; still able to walk or stand unassisted") (Goetz et al., 2004); (iv) ability to walk independently without walking aids; (v) ability to perform the experimental procedure. The exclusion criteria were as follows: (i) cognitive impairment as defined by a Montreal Cognitive Assessment (MoCA) score < 24; (ii) orthopedic, rheumatologic, or systemic conditions affecting mobility as judged by the assessor.

Experimental Procedure

Participants were evaluated during scheduled visits on Wednesday, Thursday, or Friday, at the hospital. Demographics (age, sex) and anthropometric measures (weight, height, body mass index (BMI)) were collected. Disease duration, disease stage according to the modified Hoehn and Yahr scale (mHY), and Levodopa Equivalent Daily Dose (LEDD) (Jost et al., 2023), were also collected. The Movement Disorder Society—Unified Parkinson's Disease Rating Scale (MDS-UPDRS)—part III (Goetz et al., 2008) was used to assess motor symptoms severity. The MDS-UPDRS—part IV was used to assess the presence of motor complications. Participants received the smartwatch Garmin Vivosmart 4 (Garmin, Olathe, KS, USA), to be worn at home for at least 5 days, including at least one weekend day, on the wrist on the side least affected by the disease, following a previous study

from our group (Bianchini et al., 2022). The smartwatch was configured according to the producer’s recommendations (“vivosmart 4 - Introduction,” n.d.) by indicating the users’ age, height, weight, and the wrist on which the smartwatch was worn (i.e., left or right). Patients were asked to perform daily activities as usual. From the smartwatch dashboard, the total daily steps for each day was recorded. The average daily steps was calculated as well as the working days (i.e., Monday to Friday) and weekend days (i.e., Saturday and Sunday) average steps.

Statistical analyses

The statistical analyses were performed using JASP v0.17.2.1 (JASP Team, University of Amsterdam), R v4.3.1, and RStudio v2023.06.0+421 for Windows (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were calculated for the examined variables. The normality of the distributions was assessed by histogram and residual plots inspection. A one-way analysis of variance (ANOVA) was performed to assess the difference in the daily step count, across the 5 days. To evaluate the relative reliability for each combination of 2–5 days, a two-way intraclass correlation coefficient (ICC) with a fixed set of raters and averaged ratings was used (ICC (3,k), where k was the number of days of measurement), together with a custom R script. The following reference cut-off values for ICC interpretation were used (Koo & Li, 2016): Excellent: >0.90 ; Good: $0.75\text{--}0.90$; Moderate: $0.50\text{--}0.75$; Poor: <0.50 . The a priori threshold for an acceptable ICC was set at a point estimate ≥ 0.80 with a lower bound of 95% confidence interval (CI 95%) ≥ 0.75 . Standard error of measurement (SEM) and minimal detectable change with a confidence interval of 95% (MDC95) were used to compute the absolute reliability for all combinations of 2–4 days (Lexell & Downham, 2005) and were reported as absolute value and percentage of criterion measure (SEM% and MDC95%, respectively). The criterion was the average daily step count derived from the 5 days. SEM% values lower than 10% were considered acceptable (Pedersen et al., 2022). Bland–Altman plots were used to assess the average magnitude bias between the 2–4 days combinations and criterion as well as 95% limits of agreement, calculated as bias ± 1.96 SD. For all analyses, the significance threshold was set at < 0.05 . All data were reported as mean $\pm$ SD or median (Q1–Q3) for numerical data and N (%) for categorical variables.

Results

A total of 56 PD patients were enrolled in the study. All patients were monitored through Garmin Vivosmart 4 at home for a period of 5 consecutive days. Participants took on average 5861 ± 3086 daily steps ranging from 357 to 12,509. Details of demographic, anthropometric, and clinical variables are shown in table 5.1. Details of the daily steps, working and weekend day steps, and average daily steps across the 5-day period are shown in table 5.2. The ANOVA test showed no significant differences in the daily steps across the 5 days ($F_{2,272} = 1.997$; $p = 0.095$) (fig. 5.1). The Mann–Whitney test showed no significant difference between the working days and weekend days for daily steps ($W = 9051.52$; $p = 0.774$) (fig. 5.2). table 5.3a and table 5.3b show the ICC (3,k) values for all the combinations of 2–5 days and Bland–Altman statistics, SEM, and MDC for all the combinations of 2–4 days. The consecutive 5-day recording showed an excellent ICC. All the 4-day combinations, both consecutive and non-consecutive, demonstrated a good ICC above the predefined criterion, a SEM below 10% and a small bias from the Bland–Altman statistics. Two- and three-day combinations did not consistently show an ICC above the a priori threshold (fig. 5.3).

Table 5.1. Demographic, anthropometric, and clinical characteristics of the enrolled population.

	PD Patients (N = 56)
Age (years)	69.5 $\pm$ 7.8
Retired	44 (79%)
Height (cm)	174 $\pm$ 7.6
Weight (kg)	79.0 $\pm$ 13.0
BMI (kg/m ²)	26.2 $\pm$ 3.8
Sex	M: 43 (77%) F: 13 (23%)
Disease duration (years)	7.1 $\pm$ 4.7
LEDD (mg)	604 $\pm$ 325
mHY	2 (2–2.5)
Motor complications	15 (27%)
MDS-UPDRS-III	29 (23–32)

BMI: body mass index; F: females; LEDD: Levodopa equivalent daily dose; M: males; MDS-UPDRS-III: Movement Disorder Society Unified Parkinson's Disease Rating Scale part III; mHY: modified Hoehn and Yahr scale; PD: Parkinson's disease.

Table 5.2. Daily steps for each monitoring day, average steps during working and weekend days, and average daily steps across the 5-day period in the enrolled population. ANOVA: Analysis of variance; PD: Parkinson's disease.

	PD Patients (N = 56)	
Steps day 1	6858 $\pm$ 4230	
Steps day 2	6280 $\pm$ 4094	
Steps day 3	5203 $\pm$ 3034	$F_{2,272} = 1.997, p = 0.095^a$
Steps day 4	5401 $\pm$ 3411	
Steps day 5	5520 $\pm$ 3436	
Working days	5805 $\pm$ 3693	$W = 9051.52, p = 0.774^b$
Weekend days	5932 $\pm$ 3719	
Average daily steps	5861 $\pm$ 3086	

^a One-way ANOVA, ^b Mann-Whitney U test.

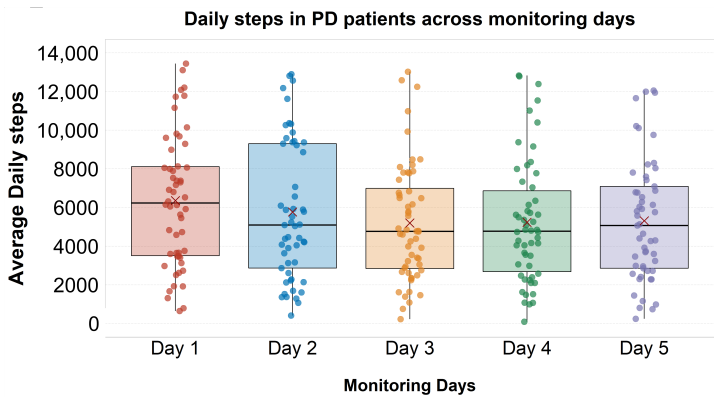


Figure 5.1. Boxplots showing daily steps for each monitoring day in PD patients. Thick line in the boxes indicates the median; lower and upper box limits indicate first (Q1) and third quartile (Q3), respectively; black vertical lines indicate lower and upper outliers boundaries calculated as $Q1 - (1.5 \times IQR)$ and $Q3 + (1.5 \times IQR)$, respectively. Red X indicates mean values for each disease stage. PD: Parkinson's disease.

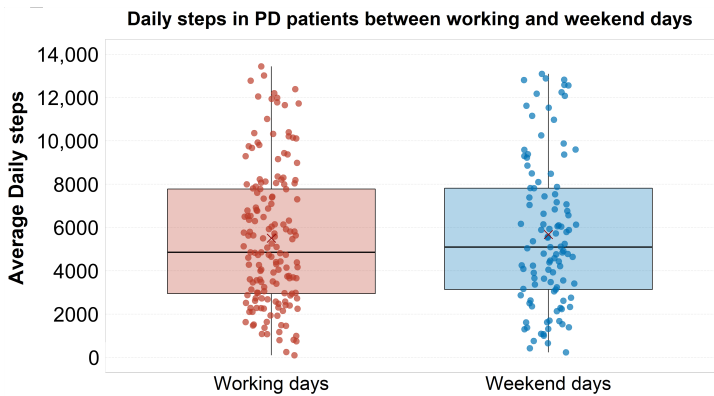


Figure 5.2. Boxplots showing daily steps for working and weekend days in PD patients. The thick line in the boxes indicates the median; lower and upper box limits indicate first (Q1) and third quartile (Q3), respectively; black vertical lines indicate lower and upper outliers boundaries calculated as $Q1 - (1.5 \times IQR)$ and $Q3 + (1.5 \times IQR)$, respectively. Red X indicates mean values for each disease stage. PD: Parkinson's disease.

Table 5.3a. ICC (3,k), Bland–Altman statistics, SEM, and MDC for all combinations of 2–3 days. ICC values are reported as point estimate (95%CI lower bound–95% CI upper bound). Bland–Altman statistics are reported as bias (upper limit of agreement; lower limit of agreement). SEM and MDC are reported as absolute number of steps (percentage of criterion measure). ICC and SEM values within the a priori thresholds for acceptability are displayed in bold.

Combinations of Days	ICC (3,k)	Bland–Altman Statistics	SEM (SEM%)	MDC95 (MDC95%)
Days 1-2	0.85 (0.74–0.91)	-707.9 (-3340.2; 1924.4)	1510 (25.8)	4185 (71.4)
Days 1-3	0.71 (0.51–0.83)	-169.3 (-2337.2; 1998.6)	1109 (18.9)	3074 (52.5)
Days 1-4	0.62 (0.35–0.78)	-269.3 (-2195.3; 1656.7)	1010 (17.2)	2801 (47.8)
Days 1-5	0.83 (0.70–0.90)	-361.1 (-3245.7; 2523.6)	1503 (25.6)	4165 (71.1)
Days 2-3	0.82 (0.69–0.89)	119.8 (-1829.7; 2069.3)	993 (16.9)	2752 (47.0)
Days 2-4	0.80 (0.66–0.88)	15.6 (-2312.2; 2343.4)	1177 (20.1)	3263 (55.7)
Days 2-5	0.86 (0.76–0.92)	-76.3 (-2353.2; 2200.7)	1154 (19.7)	3198 (54.6)
Days 3-4	0.83 (0.72–0.90)	578.3 (-2492.3; 3648.8)	1657 (28.3)	4592 (78.4)
Days 3-5	0.72 (0.51–0.84)	508.4 (-1488.0; 2504.8)	1130 (19.3)	3133 (53.5)
Days 4-5	0.67 (0.42–0.81)	368.3 (-1844.4; 2581.0)	1337 (22.8)	3705 (63.2)
Days 1-2-3	0.86 (0.78–0.91)	-252.5 (-1678.8; 1173.9)	764 (13.0)	2118 (36.1)
Days 1-2-4	0.83 (0.74–0.90)	-320.5 (-1609.8; 968.7)	726 (12.4)	2014 (34.4)
Days 1-2-5	0.89 (0.83–0.93)	-381.7 (-2422.9; 1659.4)	1100 (18.8)	3050 (52.0)
Days 1-3-4	0.79 (0.67–0.87)	46.6 (-1466.6; 1559.8)	767 (13.1)	2125 (36.3)
Days 1-3-5	0.82 (0.72–0.89)	-7.3 (-1565.0; 1553.4)	789 (13.5)	2187 (37.3)
Days 1-4-5	0.79 (0.67–0.87)	-93.0 (-1413.5; 1227.4)	674 (11.5)	1869 (31.9)
Days 2-3-4	0.87 (0.80–0.92)	237.9 (-1685.2; 2161.0)	1001 (17.1)	2775 (47.3)
Days 2-3-5	0.86 (0.79–0.92)	184.0 (-1112.1; 1480.0)	681 (11.6)	1887 (32.2)
Days 2-4-5	0.85 (0.76–0.91)	94.1 (-1394.5; 1582.6)	758 (12.9)	2102 (35.9)
Days 3-4-5	0.81 (0.70–0.88)	492.6 (-1288.0; 2273.1)	1026 (17.5)	2845 (48.5)

CI: confidence interval; ICC: intraclass correlation coefficient; MDC95: minimum detectable change with 95% CI; MDC95%: minimum detectable change with 95% CI expressed as percentage of criterion measure SEM: standard error of measurement; SEM%: standard error of measurement expressed as percentage of criterion measure.

Table 5.3b. ICC (3,k), Bland–Altman statistics, SEM, and MDC for all combinations of 4-5 days. ICC values are reported as point estimate (95%CI lower bound—95% CI upper bound). Bland–Altman statistics are reported as bias (upper limit of agreement; lower limit of agreement). SEM and MDC are reported as absolute number of steps (percentage of criterion measure). ICC and SEM values within the a priori thresholds for acceptability are displayed in bold.

Combinations of Days	ICC (3,k)	Bland–Altman Statistics	SEM (SEM%)	MDC95 (MDC95%)
Days 1-2-3-4	0.87 (0.81–0.92)	-72.1 (-968.0; 823.7)	459 (7.8)	1271 (21.7)
Days 1-2-3-5	0.89 (0.84–0.93)	-114.4 (-1177.9; 949.1)	550 (9.4)	1524 (26.0)
Days 1-2-4-5	0.88 (0.81–0.92)	-175.3 (-1068.2; 717.6)	484 (8.3)	1342 (22.9)
Days 1-3-4-5	0.84 (0.76–0.90)	109.7 (-717.1; 936.5)	432 (7.4)	1198 (20.4)
Days 2-3-4-5	0.88 (0.82–0.93)	252.1 (-879.4; 1383.6)	539 (9.2)	1495 (25.5)
Days 1-2-3-4-5	0.90 (0.85–0.94)	—	—	—

CI: confidence interval; ICC: intraclass correlation coefficient; MDC95: minimum detectable change with 95% CI; MDC95%: minimum detectable change with 95% CI expressed as percentage of criterion measure SEM: standard error of measurement; SEM%: standard error of measurement expressed as percentage of criterion measure.

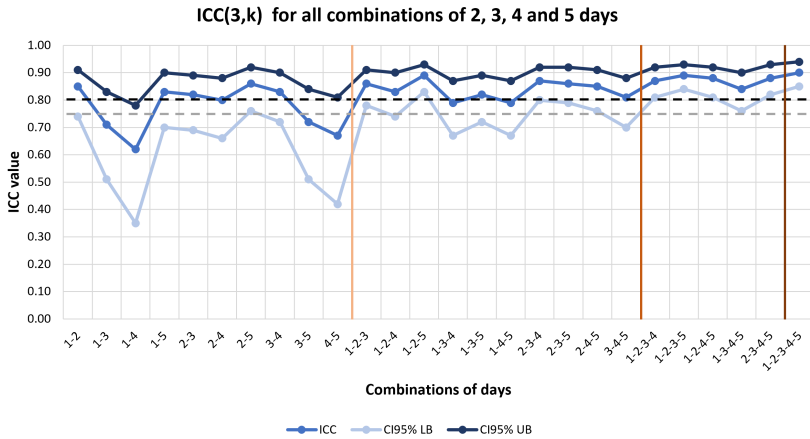


Figure 5.3. Graph showing the ICC(3,k) values across the different combinations of monitoring days. The top dark blue line represents 95% CI upper bound. The middle blue line represents the ICC (3,k) point estimate. The bottom light blue line represents 95% CI lower bound. Vertical brown lines were added to mark 2-day, 3-day, 4, day, and 5-day combinations. Dashed horizontal dark and light grey lines were added to mark the 0.8 threshold for the point estimate and the 0.75 threshold for 95% CI lower bound, respectively. CI: confidence interval; ICC: intraclass correlation coefficient. LB: lower bound; UB: upper bound.

Discussion

This cross-sectional study aimed at investigating the minimum number of days needed to reliably estimate the daily step count using a commercial smartwatch, in an unsupervised, real-world setting, in people with mild to moderate PD. To our knowledge, this is the first study to investigate this aspect using a commercial smartwatch in PD patients. We conclude the following: (i) 4 days are needed to reliably estimate the average daily steps in mild to moderate PD, and (ii) daily steps did not differ across the 5 monitoring days and between working days and weekend days. These results are discussed in detail in the following sections.

Reliability of Smartwatch-Based Average Daily Steps in PD Patients

We found that a minimum of 4 days was needed to reliably estimate the average daily steps in mild to moderate PD using a consumer-grade, wrist-worn smartwatch. Only one study has examined this aspect before in a similar group of 92 people with PD (Age: 67.3 ± 7.8 years; females: 41/92 (45%); mHY: 2.3 ± 0.6) (Paul et al., 2016). In this report, the authors concluded that two days of monitoring were sufficient to obtain a reliable daily step count estimate with an ICC (2,1) >0.9 , using a research-grade, ankle-mounted step counter (step activity monitor, SAM) worn for 7 continuous days (Paul et al., 2016). The lower minimum required number of days found in this study could be due to the different devices used and the position where the instrument was worn. It is generally expected that an ankle-mounted device achieves higher reliability than a wrist-worn one (Hergenroeder et al., 2018). Such research-grade devices undergo rigorous validation processes, and have displayed high accuracy and reliability under a broad range of walking conditions in different diseases, including PD (Hergenroeder et al., 2018; Mudge et al., 2007; Schmidt et al., 2011). Previous studies on patients with different neurological conditions, such as multiple sclerosis (Norris et al., 2017) and post-stroke (Fini et al., 2019), also reported that 2 days could be sufficient to reliably estimate daily steps using an arm-mounted research-grade device (SenseWear Armband J. A. Lee & Laurson, 2015). However, in line with our results, other studies reported a minimum number of monitoring days of 3–7 in healthy elderly patients using hip- and wrist-mounted devices (Clemes & Griffiths, 2008; Hart et al., 2011; Sigmundová et al., 2013; Yao et al., 2021). In PD, motor symptoms could hamper the performance of the step detection algorithm. In particular, the step detection performances of wearable sensors have been reported to be lower with a reduced gait speed (Chow et al., 2017; Fokkema et al., 2017; Svarre et al., 2020) and increased cadence (Lamont et al., 2018), both features of a parkinsonian gait, and during discontinuous walking periods (Wendel et al., 2018) that likely occur in PD patients due to reduced automaticity and episodes of FOG. Moreover, bradykinesia and reduced arm swing during ambulation could lead to an underestimation of the number of steps (Wendel et al., 2018), whereas tremor and dyskinesia may induce overestimation of the step count (Bianchini et al., 2022; Kim et al., 2019), particularly when the device is worn on the wrist (Kim et al., 2019). Furthermore, inter- and intra-day symptom fluctuations (Jankovic, 2005) and increased gait variability are common aspects of PD (Mirelman et al., 2019). Indeed, motor complications were present in 27% of our patients. All these elements and the use of a research-grade device could explain why the minimum number of days required to reliably estimate the average daily steps was higher in our study than in the previous literature on other neurological conditions.

The result that 4 days of monitoring was sufficient to obtain a reliable average daily step count is extremely relevant, as shorter monitoring periods could make it easier to collect step counts in daily clinical practice. Additionally, this is the first study to report Bland–Altman statistics, SEM, and MDC95 for daily step count in PD patients. The Bland–Altman plots revealed a good agreement in terms of magnitudes of bias and 95% limits of agreement for the 4-day combinations; the SEM showed that the 4-day combinations reached an absolute

reliability within the a priori threshold of 10% (table 5.3b). The 4-day combinations also showed the lowest degree of MDC95, with the values ranging from 1198 to 1524 steps/day (20–26% of the criterion). MDC is defined as the minimal change that falls outside the measurement error of an instrument used to collect a given parameter (Hansen et al., 2022; Lexell & Downham, 2005). This metric is extremely relevant to design future studies aiming to assess the effectiveness or cost/effectiveness of interventions, since it allows the calculation of the sample size. In our study, with 4-day monitoring windows, a difference of 1366 steps, on average, could not be attributed to random variations of the measurements, in mild–moderate PD patients measured through a commercial smartwatch.

All these findings could allow a wider implementation of step count as a reliable and easy-to-collect index of ambulatory activity and help in designing future studies including daily step count as an outcome measure in PD patients. As walking is commonly impaired in PD, it is indispensable to be able to quantify habitual walking in this population on a daily basis to develop preventive, educational, and rehabilitation strategies.

Difference in Daily Steps across Days and between Working and Weekend Days

In our study, participants took on average 5861 ± 3086 daily steps. This result is in line with previous reports showing average daily step values between 4500 and 7000 in similar PD populations (Benka Wallén et al., 2015; Christiansen et al., 2017; Ginis et al., 2023; Lord et al., 2013). There was no significant difference across the five days and between the working and weekend days. The non-significant effect of the day on average daily steps is supported by previous research on healthy elderly individuals (Hart et al., 2011) and patients with other diseases showing a moderate level of disability, such as rheumatoid arthritis (Almeida et al., 2011) and multiple sclerosis (Motl et al., 2007; Norris et al., 2017). Regarding the difference between the working and weekend days, our results are in line with previous work from Benka Wallén and collaborators on mild to moderate PD patients (Benka Wallén et al., 2015) and other reports in older adults (Hart et al., 2011; Martikainen et al., 2006; Matthews et al., 2002). The majority of PD patients are diagnosed after the age of 60 (Poewe et al., 2017), close to or after the retirement age in Italy, and it has been reported that PD patients retire 4–7 years earlier than the general population (Koerts et al., 2016). In our PD population, 44 out of 56 (nearly 80%) of the patients were retired; therefore, a difference between the working and weekend days in terms of walking pattern may not have been evident. However, our finding are in line with previous studies which also reported no physical activity and step count difference in healthy working adults between working and weekend days (Evenson et al., 2015; Smith et al., 2015). Conversely, Paul and colleagues (Paul et al., 2016), showed that PD patients take more steps on working days than on the weekend. However, it must be noted that, in that study, the difference in steps between the working and weekend days was rather small (around 600 steps/day; around 7% of the total reported daily steps), and the authors reported that they were only able to identify the time participants spent walking with moderate or greater intensity; therefore, this aspect could have influenced their results (Paul et al., 2016). Taken together, our findings support the idea that patients with PD and moderate disability display relatively consistent levels of ambulatory activity across the week, as identified by the average daily steps.

Limitations

We acknowledge that this study has limitations. First, the PD patients included in our study had, on average, relatively good levels of physical ability and cognitive functions, due to the inclusion and exclusion criteria. This could, hence, limit the generalization of our results and future studies enrolling PD participants with lower functional scores, greater disease severity, and more severe cognitive impairment are encouraged and included

in our plans. Second, we monitored the patients for 5 days only, therefore we could not draw firm conclusions regarding longer monitoring windows. However, previous studies in neurological patients used a 5-day time window to monitor daily steps and applied similar data analysis methods (Norris et al., 2017), and our results allowed us to confirm the reliability of a 4-day monitoring period for step counting. Third, the patients received a smartwatch on working days (i.e., Wednesday, Thursday, or Friday) and this could have affected our results, particularly regarding the difference between working and weekend days. However, we could hypothesize a minimal impact of this aspect on our results since our results are in line with the previous literature and we did not find any difference across the monitoring days. Fourth, we found that with a 4-day monitoring period, a difference of 1366 steps, on average, could not be attributed to random variations of the measurements. Although this aspect is relevant to design future studies, no report, to date, has investigated the minimal clinically important difference for daily steps in PD patients; therefore, no conclusions regarding the clinical relevance of a change in daily steps could be drawn and future studies will need to clarify this aspect. Finally, we tested only one smartwatch in our study, therefore more studies are needed to generalize our results and validate commercial smartwatches in clinical populations.

Conclusions

In mild to moderate PD patients, a minimum of 4 monitoring days was needed to achieve a reliable estimate of the average daily steps through a commercial smartwatch (Garmin Vivosmart 4). The step count did not significantly differ across the monitoring days and between the working and weekend days. Taken together, the short monitoring period required and the finding that PD patients with a moderate disability displayed relatively consistent levels of ambulatory activity across the week could facilitate a broader implementation of step count as an index of walking activity in this population. The present findings could be highly relevant to develop monitoring, preventive, educational, and rehabilitation strategies for people with PD.

References

- Almeida, G. J. M., Wasko, M. C. M., Jeong, K., Moore, C. G., & Piva, S. R. (2011). Physical activity measured by the SenseWear Armband in women with rheumatoid arthritis. *Physical Therapy*, 91(9), 1367–1376. <https://doi.org/10.2522/ptj.20100291>
- Armstrong, M. J., & Okun, M. S. (2020). Diagnosis and Treatment of Parkinson Disease: A Review. *JAMA*, 323(6), 548–560. <https://doi.org/10.1001/jama.2019.22360>
- Artese, A. L., Rawat, R., & Sung, A. D. (2023). The use of commercial wrist-worn technology to track physiological outcomes in behavioral interventions. *Current Opinion in Clinical Nutrition and Metabolic Care*. <https://doi.org/10.1097/MCO.0000000000000970>
- Bassett, D. R., Toth, L. P., LaMunion, S. R., & Crouter, S. E. (2017). Step Counting: A Review of Measurement Considerations and Health-Related Applications. *Sports Medicine (Auckland, N.Z.)*, 47(7), 1303–1315. <https://doi.org/10.1007/s40279-016-0663-1>
- Bate, G. L., Kirk, C., Rehman, R. Z. U., Guan, Y., Yarnall, A. J., Del Din, S., & Lawson, R. A. (2023). The Role of Wearable Sensors to Monitor Physical Activity and Sleep Patterns in Older Adult Inpatients: A Structured Review. *Sensors (Basel, Switzerland)*, 23(10), 4881. <https://doi.org/10.3390/s23104881>
- Benka Wallén, M., Franzén, E., Nero, H., & Hagströmer, M. (2015). Levels and Patterns of Physical Activity and Sedentary Behavior in Elderly People With Mild to Moderate Parkinson Disease. *Physical Therapy*, 95(8), 1135–1141. <https://doi.org/10.2522/ptj.20140374>
- Bianchini, E., Calìò, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzler, W., & Pontieri, F. E. (2022). Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, 23(1), 214. <https://doi.org/10.3390/s23010214>
- Bianchini, E., & Maetzler, W. (2023, May). Wearable systems in movement disorders. In *International Review of Movement Disorders*. Academic Press. <https://doi.org/10.1016/bs.irmvd.2023.04.002>
- Chow, J. J., Thom, J. M., Weweg, M. A., Ward, R. E., & Parmenter, B. J. (2017). Accuracy of step count measured by physical activity monitors: The effect of gait speed and anatomical placement site. *Gait & Posture*, 57, 199–203. <https://doi.org/10.1016/j.gaitpost.2017.06.012>
- Christiansen, C., Moore, C., Schenkman, M., Kluger, B., Kohrt, W., Delitto, A., Berman, B., Hall, D., Josbeno, D., Poon, C., Robichaud, J., Wellington, T., Jain, S., Comella, C., Corcos, D., & Melanson, E. (2017). Factors Associated With Ambulatory Activity in De Novo Parkinson Disease. *Journal of neurologic physical therapy: JNPT*, 41(2), 93–100. <https://doi.org/10.1097/NPT.0000000000000169>
- Clemes, S. A., & Griffiths, P. L. (2008). How many days of pedometer monitoring predict monthly ambulatory activity in adults? *Medicine and Science in Sports and Exercise*, 40(9), 1589–1595. <https://doi.org/10.1249/MSS.0b013e318177eb96>
- Correno, M. B., Hansen, C., Chardon, M., Milane, T., Bianchini, E., & Vuillerme, N. (2022). Association between Backward Walking and Cognition in Parkinson Disease: A Systematic Review. *International Journal of Environmental Research and Public Health*, 19(19), 12810. <https://doi.org/10.3390/ijerph191912810>
- Creaby, M. W., & Cole, M. H. (2018). Gait characteristics and falls in Parkinson's disease: A systematic review and meta-analysis. *Parkinsonism & Related Disorders*, 57, 1–8. <https://doi.org/10.1016/j.parkreldis.2018.07.008>
- Del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK. *JAMA neurology*, 79(10), 1059–1063. <https://doi.org/10.1001/jamaneurol.2022.2672>
- Del Pozo Cruz, B., Ahmadi, M. N., Lee, I.-M., & Stamatakis, E. (2022). Prospective

- Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. *JAMA internal medicine*. <https://doi.org/10.1001/jamainternmed.2022.4000>
- Evenson, K. R., Wen, F., Metzger, J. S., & Herring, A. H. (2015). Physical activity and sedentary behavior patterns using accelerometry from a national sample of United States adults. *The International Journal of Behavioral Nutrition and Physical Activity*, 12, 20. <https://doi.org/10.1186/s12966-015-0183-7>
- Fini, N. A., Burge, A. T., Bernhardt, J., & Holland, A. E. (2019). Two Days of Measurement Provides Reliable Estimates of Physical Activity Poststroke: An Observational Study. *Archives of Physical Medicine and Rehabilitation*, 100(5), 883–890. <https://doi.org/10.1016/j.apmr.2018.10.006>
- Fokkema, T., Kooiman, T. J. M., Krijnen, W. P., VAN DER Schans, C. P., & DE Groot, M. (2017). Reliability and Validity of Ten Consumer Activity Trackers Depend on Walking Speed. *Medicine and Science in Sports and Exercise*, 49(4), 793–800. <https://doi.org/10.1249/MSS.0000000000001146>
- Germini, F., Noronha, N., Borg Debono, V., Abraham Philip, B., Pete, D., Navarro, T., Keenanasseril, A., Parpia, S., de Wit, K., & Iorio, A. (2022). Accuracy and Acceptability of Wrist-Wearable Activity-Tracking Devices: Systematic Review of the Literature. *Journal of Medical Internet Research*, 24(1), e30791. <https://doi.org/10.2196/30791>
- Ginis, P., Goris, M., De Groef, A., Blondeel, A., Gilat, M., Demeyer, H., Troosters, T., & Nieuwboer, A. (2023). Validation of Commercial Activity Trackers in Everyday Life of People with Parkinson's Disease. *Sensors*, 23(8). <https://doi.org/10.3390/s23084156>
Export Date: 14 April 2025; Cited By: 6.
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., Giladi, N., Holloway, R. G., Moore, C. G., Wenning, G. K., Yahr, M. D., Seidl, L., & Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 19(9), 1020–1028. <https://doi.org/10.1002/mds.20213>
- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Hansen, C., Ortlieb, C., Romijnders, R., Warmerdam, E., Welzel, J., Geritz, J., & Maetzler, W. (2022). Reliability of IMU-Derived Temporal Gait Parameters in Neurological Diseases. *Sensors (Basel, Switzerland)*, 22(6), 2304. <https://doi.org/10.3390/s22062304>
- Hart, T. L., Swartz, A. M., Cashin, S. E., & Strath, S. J. (2011). How many days of monitoring predict physical activity and sedentary behaviour in older adults? *The International Journal of Behavioral Nutrition and Physical Activity*, 8, 62. <https://doi.org/10.1186/1479-5868-8-62>
- Hergenroeder, A. L., Barone Gibbs, B., Kotlarczyk, M. P., Kowalsky, R. J., Perera, S., & Brach, J. S. (2018). Accuracy of Objective Physical Activity Monitors in Measuring Steps in Older Adults. *Gerontology & Geriatric Medicine*, 4, 2333721418781126. <https://doi.org/10.1177/2333721418781126>
- Inoue, K., Tsugawa, Y., Mayeda, E. R., & Ritz, B. (2023). Association of Daily Step Patterns With Mortality in US Adults. *JAMA network open*, 6(3), e235174. <https://doi.org/10.1001/jamanetworkopen.2023.5174>
- Jankovic, J. (2005). Motor fluctuations and dyskinesias in Parkinson's disease: Clinical manifestations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 20 Suppl 11, S11–16. <https://doi.org/10.1002/mds.20458>

- Jost, S. T., Kaldenbach, M.-A., Antonini, A., Martinez-Martin, P., Timmermann, L., Odin, P., Katzenschlager, R., Borghain, R., Fasano, A., Stocchi, F., Hattori, N., Kukkle, P. L., Rodriguez-Violante, M., Falup-Pecurariu, C., Schade, S., Petry-Schmelzer, J. N., Metta, V., Weintraub, D., Deuschl, G., ... International Parkinson and Movement Disorders Society Non-Motor Parkinson Disease Study Group. (2023). Levodopa Dose Equivalency in Parkinson's Disease: Updated Systematic Review and Proposals. *Movement Disorders: Official Journal of the Movement Disorder Society*, 38(7), 1236–1252. <https://doi.org/10.1002/mds.29410>
- Kang, M., Bassett, D. R., Barreira, T. V., Tudor-Locke, C., Ainsworth, B., Reis, J. P., Strath, S., & Swartz, A. (2009). How many days are enough? A study of 365 days of pedometer monitoring. *Research Quarterly for Exercise and Sport*, 80(3), 445–453. <https://doi.org/10.1080/02701367.2009.10599582>
- Kim, D. W., Hassett, L. M., Nguy, V., & Allen, N. E. (2019). A Comparison of Activity Monitor Data from Devices Worn on the Wrist and the Waist in People with Parkinson's Disease. [Place: United States]. *Movement disorders clinical practice*, 6(8), 693–699. <https://doi.org/10.1002/mdc3.12850>
- Koerts, J., König, M., Tucha, L., & Tucha, O. (2016). Working capacity of patients with Parkinson's disease - A systematic review. *Parkinsonism & Related Disorders*, 27, 9–24. <https://doi.org/10.1016/j.parkreldis.2016.03.017>
- Koo, T. K., & Li, M. Y. (2016). A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *Journal of Chiropractic Medicine*, 15(2), 155–163. <https://doi.org/10.1016/j.jcm.2016.02.012>
- Lamont, R. M., Daniel, H. L., Payne, C. L., & Brauer, S. G. (2018). Accuracy of wearable physical activity trackers in people with Parkinson's disease. [Place: England]. *Gait & posture*, 63, 104–108. <https://doi.org/10.1016/j.gaitpost.2018.04.034>
- Lee, I.-M., Shiroma, E. J., Kamada, M., Bassett, D. R., Matthews, C. E., & Buring, J. E. (2019). Association of Step Volume and Intensity With All-Cause Mortality in Older Women. *JAMA internal medicine*, 179(8), 1105–1112. <https://doi.org/10.1001/jamainternmed.2019.0899>
- Lee, J. A., & Laursen, K. R. (2015). Validity of the SenseWear armband step count measure during controlled and free-living conditions. *Journal of Exercise Science and Fitness*, 13(1), 16–23. <https://doi.org/10.1016/j.jesf.2014.11.002>
- Lee, M., Noh, Y., Youm, C., Kim, S., Park, H., Noh, B., Kim, B., Choi, H., & Yoon, H. (2021). Estimating Health-Related Quality of Life Based on Demographic Characteristics, Questionnaires, Gait Ability, and Physical Fitness in Korean Elderly Adults. *International Journal of Environmental Research and Public Health*, 18(22), 11816. <https://doi.org/10.3390/ijerph182211816>
- Lexell, J. E., & Downham, D. Y. (2005). How to assess the reliability of measurements in rehabilitation. *American Journal of Physical Medicine & Rehabilitation*, 84(9), 719–723. <https://doi.org/10.1097/01.phm.0000176452.17771.20>
- Lim, S. E. R., Dodds, R., Bacon, D., Sayer, A. A., & Roberts, H. C. (2018). Physical activity among hospitalised older people: Insights from upper and lower limb accelerometry. *Aging Clinical and Experimental Research*, 30(11), 1363–1369. <https://doi.org/10.1007/s40520-018-0930-0>
- Lord, S., Godfrey, A., Galna, B., Mhiripiri, D., Burn, D., & Rochester, L. (2013). Ambulatory activity in incident Parkinson's: More than meets the eye? *Journal of Neurology*, 260(12), 2964–2972. <https://doi.org/10.1007/s00415-013-7037-5>
- Export Date: 14 April 2025; Cited By: 135.
- Maggioni, M. A., Veicsteinas, A., Rampichini, S., Cè, E., Nemni, R., Riboldazzi, G., & Merati, G. (2012). Energy cost of spontaneous walking in Parkinson's disease patients. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 33(4), 779–784. <https://doi.org/10.1007/s10072-011-0827-6>
- Mantri, S., Wood, S., Duda, J., & Morley, J. (2019). Comparing self-reported and objective monitoring of physical activity in Parkinson disease. *Parkinsonism and Re-*

- lated Disorders*, 67, 56–59. <https://doi.org/10.1016/j.parkreldis.2019.09.004>
Export Date: 14 April 2025; Cited By: 36.
- Martikainen, K. K., Luukkaala, T. H., & Marttila, R. J. (2006). Parkinson's disease and working capacity. *Movement Disorders: Official Journal of the Movement Disorder Society*, 21(12), 2187–2191. <https://doi.org/10.1002/mds.21171>
- Matthews, C. E., Ainsworth, B. E., Thompson, R. W., & Bassett, D. R. (2002). Sources of variance in daily physical activity levels as measured by an accelerometer. *Medicine and Science in Sports and Exercise*, 34(8), 1376–1381. <https://doi.org/10.1097/00005768-200208000-00021>
- Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L., Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)
- Motl, R. W., Zhu, W., Park, Y., McAuley, E., Scott, J. A., & Snook, E. M. (2007). Reliability of scores from physical activity monitors in adults with multiple sclerosis. *Adapted physical activity quarterly: APAQ*, 24(3), 245–253. <https://doi.org/10.1123/apaq.24.3.245>
- Mudge, S., Stott, N. S., & Walt, S. E. (2007). Criterion validity of the StepWatch Activity Monitor as a measure of walking activity in patients after stroke. *Archives of Physical Medicine and Rehabilitation*, 88(12), 1710–1715. <https://doi.org/10.1016/j.apmr.2007.07.039>
- Norris, M., Anderson, R., Motl, R. W., Hayes, S., & Coote, S. (2017). Minimum number of days required for a reliable estimate of daily step count and energy expenditure, in people with MS who walk unaided. *Gait & Posture*, 53, 201–206. <https://doi.org/10.1016/j.gaitpost.2017.02.005>
- Paluch, A. E., Bajpai, S., Bassett, D. R., Carnethon, M. R., Ekelund, U., Evenson, K. R., Galuska, D. A., Jefferis, B. J., Kraus, W. E., Lee, I.-M., Matthews, C. E., Omura, J. D., Patel, A. V., Pieper, C. F., Rees-Punia, E., Dallmeier, D., Klenk, J., Whincup, P. H., Dooley, E. E., ... Fulton, J. E. (2022). Daily steps and all-cause mortality: A meta-analysis of 15 international cohorts [Publisher: Elsevier]. *The Lancet Public Health*, 7(3), e219–e228. [https://doi.org/10.1016/S2468-2667\(21\)00302-9](https://doi.org/10.1016/S2468-2667(21)00302-9)
- Paluch, A. E., Gabriel, K. P., Fulton, J. E., Lewis, C. E., Schreiner, P. J., Sternfeld, B., Sidney, S., Siddique, J., Whitaker, K. M., & Carnethon, M. R. (2021). Steps per Day and All-Cause Mortality in Middle-aged Adults in the Coronary Artery Risk Development in Young Adults Study. *JAMA network open*, 4(9), e2124516. <https://doi.org/10.1001/jamanetworkopen.2021.24516>
- Paul, S. S., Ellis, T. D., Dibble, L. E., Earhart, G. M., Ford, M. P., Foreman, K. B., & Cavanaugh, J. T. (2016). Obtaining Reliable Estimates of Ambulatory Physical Activity in People with Parkinson's Disease. *Journal of Parkinson's Disease*, 6(2), 301–305. <https://doi.org/10.3233/JPD-160791>
- Pedersen, B. S., Kristensen, M. T., Josefsen, C. O., Lykkegaard, K. L., Jønsson, L. R., & Pedersen, M. M. (2022). Validation of Two Activity Monitors in Slow and Fast Walking Hospitalized Patients. *Rehabilitation Research and Practice*, 2022, 9230081. <https://doi.org/10.1155/2022/9230081>
- Poewe, W., Seppi, K., Tanner, C. M., Halliday, G. M., Brundin, P., Volkmann, J., Schrag, A.-E., & Lang, A. E. (2017). Parkinson disease. *Nature Reviews. Disease Primers*, 3, 17013. <https://doi.org/10.1038/nrdp.2017.13>
- Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., Obeso, J., Marek, K., Litvan, I., Lang, A. E., Halliday, G., Goetz, C. G., Gasser, T., Dubois, B., Chan, P., Bloem, B. R., Adler, C. H., & Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 30(12), 1591–1601. <https://doi.org/10.1002/mds.26424>
- Rousham, E. K., Clarke, P. E., & Gross, H. (2006). Significant changes in physical activity among pregnant women in the UK as assessed by accelerometry and self-reported activity. *European Journal of Clinical Nutrition*, 60(3), 393–400. <https://doi.org/10.1038/sj.ejcn.1602329>

- Saint-Maurice, P. F., Troiano, R. P., Bassett, D. R., Graubard, B. I., Carlson, S. A., Shiro, E. J., Fulton, J. E., & Matthews, C. E. (2020). Association of Daily Step Count and Step Intensity With Mortality Among US Adults. *JAMA*, *323*(12), 1151–1160. <https://doi.org/10.1001/jama.2020.1382>
- Schmidt, A. L., Pennypacker, M. L., Thrush, A. H., Leiper, C. I., & Craik, R. L. (2011). Validity of the StepWatch Step Activity Monitor: Preliminary findings for use in persons with Parkinson disease and multiple sclerosis. *Journal of Geriatric Physical Therapy* (2001), *34*(1), 41–45. <https://doi.org/10.1519/JPT.0b013e31820aa921>
- Sigmundová, D., Vašíčková, J., Stelzer, J., & Repka, E. (2013). The influence of monitoring interval on data measurement: An analysis of step counts of university students. *International Journal of Environmental Research and Public Health*, *10*(2), 515–527. <https://doi.org/10.3390/ijerph10020515>
- Skidmore, F. M., Mackman, C. A., Pav, B., Shulman, L. M., Garvan, C., Macko, R. F., & Heilman, K. M. (2008). Daily ambulatory activity levels in idiopathic Parkinson disease. *Journal of Rehabilitation Research and Development*, *45*(9), 1343–1348.
- Smith, L., Hamer, M., Ucci, M., Marmot, A., Gardner, B., Sawyer, A., Wardle, J., & Fisher, A. (2015). Weekday and weekend patterns of objectively measured sitting, standing, and stepping in a sample of office-based workers: The active buildings study. *BMC public health*, *15*, 9. <https://doi.org/10.1186/s12889-014-1338-1>
- Soulard, J., Carlin, T., Knitza, J., & Vuillerme, N. (2022). Wearables for Measuring the Physical Activity and Sedentary Behavior of Patients With Axial Spondyloarthritis: Systematic Review. *JMIR mHealth and uHealth*, *10*(8), e34734. <https://doi.org/10.2196/34734>
- Studenski, S., Perera, S., Patel, K., Rosano, C., Faulkner, K., Inzitari, M., Brach, J., Chandler, J., Cawthon, P., Connor, E. B., Nevitt, M., Visser, M., Kritchevsky, S., Badinelli, S., Harris, T., Newman, A. B., Cauley, J., Ferrucci, L., & Guralnik, J. (2011). Gait speed and survival in older adults. *JAMA*, *305*(1), 50–58. <https://doi.org/10.1001/jama.2010.1923>
- Svarre, F. R., Jensen, M. M., Nielsen, J., & Villumsen, M. (2020). The validity of activity trackers is affected by walking speed: The criterion validity of Garmin Vivosmart® HR and StepWatch™ 3 for measuring steps at various walking speeds under controlled conditions. *PeerJ*, *8*, e9381. <https://doi.org/10.7717/peerj.9381>
- van Schooten, K. S., Rispens, S. M., Elders, P. J., Lips, P., van Dieën, J. H., & Pijnappels, M. (2015). Assessing physical activity in older adults: Required days of trunk accelerometer measurements for reliable estimation. *Journal of Aging and Physical Activity*, *23*(1), 9–17. <https://doi.org/10.1123/japa.2013-0103>
- Vivosmart 4 - Introduction. (n.d.). Retrieved July 16, 2025, from <https://www8.garmin.com/manuals/webhelp/vivosmart4/EN-US/GUID-8B9070D6-C0EA-45EE-8F62-1602492BF264.html>
- Walton, C. C., Shine, J. M., Hall, J. M., O'Callaghan, C., Mowszowski, L., Gilat, M., Szeto, J. Y. Y., Naismith, S. L., & Lewis, S. J. G. (2015). The major impact of freezing of gait on quality of life in Parkinson's disease. *Journal of Neurology*, *262*(1), 108–115. <https://doi.org/10.1007/s00415-014-7524-3>
- Wendel, N., Macpherson, C. E., Webber, K., Hendron, K., DeAngelis, T., Colon-Semenza, C., & Ellis, T. (2018). Accuracy of Activity Trackers in Parkinson Disease: Should We Prescribe Them? [Place: United States]. *Physical therapy*, *98*(8), 705–714. <https://doi.org/10.1093/ptj/pzy054>
- Yao, J., Tan, C. S., Lim, N., Tan, J., Chen, C., & Müller-Riemenschneider, F. (2021). Number of daily measurements needed to estimate habitual step count levels using wrist-worn trackers and smartphones in 212,048 adults. *Scientific Reports*, *11*(1), 9633. <https://doi.org/10.1038/s41598-021-89141-3>

Chapter 6

Contribution 3: Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study

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Abstract

Average daily steps (avDS) could be a valuable indicator of real-world ambulation in people with Parkinson disease (PD), and previous studies have reported the validity and reliability of this measure. Nonetheless, no study has considered disease phenotype, stage, and severity when assessing the reliability of consumer wrist-worn devices to estimate daily step count in unsupervised, free-living conditions in PD. This study aims to assess and compare the reliability of a consumer wrist-worn smartwatch (Garmin Vivosmart 4) in counting avDS in people with PD in unsupervised, free-living conditions among disease phenotypes, stages, and severity groups. A total of 104 people with PD were monitored through Garmin Vivosmart 4 for 5 consecutive days. Total daily steps were recorded and avDS were calculated. Participants were dichotomized into tremor dominant (TD; n=39) or postural instability and gait disorder (PIGD; n=65), presence (n=57) or absence (n=47) of tremor, and mild (n=65) or moderate (n=39) disease severity. Based on the modified Hoehn and Yahr scale (mHY), participants were further dichotomized into earlier (mHY 1-2; n=68) or intermediate (mHY 2.5-3; n=36) disease stages. Intraclass correlation coefficient (ICC; 3,k), standard error of measurement (SEM), and minimal detectable change (MDC) were used to evaluate the reliability of avDS for each subgroup. The threshold for acceptability was set at an ICC ≥ 0.8 with a lower bound of 95% CI ≥ 0.75 . The 2-tailed Student t tests for independent groups and analysis of 83.4% CI overlap were used to compare ICC between each group pair. Reliability of avDS measured through Garmin Vivosmart 4 for 5 consecutive days in unsupervised, free-living conditions was acceptable in the overall population with an ICC of 0.89 (95% CI 0.85-0.92), SEM below 10%, and an MDC of 1580 steps per day (27% of criterion). In all investigated subgroups, the reliability of avDS was also acceptable (ICC range 0.84-0.94). However, ICCs were significantly lower in participants with tremor (P=.03), with mild severity (P=.04), and earlier stage (P=.003). Moreover, SEM was below 10% in participants with PIGD phenotype, without tremor, moderate disease severity, and intermediate disease stage, with an MDC ranging from 1148 to 1687 steps per day (18%-25% of criterion). Conversely, in participants with TD phenotype, tremor, mild disease severity, and earlier disease stage, SEM was $>10\%$ of the criterion and MDC values ranged from 1401 to 2263 steps per day (30%-33% of the criterion). In mild-to-moderate PD, avDS measured through a consumer smartwatch in unsupervised, free-living conditions for 5 consecutive days are reliable irrespective of disease phenotype, stage, and severity. However, in individuals with TD phenotype, tremor, mild disease severity, and earlier disease stages, reliability could be lower. These findings could facilitate a broader and informed implementation of avDS as an index of ambulatory activity in PD.

Introduction

Walking is a fundamental motor ability, and it is pivotal for functional independence and social well-being (MacKinnon, 2018). Gait disturbances are common in people with Parkinson disease (PD), and include shuffling gait, shortened step length, altered automaticity, decreased arm swing, and freezing of gait (Mirelman et al., 2019). These represent a particularly disabling group of symptoms, significantly hampering the quality of life of people with PD (M. Lee et al., 2021) and increasing the risk of falls (Creaby & Cole, 2018).

Daily steps are an easy-to-collect and useful measure of ambulatory activity and mobility (Bassett et al., 2017). Although this parameter could not provide details regarding subtle gait features, several evidence linked a reduced daily step count to overall mortality risk (Inoue et al., 2023; I.-M. Lee et al., 2019; Paluch et al., 2022; Saint-Maurice et al., 2020), as well as to a range of health conditions, such as dementia (Del Pozo Cruz, Ahmadi, et al., 2022) and oncological and cardiovascular diseases (Banach et al., 2023; Del Pozo Cruz, Ahmadi, et al., 2022). Previous studies have also reported a negative correlation between daily steps and disease severity in PD (Skidmore et al., 2008) and proposed a minimum daily step goal of 4200 to match with physical activity recommendations in the early stages of the disease (Handlery et al., 2021).

Wearable devices, including smartwatches, could represent a useful option to estimate daily steps in an unobtrusive, ecological way (Mattison et al., 2022). Moreover, wearables are widely available on the market, easily used by the general population, and enable unobtrusive continuous long-term data collection (Bianchini & Maetzler, 2023). However, since these devices are usually tested in healthy populations, knowledge of the validity and reliability of collected data is generally limited when applied to different groups of patients. Therefore, a growing body of literature focused on the validity and reliability of consumer wearable devices for step counting, with generally positive results (Chevance et al., 2022; Fuller et al., 2020; Nakagata et al., 2022).

In PD, motor and gait manifestations could render step detection and step count challenging and hence significantly diminish the validity and reliability of device algorithms (Bianchini et al., 2022; Kim et al., 2019; Wendel et al., 2018). Nevertheless, a prior study by Ginis et al. (Ginis et al., 2023) demonstrated a good criterion validity in estimating average daily steps (avDS) of 2 Fitbit devices (Fitbit Alta and Fitbit Inspire 3) in 28 people with PD in a real-life setting, compared to a research-grade device (Dynaport Movemonitor, McRoberts, NL).

Similarly, a prior study from our group involving 47 individuals with PD demonstrated a good criterion validity in step counting using a consumer smartwatch (Garmin Vivosmart 4), when worn on the side least affected by the disease and under well-controlled pharmacological conditions in a supervised, in-clinic setting (Bianchini et al., 2022).

Besides criterion validity, we recently demonstrated that optimal reliability of avDS recorded by Garmin Vivosmart 4 in real-life conditions could be achieved if the smartwatch is worn for a minimum of 4 days (Bianchini et al., 2023).

However, the clinical heterogeneity of PD when evaluating metrological characteristics of step-counting devices has been neglected so far. Indeed, the clinical presentation of PD is highly variable among individuals, thus, significant efforts have been made to identify distinct clusters and subtypes (Outeiro et al., 2023). Several classifications have been proposed over the years from clinical-based (Jankovic et al., 1990; Stebbins et al., 2013; Zetuský et al., 1985) to more recent biomarker-based classifications (Cardoso et al., 2024; Höglinger et al., 2024; Horsager & Borghammer, 2024). In this regard, one of the most used classifications distinguishes PD with predominant features of tremor (ie, tremor dominant [TD]) or gait, posture, and balance issues (ie, postural instability and gait disorder [PIGD]) (Jankovic et al., 1990; Stebbins et al., 2013; Zetuský et al., 1985) based on subitems scores of the Unified Parkinson's Disease Rating Scale (UPDRS) and its revision by the Movement Disorder Society (MDS-UPDRS) (Goetz et al., 2008). This classification could be relevant when measuring avDS in PD since tremors could increase the noise-to-signal ratio, making step detection more challenging (Kim et al., 2019). Similarly, in PIGD individuals, the higher degree of gait alterations could alter the performance of step-detection algorithms (Bianchini et al., 2022; Wendel et al., 2018).

Symptom severity and disease stage could also represent other relevant parameters to be considered when assessing the reliability of any wearable devices in counting avDS. Indeed, with disease progression, gait features increasingly deviate from normality (Mirelman et al., 2019; Schlachetzki et al., 2017), and tremor and bradykinesia could further alter the spatiotemporal and kinematic characteristics of walking, dampening, in turn, algorithm performance in step detection (Bianchini et al., 2022; Kim et al., 2019; Wendel et al., 2018).

Nevertheless, no study to date considered disease phenotype, stage, and symptom severity when assessing the reliability of consumer wrist-worn devices for step counting in unsupervised, free-living conditions in mild-to-moderate people with PD. This study was hence specifically designed to address this issue. We hypothesized that reduced reliability might be observed in TD individuals and people with PD with more severe symptoms and in more advanced disease stages due to the aforementioned increased signal noise due to tremor, the higher degree of motor symptoms, and the more marked gait alterations. In addition, since no previous study specifically investigated the criterion validity of Garmin Vivosmart 4 in estimating avDS, we performed a proof-of-concept experiment in a subgroup of participants. Details of methods and results of this latter experiment are presented in Appendix 2.

Material and Methods

Population

Participants were consecutively screened and recruited during scheduled visits at the Movement Disorder Outpatient Service of the Sant'Andrea University Hospital (Rome, Italy) in the period between March 2023 and March 2024. Inclusion criteria were: (1) diagnosis of idiopathic PD according to the MDS criteria (Postuma et al Postuma et al., 2015); (2) aged 18 years or older; (3) disease stage <4 according to the modified Hoehn and Yahr scale (mHY) (Goetz et al., 2004); (4) classification as TD or PIGD according to Stebbins et al (Stebbins et al., 2013); and (5) stable medication in the 4 weeks before the experimental procedure. Exclusion criteria were: (1) cognitive impairment, defined by Montreal Cognitive Assessment (Nasreddine et al., 2005) score <21; and (2) orthopedic, rheumatologic, or systemic conditions affecting mobility as judged by the assessor.

Ethical Considerations

This cross-sectional study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Approval was granted by the local Ethical Committee of Sapienza, University of Rome, Italy (0372/2022). Data collection and processing followed the current European regulations for data protection. All participants provided written informed consent before the beginning of measurements. All data were deidentified. Participants did not receive any form of compensation.

Demographic and Clinical Data

Participants were evaluated during scheduled visits. Demographics and anthropometric measures (including age, sex, weight, height, and BMI) were collected. Disease duration and disease stage according to mHY and levodopa equivalent daily dose (Jost et al., 2023) were also collected. MDS-UPDRS (Goetz et al., 2008) part III was used to assess motor symptoms severity. Participants were divided into 4 subgroup pairs. Based on MDS-UPDRS part II and III scores, participants were classified into TD or PIGD disease subtypes according to Stebbins et al (Stebbins et al., 2013). To evaluate the effect of tremor presence on device reliability, participants were also classified as those with and without tremor based on a score of ≥ 1 at item 2.10 of MDS-UPDRS part II. Concerning disease severity, participants were grouped into those with mild or moderate disease severity based on the MDS-UPDRS score as proposed by Martínez-Martín et al (Martínez-Martín et al., 2015). Similarly, participants were dichotomized in earlier (mHY 1-2) or intermediate (mHY 2.5-3) stages, based on mHY score.

Experimental Procedure

Participants received the smartwatch Garmin Vivosmart 4 after the visit and were instructed to wear it at home for a minimum of 5 consecutive days, including at least 1 weekend day, on the wrist of the body side least affected by the disease (Bianchini et al., 2022). No reminders or further instructions were provided to participants during registration. We chose a 5-day period since we demonstrated previously that a minimum of 4 days of monitoring is needed to reliably estimate daily step count in PD (Bianchini et al., 2023). Each smartwatch was configured according to the producer's recommendations and participants were asked to perform daily activities as usual.

After 5 days, participants returned the smartwatch. The total daily number of steps for each day was recorded and avDS were calculated (Bianchini et al., 2023). Compliance was assessed based on the participants' dashboard data. The device recognizes that it is worn through heart rate and inertial motion unit signal. We considered all recording days with >80% wear time while awake and no interruption of device use greater than 3 hours to be valid. Details of methods of the proof-of-concept experiment regarding criterion validity of Garmin Vivosmart 4 are presented in Appendix 2.

Data and Statistical analyses

The statistical analyses were performed using JASP (version 0.18.3.0; JASP Team), R (version 4.0.3; R Core Team), and RStudio (version 2023.12.0+369; R Foundation for Statistical Computing) for Windows. Descriptive statistics were calculated for the examined variables. The normality of distributions was assessed by histogram and residual plots inspection.

To evaluate the relative reliability for the 5-day monitoring period in the overall population and each subgroup, a 2-way intraclass correlation coefficient (ICC) with a fixed set of raters and averaged ratings was used (ICC (3,k), where k was the number of days of measurement), together with a custom R script. The following reference cut-off values for ICC interpretation were used (Koo & Li, 2016): excellent: >0.90; good: 0.75-0.90; moderate: 0.50-0.75; and poor: <0.50. The a priori threshold for acceptable ICC was set at a point estimate ≥ 0.80 with a lower bound of 95% CI ≥ 0.75 in accordance with a previous study from our group (Bianchini et al., 2023).

To compare ICCs between the 4 subgroup pairs, 2 methods were applied. First, standard errors and point estimates of ICCs were used to compute t statistics and perform 2-tailed independent groups Student t tests. Second, the CI overlap between each group pair was graphically and numerically assessed. Nonoverlapping CIs were considered indicators of significantly different ICCs (Knol et al., 2011). Previous evidence underscored that a 95% CI overlap assessment could inflate the risk of type II error and suggested that an 83.4% CI could be a more powerful option (Austin & Hux, 2002; Cho et al., 2020; Knol et al., 2011). Therefore, we adopted this method for CI overlap evaluation.

Standard error of measurement (SEM) and minimal detectable change (MDC) with a CI of 95% were used to compute the absolute reliability for the 5-day recordings in the overall population and each subgroup (Balaguier et al., 2016). SEM and MDC were reported as absolute value and percentage of criterion measure (SEM% and MDC%, respectively). The criterion was the avDS count derived from the 5 days. For all analyses, the significance threshold was set at $<.05$. All data were reported as mean (SD) or median (IQR) for numerical data and n (%) for categorical variables.

Results

Overview

A total of 104 people with PD were included in the study. All participants were monitored through Garmin Vivosmart 4 at home for a period of 5 consecutive days. No participants or days were excluded based on the prespecified compliance criteria. Participants took on average 5923 (SD 3014) daily steps, ranging from 357 to 12,620. Details of demographic, anthropometric, and clinical variables of the study population are shown in table 6.1. The overlap between the subgroups is shown in Appendix 1 (table S6.1 and table S6.2).

Overall, the results of the proof-of-concept experiment suggest that the smartwatch Garmin Vivosmart 4 is valid and decently accurate in estimating avDS in PD. Details are presented in Appendix 2.

Reliability of avDS in People With PD

Relative Reliability

AvDS collected during 5 consecutive days showed a level of relative reliability above the threshold of acceptability, as indicated by an ICC point estimate of ≥ 0.80 and a lower 95% CI limit of ≥ 0.75 , in the overall population and all subgroups. Moreover, daily step count showed excellent reliability in PD in the intermediate disease stage. Details of ICC and CI limits are shown in table 6.2.

Relative Reliability

AvDS showed an SEM below 10% in the overall population with an MDC of 1580 (26.7% of the criterion). AvDS also showed an SEM below 10% in the PIGD disease subtype, in participants without tremor, with a moderate disease severity, and in an intermediate disease stage with an MDC ranging from 1148 to 1687 steps per day (18% to 25% of criterion). Conversely, in the TD disease subtype, in participants with tremor, with mild disease severity and in an early disease stage, SEM was $>10\%$ of criterion and MDC values ranged from 1401 to 2263 steps per day (30% to 33% of the criterion). Details of SEM and MDC are shown in table 6.3.

Table 6.1. Demographic, anthropometric, and clinical characteristics of the study population.

	Overall (N=104)	TD ^a (n=39)	PIGD ^b (n=65)	Tremor (n=57)	No tremor (n=47)	Mild (n=65)	Mod- erate (n=39)	mHY ^c 1-2 (n=68)	mHY 2.5-3 (n=36)
Age (years)	68.0 (8.4)	66.4 (9.0)	68.9 (8.0)	69.5 (7.9)	66.7 (8.8)	66.8 (8.7)	69.9 (7.7)	65.3 (7.8)	73.0 (7.3)
Height (cm)	171 (9.0)	173 (7.6)	170 (9.6)	170 (9.6)	172 (8.4)	173 (9.3)	168 (7.6)	173 (8.1)	168 (9.8)
Weight (kg)	75.7 (13.1)	76.7 (13.0)	75.1 (13.2)	75.0 (12.1)	76.3 (13.9)	77.2 (13.7)	73.2 (11.8)	77.7 (13.8)	71.9 (10.8)
BMI (kg/m ²)	25.7 (3.4)	25.5 (3.6)	25.8 (3.4)	25.8 (3.0)	25.7 (3.8)	25.7 (3.5)	25.8 (3.4)	25.9 (3.7)	25.4 (3.0)
Sex (female)	34 (33)	11 (28)	23 (35)	19 (33)	15 (32)	22 (34)	12 (31)	22 (32)	12 (33)
Disease duration (years)	6.4 (4.4)	5.2 (4.4)	7.0 (4.4)	7.2 (3.9)	5.7 (4.8)	5.7 (4.5)	7.5 (4.2)	5.3 (4.3)	8.4 (4.1)
LEDD ^d (mg)	553 (302)	418 (247)	634 (304)	623 (271)	495 (316)	489 (289)	659 (296)	453 (248)	741 (307)
mHY	2 (2-2.5)	2 (1-2)	2 (2-2.5)	2 (2-2.5)	2 (2-2)	2 (2-2)	2.5 (2-3)	2 (2-2)	2.5 (2.5-3)
MDS-UPDRS-III ^e	27 (21-32)	26 (18-31)	29 (22-33)	29 (22-33)	26 (21-32)	23 (19-29)	33 (29-37)	23 (18-29)	33 (29-36)
avDS ^f	5923 (301.4)	6654 (2733)	5485 (3109)	4594 (2612)	7020 (2898)	6512 (2857)	4942 (3049)	6838 (2908)	4195 (2419)

^aTD: tremor dominant.
^bPIGD: postural instability and gait disorder.
^cmHY: modified Hoehn and Yahr scale.
^dLEDD: levodopa equivalent daily dose.
^eMDS-UPDRS III: Movement Disorder Society Unified Parkinson's Disease Rating Scale part III.
^favDS: average daily steps.

Reliability Comparison Between Subgroups

When comparing ICCs between subgroups pairs, 2-tailed Student t test for independent groups showed a significant difference between participants with and without tremor ($t_{102}=1.897$; $P=.03$), between PD with mild and moderate disease severity ($t_{102}=1.765$; $P=.04$), and between individuals in early and intermediate disease stage ($t_{102}=2.817$; $P=.003$). Conversely, no significant difference was found between TD and PIGD participants ($t_{102}=1.048$; $P=.15$).

The analysis of 83.4% CI showed no overlap between interval limits between participants with and without tremor (fig. 6.1A), in early and intermediate disease stage (fig. 6.1C), and only a negligible overlap between individuals with mild and moderate disease severity (fig. 6.1B). Conversely, a degree of overlap of the two 83.4% CIs was observed between TD and PIGD participants (fig. 6.1D). Details of 83.4% CI limits are shown in table 6.2.

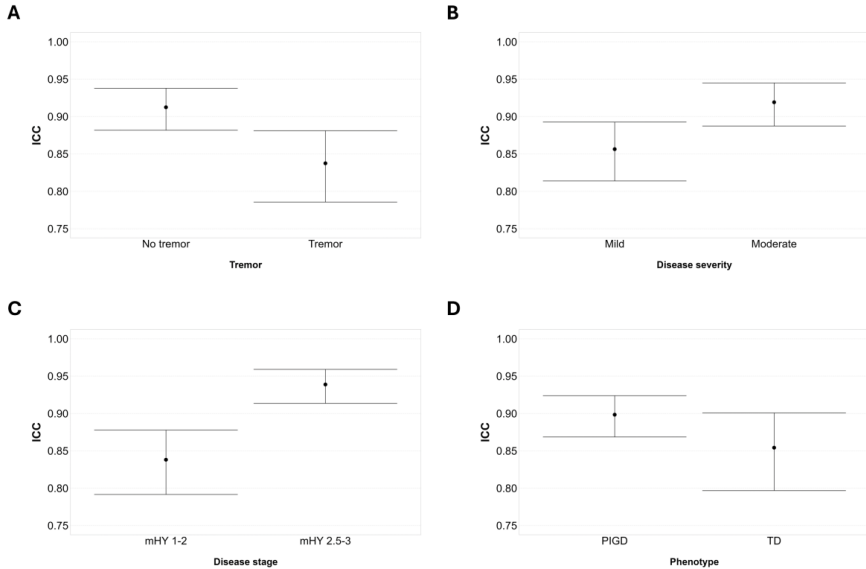


Figure 6.1. ICC and 83.4% CI comparison for each subgroup pair. (A) Participants with reported presence or absence of tremor. (B) Participants with mild and moderate disease severity as indicated by MDS-UPDRS. (C) Participants with earlier (mHY 1-2) and intermediate (mHY 2.5-3) disease stage. (D) PIGD and TD phenotypes. ICC (3,k) point estimate is indicated by the black dot, CI limits are represented by the vertical bars. ICC: intraclass correlation coefficient; MDS-UPDRS: International Movement Disorders Society Unified Parkinson's Disease Rating Scale; mHY: modified Hoehn and Yahr stage; PIGD: postural instability and gait disorder; TD: tremor dominant.

Table 6.2. ICC (3,k) values with 95% CI for the overall population and each subgroup. For subgroups, 83.4% CI to assess intervals overlap are also reported.

	Overall (N=104)	TD ^c (n=39)	PIGD ^d (n=65)	Tremor (n=57)	No tremor (n=47)	Mild (n=65)	Mod- erate (n=39)	mHY ^e 1-2 (n=68)	mHY 2.5-3 (n=36)
ICC (3,k)	0.888	0.854	0.899	0.838	0.914	0.856	0.919	0.839	0.939
Lower 95% CI	0.850	0.767	0.855	0.760	0.868	0.793	0.871	0.769	0.900
Upper 95% CI	0.919	0.916	0.933	0.896	0.947	0.905	0.953	0.892	0.966
Lower 83.4% CI	N/A ^f	0.797	0.869	0.786	0.883	0.814	0.887	0.792	0.914
Upper 83.4% CI	N/A	0.901	0.925	0.881	0.939	0.893	0.945	0.878	0.959

^aICC: intraclass correlation coefficient.

^cTD: tremor dominant.

^dPIGD: postural instability and gait disorder.

^emHY: modified Hoehn and Yahr scale.

^fNot applicable.

Table 6.3. Absolute and percentage values of SEM^a and MDC^b for the overall population and each subgroup.

	Overall (N=104)	TD ^c (n=39)	PIGD ^d (n=65)	Tremor (n=57)	No tremor (n=47)	Mild (n=65)	Mod- erate (n=39)	mHY ^e 1-2 (n=68)	mHY 2.5-3 (n=36)
SEM	570	742	495	506	609	701	414	817	267
SEM%	9.6	11.1	9.0	11.0	8.7	10.8	8.4	11.9	6.4
MDC	1580	2056	1372	1401	1687	1944	1148	2263	741
MDC%	26.7	30.9	25.0	30.5	24.0	29.8	23.2	33.1	17.7

^aSEM: standard error of measurement.

^bMDC: minimal detectable change.

^cTD: tremor dominant.

^dPIGD: postural instability and gait disorder.

^emHY: modified Hoehn and Yahr scale.

Discussion

Principal Findings

This cross-sectional study aimed at assessing and comparing the reliability of a consumer wrist-worn smartwatch (Garmin Vivosmart 4) in counting avDS in PD in unsupervised, free-living conditions for 5 consecutive days between disease phenotypes, stages, and severity groups.

Overall, our results showed, for the first time, that avDS were acceptably reliable in mild-to-moderate PD irrespective of disease severity, stage, or phenotype. Nevertheless, our results further indicated lower reliability in people with PD with TD phenotype, tremor, lower disease severity, and earlier stage.

Reliability of avDS in the Overall PD Population

We found that the relative reliability of avDS, measured in unsupervised, free-living conditions, by Garmin Vivosmart 4 for 5 consecutive days was within the a priori criteria for acceptability in the overall PD population. We identified only 2 studies investigating the reliability of wearable devices in measuring avDS in people with PD (Bianchini et al., 2023; Paul et al., 2016). Paul et al (Paul et al., 2016) reported that 2 consecutive days of monitoring were sufficient to obtain an ICC of >0.9 , using a research-grade, ankle-mounted, step counter (Step Activity Monitor) in 92 people with PD. One study from our group investigated the reliability of a wrist-worn consumer device in measuring avDS in PD before. In that study, we found an ICC (3,k) of 0.88 (0.82-0.93) for 4 days of monitoring in 56 mild-to-moderate people with PD using Garmin Vivosmart 4 (Bianchini et al., 2023). The present results are consistent with our previous study, but also with other studies investigating the reliability of avDS through wrist-worn wearables in healthy older people (Clemes & Griffiths, 2008; Paul et al., 2016; Sigmundová et al., 2013; Yao et al., 2021), and in people with various neurological conditions, such as multiple sclerosis (Norris et al., 2017) and stroke (Fini et al., 2019). Regarding absolute reliability, we found that SEM% was below 10% (9.6%) with an MDC of 1580 steps per day (27% of criterion). Only 1 study, from our group, investigated SEM and MDC for avDS in PD (Bianchini et al., 2023). The present results are consistent with our previous study in which we reported an SEM% of 9.2% and an MDC of 1495 steps per day (or 26% of criterion) (Bianchini et al., 2023). Taken together, these results confirm the reliability of avDS measured through Garmin Vivosmart 4 in unsupervised, free-living conditions in mild-to-moderate PD for 5 consecutive days.

Reliability of avDS in People With PD Subgroups

To our knowledge, this is the first study to investigate and compare the reliability of a consumer smartwatch in measuring avDS in different subgroups of PD based on disease phenotype, severity, and stage. We found that in all investigated subgroups (ie, TD vs PIGD, mild vs moderate, tremor vs nontremor, and earlier vs intermediate), ICC values were within the a priori criteria for acceptability (ICC range 0.84-0.94). However, a significantly lower ICC was observed in people with PD with tremor, mild disease severity, and earlier disease stage. Moreover, SEM% was below 10% in participants with PIGD phenotype, moderate disease severity, intermediate disease stage, and without tremor, with an MDC ranging from 1148 to 1687 steps per day (18%-25% of criterion). Conversely, in individuals with TD phenotype, tremor, mild disease severity, and earlier disease stage, SEM was $>10\%$ of criterion and MDC values ranged from 1401 to 2263 steps per day (30%-33% of the criterion).

MDC, defined as the minimal change that falls outside the measurement error of an instrument, is extremely relevant in study design since it allows to calculate the sample size of studies aiming to assess the effectiveness of interventions (Lexell & Downham, 2005). MDC could be also crucial to define the appropriateness and feasibility of using a determinate device to measure a given construct. A prior work from Handlery et al. (Handlery et al., 2021) reported an increase in 1250 steps per day following a high-intensity physical activity intervention in PD measured through a research-grade wrist-worn device (Actigraph GT3X). In this study, we found that in individuals with TD phenotype, mild disease severity, and earlier disease stage, MDC was 2000 steps per day. Although a direct comparison with the metrics reported in the work from Handlery et al. (Handlery et al., 2021) could not be performed due to the different devices, we could hypothesize that only large modifications in avDS could be reliably measured through Garmin Vivosmart 4 in the aforementioned PD subgroups. To this end, future studies will be needed to define the minimal clinically important difference for avDS measured through consumer wrist-worn devices

and to assess the attainability of avDS modifications sufficiently large to be reliably detected by these devices.

The reduced reliability in participants with tremor is in line with our hypothesis that tremor could reduce the performance of the step-detection algorithm. In fact, tremor could increase the noise-to-signal ratio in the accelerometer signal, and in turn, render step detection more challenging (Kim et al., 2019). Indeed, a previous study highlighted that tremor and dyskinesia together contributed to more than 19% of the variation in daily step counts when comparing measurements from waist-worn and wrist-worn devices in 46 people with PD with similar characteristics to those included in this study (Kim et al., 2019). In this regard, our study further supports the assumption that tremor could reduce the step-detection performance of wrist-worn devices in PD.

On the other hand, our hypothesis that a reduced reliability might be observed in participants with higher symptom severity and more advanced stages was not supported by our results. Indeed, the reduced reliability of avDS observed in individuals with mild disease severity and earlier disease stage is somehow counterintuitive. In fact, previous evidence highlighted that step count was less accurate in people walking at slower gait speed and with shorter step length in several neurological and musculoskeletal conditions, including PD (Bianchini et al., 2022; Chow et al., 2017; Fokkema et al., 2017; Lamont et al., 2018; Treacy et al., 2017; Wendel et al., 2018). Reduced step length and slower walking speed are typical features of Parkinsonian gait, with a higher prevalence along the disease course (Mirelman et al., 2019; Schlachetzki et al., 2017). Moreover, another typical characteristic of walking in PD is the reduced automaticity that leads to a more discontinuous and irregular gait pattern that can further reduce device accuracy in step detection (Mirelman et al., 2019; Wendel et al., 2018).

Despite these considerations, our results showed that avDS estimation was more reliable in people with PD with moderate disease severity and intermediate disease stage, compared with individuals with mild disease severity and earlier disease stage. In this regard, it must be considered that reliability is a measure of consistency and reproducibility of measurement and not a measure of accuracy (Mokkink et al., 2010). Therefore, a reduced accuracy could not directly translate into reduced reliability. We could hypothesize that in more advanced stages of PD, the variability of clinical presentation could be lower. In an earlier stage, indeed, symptom heterogeneity, both in terms of motor and nonmotor features, could be extremely high (Berg et al., 2021; Erro et al., 2013; Wüllner et al., 2023). However, this variability could decrease with disease progression since motor symptoms tend to consistently worsen along the disease course and motor features such as gait and balance impairment become increasingly prevalent (Fasano et al., 2019; Stefani et al., 2022). In addition, the phenotype is dynamic along the disease course and some researchers have proposed that the classification into PIGD/TD evolves over time (Alves et al., 2006; Che et al., 2024). One study, indeed, reported that over a period of 8 years, approximately 70% of TD individuals transitioned to PIGD, whereas only 4% of PIGD individuals transitioned to TD (Alves et al., 2006). Another study reported that 45% of TD participants at baseline had a subtype shift along a 2-year follow-up while 85% of PIGD participants remained as PIGD (Che et al., 2024). This is mirrored in our study cohort, where 32 out of 65 (49%) individuals with mild disease severity were classified as TD, whereas only 7 out of 39 (18%) were in the moderate group. Similarly, 33 out of 68 (49%) participants with earlier disease stage were classified as TD, whereas only 6 out of 36 (17%) were in the intermediate group. Therefore, a regression toward a more uniform motor impairment along the disease course might be considered. Moreover, since we found that tremor could be a relevant factor in reducing avDS reliability, the different prevalence of TD phenotype could also contribute to explaining our results. However, it must be underlined that no study, to our knowledge, systematically compared the heterogeneity of PD features across early, intermediate, and advanced disease stages. Therefore, our hypothesis should be taken with caution and future studies are needed to confirm it.

In conclusion, our findings highlight that, although avDS were reliable across the examined subgroups, clinicians and researchers should consider disease phenotype, stage, and severity when implementing wrist-worn wearables and interpreting mobility data collected through these devices in PD.

Limitations

We acknowledge that this study has some limitations. First, the participants included in our study displayed relatively preserved cognitive functions, due to our exclusion of participants with a Montreal Cognitive Assessment of <21. Additionally, those with more advanced disease stages or requiring walking aids were not included. This potentially limits the generalizability of our

findings. However, it should be considered that the sample in our study can be seen as representative of the typical target for interventions using consumer-grade wearable technology. Moreover, including individuals with a disease stage >3 , using walking aids, or with more severe cognitive impairments poses significant challenges in the utilization of consumer technology and is beyond our scope. Nevertheless, future research incorporating PD with lower functional scores, higher disease severity, and more impactful cognitive impairments would be valuable. Furthermore, we used only PD subtyping based on clinical features, yet other classification methods and clustering techniques have been proposed incorporating instrumental and biological data. Future studies are warranted to investigate the reliability of consumer smartwatches in PD subgroups defined using multimodal biomarkers. Finally, we did not account for antiparkinsonian treatment to control tremor. All included participants were under dopaminergic medical treatment and stable medical treatment in the 4 weeks before data collection, and we did not enroll drug-naïve individuals. In addition, we did not account for different drug classes since it would have required a much higher sample size to cover all the possible combinations. Future studies might investigate the metrological features of commercial smartwatches in drug-naïve PD to avoid the influencing factor of dopaminergic treatment. However, since almost all patients with a diagnosis of PD are medically treated, we considered it relevant to assess the measurement properties of commercial devices in a setting more representative of the real-world experience.

Conclusions

In mild-to-moderate PD, avDS measured through a consumer smartwatch in unsupervised, free-living conditions for 5 consecutive days are reliable irrespective of disease phenotype, stage, and severity. Researchers and clinicians who want to implement these instruments should consider that in individuals with TD phenotype, tremor, mild disease severity, and earlier disease stage, reliability could be lower and MDC could be higher. Future studies are needed to define the minimal clinically important difference for avDS measured through consumer wrist-worn devices and to assess the attainability of avDS modifications sufficiently large to be reliably detected by wrist-worn consumer devices. Taken together, we believe that these results could facilitate a broader implementation and an informed application of avDS as an index of ambulatory activity in PD and could be highly relevant to developing monitoring, preventive, educational, and rehabilitation strategies for PD.

Appendix 1 - Supplementary tables

Table S6.1. Overlap between the groups of patients with and without self-reported tremor and TD/PIGD phenotypes.

	TD (N=39)	PIGD (N=65)	Tremor (N=57)	No tremor (N=47)
TD	–	–	36/57 (63%)	3/47 (6%)
PIGD	–	–	21/57 (37%)	44/47 (93%)
Tremor	36/39 (92%)	44/65 (68%)	–	–
No tremor	3/39 (8%)	21/65 (32%)	–	–

PIGD: postural instability and gait disorder; TD: tremor dominant.

Table S6.2. Overlap between the groups of patients with mild/moderate disease severity and early/intermediate disease stage.

	Mild (N=65)	Moderate (N=39)	mHY (N=39)	1-2	mHY (N=36)	2.5-3
Mild	–	–	52/68 (76%)		13/36 (36%)	
Moderate	–	–	16/68 (24%)		23/36 (64%)	
mHY 1-2	52/68 (80%)	16/39 (41%)	–		–	
mHY 2.5-3	13/68 (20%)	23/39 (59%)	–		–	

mHY: modified Hoehn and Yahr scale.

Appendix 2 - Supplementary experiment

Since no previous study specifically investigated the criterion validity of the smartwatch Garmin Vivosmart 4 in estimating average daily steps (avDS), we performed this proof-of-concept experiment in a small subgroup people with Parkinson's disease (PwPD).

Methods

Details regarding population, ethics and collected clinical measures are presented in the main manuscript.

Experimental procedure

Participants were provided with a smartwatch Garmin Vivosmart 4 and a lower-back mounted research-grade inertial sensor for mobility analysis (McRoberts MoveMonitor, McRoberts B.V., Den Haag, The Netherlands) to wear concurrently for 7 consecutive days in their home environment. They were instructed to wear both the smartwatch on the wrist of the body side least affected by the disease and MoveMonitor all time during day and night and remove them only when involved in water activities (e.g., bathing, showering, swimming, etc.). As far as Garmin Vivosmart 4 is concerned, data extraction and compliance assessment are described in the main section of the manuscript. For MoveMonitor, the number of steps taken each day were extracted from device report and the avDS were calculated. Compliance was assessed through the “no wear time” provided by device report. We considered all recording days with $\geq 80\%$ wear time while awake for both devices to be valid.

Data and statistical analysis

The statistical analyses were performed using JASP v0.18.3.0 (JASP Team, University of Amsterdam, The Netherlands). Statistical analyses were performed using JASP v0.18.3 (JASP Team, University of Amsterdam, Amsterdam, The Netherlands). To assess the agreement between the number of steps counted by Garmin Vivosmart 4 and MoveMonitor (gold standard), the intra-class correlation coefficient (ICC) (2,1) was used and the point estimate and lower and upper 95% confidence interval reported. The following reference cut-off values for the ICC interpretation were used (Koo & Li, 2016): Excellent: >0.90 ; Good: $0.75-0.90$; Moderate: $0.50-0.75$; Poor: <0.50 . From the number of steps counted by Garmin Vivosmart 4 and MoveMonitor, the mean percentage error (MPE) and the mean absolute percentage error (MAPE) were calculated for avDS as follows:

$$\text{MPE} = \frac{(\text{steps counted manually}) - (\text{steps counted by smartwatch})}{(\text{steps counted manually})} \times 100$$

$$\text{MAPE} = \frac{|(\text{steps counted manually}) - (\text{steps counted by smartwatch})|}{(\text{steps counted manually})} \times 100$$

The MPE was used to evaluate the direction-of-error of the smartwatch Garmin Vivosmart 4 compared with MoveMonitor. A negative value indicated an overestimate of counting and vice versa. The MAPE was used to assess the magnitude-of-error of the smartwatch Garmin Vivosmart 4 in step counting compared with MoveMonitor.

Results

Data from a subgroup of 11 PwPD [Age: 66.4 ± 7.0 years; Females: 4 (36%); Disease duration: 7.9 ± 3.9 years; Hoehn & Yahr: 2 (2-2.5)] were analyzed for a total of 64 valid days of recording for both devices. The median recording time was 6 days (range 5-7). The smartwatch Garmin Vivosmart 4 demonstrated an excellent agreement with MoveMonitor for avDS [ICC2,1 $0.984 = (0.946 - 0.996)$]. MPE was -1.3% (CI95%: $-11.0 - 8.4$) and MAPE was 10.2% (CI95%: $3.6 - 16.8$) for avDS.

Discussion

In this proof-of-concept experiment, the smartwatch Garmin Vivosmart 4 demonstrated an excellent agreement with MoveMonitor research-grade inertial sensor. It is important to mention that MoveMonitor was extensively validated both technically and clinically (Mazzà et al., 2021; Micó-Amigo et al., 2023) and was used for several large multicentric studies in PwPD to monitor gait in free-living, real-world conditions as part of international consortia (e.g., Mobilize-D). Moreover, MoveMonitor was used in a previous study to demonstrate the criterion validity of Fitbit Inspire in measuring avDS (Ginis et al., 2023). Our result is in line with those reported in this previous study which showed a good-to-excellent ICC (>0.83) between the smartwatch and the research-grade device. Moreover, although preliminary, the present results confirm the findings from a previous study from our group showing a good agreement between steps measured through Garmin Vivosmart 4 and manual counting in a supervised setting (Bianchini et al., 2022). Regarding MPE and MAPE, our preliminary findings point towards a slight overestimation of avDS by the smartwatch. This result is in line with our preliminary findings in supervised setting. Regarding MAPE Garmin Vivosmart 4 showed an error around 10% in estimating avDS. To the best of our knowledge, no previous study reported this aspect in PwPD. However, our results are in line with or lower than previous studies on healthy individuals (Germini et al., 2022). Moreover, it is worth noting that the MAPE is within the threshold of acceptability as indicated by the cut-off value of 15% recommended for devices intended to be used by the general population (Johnston et al., 2021). In conclusion, our proof-of-concept experiment suggests that the smartwatch Garmin Vivosmart 4 is valid and decently accurate in estimating avDS in PwPD. It must be stressed, however, that this is a proof-of-concept experiment, and the results hereby presented were included since no previous study are available to support the criterion validity of the used smartwatch. Therefore, these findings are not sufficient to conclusively demonstrate the accuracy and validity of the smartwatch Garmin Vivosmart 4. Further studies are hence warranted to fully address this issue.

References

- Alves, G., Larsen, J. P., Emre, M., Wentzel-Larsen, T., & Aarsland, D. (2006). Changes in motor subtype and risk for incident dementia in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 21(8), 1123–1130. <https://doi.org/10.1002/mds.20897>
- Austin, P. C., & Hux, J. E. (2002). A brief note on overlapping confidence intervals. *Journal of Vascular Surgery*, 36(1), 194–195. <https://doi.org/10.1067/mva.2002.125015>
- Balaguier, R., Madeleine, P., & Vuillerme, N. (2016). Intra-session absolute and relative reliability of pressure pain thresholds in the low back region of vine-workers: Effect of the number of trials. *BMC musculoskeletal disorders*, 17(1), 350. <https://doi.org/10.1186/s12891-016-1212-7>
- Banach, M., Lewek, J., Surma, S., Penson, P. E., Sahebkar, A., Martin, S. S., Bajraktari, G., Henein, M. Y., Reiner, Ž., Bielecka-Dąbrowa, A., & Bytyçi, I. (2023). The association between daily step count and all-cause and cardiovascular mortality: A meta-analysis. *European Journal of Preventive Cardiology*, 30(18), 1975–1985. <https://doi.org/10.1093/eurjpc/zwad229>
- Bassett, D. R., Toth, L. P., LaMunion, S. R., & Crouter, S. E. (2017). Step Counting: A Review of Measurement Considerations and Health-Related Applications. *Sports Medicine (Auckland, N.Z.)*, 47(7), 1303–1315. <https://doi.org/10.1007/s40279-016-0663-1>
- Berg, D., Borghammer, P., Ferestehnejad, S.-M., Heinzel, S., Horsager, J., Schaeffer, E., & Postuma, R. B. (2021). Prodromal Parkinson disease subtypes - key to understanding heterogeneity. *Nature Reviews. Neurology*, 17(6), 349–361. <https://doi.org/10.1038/s41582-021-00486-9>
- Bianchini, E., Calì, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzler, W., & Pontieri, F. E. (2022). Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, 23(1), 214. <https://doi.org/10.3390/s23010214>
- Bianchini, E., Galli, S., Alborghetti, M., De Carolis, L., Zampogna, A., Hansen, C., Vuillerme, N., Suppa, A., & Pontieri, F. E. (2023). Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch [Number: 21 Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 23(21), 8971. <https://doi.org/10.3390/s23218971>
- Bianchini, E., & Maetzler, W. (2023, May). Wearable systems in movement disorders. In *International Review of Movement Disorders*. Academic Press. <https://doi.org/10.1016/bs.irmvd.2023.04.002>
- Cardoso, F., Goetz, C. G., Mestre, T. A., Sampaio, C., Adler, C. H., Berg, D., Bloem, B. R., Burn, D. J., Fitts, M. S., Gasser, T., Klein, C., de Tijssen, M. A. J., Lang, A. E., Lim, S.-Y., Litvan, I., Meissner, W. G., Mollehuier, B., Okubadejo, N., Okun, M. S., ... Trenkwalder, C. (2024). A Statement of the MDS on Biological Definition, Staging, and Classification of Parkinson's Disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 39(2), 259–266. <https://doi.org/10.1002/mds.29683>
- Che, N., Ou, R., Li, C., Zhang, L., Wei, Q., Wang, S., Jiang, Q., Yang, T., Xiao, Y., Lin, J., Zhao, B., Chen, X., & Shang, H. (2024). Plasma GFAP as a prognostic biomarker of motor subtype in early Parkinson's disease. *NPJ Parkinson's disease*, 10(1), 48. <https://doi.org/10.1038/s41531-024-00664-8>
- Chevance, G., Golaszewski, N. M., Tippett, E., Hekler, E. B., Buman, M., Welk, G. J., Patrick, K., & Godino, J. G. (2022). Accuracy and Precision of Energy Expenditure, Heart Rate, and Steps Measured by Combined-Sensing Fitbits Against Reference Measures: Systematic Review and Meta-analysis. *JMIR mHealth and uHealth*, 10(4), e35626. <https://doi.org/10.2196/35626>
- Cho, J., Seo, D. M., & Uh, Y. (2020). Clinical Application of Overlapping Confidence Intervals for Monitoring Changes in Serial Clinical Chemistry Test Results. *Annals of Laboratory Medicine*, 40(3), 201–208. <https://doi.org/10.3343/alm.2020.40.3.201>

- Chow, J. J., Thom, J. M., Wewege, M. A., Ward, R. E., & Parmenter, B. J. (2017). Accuracy of step count measured by physical activity monitors: The effect of gait speed and anatomical placement site. *Gait & Posture*, 57, 199–203. <https://doi.org/10.1016/j.gaitpost.2017.06.012>
- Clemes, S. A., & Griffiths, P. L. (2008). How many days of pedometer monitoring predict monthly ambulatory activity in adults? *Medicine and Science in Sports and Exercise*, 40(9), 1589–1595. <https://doi.org/10.1249/MSS.0b013e318177eb96>
- Creaby, M. W., & Cole, M. H. (2018). Gait characteristics and falls in Parkinson's disease: A systematic review and meta-analysis. *Parkinsonism & Related Disorders*, 57, 1–8. <https://doi.org/10.1016/j.parkreldis.2018.07.008>
- Del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK. *JAMA neurology*, 79(10), 1059–1063. <https://doi.org/10.1001/jamaneurol.2022.2672>
- Del Pozo Cruz, B., Ahmadi, M. N., Lee, I.-M., & Stamatakis, E. (2022). Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. *JAMA internal medicine*. <https://doi.org/10.1001/jamainternmed.2022.4000>
- Erro, R., Vitale, C., Amboni, M., Picillo, M., Moccia, M., Longo, K., Santangelo, G., De Rosa, A., Allocca, R., Giordano, F., Orefice, G., De Michele, G., Santoro, L., Pellecchia, M. T., & Barone, P. (2013). The heterogeneity of early Parkinson's disease: A cluster analysis on newly diagnosed untreated patients. *PloS One*, 8(8), e70244. <https://doi.org/10.1371/journal.pone.0070244>
- Fasano, A., Fung, V. S. C., Lopiano, L., Elibol, B., Smolentseva, I. G., Seppi, K., Takáts, A., Onuk, K., Parra, J. C., Bergmann, L., Sail, K., Jalundhwala, Y., & Pirtosek, Z. (2019). Characterizing advanced Parkinson's disease: OBSERVE-PD observational study results of 2615 patients. *BMC neurology*, 19(1), 50. <https://doi.org/10.1186/s12883-019-1276-8>
- Finis, N. A., Burge, A. T., Bernhardt, J., & Holland, A. E. (2019). Two Days of Measurement Provides Reliable Estimates of Physical Activity Poststroke: An Observational Study. *Archives of Physical Medicine and Rehabilitation*, 100(5), 883–890. <https://doi.org/10.1016/j.apmr.2018.10.006>
- Fokkema, T., Kooiman, T. J. M., Krijnen, W. P., VAN DER Schans, C. P., & DE Groot, M. (2017). Reliability and Validity of Ten Consumer Activity Trackers Depend on Walking Speed. *Medicine and Science in Sports and Exercise*, 49(4), 793–800. <https://doi.org/10.1249/MSS.0000000000001146>
- Fuller, D., Colwell, E., Low, J., Orychock, K., Tobin, M. A., Simango, B., Buote, R., Van Heerden, D., Luan, H., Cullen, K., Slade, L., & Taylor, N. G. A. (2020). Reliability and Validity of Commercially Available Wearable Devices for Measuring Steps, Energy Expenditure, and Heart Rate: Systematic Review. *JMIR mHealth and uHealth*, 8(9), e18694. <https://doi.org/10.2196/18694>
- Germini, F., Noronha, N., Borg Debono, V., Abraham Philip, B., Pete, D., Navarro, T., Keepanasseril, A., Parpia, S., de Wit, K., & Iorio, A. (2022). Accuracy and Acceptability of Wrist-Wearable Activity-Tracking Devices: Systematic Review of the Literature. *Journal of Medical Internet Research*, 24(1), e30791. <https://doi.org/10.2196/30791>
- Ginis, P., Goris, M., De Groef, A., Blondeel, A., Gilat, M., Demeyer, H., Troosters, T., & Nieuwboer, A. (2023). Validation of Commercial Activity Trackers in Everyday Life of People with Parkinson's Disease. *Sensors*, 23(8). <https://doi.org/10.3390/s23084156> Export Date: 14 April 2025; Cited By: 6.
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., Giladi, N., Holloway, R. G., Moore, C. G., Wenning, G. K., Yahr, M. D., Seidl, L., & Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 19(9), 1020–1028. <https://doi.org/10.1002/mds.20213>

- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Handlery, R., Stewart, J. C., Pellegrini, C., Monroe, C., Hainline, G., Flach, A., Handlery, K., & Fritz, S. (2021). Physical Activity in De Novo Parkinson Disease: Daily Step Recommendation and Effects of Treadmill Exercise on Physical Activity. *Physical Therapy*, 101(10), pzab174. <https://doi.org/10.1093/ptj/pzab174>
- Höglinger, G. U., Adler, C. H., Berg, D., Klein, C., Outeiro, T. F., Poewe, W., Postuma, R., Stoessl, A. J., & Lang, A. E. (2024). A biological classification of Parkinson's disease: The SynNeurGe research diagnostic criteria. *The Lancet. Neurology*, 23(2), 191–204. [https://doi.org/10.1016/S1474-4422\(23\)00404-0](https://doi.org/10.1016/S1474-4422(23)00404-0)
- Horsager, J., & Borghammer, P. (2024). Brain-first vs. body-first Parkinson's disease: An update on recent evidence. *Parkinsonism & Related Disorders*, 106101. <https://doi.org/10.1016/j.parkreldis.2024.106101>
- Inoue, K., Tsugawa, Y., Mayeda, E. R., & Ritz, B. (2023). Association of Daily Step Patterns With Mortality in US Adults. *JAMA network open*, 6(3), e235174. <https://doi.org/10.1001/jamanetworkopen.2023.5174>
- Jankovic, J., McDermott, M., Carter, J., Gauthier, S., Goetz, C., Golbe, L., Huber, S., Koller, W., Olanow, C., & Shoulson, I. (1990). Variable expression of Parkinson's disease: A base-line analysis of the DATATOP cohort. The Parkinson Study Group. *Neurology*, 40(10), 1529–1534. <https://doi.org/10.1212/wnl.40.10.1529>
- Johnston, W., Judice, P. B., Molina García, P., Mühlen, J. M., Lykke Skovgaard, E., Stang, J., Schumann, M., Cheng, S., Bloch, W., Brønd, J. C., Ekelund, U., Grøntved, A., Caulfield, B., Ortega, F. B., & Sardinha, L. B. (2021). Recommendations for determining the validity of consumer wearable and smartphone step count: Expert statement and checklist of the INTERLIVE network. *British Journal of Sports Medicine*, 55(14), 780–793. <https://doi.org/10.1136/bjsports-2020-103147>
- Jost, S. T., Kaldenbach, M.-A., Antonini, A., Martinez-Martin, P., Timmermann, L., Odin, P., Katzenschlager, R., Borgohain, R., Fasano, A., Stocchi, F., Hattori, N., Kukkle, P. L., Rodríguez-Violante, M., Falup-Pecurariu, C., Schade, S., Petry-Schmelzer, J. N., Metta, V., Weintraub, D., Deuschl, G., ... International Parkinson and Movement Disorders Society Non-Motor Parkinson Disease Study Group. (2023). Levodopa Dose Equivalency in Parkinson's Disease: Updated Systematic Review and Proposals. *Movement Disorders: Official Journal of the Movement Disorder Society*, 38(7), 1236–1252. <https://doi.org/10.1002/mds.29410>
- Kim, D. W., Hassett, L. M., Nguy, V., & Allen, N. E. (2019). A Comparison of Activity Monitor Data from Devices Worn on the Wrist and the Waist in People with Parkinson's Disease. [Place: United States]. *Movement disorders clinical practice*, 6(8), 693–699. <https://doi.org/10.1002/mdc3.12850>
- Knol, M. J., Pestman, W. R., & Grobbee, D. E. (2011). The (mis)use of overlap of confidence intervals to assess effect modification. *European Journal of Epidemiology*, 26(4), 253–254. <https://doi.org/10.1007/s10654-011-9563-8>
- Koo, T. K., & Li, M. Y. (2016). A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *Journal of Chiropractic Medicine*, 15(2), 155–163. <https://doi.org/10.1016/j.jcm.2016.02.012>
- Lamont, R. M., Daniel, H. L., Payne, C. L., & Brauer, S. G. (2018). Accuracy of wearable physical activity trackers in people with Parkinson's disease. [Place: England]. *Gait & posture*, 63, 104–108. <https://doi.org/10.1016/j.gaitpost.2018.04.034>

- Lee, I.-M., Shiroma, E. J., Kamada, M., Bassett, D. R., Matthews, C. E., & Buring, J. E. (2019). Association of Step Volume and Intensity With All-Cause Mortality in Older Women. *JAMA internal medicine*, 179(8), 1105–1112. <https://doi.org/10.1001/jamainternmed.2019.0899>
- Lee, M., Noh, Y., Youm, C., Kim, S., Park, H., Noh, B., Kim, B., Choi, H., & Yoon, H. (2021). Estimating Health-Related Quality of Life Based on Demographic Characteristics, Questionnaires, Gait Ability, and Physical Fitness in Korean Elderly Adults. *International Journal of Environmental Research and Public Health*, 18(22), 11816. <https://doi.org/10.3390/ijerph182211816>
- Lexell, J. E., & Downham, D. Y. (2005). How to assess the reliability of measurements in rehabilitation. *American Journal of Physical Medicine & Rehabilitation*, 84(9), 719–723. <https://doi.org/10.1097/01.phm.0000176452.17771.20>
- MacKinnon, C. D. (2018). Sensorimotor anatomy of gait, balance, and falls. *Handbook of Clinical Neurology*, 159, 3–26. <https://doi.org/10.1016/B978-0-444-63916-5.00001-X>
- Martínez-Martín, P., Rodríguez-Blázquez, C., Mario Alvarez, n., Arakaki, T., Arillo, V. C., Chaná, P., Fernández, W., Garretto, N., Martínez-Castrillo, J. C., Rodríguez-Violante, M., Serrano-Dueñas, M., Ballesteros, D., Rojo-Abuin, J. M., Chaudhuri, K. R., & Merello, M. (2015). Parkinson's disease severity levels and MDS-Unified Parkinson's Disease Rating Scale. *Parkinsonism & Related Disorders*, 21(1), 50–54. <https://doi.org/10.1016/j.parkreldis.2014.10.026>
- Mattison, G., Canfell, O., Forrester, D., Dobbins, C., Smith, D., Töyräs, J., & Sullivan, C. (2022). The Influence of Wearables on Health Care Outcomes in Chronic Disease: Systematic Review. *Journal of Medical Internet Research*, 24(7), e36690. <https://doi.org/10.2196/36690>
- Mazzà, C., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Bonci, T., Brown, P., Brozgol, M., Buckley, E., Carsin, A.-E., Caruso, M., Caulfield, B., Cereatti, A., Chiari, L., Chynkiamis, N., Ciravegna, F., Del Din, S., Eskofier, B., Evers, J., ... Rochester, L. (2021). Technical validation of real-world monitoring of gait: A multicentric observational study. *BMJ open*, 11(12), e050785. <https://doi.org/10.1136/bmjopen-2021-050785>
- Micó-Amigo, M. E., Bonci, T., Paraschiv-Ionescu, A., Ullrich, M., Kirk, C., Soltani, A., Küderle, A., Gazit, E., Salis, F., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Brown, P., Buckley, E., Cantu, A., Carsin, A.-E., Caruso, M., Caulfield, B., ... Mobilise-D consortium. (2023). Assessing real-world gait with digital technology? Validation, insights and recommendations from the Mobilise-D consortium. *Journal of Neuroengineering and Rehabilitation*, 20(1), 78. <https://doi.org/10.1186/s12984-023-01198-5>
- Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L., Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)
- Mokkink, L. B., Terwee, C. B., Patrick, D. L., Alonso, J., Stratford, P. W., Knol, D. L., Bouter, L. M., & de Vet, H. C. W. (2010). The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: An international Delphi study. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, 19(4), 539–549. <https://doi.org/10.1007/s11136-010-9606-8>
- Nakagata, T., Murakami, H., Kawakami, R., Tripette, J., Nakae, S., Yamada, Y., Ishikawa-Takata, K., Tanaka, S., & Miyachi, M. (2022). Step-count outcomes of 13 different activity trackers: Results from laboratory and free-living experiments. *Gait & Posture*, 98, 24–33. <https://doi.org/10.1016/j.gaitpost.2022.08.004>
- Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>

- Norris, M., Anderson, R., Motl, R. W., Hayes, S., & Coote, S. (2017). Minimum number of days required for a reliable estimate of daily step count and energy expenditure, in people with MS who walk unaided. *Gait & Posture*, *53*, 201–206. <https://doi.org/10.1016/j.gaitpost.2017.02.005>
- Outeiro, T. F., Alcalay, R. N., Antonini, A., Attems, J., Bonifati, V., Cardoso, F., Cheselet, M.-F., Hardy, J., Madeo, G., McKeith, I., Mollenhauer, B., Moore, D. J., Rascol, O., Schlossmacher, M. G., Soreq, H., Stefanis, L., & Ferreira, J. J. (2023). Defining the Riddle in Order to Solve It: There Is More Than One "Parkinson's Disease". *Movement Disorders: Official Journal of the Movement Disorder Society*, *38*(7), 1127–1142. <https://doi.org/10.1002/mds.29419>
- Paluch, A. E., Bajpai, S., Bassett, D. R., Carnethon, M. R., Ekelund, U., Evenson, K. R., Galuska, D. A., Jefferis, B. J., Kraus, W. E., Lee, I.-M., Matthews, C. E., Omura, J. D., Patel, A. V., Pieper, C. F., Rees-Punia, E., Dallmeier, D., Klenk, J., Whincup, P. H., Dooley, E. E., ... Fulton, J. E. (2022). Daily steps and all-cause mortality: A meta-analysis of 15 international cohorts [Publisher: Elsevier]. *The Lancet Public Health*, *7*(3), e219–e228. [https://doi.org/10.1016/S2468-2667\(21\)00302-9](https://doi.org/10.1016/S2468-2667(21)00302-9)
- Paul, S. S., Ellis, T. D., Dibble, L. E., Earhart, G. M., Ford, M. P., Foreman, K. B., & Cavanaugh, J. T. (2016). Obtaining Reliable Estimates of Ambulatory Physical Activity in People with Parkinson's Disease. *Journal of Parkinson's Disease*, *6*(2), 301–305. <https://doi.org/10.3233/JPD-160791>
- Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., Obeso, J., Marek, K., Litvan, I., Lang, A. E., Halliday, G., Goetz, C. G., Gasser, T., Dubois, B., Chan, P., Bloem, B. R., Adler, C. H., & Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, *30*(12), 1591–1601. <https://doi.org/10.1002/mds.26424>
- Saint-Maurice, P. F., Troiano, R. P., Bassett, D. R., Graubard, B. I., Carlson, S. A., Shiro, E. J., Fulton, J. E., & Matthews, C. E. (2020). Association of Daily Step Count and Step Intensity With Mortality Among US Adults. *JAMA*, *323*(12), 1151–1160. <https://doi.org/10.1001/jama.2020.1382>
- Schlachetzki, J. C. M., Barth, J., Marxreiter, F., Gossler, J., Kohl, Z., Reinfelder, S., Gassner, H., Aminian, K., Eskofier, B. M., Winkler, J., & Klucken, J. (2017). Wearable sensors objectively measure gait parameters in Parkinson's disease. *PLoS One*, *12*(10), e0183989. <https://doi.org/10.1371/journal.pone.0183989>
- Sigmundová, D., Vašíčková, J., Stelzer, J., & Repka, E. (2013). The influence of monitoring interval on data measurement: An analysis of step counts of university students. *International Journal of Environmental Research and Public Health*, *10*(2), 515–527. <https://doi.org/10.3390/ijerph10020515>
- Skidmore, F. M., Mackman, C. A., Pav, B., Shulman, L. M., Garvan, C., Macko, R. F., & Heilman, K. M. (2008). Daily ambulatory activity levels in idiopathic Parkinson disease. *Journal of Rehabilitation Research and Development*, *45*(9), 1343–1348.
- Stebbins, G. T., Goetz, C. G., Burn, D. J., Jankovic, J., Khoo, T. K., & Tilley, B. C. (2013). How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: Comparison with the unified Parkinson's disease rating scale. *Movement Disorders: Official Journal of the Movement Disorder Society*, *28*(5), 668–670. <https://doi.org/10.1002/mds.25383>
- Stefani, A., Tassitore, A., Tambasco, N., Cossu, G., Ceravolo, M. G., Defazio, G., Morgante, F., Ramat, S., Melzi, G., Gualberti, G., Merolla, R., Onuk, K., & Lopiano, L. (2022). Criteria for identification of advanced Parkinson's disease: The results of the Italian subgroup of OBSERVE-PD observational study. *BMC neurology*, *22*(1), 41. <https://doi.org/10.1186/s12883-022-02554-z>
- Treacy, D., Hassett, L., Schurr, K., Chagpar, S., Paul, S. S., & Sherrington, C. (2017). Validity of Different Activity Monitors to Count Steps in an Inpatient Rehabilitation Setting. *Physical Therapy*, *97*(5), 581–588. <https://doi.org/10.1093/ptj/ptxz010>

Wendel, N., Macpherson, C. E., Webber, K., Hendron, K., DeAngelis, T., Colon-Semenza, C., & Ellis, T. (2018). Accuracy of Activity Trackers in Parkinson Disease: Should We Prescribe Them? [Place: United States]. *Physical therapy*, 98(8), 705–714. <https://doi.org/10.1093/ptj/pzy054>

Wüllner, U., Borghammer, P., Choe, C.-U., Csoti, I., Falkenburger, B., Gasser, T., Lingor, P., & Riederer, P. (2023). The heterogeneity of Parkinson's disease. *Journal of Neural Transmission (Vienna, Austria: 1996)*, 130(6), 827–838. <https://doi.org/10.1007/s00702-023-02635-4>

Yao, J., Tan, C. S., Lim, N., Tan, J., Chen, C., & Müller-Riemenschneider, F. (2021). Number of daily measurements needed to estimate habitual step count levels using wrist-worn trackers and smartphones in 212,048 adults. *Scientific Reports*, 11(1), 9633. <https://doi.org/10.1038/s41598-021-89141-3>

Zetuský, W. J., Jankovic, J., & Pirozzolo, F. J. (1985). The heterogeneity of Parkinson's disease: Clinical and prognostic implications. *Neurology*, 35(4), 522–526. <https://doi.org/10.1212/wnl.35.4.522>

Chapter 7

Contribution 4: Minimal Clinically Important Difference of Average Daily Steps Measured Through a Consumer Smartwatch in People With Mild-to-Moderate Parkinson Disease: Cross-Sectional Study

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Abstract

Recent studies demonstrated the validity, reliability, and accuracy of consumer smartwatches for measuring daily steps in people with Parkinson disease (PD). However, no study to date estimated the minimal clinically important difference (MCID) for average daily steps (avDS), measured through a consumer smartwatch in people with PD. This study aimed to calculate the MCID of avDS, measured through a commercial smartwatch (Garmin Vivosmart 4) in people with PD. People with PD with a disease stage <4, without cognitive impairment, and who were able to walk unaided wore a Garmin Vivosmart 4 smartwatch for 5 consecutive days on the wrist least affected by the disease allowing the computation of avDS. To define the 3 levels of MCID for avDS, we used an anchor-based method linked to: (1) scales capturing subtle changes in global mobility and motor functions, (2) clinical and health-related measures, and (3) disease-related patient reported outcomes. Linear regressions, Student t test, and ANOVA were used to estimate the minimal change in avDS based on anchors relevant change. For each level, overall MCID was calculated as the average of the variables included and range was reported. A total of 100 people with PD were enrolled. Participants took on average 5949 (SD 3034) daily steps ranging from 357 to 12,620. MCID of avDS anchored to standardized measures of motor symptoms and mobility was 581 steps/day (range 554-608) or around 10% of mean avDS in our population. MCID of avDS anchored to clinical and health-related variables was 1200 steps/day (range 350-1683), or around 20% of mean avDS in our population. Finally, MCID of avDS anchored to disease-related patient reported outcomes was 1592 steps/day (range 594-2589), or around 27% of the mean avDS in our population. These findings could be relevant for designing future clinical trials involving avDS as a digital mobility outcome in daily life for people with PD and evaluating the effectiveness of intervention promoting free-living walking in this population.

Introduction

Parkinson disease (PD) is a neurodegenerative disease characterized by both motor and nonmotor symptoms. Among the motor manifestations of PD, gait disturbances are notably prevalent and encompass a variety of issues, such as a shuffling gait, reduced step length and diminished automaticity, decreased arm swing, increased double support time, altered cadence, and periodic episodes such as freezing of gait (FOG) (Mirelman et al., 2019). Walking, a fundamental daily activity, is crucial for maintaining functional independence and social wellbeing (MacKinnon, 2018). Gait disturbances, therefore, represent a particularly disabling category of symptoms in PD, significantly impacting the autonomy and quality of life of patients (M. Lee et al., 2021).

Gait characteristics can be examined through various methods, both in controlled and ecological settings. Recently, the use of wearable inertial sensors for gait analysis has gained considerable traction (Bate et al., 2023; Correno et al., 2022; Soulard et al., 2022). Specifically, the daily step count serves as an indirect yet rather easily obtainable indicator of walking and physical activity (Bassett et al., 2017). While this metric does not provide detailed gait analysis, there is established evidence linking a reduced daily step count to a range of health issues, including oncological and cardiovascular diseases (Del Pozo Cruz, Ahmadi, et al., 2022), dementia (Del Pozo Cruz, Ahmadi, et al., 2022), as well as an elevated risk of overall mortality (Inoue et al., 2023; I.-M. Lee et al., 2019; Paluch et al., 2022; Saint-Maurice et al., 2020). In the context of PD, studies have consistently demonstrated a correlation between a decrease in daily steps and increased disease severity (Skidmore et al., 2008) as well as with levels of physical activity (Liu et al., 2023; Mantri et al., 2019). These studies have also proposed a minimum daily step goal of around 4200 to align with physical activity recommendations in the early stages of PD (Handlery et al., 2021). Step measurement can be accomplished using either research-grade or consumer devices. Research-grade devices are specifically developed for use by professionals in research or clinical settings and are generally recognized for their superior accuracy and reliability (Brewer et al., 2017; Degroote et al., 2018; Hergenroeder et al., 2018; Topalidis et al., 2021). Despite this, they come with drawbacks such as higher costs, limited market availability, the need for specialized expertise for operation, and less focus on aesthetic appeal and user-friendliness. In contrast, consumer wearable devices are designed for the general public. These devices are easily accessible in the market and user-friendly, requiring no specialized knowledge for operation. However, they typically lack validation for research purposes and often do not include sophisticated algorithms or analysis software (Bianchini & Maetzler, 2023). Despite this, there is an increasing focus in the literature on using consumer wearables for data collection and monitoring in neurological patients (Chandrabhatla et al., 2022; Löhle et al., 2023; Powers et al., 2021). Both device types demonstrate reliable step counting in individuals with normal gait patterns (Lamont et al., 2018), though research-grade devices show higher reliability across a wider range of conditions (Treacy et al., 2017). However, for individuals with nonphysiological gait, such as those with reduced walking speeds or those using walking aids, the performance of consumer wearables tends to diminish (Bianchini et al., 2022; Chow et al., 2017; Fokkema et al., 2017; Hergenroeder et al., 2018; Svarre et al., 2020).

PD poses a unique challenge for gait analysis, as its associated disturbed gait patterns could adversely impact the reliability of device algorithms. Furthermore, the occurrence of tremors and dyskinesias in patients with PD may introduce additional background noise in recordings, potentially resulting in an overestimation of step counts (Bianchini et al., 2022; Kim et al., 2019). Conversely, the presence of rigidity and bradykinesia, characteristic of PD, might lead to an underestimation of steps, especially when the activity monitor is worn on the wrist (Wendel et al., 2018). In our previous in-laboratory study involving 47 people with PD, we demonstrated a good criterion validity (intraclass correlation coefficient=0.76) and an acceptable level of error (mean absolute percentage error=5%) in step counting using a consumer smartwatch (Garmin Vivosmart 4), when worn on the side least affected

by the disease and under well-controlled pharmacological conditions (Bianchini et al., 2022). In the context of real-life settings, a separate study underscored the criterion validity of average daily steps (avDS) measured by several wrist-worn consumer devices (Fitbit Alta [Google] and Fitbit Inspire 3 [Google]) in 28 people with PD at home, compared with a research-grade device (Dynaport movemonitor) (Ginis et al., 2023). We recently replicated these results, using Garmin Vivosmart 4, in a proof-of-concept experiment (Bianchini et al., 2025). Beyond criterion validity, the reliability of a measurement tool — the consistency of repeated measures in unchanged individuals — is equally crucial. In this regard, our recent findings indicate that a minimum of 4 days is necessary to obtain a reliable estimate of avDS recorded by a consumer smartwatch (Garmin Vivosmart 4) in free-living conditions (Bianchini et al., 2023).

An essential additional metrological characteristic of an activity monitor is its capability to reliably capture changes in measured parameters and the clinical significance of these changes. In this context, the minimum detectable change (MDC) and the minimal clinically important difference (MCID) are 2 key metrics and are pivotal for calculating clinical trial sample sizes and assessing the effectiveness of interventions (Bloom et al., 2023; Lexell & Downham, 2005). On the one hand, MDC denotes the smallest change that can be confidently identified beyond the measurement error of the instrument used for a specific parameter (Lexell & Downham, 2005). In a recent work of ours on 56 individuals with mild-to-moderate PD, we found that for a monitoring period of at least 4 days, the MDC for the Garmin Vivosmart 4 ranged between 1198 and 1524 steps/day, averaging at 1366 steps/day (Bianchini et al., 2023). On the other hand, MCID represents the smallest difference in a parameter that is meaningful from a clinical perspective (Bloom et al., 2023). In fact, a statistically significant change after an intervention may not represent a modification that has a real impact on the patient's condition and, ultimately, might not be perceived by individuals. Therefore, estimated in different ways, and there is no definite consensus for the best method (Byrom et al., 2020; Sedaghat, 2019). Globally, two calculation methods exist: (1) distribution-based and (2) anchor-based. Distribution-based methods rely on the statistical characteristics of the variables of interest within the given population to identify the magnitude of change that would be unlikely to be observed by chance. Spread parameters, such as SD and SE of measurements, are commonly used indexes to calculate MCID using distribution-based methods (Byrom et al., 2020; Sedaghat, 2019). However, several authors underlined the limitation of distribution-based methods in capturing truly meaningful change and consider the use of these techniques only as an addition to anchor-based methods (Byrom et al., 2020; McLeod et al., 2011). Anchor-based methods compare the change in patients' variable of interest with how patients score on a second, explicit metric of improvement (ie, the anchor) (Byrom et al., 2020; Sedaghat, 2019; Zhang et al., 2023). Usually, when applying anchor-based method, improvement is evaluated longitudinally following an intervention and a time period for which a change in the anchor measure is expected (Byrom et al., 2020). However, cross-sectional evaluation is also possible, as reported by Motl and collaborators (Motl et al., 2013). With this second approach, a value, or a range of values, are defined for the anchor that correspond to the MCID and then the target score of the variable of interest that corresponds to anchor value is calculated. With cross-sectional method, the between-subjects variability in the relationship between the anchor and the new measure is often high therefore multiple anchors are often needed to provide a well-triangulated MCID value (Byrom et al., 2020). However, this could offer the advantage of delineating several levels of MCID depending on their specific goals and expected outcomes, providing a more versatile framework (Motl et al., 2013). While generally considered more reliable than distribution-based, potential limitations of anchor-based methods include recall bias and the need for at least a moderate correlation between the anchor and the variable of interest (Byrom et al., 2020).

As of now, there are no published studies that have evaluated the MCID for avDS in people with PD. Therefore, considering these identified research gaps and the clinical significance of the psychometric and clinometric properties of daily steps measured by consumer smartwatches in free-living conditions for people with PD, the objective of this study was to

determine the MCID of avDS as recorded by a consumer smartwatch in real-world settings for this population of individuals.

Material and Methods

Population

Participants were recruited at the Movement Disorder Outpatient Service of the Sant'Andrea University Hospital, Rome, Italy, in the period between March 2023 and February 2024. Inclusion criteria were (1) diagnosis of idiopathic PD according to Movement Disorder Society (MDS) criteria (Postuma et al., 2015), (2) aged 18 years or older, (3) disease stage ≤ 4 according to the modified Hoehn and Yahr scale (mHY; "severe disability; still able to walk or stand unassisted") (Goetz et al., 2004), and (4) ability to perform the experimental procedure. Exclusion criteria were (1) cognitive impairment as defined by a Montreal Cognitive Assessment (MoCA) score < 21 , and (2) orthopedic, rheumatologic, or systemic conditions affecting mobility as judged by the assessor.

Ethical Considerations

This cross-sectional study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. Approval was granted by the local Ethical Committee of Sapienza, University of Rome (Reference 0372/2022). Data collection and processing followed the current European regulation for data protection. All participants provided written informed consent before the beginning of measurements. All data were deidentified. Participants did not receive any form of compensation.

Demographic and Clinical Data

Participants were evaluated during scheduled visits. Demographics (age and sex) and anthropometric measures (weight, height, and BMI) were collected. Disease duration, disease stage according to mHY scale, and levodopa equivalent daily dose (LEDD) (Jost et al., 2023) were also collected. Participants then were evaluated with the following rating scales: The sum of the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Goetz et al., 2008) parts I and II were used to assess the impact of motor and nonmotor symptoms on daily life (Zou et al., 2023). MDS-UPDRS part III was used to assess motor symptoms severity. From MDS-UPDRS part II and III scores, participants were classified into tremor dominant (TD), postural instability and gait disorder (PIGD), or indeterminate disease subtypes, according to Stebbins et al (Stebbins et al., 2013). Participants were also grouped in those with mild and moderate disease severity based on the MDS-UPDRS score as proposed by Martínez-Martín and colleagues (Martínez-Martín et al., 2015). The Parkinson's Disease Questionnaire-39 (PDQ-39) was used to evaluate participants' quality of life (Peto et al., 1995). The Short Physical Performance Battery (SPPB) was used to assess lower limb function and general physical capacity (Tanji et al., 2008). The Wearing-Off Questionnaire-19 (WOQ-19) was used to assess presence of wearing off. A score *geq* 2 was used as cutoff to define the presence of wearing off (Mantese et al., 2018). The Fatigue Severity Scale (FSS) was used to assess fatigue severity, a score *geq* 4.67 was used to define clinically relevant fatigue (Siciliano et al., 2019). The item 1 of the New Freezing of Gait Questionnaire (N-FOGQ) (Nieuwboer et al., 2009) was used to assess the presence of FOG, defined as a score > 0 . Finally, the MDS-UPDRS item 2.10 was used to assess the absolute presence or absence of tremor as reported by participants.

Experimental Procedure

Participants then received the smartwatch Garmin Vivosmart 4 to be worn at home for 5 consecutive days, including at least 1 weekend day, on the wrist of the body side least affected by the disease (Bianchini et al., 2022). Participants were instructed to wear the smartwatch all time during day and night and remove it only when involved in water activities (eg, bathing, showering, and swimming). Participants were also asked to perform daily activities as usual. No additional reminder or instructions were provided to participants during the monitoring period. We choose a 5-day period since we demonstrated previously that a minimum of 4 days of monitoring is needed to reliably estimate daily step count in people with PD (Bianchini et al., 2023). Each smartwatch was configured according to the producer's recommendations by indicating patient's age, height, weight, and the wrist on which the smartwatch was worn (ie, left or right). During the monitoring period, participants could access information on the smartwatch screen, including the total number of steps, heart rate, and sleep time. The device did not provide instructions, alerts, or other messages to participants. After 5 days, they returned the smartwatch to the hospital. From smartwatch dashboard, total daily number of steps for each day was recorded and the avDS were calculated (Bianchini et al., 2023). Compliance was assessed based on the participants' dashboard data. We could assess that the device was worn through heart rate and activity data. We considered all recording days with *geq* 80% wear time while awake to be valid. We estimated the awake time as 24 hours minus the total sleep time as indicated by the device.

Data and Statistical Analysis

The statistical analyses were performed using JASP v0.18.3.0 (JASP Team, University of Amsterdam), R v4.0.3 (R Core Team), and RStudio v2022.07.1+554 for Windows (R Foundation for Statistical Computing). Descriptive statistics were calculated for the examined variables. Normality of distributions were assessed by histogram and residual plots inspection. To define MCID, we used an anchor-based method identifying three levels of variables, following the approach of Motl and collaborators (Motl et al., 2013): (1) scales capturing subtle changes in global mobility and motor functions (ie, MDS-UPDRS part III and SPPB); (2) clinical and health-related measures including disease duration, mHY, LEDD, PD subtype, disease severity as assessed by MDS-UPDRS, age, sex, and BMI; and (3) disease-related patient reported outcomes (PROs) including MDS-UPDRS parts I and II, PDQ-39, presence of FOG, presence of wearing off, presence of fatigue, and presence of tremor. Such an approach could provide ranges of MCIDs, and options for MCID selection that are appropriate for specific populations and circumstances, including both assessor-based and PROs, in clinical trials and interventions involving people with PD [39]. Since previous studies have recommended a correlation coefficient of at least 0.3-0.35 between the change score and the anchor (Revicki et al., 2008), we first conducted a correlation analysis between avDS and the included variables using Spearman test. Only association with a correlation coefficient >0.3 were considered for MCID estimation. We then conducted a linear regression between avDS and MDS-UPDRS part I+II and part III, mHY, SPPB, LEDD, and age for estimating the incremental change in daily steps per relevant variable change. To evaluate the relevant change, we used the already known MCID for each scale included in regression analysis. Scales for which an MCID was not reported were excluded from the analysis. In case of asymmetric MCID (ie, different values for improvement and deterioration) we used the average value rounded to the higher next whole number. For the remaining variables, we calculated mean and SE differences in avDS between groups by performing between-subjects analyses of variance (ANOVA) with Bonferroni-Holm post hoc pairwise comparisons in case of overall significance, when the variables included more than 2 classes. For 2-class variables, we used the Student t test for independent groups to compute the mean differences and SE in avDS. Cohen d was used to estimate the standardized effect size. MCID for the 3 levels was then calculated and the average of the included

variables, and range was reported. The level of significance was set at $<.05$.

Results

Overview

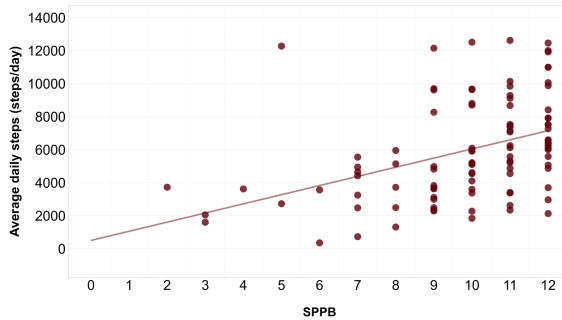
A total of 100 people with PD were enrolled in the study. All participants were monitored through Garmin Vivosmart 4 at home for a period of 5 consecutive days. No participants or days were excluded based on the prespecified compliance criteria. Participants took on average 5949 (SD 3034) daily steps ranging from 357 to 12620. Details of demographic, anthropometric, and clinical variables in the enrolled population are illustrated in fig. 7.1.

Table 7.1. Clinical, anthropometric, and demographic characteristics of enrolled population.

	People with PD (n=100)
Age (y), mean (SD)	67.8 (8.5)
Height (cm), mean (SD)	171 (9.0)
Weight (kg), mean (SD)	76.0 (13.2)
BMI (kg/m ²), mean (SD)	25.8 (3.5)
Sex, n (%)	
Male	67 (67)
Female	33 (33)
Disease duration (y), mean (SD)	6.2 (4.4)
LEDD (mg), mean (SD)	544 (298)
mHY, median (IQR)	2 (2-2.5)
MDS-UPDRS I+II, median (IQR)	11 (6-16)
MDS-UPDRS-III, median (IQR)	27 (21-32)
PDQ39, mean (SD)	12.1 (9.4)
Disease subtypes, n (%)	
TD	31 (31)
IND	8 (8)
PIGD	61 (61)
WO	28 (28)
FOG	13 (13)
Fatigue	23 (23)
Tremor	55 (55)
Disease severity, n (%)	
Mild	63 (63)
Moderate	37 (37)
SPPB, median (IQR)	10 (9-12)
avDS, mean (SD)	5949 (3034)

avDS: average daily steps; FOG: freezing of gait; IND: indeterminate; LEDD: levodopa equivalent daily dose; MDS-UPDRS: Movement Disorder Society Unified Parkinson Disease Rating Scale; mHY: modified Hoehn and Yahr scale; PD: Parkinson disease; PDQ39: Parkinson disease questionnaire; PIGD: postural instability and gait disorder; SPPB: Short Physical Performance Battery; TD: tremor dominant; WO: wearing-off.

A



B

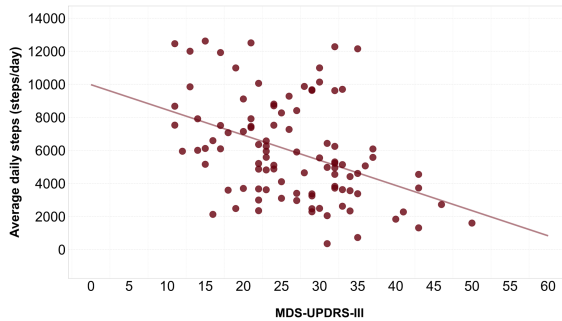


Figure 7.1. Correlation of average daily steps with Short Physical Performance Battery and Movement Disorder Society Unified Parkinson Disease Rating Scale-III. Scatterplot showing correlation between average daily steps and Short Physical Performance Battery score (panel A) and between average daily steps and Movement Disorder Society Unified Parkinson Disease Rating Scale-III score (panel B). A linear regression line was added to show the linear tendency. MDS-UPDRS: Movement Disorder Society Unified Parkinson Disease Rating Scale; SPPB: Short Physical Performance Battery.

MCID

Global Mobility and Motor Functions

All included variables showed a correlation coefficient >0.3 with avDS. The 2 linear regression models between avDS and MDS-UPDRS-III and SPPB were statistically significant (MDS-UPDRS-III: $F_{1,98}=20.46$, $P<.001$, $R^2=0.16$; SPPB: $F_{1,98}=19.84$, $P<.001$; $R^2=0.16$) (fig. 7.1).

The resulting regression equations indicated that every 1-point increase in MDS-UPDRS-III corresponded to a 152 steps/day decrease ($\text{avDS}=9778-152\times\text{MDS-UPDRS-III}$). MCID for MDS-UPDRS was reported as 3.25 for score decrease and 4.63 for score increase (Horváth et al., 2015), therefore we calculated a rounded average of 4 points and we estimated a 608 steps/day modification for each 4-point change in MDS-UPDRS-III. Finally, each 1-point increase in SPPB score corresponded to an increase of 554 step/day ($\text{avDS}=503+554\times\text{SPPB}$). Changes in 1 point is also the reported MCID for SPPB in older adults, therefore we adopted this value (Perera et al., 2006). Overall, the mean MCID across the 3 clinical scales that capture meaningful changes in motor and mobility condition was 581 steps/day (range 554-608) corresponding to 10% of the avDS in our population.

Clinical and Health-Related Measures

All included variables except BMI showed a correlation coefficient >0.3 with avDS. Regression models of mHY, LEDD, age, and disease duration were statistically significant (mHY: $F_{1,98}=26.26$, $P<.001$, $R^2=0.20$; LEDD: $F_{1,98}=12.97$, $P<.001$, $R^2=0.11$; age: $F_{1,98}=18.22$, $P<.001$, $R^2=0.15$; disease duration: $F_{1,98}=7.01$, $P=.009$, $R^2=0.06$) (fig. 7.2).

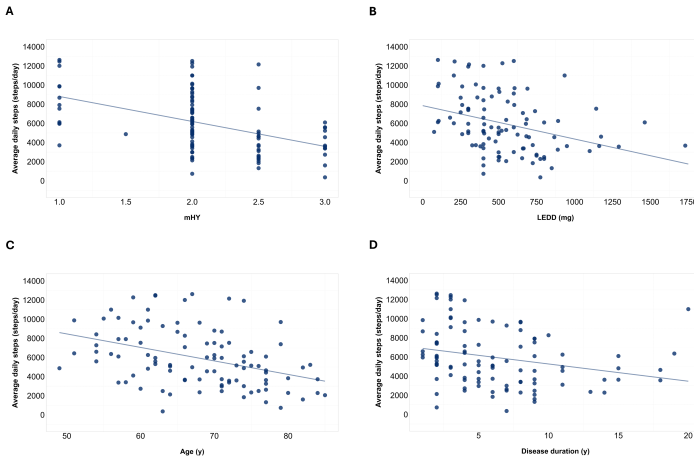


Figure 7.2. Correlation of average daily steps with modified Hoehn and Yahr stage, levodopa equivalent daily dose, age and disease duration. Scatterplot are reported showing correlation between average daily steps and modified Hoehn and Yahr stage (panel A), levodopa equivalent daily dose (panel B), age (panel C), and disease duration (panel D). A linear regression line was added to show the linear tendency. LEDD: levodopa equivalent dose; mHY: modified Hoehn and Yahr stage.

The resulting regression equations indicated that every 1-point increase in mHY stage yielded a reduction of 2607 steps/day ($\text{avDS}=11,409-2607\times\text{mHY}$). Since mHY included 0.5 steps increases between scores 1 and 3, we calculated that each step corresponded to a 1304 steps/day reduction. For LEDD, regression equations indicated that every 1 equivalent mg increase led to a reduction of 3.5 steps/day ($\text{avDS}=7846-3.5\times\text{mHY}$). Since the usual single dose of levodopa corresponds to 100 mg, we used this value as reference, and we estimated a 350 steps/day modification for each 100 mg change in LEDD. For age, regression equations

indicated that 1-year increase in age yielded a reduction of 141 steps/day ($\text{avDS}=15,512-141\times\text{age}$). Furthermore, 10-year increases are usually used to divide participants in age groups; therefore, we estimated a 1410 steps/day modification each 10-year change of age. For disease duration, regression equations indicated that 1-year increase in disease duration resulted in a reduction of 180 steps/day ($\text{avDS}=7071-180\times\text{age}$). We chose 5 years as a significant increment in disease duration since this was a common cutoff to categorize disease duration in previous studies (Adler et al., 2021; De Carolis et al., 2023; Prange et al., 2019). Therefore, we estimated a 900 steps/day modification for each 5-year change of disease duration. Considering categorical descriptors, ANOVA showed a significant difference in avDS among TD, PIGD and indeterminate participants ($F_{2,97}=4.55$, $P=.01$). Post hoc pairwise comparisons showed a significant difference between TD and PIGD participants ($t(90)=2.60$, $P=.03$) with a mean difference of 1683 (SD 646) steps/day and moderate effect size (Cohen $d=0.57$) (fig. 7.3A). Student t test showed a significant difference between mild and moderate disease severity, as categorized based on MDS-UPDRS cutoffs ($t(98)=2.54$, $P=.01$) with a mean difference of 1554 (SD 612) steps/day and moderate effect size (Cohen $d=0.53$) (fig. 7.3B).

No significant differences were found between males and females ($t(98)=-0.12$, $P=.90$). Overall, the mean MCID across the clinical and health-related variables was 1200 steps/day (range 350-1683) corresponding to 20% of the avDS in our population.

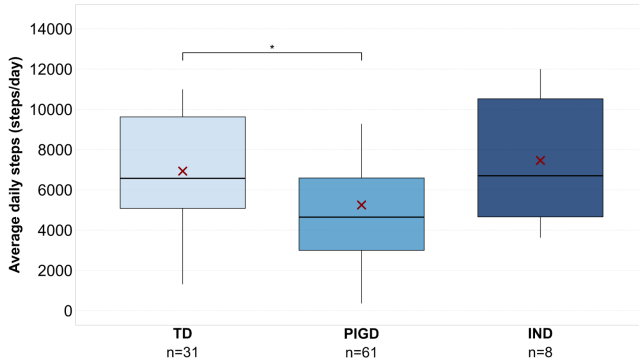
Clinical and Health-Related Measures

Only MDS-UPDRS I+II showed a correlation coefficient >0.3 with avDS and was included in the regression analysis. Regression models of MDS-UPDRS part I+II was statistically significant (MDS-UPDRS I+II: $F_{1,98}=7.03$, $P=.009$, $R^2=0.06$) (fig. 7.4).

For MDS-UPDRS I+II regression equations indicated that every 1-point increase led to a reduction of 99 steps/day ($\text{avDS}=7188-99\times\text{MDS-UPDRS I+II}$). For the sum of MDS-UPDRS I and II, the reported MCID is 5.73 points for improvement and 4.70 points for worsening, therefore we calculated a rounded average of 6 points, and we estimated a 594 steps/day modification for each 6-point change in MDS-UPDRS I+II. Student t test showed a significant difference between patients reporting tremor and those not reporting it ($t(98)=-4.67$, $P<.001$) with a mean difference of 2589 (SD 554) steps/day and large effect size (Cohen $d=-0.94$) (fig. 7.5).

No significant differences were found in avDS between participants with and without FOG ($t(98)=0.74$, $P=.46$), between participants with and without fatigue ($t(98)=0.61$, $P=.55$), between participants with and without wearing-off ($t(98)=-0.39$, $P=.70$). Overall, the mean MCID across the disease-related PROs variables was 1592 steps/day (range 594-2589) corresponding to 27% of the avDS in our population. The 3 calculated MCIDs, as well as the anchors and the avDS modification related to anchors significant changes are reported in fig. 7.2.

A



B

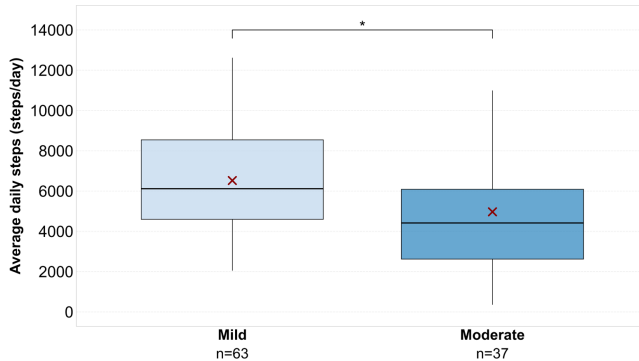


Figure 7.3. Differences across disease phenotypes, severity, and duration groups. Boxplots showing average daily steps in people with Parkinson disease across disease phenotypes (panel A) and disease severity (panel B). Thick line in the boxes indicates median; lower and upper box limits indicate first quartile (Q1) and third quartile (Q3), respectively; black vertical lines indicate lower and upper outliers boundaries calculated as $Q1 - (1.5 \times IQR)$ and $Q3 + (1.5 \times IQR)$, respectively. Red X indicates mean values for each disease group. Significant pairwise comparisons are marked by brackets and asterisks. IND: indeterminate; PIGD: postural instability and gait disorder; TD: tremor dominant. * $P < .05$; ** $P < .01$; *** $P < .001$; **** $P < .0001$.

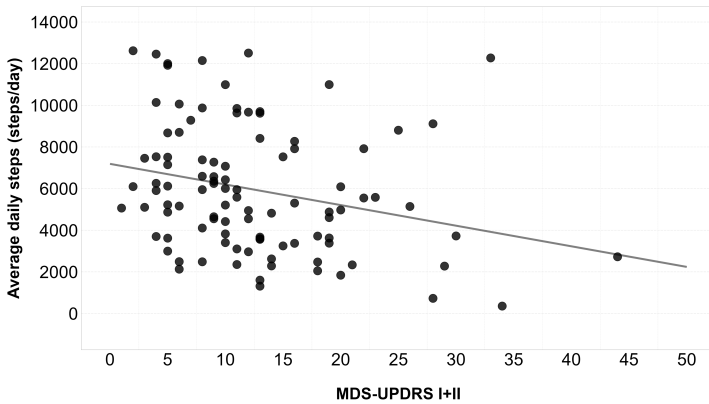


Figure 7.4. Correlation between average daily steps and Movement Disorder Society Unified Parkinson Disease Rating Scale I+II. A linear regression line was added to show the linear tendency. MDS-UPDRS: Movement Disorder Society Unified Parkinson Disease Rating Scale.

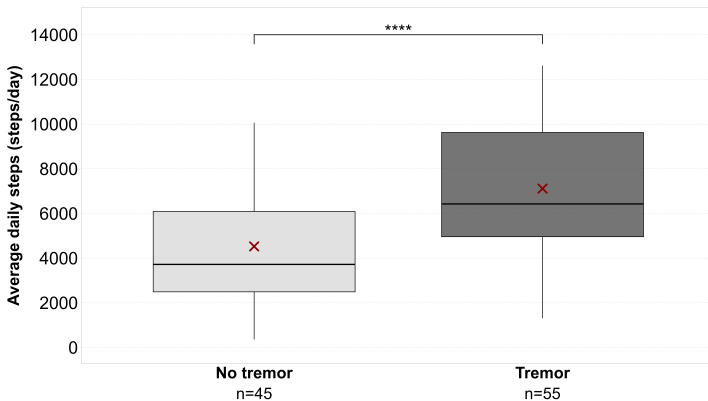


Figure 7.5. Differences between people with Parkinson disease with and without tremor. Boxplots are reported showing average daily steps in people with Parkinson disease with and without tremor. Thick line in the boxes indicates median; lower and upper box limits indicate first quartile (Q1) and third quartile (Q3), respectively; black vertical lines indicate lower and upper outliers boundaries calculated as $Q1 - (1.5 \times IQR)$ and $Q3 + (1.5 \times IQR)$, respectively. Red X indicates mean values for each disease group. Significant pairwise comparisons are marked by brackets and asterisks. PD: Parkinson disease. * $P < .05$; ** $P < .01$; *** $P < .001$; **** $P < .0001$.

Table 7.2. Minimal clinically important differences for average daily steps for each of the 3 identified levels. The clinically significant anchor change and the corresponding average daily steps variation is reported next to each variable.

Anchors	avDS changes	MCIDs
Global mobility and motor functions		
MDS-UPDRS-III (4 points)	608	581
SPPB (1 point)	554	
Clinical and health-related measures		
mHY (0.5 points)	1304	1200
LEDD (100 mg)	350	
Age (10 y)	1410	
Disease duration (5 y)	900	
Phenotype (TD, PIGD, or IND)	1683	
Symptoms severity (mild or moderate)	1554	
Disease-related PRO		
MDS-UPDRS I+II	594	1592
Tremor or no tremor (MDS-UPDRS 2.10)	2589	

avDS: average daily steps; IND: indeterminate; LEDD: Levodopa equivalent daily dose; MCID: minimal clinically important difference; MDS-UPDRS: Movement Disorder Society Unified Parkinson Disease Rating Scale; mHY: modified Hoehn and Yahr scale; PD: Parkinson disease; PIGD: postural instability and gait disorder; PRO: patient-reported outcome; SPPB: short physical performance battery; TD: tremor dominant.

Discussion

Principal Findings

In this cross-sectional study, we aimed to calculate, for the first time, the MCID for avDS as an indicator of free-living walking behavior in people with PD using a consumer smartwatch under real-world conditions. We identified 3 distinct levels of MCID for avDS. The first level, of around 580 steps/day, is anchored to standardized measures of motor symptoms and mobility. The second level, of around 1200 steps/day, is based on clinical and health-related variables. Finally, the third level, of around 1590 steps/day, is anchored on disease-related PROs.

Globally, the MCID values ranged from 581 to 1592 steps/day, representing 10%-27% of the average in our study population. We used the method used by Motl and colleagues (Motl et al., 2013), which offers the advantage of delineating distinct levels of clinically meaningful changes in real-world walking behavior for people with PD. These 3 thresholds provide a versatile framework for assessing the impact of clinical interventions in people with PD, depending on their specific goals and expected outcomes. Furthermore, the MCID estimates for avDS can be used either independently or in conjunction with other MCIDs, as presented in this manuscript for clinical assessment tools, to offer a more comprehensive evaluation of clinically meaningful changes in individuals with PD.

Our results suggest that a value of around 580 steps/day might reflect the smallest clinically meaningful change in avDS when measured by a consumer smartwatch and should be considered when designing a study including interventions focused on mobility or motor condition improvement. Differently, when global disease and health status are the main outcomes, our results showed that a larger value of around 1200 steps/day might be considered to define a clinically meaningful change. In the last decades, a growing importance has been attributed to PROs, such as patient-reported scales, quality of life questionnaires, etc, as vital indicators of people perception of their own condition (Martinez-Martin et al., 2008). PROs are often central outcomes in patients' perspectives and might capture some aspects that cannot be evaluated through objective measurements. The use of these outcomes is encouraged to guide research and clinical practice in the context of a patient-centered model of care and several PROs were included in a recent consensus on outcome measures for PD (de Roos et al., 2017). To this end, in this paper, we calculated that a change of around 1590 steps/day might be considered to define a clinically meaningful intervention when patients' self-perception is the main outcome.

It is also vital to consider the feasibility of achieving changes in avDS of the magnitudes identified in this study. Previous research has explored interventions in people with PD that use daily steps as an outcome measure (Ellis et al., 2019; Handlery et al., 2021). In a study by Handlery and colleagues (Handlery et al., 2021), people with PD who initially took fewer than 4200 steps per day managed to increase their daily step count by approximately 1250 steps/day 6 months after participating in high-intensity treadmill exercises (Handlery et al., 2021). Similarly, another randomized controlled trial by Ellis and colleagues (Ellis et al., 2019) involving 44 people with PD found that participants who initially averaged fewer than 7500 steps per day increased their avDS by about 763 steps/day over a year, following an mobile health-supported exercise program. These findings suggest that achieving changes comparable with the MCID values identified in our study is feasible through interventions aimed at promoting physical activity.

Nevertheless, the capability of consumer devices to accurately detect changes of the magnitude reported here is crucial for their clinical utility. In a recent study of ours, we found that for a monitoring duration of at least 4 days, the MDC for the Garmin Vivosmart 4 ranged between 1198 and 1524 steps/day, averaging at 1366 steps/day (Bianchini et al., 2023). This MDC value is higher than the smaller MCID we calculated, indicating that any observed change exceeding this threshold is not only beyond the realm of measurement

error but also clinically significant. However, this also implies that the device might not be sensitive enough to consistently detect subtler yet clinically meaningful changes in avDS, as indicated by the lower MCID limit of approximately 580 steps/day. Consequently, while the Garmin Vivosmart 4 can be effective in measuring significant differences in avDS in people with PD, for smaller anticipated changes, other instruments with higher reliability need to be considered. Future research should therefore investigate the performance of various consumer smartwatches and other devices such as smart socks, insoles, etc, and their applicability across different neurological conditions to validate, refine, and possibly extend our findings.

Limitations

We recognize certain limitations in our study. First, the people with PD included in our study displayed relatively high levels of physical capacity, as evidenced by a median SPPB score of 10 (9-12), and adequate cognitive functions, due to our exclusion of participants with a MoCA score below 21. In addition, those with more advanced disease stages or requiring walking aids were not part of our study group. This selection criteria potentially limits the generalizability of our findings to only mild-to-moderate people with PD. Indeed, in a population of individuals with worse cognitive and motor conditions, we might expect lower accuracy and reliability of avDS estimate by smartwatches and less steps/day due to greater walking impairments (Cohen & Verghese, 2019; Hobert et al., 2019; Rosenfeldt et al., 2024). Therefore, higher absolute and relative MCID values as well as different anchors combinations could be observed. Nevertheless, the sample in our study can be seen as representative of the typical target demographic for interventions using consumer-grade wearable technology. In fact, including people with PD with a disease stage greater than 3, those using walking aids, or with more severe cognitive impairments, poses significant challenges in the use of consumer technology and was beyond our study's scope. Eventually, the evaluation of people using walking aids with commercial out-of-the-shelf devices, without more advanced data processing, might not even be feasible due to the potential inadequate accuracy of smartwatch for measuring daily steps among this patient population, whose mobility characteristics differ substantially from those of individuals with physiological ambulation (García-Bustillo et al., 2022). Future research incorporating participants with PD with lower functional scores, increased disease severity, and more pronounced cognitive impairments would be valuable.

In addition, while we incorporated a range of general and disease-specific measurements, other factors that might affect daily life mobility, such as fear of falling, frontal executive cognitive dysfunction, and objectively measured gait parameters (eg, gait speed, cadence, and step length), were not examined. Furthermore, specific subdomains of adopted measurement tools could be further explored (eg, walking speed or balance subitems of SPPB and PIGD subscore of MDS-UPDRS part III). Further studies exploring the relationship between these factors and smartwatch-recordable parameters are recommended to provide a more comprehensive understanding of mobility in people with PD.

In addition, we did not extract the raw data from the smartwatches, but used the information reported by the device's dashboard. While acknowledging the technical limitations of this approach, we designed the study to mimic as closely as possible the actual use of the device in a real-world context and to use parameters as similar as possible to those that a general user would have access to. Finally, in this work, we used an anchor-based cross-sectional method to define different levels MCID as presented by Motl et al (Motl et al., 2013). However, other anchor-based methods are available. In particular, a widely used method consists in the longitudinal calculation of MCID following an intervention (Byrom et al., 2020; Sedaghat, 2019). However, while this latter method could allow to draw more sound conclusions, it must be considered that it might be dependent on the type of interventions used, thus hampering the generalizability. Furthermore, previous evidence highlighted the sample-specificity of MCID estimates (particularly for distribution-

based methods) (Wright et al., 2012) and the dependency on the baseline scores of the enrolled population (Wang et al., 2011). This further stresses the importance of conducting future longitudinal, multicenter, studies in a free-living context including independent cohorts of people with PD with different clinical baseline conditions, from different clinical centers—and even different countries—and using different evaluation tools to confirm and expand the results hereby presented. In addition, since different methods to calculate MCID could lead to different results (Franceschini et al., 2023), using different techniques and comparing them will be important to provide the best scientific evidence on this topic. Nevertheless, we considered it relevant to provide researchers with a first indication of MCID for avDS as measured by a consumer smartwatch in order to build a framework to interpret findings in studies incorporating this outcome measure. In fact, researchers designing a study (eg, a clinical trial that aims at assessing the effectiveness of an intervention specifically designed to increase physical activity in PD) and incorporating smartwatch-based avDS as an outcome measure of physical activity will be able to define end points that are clinically relevant, beyond statistical significance. Furthermore, based on the other included endpoints (ie, mobility, clinical indicators, or PROs), investigators will be able to select the more appropriate MCID level.

Conclusions

We reported 3 levels of MCID for avDS measured through Garmin Vivosmart 4, for 5 consecutive days, 1 of approximately 580 steps/day (or about 10% of our population's average) anchored to standardized measures of motor symptoms and mobility. A second, of around 1200 steps/day (or about 20% of the mean in our population), anchored to clinical and health-related variables. Finally, a third, or around 1590 steps/day (or about 27% of the mean in our population) anchored to disease-related PROs. Considering that the previously reported MCD for Garmin Vivosmart 4 was 1366 steps/day, this indicate that any observed change exceeding this threshold is not only beyond the realm of measurement error but also clinically meaningful. Furthermore, based on previous studies, we could suppose that achieving changes comparable with the smaller MCID identified in our study might be feasible following interventions aimed at promoting physical activity in people with PD. These findings, together with existing evidence for reliability and validity on consumer smartwatches, could be relevant for designing future clinical trials involving avDS as an outcome measure of real-world walking behavior in PD, and evaluating the effectiveness of intervention promoting free-living walking.

References

- Adler, C. H., Beach, T. G., Zhang, N., Shill, H. A., Driver-Dunkley, E., Mehta, S. H., Atri, A., Caviness, J. N., Serrano, G., Shprecher, D. R., Sue, L. I., & Belden, C. M. (2021). Clinical Diagnostic Accuracy of Early/Advanced Parkinson Disease: An Updated Clinicopathologic Study. *Neurology. Clinical Practice*, 11(4), e414–e421. <https://doi.org/10.1212/CPJ.0000000000001016>
- Bassett, D. R., Toth, L. P., LaMunion, S. R., & Crouter, S. E. (2017). Step Counting: A Review of Measurement Considerations and Health-Related Applications. *Sports Medicine (Auckland, N.Z.)*, 47(7), 1303–1315. <https://doi.org/10.1007/s40279-016-0663-1>
- Bate, G. L., Kirk, C., Rehman, R. Z. U., Guan, Y., Yarnall, A. J., Del Din, S., & Lawson, R. A. (2023). The Role of Wearable Sensors to Monitor Physical Activity and Sleep Patterns in Older Adult Inpatients: A Structured Review. *Sensors (Basel, Switzerland)*, 23(10), 4881. <https://doi.org/10.3390/s23104881>
- Bianchini, E., Rinaldi, D., De Carolis, L., Galli, S., Alborghetti, M., Hansen, C., Suppa, A., Salvetti, M., Pontieri, F., & Vuillerme, N. (2025). Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study. *JMIR Formative Research*, 9. <https://doi.org/10.2196/63153>
Export Date: 14 April 2025; Cited By: 0.
- Bianchini, E., Calì, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzler, W., & Pontieri, F. E. (2022). Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, 23(1), 214. <https://doi.org/10.3390/s23010214>
- Bianchini, E., Galli, S., Alborghetti, M., De Carolis, L., Zampogna, A., Hansen, C., Vuillerme, N., Suppa, A., & Pontieri, F. E. (2023). Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch [Number: 21 Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 23(21), 8971. <https://doi.org/10.3390/s23218971>
- Bianchini, E., & Maetzler, W. (2023, May). Wearable systems in movement disorders. In *International Review of Movement Disorders*. Academic Press. <https://doi.org/10.1016/bs.irmvd.2023.04.002>
- Bloom, D. A., Kaplan, D. J., Mojica, E., Strauss, E. J., Gonzalez-Lomas, G., Campbell, K. A., Alaia, M. J., & Jazrawi, L. M. (2023). The Minimal Clinically Important Difference: A Review of Clinical Significance. *The American Journal of Sports Medicine*, 51(2), 520–524. <https://doi.org/10.1177/03635465211053869>
- Brewer, W., Swanson, B. T., & Ortiz, A. (2017). Validity of Fitbit's active minutes as compared with a research-grade accelerometer and self-reported measures. *BMJ open sport & exercise medicine*, 3(1), e000254. <https://doi.org/10.1136/bmjsem-2017-000254>
- Byrom, B., Breedon, P., Tulkki-Wilke, R., & Platko, J. V. (2020). Meaningful change: Defining the interpretability of changes in endpoints derived from interactive and mHealth technologies in healthcare and clinical research. *Journal of Rehabilitation and Assistive Technologies Engineering*, 7, 2055668319892778. <https://doi.org/10.1177/2055668319892778>
- Chandrabhatla, A. S., Pomeranec, I. J., & Ksendzovsky, A. (2022). Co-evolution of machine learning and digital technologies to improve monitoring of Parkinson's disease motor symptoms. *NPJ digital medicine*, 5(1), 32. <https://doi.org/10.1038/s41746-022-00568-y>
- Chow, J. J., Thom, J. M., Weweg, M. A., Ward, R. E., & Parmenter, B. J. (2017). Accuracy of step count measured by physical activity monitors: The effect of gait speed and anatomical placement site. *Gait & Posture*, 57, 199–203. <https://doi.org/10.1016/j.gaitpost.2017.06.012>
- Cohen, J. A., & Verghese, J. (2019). Gait and dementia. *Handbook of Clinical Neurology*, 167, 419–427. <https://doi.org/10.1016/B978-0-12-804766-8.00022-4>

- Correno, M. B., Hansen, C., Chardon, M., Milane, T., Bianchini, E., & Vuillerme, N. (2022). Association between Backward Walking and Cognition in Parkinson Disease: A Systematic Review. *International Journal of Environmental Research and Public Health*, 19(19), 12810. <https://doi.org/10.3390/ijerph191912810>
- De Carolis, L., Galli, S., Bianchini, E., Rinaldi, D., Raju, M., Calì, B., Alborghetti, M., & Pontieri, F. E. (2023). Age at Onset Influences Progression of Motor and Non-Motor Symptoms during the Early Stage of Parkinson's Disease: A Monocentric Retrospective Study. *Brain Sciences*, 13(2), 157. <https://doi.org/10.3390/brainsci13020157>
- de Roos, P., Bloem, B. R., Kelley, T. A., Antonini, A., Dodel, R., Hagell, P., Marras, C., Martinez-Martin, P., Mehta, S. H., Odin, P., Chaudhuri, K. R., Weintraub, D., Wilson, B., & Uitti, R. J. (2017). A Consensus Set of Outcomes for Parkinson's Disease from the International Consortium for Health Outcomes Measurement. *Journal of Parkinson's disease*, 7(3), 533–543. <https://doi.org/10.3233/JPD-161055>
- Degroote, L., De Bourdeaudhuij, I., Verloigne, M., Poppe, L., & Crombez, G. (2018). The Accuracy of Smart Devices for Measuring Physical Activity in Daily Life: Validation Study. *JMIR mHealth and uHealth*, 6(12), e10972. <https://doi.org/10.2196/10972>
- Del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK. *JAMA neurology*, 79(10), 1059–1063. <https://doi.org/10.1001/jamaneurol.2022.2672>
- Del Pozo Cruz, B., Ahmadi, M. N., Lee, I.-M., & Stamatakis, E. (2022). Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. *JAMA internal medicine*. <https://doi.org/10.1001/jamainternmed.2022.4000>
- Ellis, T. D., Cavanaugh, J. T., DeAngelis, T., Hendron, K., Thomas, C. A., Saint-Hilaire, M., Pencina, K., & Latham, N. K. (2019). Comparative Effectiveness of mHealth-Supported Exercise Compared With Exercise Alone for People With Parkinson Disease: Randomized Controlled Pilot Study. *Physical Therapy*, 99(2), 203–216. <https://doi.org/10.1093/ptj/pzy131>
- Fokkema, T., Kooiman, T. J. M., Krijnen, W. P., VAN DER Schans, C. P., & DE Groot, M. (2017). Reliability and Validity of Ten Consumer Activity Trackers Depend on Walking Speed. *Medicine and Science in Sports and Exercise*, 49(4), 793–800. <https://doi.org/10.1249/MSS.0000000000001146>
- Franceschini, M., Boffa, A., Pignotti, E., Andriolo, L., Zaffagnini, S., & Filardo, G. (2023). The Minimal Clinically Important Difference Changes Greatly Based on the Different Calculation Methods. *The American Journal of Sports Medicine*, 51(4), 1067–1073. <https://doi.org/10.1177/03635465231152484>
- García-Bustillo, Á., Valiñas-Sieiro, F., Allende-Río, M., González-Santos, J., Cubo, E., & and the Multidisciplinary Telemedicine Group. (2022). Assistive Devices for Personal Mobility in Parkinson's Disease: A Systematic Review of the Literature. *Movement Disorders Clinical Practice*, 9(8), 1040–1046. <https://doi.org/10.1002/mdc3.13568>
- Ginis, P., Goris, M., De Groef, A., Blondeel, A., Gilat, M., Demeyer, H., Troosters, T., & Nieuwboer, A. (2023). Validation of Commercial Activity Trackers in Everyday Life of People with Parkinson's Disease. *Sensors*, 23(8). <https://doi.org/10.3390/s23084156> Export Date: 14 April 2025; Cited By: 6.
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., Giladi, N., Holloway, R. G., Moore, C. G., Wenning, G. K., Yahr, M. D., Seidl, L., & Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 19(9), 1020–1028. <https://doi.org/10.1002/mds.20213>
- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R.,

- Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Handlery, R., Stewart, J. C., Pellegrini, C., Monroe, C., Hainline, G., Flach, A., Handlery, K., & Fritz, S. (2021). Physical Activity in De Novo Parkinson Disease: Daily Step Recommendation and Effects of Treadmill Exercise on Physical Activity. *Physical Therapy*, 101(10), pzab174. <https://doi.org/10.1093/ptj/pzab174>
- Hergenroeder, A. L., Barone Gibbs, B., Kotlarczyk, M. P., Kowalsky, R. J., Perera, S., & Brach, J. S. (2018). Accuracy of Objective Physical Activity Monitors in Measuring Steps in Older Adults. *Gerontology & Geriatric Medicine*, 4, 2333721418781126. <https://doi.org/10.1177/2333721418781126>
- Hobert, M. A., Nussbaum, S., Heger, T., Berg, D., Maetzler, W., & Heinzel, S. (2019). Progressive Gait Deficits in Parkinson's Disease: A Wearable-Based Biannual 5-Year Prospective Study. *Frontiers in Aging Neuroscience*, 11, 22. <https://doi.org/10.3389/fnagi.2019.00022>
- Horváth, K., Aschermann, Z., Ács, P., Deli, G., Janszky, J., Komoly, S., Balázs, É., Takács, K., Karádi, K., & Kovács, N. (2015). Minimal clinically important difference on the Motor Examination part of MDS-UPDRS. *Parkinsonism & Related Disorders*, 21(12), 1421–1426. <https://doi.org/10.1016/j.parkreldis.2015.10.006>
- Inoue, K., Tsugawa, Y., Mayeda, E. R., & Ritz, B. (2023). Association of Daily Step Patterns With Mortality in US Adults. *JAMA network open*, 6(3), e235174. <https://doi.org/10.1001/jamanetworkopen.2023.5174>
- Jost, S. T., Kaldenbach, M.-A., Antonini, A., Martinez-Martin, P., Timmermann, L., Odin, P., Katzenschlager, R., Borgohain, R., Fasano, A., Stocchi, F., Hattori, N., Kukkle, P. L., Rodríguez-Violante, M., Falup-Pecurariu, C., Schade, S., Petry-Schmelzer, J. N., Metta, V., Weintraub, D., Deuschl, G., ... International Parkinson and Movement Disorders Society Non-Motor Parkinson Disease Study Group. (2023). Levodopa Dose Equivalency in Parkinson's Disease: Updated Systematic Review and Proposals. *Movement Disorders: Official Journal of the Movement Disorder Society*, 38(7), 1236–1252. <https://doi.org/10.1002/mds.29410>
- Kim, D. W., Hassett, L. M., Nguy, V., & Allen, N. E. (2019). A Comparison of Activity Monitor Data from Devices Worn on the Wrist and the Waist in People with Parkinson's Disease. [Place: United States]. *Movement disorders clinical practice*, 6(8), 693–699. <https://doi.org/10.1002/mdc3.12850>
- Lamont, R. M., Daniel, H. L., Payne, C. L., & Brauer, S. G. (2018). Accuracy of wearable physical activity trackers in people with Parkinson's disease. [Place: England]. *Gait & posture*, 63, 104–108. <https://doi.org/10.1016/j.gaitpost.2018.04.034>
- Lee, I.-M., Shiroma, E. J., Kamada, M., Bassett, D. R., Matthews, C. E., & Buring, J. E. (2019). Association of Step Volume and Intensity With All-Cause Mortality in Older Women. *JAMA internal medicine*, 179(8), 1105–1112. <https://doi.org/10.1001/jamainternmed.2019.0899>
- Lee, M., Noh, Y., Youm, C., Kim, S., Park, H., Noh, B., Kim, B., Choi, H., & Yoon, H. (2021). Estimating Health-Related Quality of Life Based on Demographic Characteristics, Questionnaires, Gait Ability, and Physical Fitness in Korean Elderly Adults. *International Journal of Environmental Research and Public Health*, 18(22), 11816. <https://doi.org/10.3390/ijerph182211816>
- Lexell, J. E., & Downham, D. Y. (2005). How to assess the reliability of measurements in rehabilitation. *American Journal of Physical Medicine & Rehabilitation*, 84(9), 719–723. <https://doi.org/10.1097/01.phm.0000176452.17771.20>
- Liu, M., Gan, X., Ye, Z., Zhang, Y., He, P., Zhou, C., Yang, S., Zhang, Y., & Qin, X. (2023). Association of accelerometer-measured physical activity intensity, sedentary time, and exercise time with incident Parkinson's disease. *NPJ digital medicine*,

- 6(1), 224. <https://doi.org/10.1038/s41746-023-00969-7>
- Löhle, M., Timpka, J., Bremer, A., Khodakarami, H., Gandor, F., Horne, M., Ebersbach, G., Odin, P., & Storch, A. (2023). Application of single wrist-wearable accelerometry for objective motor diary assessment in fluctuating Parkinson's disease. *NPJ digital medicine*, 6(1), 194. <https://doi.org/10.1038/s41746-023-00937-1>
- MacKinnon, C. D. (2018). Sensorimotor anatomy of gait, balance, and falls. *Handbook of Clinical Neurology*, 159, 3–26. <https://doi.org/10.1016/B978-0-444-63916-5.00001-X>
- Mantese, C. E., Schumacher-Schuh, A., & Rieder, C. R. M. (2018). Clinimetrics of the 9- and 19-Item Wearing-Off Questionnaire: A Systematic Review. *Parkinson's Disease*, 2018, 5308491. <https://doi.org/10.1155/2018/5308491>
- Mantri, S., Wood, S., Duda, J., & Morley, J. (2019). Comparing self-reported and objective monitoring of physical activity in Parkinson disease. *Parkinsonism and Related Disorders*, 67, 56–59. <https://doi.org/10.1016/j.parkreldis.2019.09.004>
Export Date: 14 April 2025; Cited By: 36.
- Martinez-Martin, P., Rodriguez-Blazquez, C., & Frades-Payo, B. (2008). Specific patient-reported outcome measures for Parkinson's disease: Analysis and applications. *Expert Review of Pharmacoeconomics & Outcomes Research*, 8(4), 401–418. <https://doi.org/10.1586/14737167.8.4.401>
- Martínez-Martín, P., Rodríguez-Blázquez, C., Mario Alvarez, n., Arakaki, T., Arillo, V. C., Chaná, P., Fernández, W., Garretto, N., Martínez-Castrillo, J. C., Rodríguez-Violante, M., Serrano-Dueñas, M., Ballesteros, D., Rojo-Abuin, J. M., Chaudhuri, K. R., & Merello, M. (2015). Parkinson's disease severity levels and MDS-Unified Parkinson's Disease Rating Scale. *Parkinsonism & Related Disorders*, 21(1), 50–54. <https://doi.org/10.1016/j.parkreldis.2014.10.026>
- McLeod, L. D., Coon, C. D., Martin, S. A., Fehnel, S. E., & Hays, R. D. (2011). Interpreting patient-reported outcome results: US FDA guidance and emerging methods. *Expert Review of Pharmacoeconomics & Outcomes Research*, 11(2), 163–169. <https://doi.org/10.1586/erp.11.12>
- Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L., Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)
- Motl, R. W., Pilutti, L. A., Learmonth, Y. C., Goldman, M. D., & Brown, T. (2013). Clinical importance of steps taken per day among persons with multiple sclerosis. *PLoS One*, 8(9), e73247. <https://doi.org/10.1371/journal.pone.0073247>
- Nieuwboer, A., Rochester, L., Herman, T., Vandenberghe, W., Emil, G. E., Thomaes, T., & Giladi, N. (2009). Reliability of the new freezing of gait questionnaire: Agreement between patients with Parkinson's disease and their carers. *Gait & Posture*, 30(4), 459–463. <https://doi.org/10.1016/j.gaitpost.2009.07.108>
- Paluch, A. E., Bajpai, S., Bassett, D. R., Carnethon, M. R., Ekelund, U., Evenson, K. R., Galuska, D. A., Jefferis, B. J., Kraus, W. E., Lee, I.-M., Matthews, C. E., Omura, J. D., Patel, A. V., Pieper, C. F., Rees-Punia, E., Dallmeier, D., Klenk, J., Whincup, P. H., Dooley, E. E., ... Fulton, J. E. (2022). Daily steps and all-cause mortality: A meta-analysis of 15 international cohorts [Publisher: Elsevier]. *The Lancet Public Health*, 7(3), e219–e228. [https://doi.org/10.1016/S2468-2667\(21\)00302-9](https://doi.org/10.1016/S2468-2667(21)00302-9)
- Perera, S., Mody, S. H., Woodman, R. C., & Studenski, S. A. (2006). Meaningful change and responsiveness in common physical performance measures in older adults. *Journal of the American Geriatrics Society*, 54(5), 743–749. <https://doi.org/10.1111/j.1532-5415.2006.00701.x>
- Peto, V., Jenkinson, C., Fitzpatrick, R., & Greenhall, R. (1995). The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, 4(3), 241–248. <https://doi.org/10.1007/BF02260863>

- Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., Obeso, J., Marek, K., Litvan, I., Lang, A. E., Halliday, G., Goetz, C. G., Gasser, T., Dubois, B., Chan, P., Bloem, B. R., Adler, C. H., & Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 30(12), 1591–1601. <https://doi.org/10.1002/mds.26424>
- Powers, R., Etezadi-Amoli, M., Arnold, E. M., Kianian, S., Mance, I., Gibiansky, M., Trietsch, D., Alvarado, A. S., Kretlow, J. D., Herrington, T. M., Brillman, S., Huang, N., Lin, P. T., Pham, H. A., & Ullal, A. V. (2021). Smartwatch inertial sensors continuously monitor real-world motor fluctuations in Parkinson's disease. *Science Translational Medicine*, 13(579), eabd7865. <https://doi.org/10.1126/scitranslmed.abd7865>
- Prange, S., Danaila, T., Laurencin, C., Caire, C., Metereau, E., Merle, H., Broussolle, E., Maucourt-Boulch, D., & Thobois, S. (2019). Age and time course of long-term motor and nonmotor complications in Parkinson disease. *Neurology*, 92(2), e148–e160. <https://doi.org/10.1212/WNL.0000000000006737>
- Revicki, D., Hays, R. D., Cella, D., & Sloan, J. (2008). Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *Journal of Clinical Epidemiology*, 61(2), 102–109. <https://doi.org/10.1016/j.jclinepi.2007.03.012>
- Rosenfeldt, A. B., Jansen, A. E., Lopez-Lennon, C., Zimmerman, E., Imrey, P. B., Dibble, L. E., & Alberts, J. L. (2024). Physical Activity Declines over a 12-Month Period in Parkinson's Disease: Considerations for Longitudinal Activity Monitoring. *Medicine and Science in Sports and Exercise*. <https://doi.org/10.1249/MSS.00000000000003615>
- Saint-Maurice, P. F., Troiano, R. P., Bassett, D. R., Graubard, B. I., Carlson, S. A., Shihoma, E. J., Fulton, J. E., & Matthews, C. E. (2020). Association of Daily Step Count and Step Intensity With Mortality Among US Adults. *JAMA*, 323(12), 1151–1160. <https://doi.org/10.1001/jama.2020.1382>
- Sedaghat, A. R. (2019). Understanding the Minimal Clinically Important Difference (MCID) of Patient-Reported Outcome Measures. *Otolaryngology–Head and Neck Surgery: Official Journal of American Academy of Otolaryngology–Head and Neck Surgery*, 161(4), 551–560. <https://doi.org/10.1177/0194599819852604>
- Siciliano, M., Chiorri, C., De Micco, R., Russo, A., Tedeschi, G., Trojano, L., & Tesitore, A. (2019). Fatigue in Parkinson's disease: Italian validation of the Parkinson Fatigue Scale and the Fatigue Severity Scale using a Rasch analysis approach. *Parkinsonism & Related Disorders*, 65, 105–110. <https://doi.org/10.1016/j.parkreldis.2019.05.028>
- Skidmore, F. M., Mackman, C. A., Pav, B., Shulman, L. M., Garvan, C., Macko, R. F., & Heilman, K. M. (2008). Daily ambulatory activity levels in idiopathic Parkinson disease. *Journal of Rehabilitation Research and Development*, 45(9), 1343–1348.
- Soulard, J., Carlin, T., Knitza, J., & Vuillerme, N. (2022). Wearables for Measuring the Physical Activity and Sedentary Behavior of Patients With Axial Spondyloarthritis: Systematic Review. *JMIR mHealth and uHealth*, 10(8), e34734. <https://doi.org/10.2196/34734>
- Stebbins, G. T., Goetz, C. G., Burn, D. J., Jankovic, J., Khoo, T. K., & Tilley, B. C. (2013). How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: Comparison with the unified Parkinson's disease rating scale. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(5), 668–670. <https://doi.org/10.1002/mds.25383>
- Svarre, F. R., Jensen, M. M., Nielsen, J., & Villumsen, M. (2020). The validity of activity trackers is affected by walking speed: The criterion validity of Garmin Vivosmart® HR and StepWatch™ 3 for measuring steps at various walking speeds under controlled conditions. *PeerJ*, 8, e9381. <https://doi.org/10.7717/peerj.9381>
- Tanji, H., Gruber-Baldini, A. L., Anderson, K. E., Pretzer-Aboff, I., Reich, S. G., Fishman, P. S., Weiner, W. J., & Shulman, L. M. (2008). A comparative study of physical performance measures in Parkinson's disease. *Movement Disorders: Official Journal of the*

Movement Disorder Society, 23(13), 1897–1905. <https://doi.org/10.1002/mds.22266>

Topalidis, P., Florea, C., Eigl, E.-S., Kuraopov, A., Leon, C. A. B., & Schabus, M. (2021). Evaluation of a Low-Cost Commercial Actigraph and Its Potential Use in Detecting Cultural Variations in Physical Activity and Sleep. *Sensors (Basel, Switzerland)*, 21(11), 3774. <https://doi.org/10.3390/s21113774>

Treacy, D., Hassett, L., Schurr, K., Chagpar, S., Paul, S. S., & Sherrington, C. (2017). Validity of Different Activity Monitors to Count Steps in an Inpatient Rehabilitation Setting. *Physical Therapy*, 97(5), 581–588. <https://doi.org/10.1093/ptj/pzx010>

Wang, Y.-C., Hart, D. L., Stratford, P. W., & Mioduski, J. E. (2011). Baseline dependency of minimal clinically important improvement. *Physical Therapy*, 91(5), 675–688. <https://doi.org/10.2522/ptj.20100229>

Wendel, N., Macpherson, C. E., Webber, K., Hendron, K., DeAngelis, T., Colon-Semenza, C., & Ellis, T. (2018). Accuracy of Activity Trackers in Parkinson Disease: Should We Prescribe Them? [Place: United States]. *Physical therapy*, 98(8), 705–714. <https://doi.org/10.1093/ptj/pzy054>

Wright, A., Hannon, J., Hegedus, E. J., & Kavchak, A. E. (2012). Clinimetrics corner: A closer look at the minimal clinically important difference (MCID). *The Journal of Manual & Manipulative Therapy*, 20(3), 160–166. <https://doi.org/10.1179/2042618612Y.0000000001>

Zhang, Y., Xi, X., & Huang, Y. (2023). The anchor design of anchor-based method to determine the minimal clinically important difference: A systematic review. *Health and Quality of Life Outcomes*, 21(1), 74. <https://doi.org/10.1186/s12955-023-02157-3>

Zou, H., Goetz, C. G., Stebbins, G. T., Schrag, A., Mestre, T. A., & Luo, S. (2023). Summing MDS-UPDRS Parts 1 + 2 (Non-motor and Motor Experience of Daily Living): The Patient’s Voice. *Movement disorders : official journal of the Movement Disorder Society*, 38(7), 1363–1364. <https://doi.org/10.1002/mds.29417>

CLINICAL APPLICATIONS

Chapter 8

Contribution 5: A Bayesian model averaging analysis to compare in-clinic walking *capacity* versus real-world walking *performance* in people with Parkinson's disease from digital health technologies

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Abstract

Background: Wearable technologies enable continuous monitoring of walking behavior in people with Parkinson's disease (PwPD). While in-clinic assessments quantify walking capacity, wearable devices capture walking performance in real-life conditions. However, it remains unclear to what extent supervised mobility metrics explain free-living walking behavior in PwPD. **Objective:** To investigate the relationship between in-clinic mobility capacity and real-world walking performance in PwPD, using a Bayesian Model Averaging (BMA) framework. **Methods:** We analyzed cross-sectional data from 113 mild-to-moderate PwPD, with a disease stage <4, without cognitive impairment and able to walk unaided, recruited at a university hospital. Participants underwent three supervised tasks while wearing an inertial sensor: forward walking (20 m), instrumented Timed Up and Go (iTUG), and 3-m backward walking test. Twelve gait and turning parameters were extracted, screened for collinearity, and reduced via stepwise Akaike Information Criterion selection. Average daily steps (AvDS), collected with a Garmin Vivosmart 4 over five consecutive days, were used as the measure of real-world walking performance. BMA regression models were computed with AvDS as the dependent variable. Posterior inclusion probabilities, credible intervals, model-averaged R², and predictive R² were calculated. **Results:** Participants (mean age 68.8±8.6 years; 32% female; median Hoehn & Yahr 2 (2-2.5)) walked an average of 5800±2978 steps/day. After collinearity screening, four supervised metrics (cadence, stride length normalized to height, swing phase duration, and iTUG peak angular velocity) were retained in BMA. All showed positive associations with AvDS, with stride length emerging as the strongest determinant. The final BMA model explained 23.6% of AvDS variance, with a predictive R² of 26.7%. The cumulative posterior probability of the top five models was 57.8%, reflecting residual model uncertainty. **Conclusions:** In PwPD, clinic-based capacity explain only a limited portion of walking performance, even when incorporating multiple tasks. Real-world walking is likely influenced by additional determinants, including non-motor symptoms, motor fluctuations, motivation, cognition, and environmental barriers, not captured by standard supervised tasks. These results highlight the need for integrative assessment strategies that combine wearable-based performance monitoring with contextual and psychosocial factors. Bridging the capacity-performance gap may improve clinical evaluation, guide outcome selection in trials, and inform the design of more personalized rehabilitation interventions in PD.

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor symptoms including bradykinesia, rigidity, tremor, and postural instability (Poewe et al., 2017). These often manifest as progressive gait disturbances, such as shuffling steps, reduced step length, diminished arm swing, and freezing of gait, which are common and disabling features of PD (Mirelman et al., 2019). Such mobility deficits substantially compromise functional independence and quality of life in people with PD (PwPD) and markedly increase the risk of falls and related injuries (Fasano et al., 2017; Mirelman et al., 2019). Effective assessment of mobility in PD is therefore critical, both for monitoring disease progression and for guiding interventions aimed at improving safety and daily functioning.

Advances in wearable sensor technology have made it possible to quantify mobility objectively in both controlled clinical settings and uncontrolled real-world environments (Moreau et al., 2023). Therefore, wearable devices have the potential to collect information regarding either capacity (i.e., the individual's ability to execute a task under supervised conditions) or performance (i.e., the execution of tasks in daily life) or both, depending on their context of use (Maetzler et al., 2013, 2021). Importantly, consumer wearable devices are now widely available and easy to use, facilitating ambulatory, scalable monitoring (Bassett et al., 2017; Moreau et al., 2023; Peters et al., 2021). This creates an opportunity to compare traditional clinical mobility metrics to real-world outcomes in PD.

In PD, to the best of our knowledge, only few published articles have investigated this aspect (Atrsaei, Corrà, et al., 2021; Corrà et al., 2021; Del Din et al., 2016; Toosizadeh et al., 2015; Zajac et al., 2022). Toosizadeh et al. reported that corresponding supervised and unsupervised mobility parameters (i.e., gait speed, duration of sit-to-stand and stand-to-sit transitions) showed no association in 15 PwPD (Toosizadeh et al., 2015). Three other studies showed that free-living data showed low to moderate correlations with laboratory parameters in PwPD (Atrsaei, Corrà, et al., 2021; Corrà et al., 2021; Del Din et al., 2016). Finally, a recent study reported that standard gait tests (6-minute walking test and 10-meter walk) explained only 7–13% of the variance in PwPD daily step count (Zajac et al., 2022).

Indeed, mobility itself is a multidimensional construct. Most PD studies to date have focused on forward walking (FW) under supervised controlled conditions (Atrsaei, Corrà, et al., 2021; Corrà et al., 2021; Del Din et al., 2016; Toosizadeh et al., 2015; Zajac et al., 2022). However, everyday mobility entails much more than FW. Indeed, standing up from a chair, walking backward and turning are component of everyday mobility. PwPD commonly experience major difficulties with turning, negotiating direction changes, transitioning between postures (such as rising from a chair), and backward walking (BW), even in early disease stages (Bianchini, Warmerdam, et al., 2023; Hackney & Earhart, 2009; Mancini et al., 2015; Milane et al., 2023; Stack & Ashburn, 2008). These complex motor tasks are critical components of functional mobility and are particularly sensitive to PD deficits. However, they are not routinely captured by the simple, and often single, straight-walking tests used in many clinical assessments.

In terms of performance, average daily steps (AvDS) has emerged as a simple yet powerful indicator of unsupervised mobility. Daily step count is easy to collect continuously via wearable activity monitors and has high ecological validity as a measure of habitual ambulatory activity (Bassett et al., 2017). Though it does not capture detailed gait features, a lower daily step count is broadly associated with worse health outcomes and greater mobility limitation. Previous studies, indeed, have linked step count to general mortality (Inoue et al., 2023; Lee et al., 2019; Paluch et al., 2022) and the incidence of various medical conditions, including cancer (Del Pozo Cruz, Ahmadi, et al., 2022), cardiovascular disease (Del Pozo Cruz, Ahmadi, et al., 2022), depression (Bizzozero-Peroni et al., 2024), and dementia (Del Pozo Cruz, Ahmadi, et al., 2022) in elderly.

In PD, research has shown an association between AvDS and disease severity (Skidmore et al., 2008), as well as physical activity levels (Mantri et al., 2019), underlining the potential usefulness of this metric for the management of PwPD.

Despite these advances, to the best of our knowledge, no study has yet explored how a comprehensive panel of supervised mobility tasks, including FW, BW and turning, relates to free-living walking in PD. Previous investigations have focused on limited subsets of capacity metrics derived in the vast majority from FW, such as FW speed and other spatiotemporal parameters (Atrsaiei, Corrà, et al., 2021; Corrà et al., 2021; Del Din et al., 2016; Toosizadeh et al., 2015; Zajac et al., 2022) or endurance (Zajac et al., 2022) and therefore cannot determine whether other mobility types offer additional explanatory power. Clarifying these relationships is crucial for designing clinic assessments that reflect real-world challenges and for tailoring rehabilitation to the capacity factors most strongly linked to everyday walking. Therefore, the aim of this study was to investigate the relationship between multiple walking capacity metrics, including FW, BW and turning, and real-world walking performance in a cohort of mild-to-moderate PwPD. We could hypothesize that, expanding the range of walking capacity metrics, purposely chosen to encompass various aspects of everyday mobility, a larger portion of real-world mobility performance variability could be explained.

Materials and Methods

Study design and ethics

This was an analysis conducted on a cross-sectional dataset of mild-to-moderate PwPD collected to validate wearable-based measures and investigate the interaction between mobility, motor and non-motor symptoms in PwPD. Approval was granted by the local Ethical Committee of Sapienza, University of Rome (Ref. 0372/2022). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines. This study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki of 1964 and subsequent amendments. Data collection and processing were carried out in compliance with current European data protection regulations. All data were deidentified. Participants did not receive any form of compensation.

Population

Participants were consecutively recruited from the Movement Disorders Centre at Sant'Andrea University Hospital (A.O.U. Sant'Andrea) in Rome between February 2023 and May 2024. Inclusion criteria included: (i) diagnosis of idiopathic Parkinson's disease according to the MDS criteria (Postuma et al., 2015); (ii) age 18 years or older; (iii) disease stage < 4 according to the modified Hoehn and Yahr scale (mHY) ("severe disability; still able to walk or stand unassisted") (Goetz et al., 2004); (iv) ability to perform the experimental procedure; and (v) availability of data regarding supervised mobility parameters and AvDS. Exclusion criteria were: (i) severe cognitive impairment as defined by a Montreal Cognitive Assessment (MoCA) score < 18 (Baek et al., 2024); and (ii) orthopedic, rheumatologic, or systemic conditions affecting mobility as judged by the assessor.

Experimental Procedure

Participants meeting the inclusion and exclusion criteria were evaluated during their regular follow-up visits at the Neurology clinics of A.O.U. Sant'Andrea in Rome. All evaluations were performed in ON pharmacological state. Demographic (age, sex), anthropometric (body weight, body height, body mass index [BMI]) and clinical data (disease duration,

levodopa equivalent daily dose [LEDD], mHY) were collected. The Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) parts III (Goetz et al., 2008) was used to assess motor symptoms severity. The MoCA (Nasreddine et al., 2005) was used to evaluate global cognition. The MoCA is an extensively used screening tool to assess global cognition and the presence of cognitive impairment. The score ranges from 0 to 30 and a lower score indicates worse cognitive performance. Freezing of gait (FOG) was assessed using the New Freezing of Gait Questionnaire (NFOG-Q) (Nieuwboer et al., 2009). A score ≥ 1 at item 1 of the questionnaire was used to define the presence of FOG.

To collect data regarding capacity, participants were asked to perform two supervised mobility tasks while wearing a lower-back mounted research-grade inertial device (BTS G-WALK, BTS Engineering Inc., Milan) (Vítečková et al., 2020): (i) a 20-meter FW task; (ii) an instrumented Timed Up and Go (iTUG) (Ortega-Bastidas et al., 2023). Additionally, a 3-meter Backward Walk Test (3MBWT) was performed according with previous validation studies (Barta et al., 2025; Kocer et al., 2023). These three tasks were selected to include various mobility types in the supervised assessment, including FW, BW, turning and postural transitions. From the FW, spatiotemporal gait parameters were measured, including FW speed (m/s), cadence (steps/min), stride length normalized to height (%), cycle duration (s), stance and swing phases duration expressed as % of gait cycle. These were classified in parameters of pace (FW speed, cadence and stride length) and rhythm (cycle duration, stance and swing) according to the framework proposed by Lord et al. (Lord, Godfrey, et al., 2013; Mancini et al., 2025). For the iTUG, total iTUG duration (s), mean and peak angular velocity ($^{\circ}$ /s) (MAV and PAV, respectively) of the intermediate 180° turn as well as duration of the turning (s) were collected. Variables of iTUG were divided in turning-related parameters (turning duration, MAV and PAV) and global mobility (iTUG duration). For the 3MBWT, PwPD performed 3 trials. The average of the time (s) to complete each trial was collected (Kocer et al., 2023) and BW speed (m/s) was computed.

To collect data regarding performance, participants were then asked to wear the Garmin Vivosmart 4 smartwatch (Garmin, Olathe, KS, USA), configured according to the manufacturer's specifications by indicating the users' age, height, weight, and the wrist on which the smartwatch was worn (i.e., left or right), on the wrist of the less affected side, in line with previous research findings (Bianchini, Rinaldi, et al., 2025; Bianchini, Alborghetti, et al., 2025; Bianchini, Galli, et al., 2023; Bianchini et al., 2022) for 5 consecutive days. We choose a 5-day period since we demonstrated previously that a minimum of 4 days of monitoring is needed to reliably estimate daily step count in PwPD (Bianchini, Galli, et al., 2023) and that 5 days of monitoring led to acceptable reliability regardless of PD severity, stage and phenotype (Bianchini, Rinaldi, et al., 2025). Moreover, in a proof-of-concept experiment, we recently demonstrated that Garmin Vivosmart 4 was valid and decently accurate in estimating avDS in PD (Bianchini, Rinaldi, et al., 2025).

Participants were instructed to wear the smartwatch all time during day and night and remove it only when involved in water activities (e.g., bathing, showering, swimming, etc.). Participants were asked to perform daily activities as usual. No additional reminder or instructions were provided to participants during the monitoring period and participants could access information on the smartwatch screen, including the total number of steps, heart rate and sleep time. The device did not provide instructions, alerts or other messages to participants. The total daily steps recorded were extracted, and the average daily steps (AvDS) were calculated (Bianchini, Galli, et al., 2023). Compliance was assessed based on the participants' dashboard data. We could assess that the device was worn through heart rate and activity data. We considered all recording days with $\geq 80\%$ wear time while awake to be valid. We estimated the awake time as 24 hours minus the total sleep time as indicated by the device (Bianchini, Rinaldi, et al., 2025). Experimental procedure is summarized in Figure 8.1.

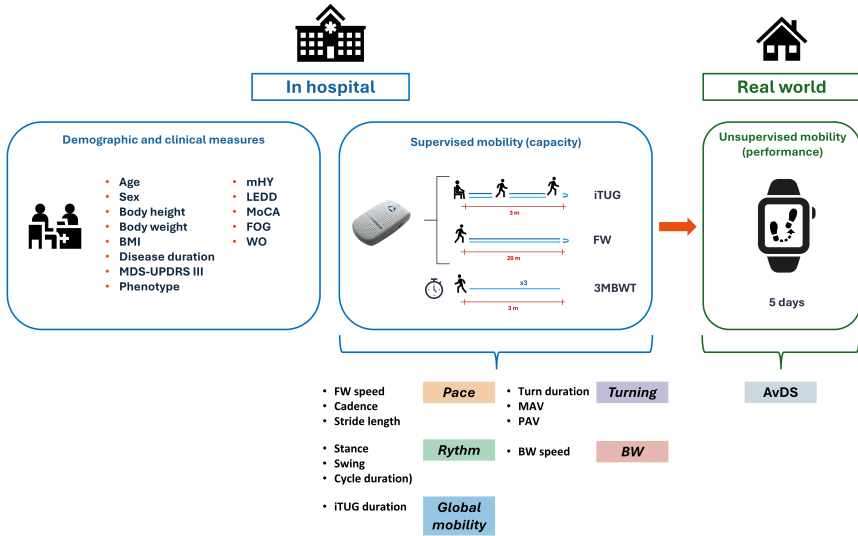


Figure 8.1. Schematic representation of study experimental procedure and outcome measures. 3MBWT: 3-meter backward walking test; AvDS: average daily steps; BMI: body mass index; BW: backward walking; FOG: Freezing of gait; FW: forward walking; iTUG: instrumented Timed Up and Go; LEDD: Levodopa equivalent daily dose; MAV: Mean angular velocity; MDS-UPDRS: Movement Disorder Society Unified Parkinson's disease rating scale; mHY: Modified Hoehn and Yahr stage; MoCA: Montreal cognitive assessment; PAV: Peak angular velocity; WO: Wearing-off.

Statistical analyses

Statistical analyses were performed using JASP (version 0.19.3.0; JASP Team, University of Amsterdam, The Nederland) and R software (version 4.4.5®) for Windows. Descriptive statistics were calculated for all variables under study. Continuous variables were reported as mean (SD) or median (Q1-Q3), and categorical variables as frequency and percentage (N (%)). To assess which supervised mobility parameters (capacity) were associated with AvDS (performance), a Bayesian Model Averaging (BMA) analysis for linear regression was conducted, with AvDS as the dependent variable and capacity metrics as independent variables. A preliminary selection of covariates was performed by assessing multicollinearity using the Variance Inflation Factor (VIF), excluding those with VIF values exceeding 2.5. An initial stepwise variable selection approach based on Akaike Information Criterion (AIC) was then applied using the `stepAIC()` function from the MASS package in R (version 7.3.64) (Venables & Ripley, 2002), to further reduce dimensionality and identify the most relevant covariates. This procedure used bidirectional elimination, iteratively adding or removing variables to minimize the AIC. BMA was then applied to the subset of selected covariates using the `bic.glm()` function from the BMA package in R (version 3.18.20). For each covariate, we computed the posterior inclusion probability ($P[\beta \neq 0]$), the posterior coefficient expected value (pEV), the posterior coefficient standard deviation (pSD) and the 95% credible intervals (CrI, calculated as $pEV \pm 1.96 \cdot pSD$). Covariates with a pos-

terior inclusion probability $\geq 10\%$ were considered determinant factors of AvDS. We also computed the posterior probability (PP) for each of the top 5 BMA models, along with their cumulative posterior probability (CPP). Finally, a model-averaged coefficient of determination (R^2) was calculated by weighting each model's R^2 by its posterior probability. A predictive R^2 was also computed to evaluate the model's generalizability.

Results

Overview

A total of 113 mild-to-moderate PwPD who met the pre-specified inclusion and exclusion criteria were included in the study. The demographic, anthropometric and clinical features are summarized in Table 8.1.

Table 8.1. Demographic, anthropometric and clinical characteristics of the enrolled population.

Variable	PwPD (N=113)
Age (years)	68.8 (8.6)
Sex (F)	36 (32%)
Body height (cm)	172 (9)
Body weight (kg)	76.1 (13.1)
BMI (m/kg^2)	25.7 (3.4)
Disease duration (years)	5.9 (3.9)
LEDD (mg)	523 (273)
mHY	2 (2–2.5)
MDS-UPDRS part III	25 (21–32)
MoCA	26 (25–28)
WO	35 (31%)
FOG	13 (12%)
Phenotype	
<i>TD</i>	35 (31%)
<i>PIGD</i>	68 (60%)
<i>Indeterminate</i>	10 (9%)

BMI: Body mass index; LEDD: Levodopa equivalent daily dose; MDS-UPDRS: Movement Disorder Society Unified Parkinson's Disease Rating Scale; mHY: Modified Hoehn and Yahr stage; MoCA: Montreal Cognitive Assessment; PwPD: people with Parkinson's disease; WO: Wearing-off; FOG: Freezing of gait; TD: Tremor-dominant; PIGD: Postural instability and gait disorder.

The summary of the twelve mobility variables in our population is shown in Table 8.2.

Table 8.2. Mobility parameters in the enrolled population.

Variable	PwPD (N=113)
AvDS (steps/day)	5800 (2978)
FW speed (m/s)	1.19 (0.22)
Cadence (steps/min)	112.3 (8.2)
Stride length% (%height)	74.3 (10.9)
Stance (%cycle)	61.1 (2.2)
Swing (%cycle)	38.9 (2.2)
Cycle duration (s)	1.09 (0.08)
iTUG duration (s)	11.8 (3.8)
Turn duration (s)	2.66 (0.96)
MAV ($^{\circ}$ /s)	71.0 (17.8)
PAV ($^{\circ}$ /s)	141.3 (40.6)
BW speed (m/s)	0.60 (0.22)

AvDS: average daily steps; BW: backward walking; FW: forward walking; iTUG: instrumented timed-up-and-go; MAV: mean angular velocity; PAV: peak angular velocity; PwPD: people with Parkinson disease.

Bayesian Model Averaging

Of the eleven mobility covariates initially considered (FW speed, cadence, stride length, stance, swing, cycle duration, iTUG duration, turn duration, MAV, PAV, BW speed), five were excluded due to collinearity (FW speed, stance, cycle duration, iTUG duration, MAV). The subsequent stepwise selection procedure identified four covariates to be included in the BMA analysis: cadence, stride length, swing and PAV. All the four above-mentioned covariates were identified as determinants of AvDS. Each of these four variables demonstrated a positive association with AvDS, indicating that higher values were associated with better walking performance. Among them, stride length percentage emerged as the strongest determinant, followed by PAV, swing, and cadence (Figure 2). The final BMA model explained 23.6% of the variance of AvDS. The CPP of the top 5 BMA models (out of 12) was 57.8%, and the model-averaged predictive R^2 , reflecting the models' ability to generalize to new data, was 26.7%. Table 8.3 summarizes the overall characteristics of the final and top 5 BMA models whereas Table 8.4 presents the features of the 4 included covariates.

Table 8.3. Overall BMA results and features of the top 5 BMA models (M1-M5).

Variable	M1	M2	M3	M4	M5
(Intercept)	-2579.6	-9026.6	-9591.1	-9819.0	-3127.3
Cadence (steps/min)				65.50	
Stride length% (%height)	76.38		61.73	111.26	120.22
Swing (%cycle)		279.27	209.75		
PAV ($^{\circ}$ /s)	19.17	27.99	18.70		
BIC	-405.16	-403.91	-403.59	-403.58	-403.53
PP	0.200	0.107	0.092	0.091	0.089
CPP (top 5 models)	0.578				
BMA R^2	0.236				
Predictive R^2	0.267				

BMA: Bayesian Model Averaging; BIC: Bayesian information criterion; PAV: peak angular velocity; PP: posterior probability; CPP: cumulative posterior probability.

Table 8.4. BMA results for the included coefficients.

Variable	$P[\beta \neq 0]$ (%)	pEV	pSD	CrI LB	CrI UP
(Intercept)	100.00	-8285.3	6710.0	-21436.9	4866.3
Cadence (steps/min)	41.10	25.33	36.24	-45.70	96.35
Stride length% (%height)	73.10	62.85	47.66	-30.57	156.27
Swing (%cycle)	45.10	113.12	148.80	-178.52	404.76
PAV ($^{\circ}$ /s)	70.30	15.36	12.40	-8.94	39.66

BMA: Bayesian Model Averaging; CrI LB: credible interval lower bound; CrI LB: credible interval upper bound; $P[\beta \neq 0]$: posterior probability to be non-zero (%); PAV: peak angular velocity; pEV: posterior coefficient expected value; pSD: posterior coefficient standard deviation (from model averaging).

Details regarding the posterior inclusion probability ($P[\beta \neq 0]$) for each of the four determinants included in the BMA as well as the PP for each of the twelve models are shown in Figure 8.2.

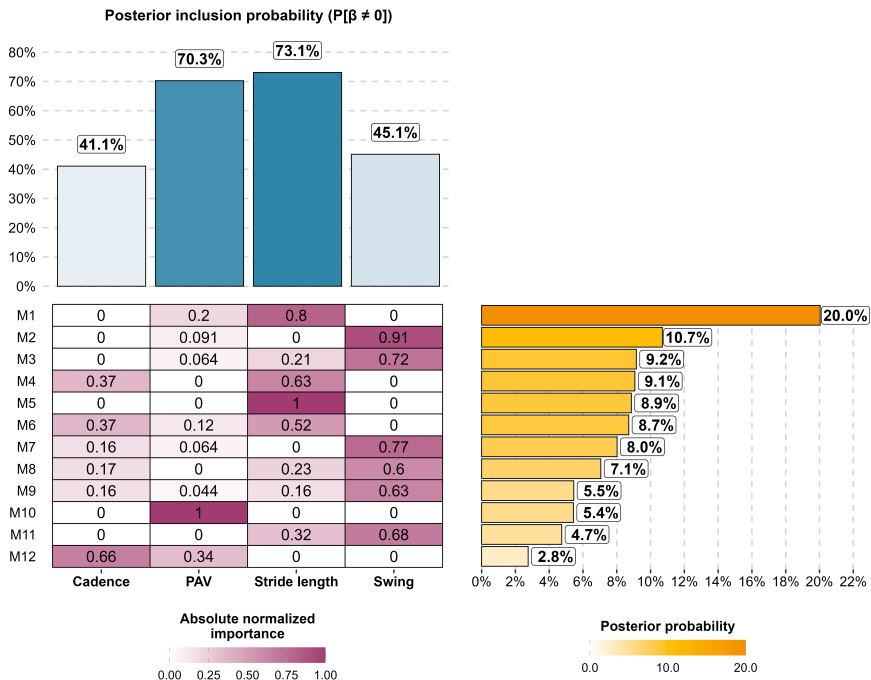


Figure 8.2. Features of models and predictors included in the BMA. Bottom left: heatmap showing the absolute normalized importance for each feature (columns) in all of the 12 models (rows). The absolute normalized importance of each feature is calculated by taking the absolute value of a feature’s maximum likelihood estimates (MLE) of its coefficient in a given model and dividing it by the sum of the absolute MLE values of all feature coefficients in that model. This yields a proportion between 0 and 1, indicating the contribution of each feature relative to the others within the same model based on its fitted coefficients, rather than integrating over uncertainty. The higher the absolute normalized importance, the more influential the feature is. Bottom right: barplot showing the posterior probability for each model. Top: barplot displaying the posterior inclusion probability of each of the four features included in the BMA (i.e., the sum of the posterior probabilities of all models that include that feature).

Discussion

This was an analysis conducted on a cross-sectional dataset of mild-to-moderate PwPD to test whether in-clinic walking capacity predicts real-world walking performance in mild-to-moderate PD. We found that capacity only explained around 20–30% of the variance in daily step count, confirming a considerable capacity/performance gap even when considering a wider range of supervised mobility tasks including FW, BW and turning.

We found that the best model accounted for roughly one quarter of AvDS variability ($R^2 =$

23.6%). Our results extend prior observations of a capacity–performance discrepancy in PD. Zajac et al. reported that standard gait tests (6-minute walk and 10-meter walk) explained only 7–13% of the variance in PD patients’ step count (Zajac et al., 2022). Toosizadeh and collaborators also reported that corresponding supervised and unsupervised mobility parameters (i.e., gait speed, duration of sit-to-stand and stand-to-sit transitions) showed no association in PwPD (Toosizadeh et al., 2015). Finally, three other studies showed that real-world walking performance data, including spatiotemporal gait parameters and spontaneous physical activity metrics, showed low to moderate correlations with laboratory-based gait spatiotemporal parameters in PwPD (Atrsaee, Corrà, et al., 2021; Corrà et al., 2021; Del Din et al., 2016). Although the population is different, our findings are also comparable to those observed in other neurological disorders (Danks et al., 2016; Mate & Mayo, 2020; Stellmann et al., 2015). In multiple sclerosis, previous studies reported that laboratory-based walk tests did not reliably correspond to the amount of walking in real world conditions (Mate & Mayo, 2020; Stellmann et al., 2015). Similarly, in stroke patients, capacity only explained around 35% of performance variance (Danks et al., 2016). Taken together, these results underscore that, even including different supervised mobility tasks (i.e., FW, BW, and turning), capacity predicts only a fraction of walking performance. Moreover, the slight increase from model R^2 to predictive R^2 shows that the covariates retain similar explanatory power in unseen data. While underscoring a limited over-fitting, these findings indicate that, practically, clinicians can expect capacity measures to explain about 25% of step-count variance in a comparable PD cohort.

When considering the CPP, the five highest-probability models together held only 57.8% of the total posterior probability. This indicates that single model uncertainty remains important and relying on just the top/best model (PP = 20.0%) would ignore more than half of the information. This warns against over-interpreting any one model and justifies the BMA approach, which averages across the full model set and yields effect estimates that are less sensitive to arbitrary variable inclusion. Globally, these findings also suggest that, in PD, factors not captured by capacity tests, even including more complex mobility tasks, dominate real-world performance, likely accounting for over 70% of AvDS variability.

To this regards, the wide spectrum on non-motor symptoms (NMS) in PD should be considered. NMS in PD include mood disturbances, anxiety, autonomic dysfunction, sleep problems, fatigue, cognitive impairment, urinary and gastrointestinal problems (Schapira et al., 2017). These could fluctuate during the day and significantly impact mobility performance. Indeed, apathy and depression, which are prevalent in PD, negatively impact walking capacity in these patients (Lord, Galna, et al., 2013). Fatigue is another critical factor and a common PD symptom. Previous studies indicated that PwPD with higher fatigue tend to be more sedentary and have worse functional mobility in daily life (Garber & Friedman, 2003). Moreover, recent evidence showed that unsupervised mobility was associated with fatigue whereas supervised mobility did not show a significant correlation (Pilotto et al., 2023). This further highlights how capacity and performance could be affected differently by NMS in PD. Anxiety and fear of falling may also cause individuals to avoid certain activities or walking opportunities. Indeed, fear of falling can negatively impact turning behaviour in a different fashion between in clinic and at home (Haertner et al., 2018). Furthermore, a previous study reported that PwPD with fear of falling showed a reduced turning velocity during the stand-to-sit phase of TUG but also showed a tendency toward lower gait speed at home and a lower amount of walking bouts (Atrsaee, Hansen, et al., 2021). Finally, executive function and attentional capacity might limit multitasking during everyday walking, an occurrence extremely common in daily mobility tasks, further reducing real-world mobility in individuals with cognitive impairment, even if their single-task gait in the clinic appears acceptable (Salazar et al., 2017).

We must also consider that PD symptoms fluctuate during the day. Usually, when assessing capacity, only a single condition is studied (i.e., ON or OFF) therefore we do not capture the entirety of the status that an individuals with PD could experiment during the day,

particularly in the intermediate and advanced stages of the disease. In our study, we only assessed ON status during capacity evaluation. Moreover, 31 (35%) of our participants resulted to have a clinically relevant WO as indicated by a score at WOQ-19 ≥ 2 . Indeed, a previous study from Corrà and collaborators showed that capacity metrics measured in ON or OFF states showed associations with specific component of real-world performance (Corrà et al., 2021). Specifically, ON assessments in the lab showed moderate-to-high correlations with faster gait speeds in unsupervised environment (linked to longer walking bouts) whereas OFF gait in the lab showed moderate correlation with slow gait speeds at home (linked to shorter walking bouts) (Corrà et al., 2021).

Beyond disease-related factors, lack of control of the home environment (e.g., uneven terrain, stairs, time constraints, weather conditions, social support, transport, walkability of the surroundings, season of the year, and lack of assistive devices or encouragement, etc.) further modulate opportunities to walk (Roussos et al., 2022). As previous work noted, patients navigate obstacles and distractions at home that are absent in the clinic, contributing to slower and more variable gait in daily life (Warmerdam et al., 2020). The International Classification of Functioning framework groups these influences under “personal” and “environmental” factors (which can be included in the broader concept of exposome Ibanez et al., 2024; Li et al., 2024), distinct from body-function capacity (Organization, 2002). Their omission likely accounts for a large share of the residual unexplained variance of AvDS. In stroke, for instance, adding balance confidence to capacity tests boosts step-prediction by around 15% (Danks et al., 2016); similar gains are plausible in PD once personal and environmental variables are included. However, these are challenging to measure and most of the technology available to collect performance data in unsupervised conditions cannot provide contextual information, particularly inertial motion units. To this regards, a great effort has been put in the last years to integrate these wearables with other sensors to improve contextual data collection (e.g., GPS, barometers, thermometers, infrared signals, etc.). From a clinical point of view, our results encourage a more global approach to evaluating and promoting mobility in PD. The observation that standard mobility tests performed under supervised, controlled setting, explain only a small fraction of daily walking behaviour means that clinicians should not rely solely on those tests to infer how active or independent a patient is in their home environment. Device-based activity monitoring (e.g., with wearable devices or smartphone apps) can provide complementary information, revealing a patient’s actual performance and day-to-day variability. Moreover, incorporating data regarding personal and environmental elements could further improve the ability to identify why a patient with adequate capacity remains sedentary. Our results could be also relevant to define endpoints to evaluate interventions in PD. In fact, an improvement of capacity not necessarily corresponds to an improvement in performance and interventions purely focused on the former may not automatically yield gains in the latter unless barriers to real-world activity are concurrently addressed. Indeed, a previous study reported that in a large cohort (N=156) of individuals with PD or post-stroke undergoing outpatient rehabilitation, around 60% improved in capacity but did not concurrently improved in performance and only around 20% of participants improved in both domains. This underscores the issue of capacity-performance gap in clinical practice and advocates for clinicians to address both domains when evaluating the effectiveness of interventions (Lang et al., 2023).

Limitations

We acknowledge several limitations in this study. Firstly, its cross-sectional design prevents us from inferring causal relationships. Moreover, the sample included only individuals in the mild-to-moderate stages of PD, excluding those with more severe cognitive or motor impairments. As a result, the generalizability of our findings to later disease stages is limited, and future research involving broader disease severity is warranted. The mobility assessment was also limited: supervised mobility was measured using spatiotemporal gait and turning metrics, while unsupervised mobility relied solely on AvDS. Incorporating a

more comprehensive range of mobility indicators, especially under real-world conditions, could enhance our understanding of ecological mobility. In recent years, international initiatives like Mobilise-D Consortium (Micó-Amigo et al., 2023) have focused on validating digital mobility outcomes captured in free-living settings. Therefore, evaluating comparable gait metrics (e.g., gait speed, step length) across both supervised and unsupervised conditions may yield important insights into their interrelation. Allowing participants to view their smartwatch data may have influenced their activity behavior during monitoring. Indeed, prior research has shown that access to activity tracker feedback can promote higher physical activity levels (Ferguson et al., 2022). We acknowledged this potential source of systematic bias, as also done in previous work by our group (Bianchini, Alborghetti, et al., 2025), but considered it acceptable since our objective was to replicate real-world conditions as closely as possible. Preventing data access would not have reflected typical everyday use. The adoption of consumer-grade smartwatches also raises concerns related to data security, privacy, and the availability of raw data. In our study, all procedures strictly followed the manufacturer's instructions, ensuring compliance with European Union data protection regulations. Because the device's proprietary algorithm is not publicly disclosed, we could not evaluate its possible influence on the outcomes. The Garmin Vivosmart 4 requires users to provide basic demographic and anthropometric information (age, weight, height). However, how these parameters are incorporated into the device's calculations remains unclear. Moreover, raw data from Garmin devices are not accessible through the standard user interface, limiting opportunities for advanced or standardized analytical processing. This limitation, however, was outside the scope of the present work, since our primary aim was to test smartwatches under conditions resembling their everyday application.

Despite these limitations, our study presents notable strengths. One is the broad range of supervised mobility tasks assessed, including FW, BW, turning and postural transitions, going beyond prior studies focused solely on linear FW (Atrsaei, Corrà, et al., 2021; Corrà et al., 2021; Zajac et al., 2022). Another key strength lies in our statistical approach. Unlike traditional multivariable regression, BMA accounts for model uncertainty by integrating across multiple plausible models, each weighted by its posterior probability. This strategy minimizes overfitting and yields more reliable estimates of variable importance. Furthermore, BMA facilitates the evaluation of the evidence supporting the inclusion of each predictor, offering a more refined interpretation. Lastly, our findings emphasize the value of integrating both supervised and unsupervised mobility assessments to achieve a comprehensive evaluation of PwPD.

Conclusions

In conclusion, this study demonstrates that even an extensive, in-clinic, supervised mobility evaluation explains only a limited portion of the variability in how much PwPD walk in their daily lives. This result highlights how real-world mobility is driven by more than just physical capacity and suggest that personal and environmental factors play a crucial role. Closing this capacity/performance gap will require broadening our perspective beyond the lab, addressing the personal and contextual determinants that ultimately determine everyday functional mobility in PD. As a whole, the present findings could be relevant to guide PwPD assessment, select outcome measures for future studies and help selecting relevant endpoints for rehabilitation programs in PD to meaningfully improve patients' daily lives.

References

- Atrsaeci, A., Corrà, M. F., Dadashi, F., Vila-Chã, N., Maia, L., Mariani, B., Maetzler, W., & Aminian, K. (2021). Gait speed in clinical and daily living assessments in Parkinson's disease patients: Performance versus capacity. *NPJ Parkinson's disease*, 7(1), 24. <https://doi.org/10.1038/s41531-021-00171-0>
- Atrsaeci, A., Hansen, C., Elshehabi, M., Solbrig, S., Berg, D., Liepelt-Scarfone, I., Maetzler, W., & Aminian, K. (2021). Effect of Fear of Falling on Mobility Measured During Lab and Daily Activity Assessments in Parkinson's Disease. *Frontiers in Aging Neuroscience*, 13, 722830. <https://doi.org/10.3389/fnagi.2021.722830>
- Baek, K., Kim, Y. M., Na, H. K., Lee, J., Shin, D. H., Heo, S.-J., Chung, S. J., Kim, K., Lee, P. H., Sohn, Y. H., Yoon, J., & Kim, Y. J. (2024). Comparing Montreal Cognitive Assessment Performance in Parkinson's Disease Patients: Age- and Education-Adjusted Cutoffs vs. Machine Learning. *Journal of Movement Disorders*, 17(2), 171–180. <https://doi.org/10.14802/jmd.23271>
- Barta, K., Boddy, A. H., Flores, M., Perry, L., Sawyer, K., & Campbell, A. (2025). Psychometric properties of 3-meter backward walk test (3MBWT) in people with Parkinson disease. *Physiotherapy Theory and Practice*, 41(3), 656–663. <https://doi.org/10.1080/09593985.2024.2348034>
- Bassett, D. R., Toth, L. P., LaMunion, S. R., & Crouter, S. E. (2017). Step Counting: A Review of Measurement Considerations and Health-Related Applications. *Sports Medicine (Auckland, N.Z.)*, 47(7), 1303–1315. <https://doi.org/10.1007/s40279-016-0663-1>
- Bianchini, E., Rinaldi, D., De Carolis, L., Galli, S., Alborghetti, M., Hansen, C., Suppa, A., Salvetti, M., Pontieri, F., & Vuillerme, N. (2025). Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study. *JMIR Formative Research*, 9. <https://doi.org/10.2196/63153>
- Export Date: 14 April 2025; Cited By: 0.
- Bianchini, E., Alborghetti, M., Galli, S., Hansen, C., Zampogna, A., Suppa, A., Salvetti, M., Pontieri, F. E., Rinaldi, D., & Vuillerme, N. (2025). Minimal Clinically Important Difference of Average Daily Steps Measured Through a Consumer Smartwatch in People With Mild-to-Moderate Parkinson Disease: Cross-Sectional Study [Company: JMIR mHealth and uHealth Distributor: JMIR mHealth and uHealth Institution: JMIR mHealth and uHealth Label: JMIR mHealth and uHealth Publisher: JMIR Publications Inc., Toronto, Canada]. *JMIR mHealth and uHealth*, 13(1), e64213. <https://doi.org/10.2196/64213>
- Bianchini, E., Calì, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzler, W., & Pontieri, F. E. (2022). Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, 23(1), 214. <https://doi.org/10.3390/s23010214>
- Bianchini, E., Galli, S., Alborghetti, M., De Carolis, L., Zampogna, A., Hansen, C., Vuillerme, N., Suppa, A., & Pontieri, F. E. (2023). Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch [Number: 21 Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 23(21), 8971. <https://doi.org/10.3390/s23218971>
- Bianchini, E., Warmerdam, E., Romijnders, R., Stürner, K. H., Baron, R., Heinzel, S., Pontieri, F. E., Hansen, C., & Maetzler, W. (2023). Turning When Using Smartphone in Persons With and Those Without Neurologic Conditions: Observational Study. *Journal of Medical Internet Research*, 25, e41082. <https://doi.org/10.2196/41082>
- Bizzozero-Peroni, B., Díaz-Goñi, V., Jiménez-López, E., Rodríguez-Gutiérrez, E., Sequí-Domínguez, I., Núñez de Arenas-Arroyo, S., López-Gil, J. F., Martínez-Vizcaíno, V., & Mesas, A. E. (2024). Daily Step Count and Depression in Adults: A Systematic Review and Meta-Analysis. *JAMA network open*, 7(12), e2451208. <https://doi.org/10.1001/jamanetworkopen.2024.51208>

- Corrà, M. F., Atrsaeci, A., Sardoreira, A., Hansen, C., Aminian, K., Correia, M., Vila-Chã, N., Maetzler, W., & Maia, L. (2021). Comparison of Laboratory and Daily-Life Gait Speed Assessment during ON and OFF States in Parkinson's Disease. *Sensors (Basel, Switzerland)*, 21(12), 3974. <https://doi.org/10.3390/s21123974>
- Danks, K. A., Pohlig, R. T., Roos, M., Wright, T. R., & Reisman, D. S. (2016). The Relationship Between Walking Capacity, Biopsychosocial Factors, Self-Efficacy and Walking Activity in Individuals Post Stroke. *Journal of neurologic physical therapy : JNPT*, 40(4), 232–238. <https://doi.org/10.1097/NPT.0000000000000143>
- Del Din, S., Godfrey, A., Galna, B., Lord, S., & Rochester, L. (2016). Free-living gait characteristics in ageing and Parkinson's disease: Impact of environment and ambulatory bout length. *Journal of NeuroEngineering and Rehabilitation*, 13, 46. <https://doi.org/10.1186/s12984-016-0154-5>
- Del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK. *JAMA neurology*, 79(10), 1059–1063. <https://doi.org/10.1001/jamaneurol.2022.2672>
- Del Pozo Cruz, B., Ahmadi, M. N., Lee, I.-M., & Stamatakis, E. (2022). Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. *JAMA internal medicine*. <https://doi.org/10.1001/jamainternmed.2022.4000>
- Fasano, A., Canning, C. G., Hausdorff, J. M., Lord, S., & Rochester, L. (2017). Falls in Parkinson's disease: A complex and evolving picture. *Movement Disorders: Official Journal of the Movement Disorder Society*, 32(11), 1524–1536. <https://doi.org/10.1002/mds.27195>
- Ferguson, T., Olds, T., Curtis, R., Blake, H., Crozier, A. J., Dankiw, K., Dumuid, D., Kasai, D., O'Connor, E., Virgara, R., & Maher, C. (2022). Effectiveness of wearable activity trackers to increase physical activity and improve health: A systematic review of systematic reviews and meta-analyses. *The Lancet. Digital Health*, 4(8), e615–e626. [https://doi.org/10.1016/S2589-7500\(22\)00111-X](https://doi.org/10.1016/S2589-7500(22)00111-X)
- Garber, C. E., & Friedman, J. H. (2003). Effects of fatigue on physical activity and function in patients with Parkinson's disease. *Neurology*, 60(7), 1119–1124. <https://doi.org/10.1212/01.wnl.0000055868.06222.ab>
- Goetz, C. G., Poewe, W., Rascol, O., Sam-paio, C., Stebbins, G. T., Counsell, C., Giladi, N., Holloway, R. G., Moore, C. G., Wenning, G. K., Yahr, M. D., Seidl, L., & Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 19(9), 1020–1028. <https://doi.org/10.1002/mds.20213>
- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Hackney, M. E., & Earhart, G. M. (2009). Backward walking in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 24(2), 218–223. <https://doi.org/10.1002/mds.22330>
- Haertner, L., Elshehabi, M., Zaunbrecher, L., Pham, M. H., Maetzler, C., van Uem, J. M. T., Hobert, M. A., Hucker, S., Nussbaum, S., Berg, D., Liepelt-Scarfone, I., & Maetzler, W. (2018). Effect of Fear of Falling on Turning Performance in Parkinson's Disease in the Lab and at Home. *Frontiers in Aging Neuroscience*, 10, 78. <https://doi.org/10.3389/fnagi.2018.00078>
- Ibanez, A., Melloni, L., Świeboda, P., Hynes, W., Ikiz, B., Ayadi, R., Thioye, M., Walss-Bass, C., Güntekin, B., Mishra, J., Salama, M., Dunlop, S., Duran-Aniotz, C., & Eyre,

- H. A. (2024). Neuroecological links of the exposome and One Health. *Neuron*, 112(12), 1905–1910. <https://doi.org/10.1016/j.neuron.2024.04.016>
- Inoue, K., Tsugawa, Y., Mayeda, E. R., & Ritz, B. (2023). Association of Daily Step Patterns With Mortality in US Adults. *JAMA network open*, 6(3), e235174. <https://doi.org/10.1001/jamanetworkopen.2023.5174>
- Kocer, B., Soke, F., Ataoglu, N. E. E., Ersoy, N., Gulsen, C., Gulsen, E. O., Yasa, M. E., Uysal, I., Comoglu, S. S., & Bora, H. A. T. (2023). The reliability and validity of the 3-m backward walk test in people with Parkinson's disease. *Irish Journal of Medical Science*. <https://doi.org/10.1007/s11845-023-03384-9>
- Lang, C. E., Holleran, C. L., Strube, M. J., Ellis, T. D., Newman, C. A., Fahey, M., DeAngelis, T. R., Nordahl, T. J., Reisman, D. S., Earhart, G. M., Lohse, K. R., & Bland, M. D. (2023). Improvement in the Capacity for Activity Versus Improvement in Performance of Activity in Daily Life During Outpatient Rehabilitation. *Journal of neurologic physical therapy: JNPT*, 47(1), 16–25. <https://doi.org/10.1097/NPT.0000000000000413>
- Lee, I.-M., Shiroma, E. J., Kamada, M., Bassett, D. R., Matthews, C. E., & Buring, J. E. (2019). Association of Step Volume and Intensity With All-Cause Mortality in Older Women. *JAMA internal medicine*, 179(8), 1105–1112. <https://doi.org/10.1001/jamainternmed.2019.0899>
- Li, D., Zhou, L., Cao, Z., Wang, J., Yang, H., Lyu, M., Zhang, Y., Yang, R., Wang, J., Bian, Y., Xu, W., & Wang, Y. (2024). Associations of environmental factors with neurodegeneration: An exposome-wide Mendelian randomization investigation. *Ageing Research Reviews*, 95, 102254. <https://doi.org/10.1016/j.arr.2024.102254>
- Lord, S., Godfrey, A., Galna, B., Mhiripiri, D., Burn, D., & Rochester, L. (2013). Ambulatory activity in incident Parkinson's: More than meets the eye? *Journal of Neurology*, 260(12), 2964–2972. <https://doi.org/10.1007/s00415-013-7037-5>
Export Date: 14 April 2025; Cited By: 135.
- Lord, S., Galna, B., Coleman, S., Burn, D., & Rochester, L. (2013). Mild depressive symptoms are associated with gait impairment in early Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(5), 634–639. <https://doi.org/10.1002/mds.25338>
- Maetzler, W., Domingos, J., Srulijes, K., Ferreira, J. J., & Bloem, B. R. (2013). Quantitative wearable sensors for objective assessment of Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(12), 1628–1637. <https://doi.org/10.1002/mds.25628>
- Maetzler, W., Rochester, L., Bhidayasiri, R., Espay, A. J., Sánchez-Ferro, A., & van Uem, J. M. (2021). Modernizing Daily Function Assessment in Parkinson's Disease Using Capacity, Perception, and Performance Measures [eprint: <https://onlinelibrary.wiley.com/doi/pdf/10.1002/mds.28377>]. *Movement Disorders*, 36(1), 76–82. <https://doi.org/10.1002/mds.28377>
- Mancini, M., El-Gohary, M., Pearson, S., McNames, J., Schlueter, H., Nutt, J. G., King, L. A., & Horak, F. B. (2015). Continuous monitoring of turning in Parkinson's disease: Rehabilitation potential. *NeuroRehabilitation*, 37(1), 3–10. <https://doi.org/10.3233/NRE-151236>
- Mancini, M., Hausdorff, J. M., Pelosin, E., Bonato, P., Camicioli, R., Ellis, T. D., Klucken, J., Gifford, L., Fasano, A., Nieuwboer, A., Kopil, C., Klapper, K., Kirsch, L., Dexter, D. T., Fuest, R., Miller, V., Asis, A., Müller, M. L., Stephenson, D., & Mirelman, A. (2025). A framework to standardize gait study protocols in Parkinson's disease. *Journal of Parkinson's Disease*, 15(1), 129–139. <https://doi.org/10.1177/1877718X241305626>
- Mantri, S., Wood, S., Duda, J., & Morley, J. (2019). Comparing self-reported and objective monitoring of physical activity in Parkinson disease. *Parkinsonism and Related Disorders*, 67, 56–59. <https://doi.org/10.1016/j.parkreldis.2019.09.004>
Export Date: 14 April 2025; Cited By: 36.
- Mate, K. K., & Mayo, N. E. (2020). Clinically Assessed Walking Capacity Versus Real-World Walking Performance in People

with Multiple Sclerosis. *International Journal of MS Care*, 22(3), 143–150. <https://doi.org/10.7224/1537-2073.2019-047>

Micó-Amigo, M. E., Bonci, T., Paraschiv-Ionescu, A., Ullrich, M., Kirk, C., Soltani, A., Küderle, A., Gazit, E., Salis, F., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Brown, P., Buckley, E., Cantu, A., Carsin, A.-E., Caruso, M., Caulfield, B., ... Mobilise-D consortium. (2023). Assessing real-world gait with digital technology? Validation, insights and recommendations from the Mobilise-D consortium. *Journal of Neuroengineering and Rehabilitation*, 20(1), 78. <https://doi.org/10.1186/s12984-023-01198-5>

Milane, T., Hansen, C., Chardon, M., Bianchini, E., & Vuillerme, N. (2023). Comparing Backward Walking Performance in Parkinson's Disease with and without Freezing of Gait-A Systematic Review. *International Journal of Environmental Research and Public Health*, 20(2), 953. <https://doi.org/10.3390/ijerph20020953>

Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L., Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)

Moreau, C., Rouaud, T., Grabli, D., Benatru, I., Remy, P., Marques, A.-R., Drapier, S., Mariani, L.-L., Roze, E., Devos, D., Dupont, G., Bereau, M., & Fabbri, M. (2023). Overview on wearable sensors for the management of Parkinson's disease. *NPJ Parkinson's disease*, 9(1), 153. <https://doi.org/10.1038/s41531-023-00585-y>

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>

Nieuwboer, A., Rochester, L., Herman, T., Vandenbergh, W., Emil, G. E., Thomaes, T., & Giladi, N. (2009). Reliability of the new freezing of gait questionnaire: Agreement between patients with Parkinson's dis-

ease and their carers. *Gait & Posture*, 30(4), 459–463. <https://doi.org/10.1016/j.gaitpost.2009.07.108>

Organization, W. H. (2002). Towards a common language for functioning, disability, and health : ICF [Publisher: World Health Organization]. *The International Classification of Functioning, Disability and Health*. Retrieved May 30, 2025, from <https://cir.nii.ac.jp/crid/1573668925447490176>

Ortega-Bastidas, P., Gómez, B., Aqueveque, P., Luarte-Martínez, S., & Cano-de-la-Cuerda, R. (2023). Instrumented Timed Up and Go Test (iTUG)-More Than Assessing Time to Predict Falls: A Systematic Review. *Sensors (Basel, Switzerland)*, 23(7), 3426. <https://doi.org/10.3390/s23073426>

Paluch, A. E., Bajpai, S., Bassett, D. R., Carnethon, M. R., Ekelund, U., Evenson, K. R., Galuska, D. A., Jefferis, B. J., Kraus, W. E., Lee, I.-M., Matthews, C. E., Omura, J. D., Patel, A. V., Pieper, C. F., Rees-Punia, E., Dallmeier, D., Klenk, J., Whincup, P. H., Dooley, E. E., ... Fulton, J. E. (2022). Daily steps and all-cause mortality: A meta-analysis of 15 international cohorts [Publisher: Elsevier]. *The Lancet Public Health*, 7(3), e219–e228. [https://doi.org/10.1016/S2468-2667\(21\)00302-9](https://doi.org/10.1016/S2468-2667(21)00302-9)

Peters, D. M., O'Brien, E. S., Kamrud, K. E., Roberts, S. M., Rooney, T. A., Thibodeau, K. P., Balakrishnan, S., Gell, N., & Mohapatra, S. (2021). Utilization of wearable technology to assess gait and mobility post-stroke: A systematic review. *Journal of Neuroengineering and Rehabilitation*, 18(1), 67. <https://doi.org/10.1186/s12984-021-00863-x>

Pilotto, A., Rizzardi, A., Zatti, C., Hansen, C., Donini, A., Romijnders, R., Maetzler, W., & Padovani, A. (2023). Unsupervised but not supervised gait parameters are related to fatigue in Parkinson's disease: A pilot study. *Frontiers in Aging Neuroscience*, 15, 1279722. <https://doi.org/10.3389/fnagi.2023.1279722>

Poewe, W., Seppi, K., Tanner, C. M., Halliday, G. M., Brundin, P., Volkman, J., Schrag, A.-E., & Lang, A. E. (2017). Parkinson disease. *Nature Reviews. Disease Primers*, 3, 17013. <https://doi.org/10.1038/nrdp.2017.13>

- Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., Obeso, J., Marek, K., Litvan, I., Lang, A. E., Halliday, G., Goetz, C. G., Gasser, T., Dubois, B., Chan, P., Bloem, B. R., Adler, C. H., & Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 30(12), 1591–1601. <https://doi.org/10.1002/mds.26424>
- Roussos, G., Herrero, T. R., Hill, D. L., Dowling, A. V., L T M Müller, M., Evers, L. J. W., Burton, J., Derungs, A., Fisher, K., Kilambi, K. P., Mehrotra, N., Bhatnagar, R., Sardar, S., Stephenson, D., Adams, J. L., Ray Dorsey, E., & Cosman, J. (2022). Identifying and characterising sources of variability in digital outcome measures in Parkinson's disease. *NPJ digital medicine*, 5(1), 93. <https://doi.org/10.1038/s41746-022-00643-4>
- Salazar, R. D., Ren, X., Ellis, T. D., Toraif, N., Barthelemy, O. J., Neargarder, S., & Cronin-Golomb, A. (2017). Dual tasking in Parkinson's disease: Cognitive consequences while walking. *Neuropsychology*, 31(6), 613–623. <https://doi.org/10.1037/neu0000331>
- Schapira, A. H. V., Chaudhuri, K. R., & Jenner, P. (2017). Non-motor features of Parkinson disease. *Nature Reviews. Neuroscience*, 18(7), 435–450. <https://doi.org/10.1038/nnr.2017.62>
- Skidmore, F. M., Mackman, C. A., Pav, B., Shulman, L. M., Garvan, C., Macko, R. F., & Heilman, K. M. (2008). Daily ambulatory activity levels in idiopathic Parkinson disease. *Journal of Rehabilitation Research and Development*, 45(9), 1343–1348.
- Stack, E., & Ashburn, A. (2008). Dysfunctional turning in Parkinson's disease. *Disability and Rehabilitation*, 30(16), 1222–1229. <https://doi.org/10.1080/09638280701829938>
- Stellmann, J. P., Neuhaus, A., Götze, N., Briken, S., Lederer, C., Schimpl, M., Heesen, C., & Daumer, M. (2015). Ecological validity of walking capacity tests in multiple sclerosis. *PloS One*, 10(4), e0123822. <https://doi.org/10.1371/journal.pone.0123822>
- Toosizadeh, N., Mohler, J., Lei, H., Parvaneh, S., Sherman, S., & Najafi, B. (2015). Motor Performance Assessment in Parkinson's Disease: Association between Objective In-Clinic, Objective In-Home, and Subjective/Semi-Objective Measures. *PLoS ONE*, 10(4), e0124763. <https://doi.org/10.1371/journal.pone.0124763>
- Venables, W. N., & Ripley, B. D. (2002, August). *Modern Applied Statistics with S* (4th edition). Springer.
- Vítečková, S., Horáková, H., Poláková, K., Krupička, R., Růžicka, E., & Brožová, H. (2020). Agreement between the GAITRite® System and the Wearable Sensor BTS G-Walk® for measurement of gait parameters in healthy adults and Parkinson's disease patients. *PeerJ*, 8, e8835. <https://doi.org/10.7717/peerj.8835>
- Warmerdam, E., Hausdorff, J. M., Atr-saei, A., Zhou, Y., Mirelman, A., Aminian, K., Espay, A. J., Hansen, C., Evers, L. J. W., Keller, A., Lamoth, C., Pilotto, A., Rochester, L., Schmidt, G., Bloem, B. R., & Maetzler, W. (2020). Long-term unsupervised mobility assessment in movement disorders. *The Lancet. Neurology*, 19(5), 462–470. [https://doi.org/10.1016/S1474-4422\(19\)30397-7](https://doi.org/10.1016/S1474-4422(19)30397-7)
- Zajac, J. A., Cavanaugh, J. T., Baker, T., Duncan, R. P., Fulford, D., Giris, J., LaValley, M., Nordahl, T., Porciuncula, F., Rawson, K. S., Saint-Hilaire, M., Thomas, C. A., Earhart, G. M., & Ellis, T. D. (2022). Does clinically measured walking capacity contribute to real-world walking performance in Parkinson's disease? *Parkinsonism & Related Disorders*, 105, 123–127. <https://doi.org/10.1016/j.parkreldis.2022.11.016>

Chapter 9

Contribution 6: Does cognition affect supervised and unsupervised mobility differently in people with Parkinson's Disease? A Cross-Sectional Study.

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Abstract

The co-existence of cognitive and mobility impairments is frequent in people with Parkinson's disease (PwPD). Cognitive functions are associated with different types of supervised mobility, but much less is known about unsupervised mobility. Mild-to-moderate PwPD, without severe cognitive impairment and not using walking aids, performed three hospital-based supervised mobility tasks: forward walking, instrumented timed-up-and-go (iTUG) with a lower-back-mounted inertial sensor and a 3-meter backward walking test. Forward walking speed (FWS), backward walking speed (BWS) and mean angular velocity (MAV) of the 180° turn during iTUG were calculated. Unsupervised mobility was monitored through average daily steps (AvDS) measured over 5 days by means of a commercial smartwatch (Garmin Vivosmart 4) in free-living conditions. Cognitive performance was evaluated using the Montreal Cognitive Assessment (MoCA) and the Word-Color Stroop Test (WCST). Multivariate linear regression models with backward elimination method were used to evaluate how much variance of each mobility measure was explained by cognitive functions and the effect of other clinical and demographic variables. A total of 105 PwPD were recruited. Regarding supervised mobility, multivariate regressions revealed that cognitive functions explained 12.3% ($P < 0.001$), 12.4% ($P < 0.001$) and 15.0% ($P < 0.001$) variance of FWS, MAV and BWS, respectively. For unsupervised mobility, cognitive functions explained only 5.5% ($P = 0.009$) of AvDS variance. WCST was included in all regression models and was a significant predictor of all mobility parameters, either supervised or unsupervised. MoCA was included only in the model for supervised BWS and was not a significant predictor. When considering clinical and demographic variables, neither MoCA nor WCST remained significant predictors. Our findings support the role of executive functions in PwPD mobility. Cognition impacted supervised mobility more than unsupervised, likely due to the role of individual and environmental factors. These findings suggest that a comprehensive approach to PD should include cognitive assessments alongside traditional motor evaluation. Mobility evaluation in PwPD should be performed in both supervised and unsupervised conditions.

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder that primarily manifests with motor symptoms such as bradykinesia, rigidity, and tremor (Poewe et al., 2017). Among motor manifestations of the disease, impaired gait and functional mobility are not uncommon, particularly with disease progression, and have a profound impact on quality of life (Mirelman et al., 2019).

Gait and functional mobility can be measured through various standardized tests in the clinical setting. However, a growing body of evidence showed that what can be seen during clinical evaluation does not closely reflect real-world mobility. Indeed, in-hospital mobility parameters of people with PD (PwPD) correlate only partially with those obtained in real-world setting environment (Giannouli et al., 2016; Lang et al., 2023; Zajac et al., 2022). Indeed, assessments in supervised setting are usually triggered by a command and done in an isolated, standardized setting with limited ecological validity. In response to these challenges, during recent years it has been a growing interest in mobile health technologies for evaluating unsupervised mobility of people with movement disorders, including PD (Bianchini & Maetzler, 2023). Indeed, inertial motion units integrated into these devices allow the collection of various mobility parameters, such as daily step count in free-living, unsupervised conditions. Although this parameter does not provide detailed insights of subtle gait disorders, a reduced number of daily steps is associated with risk of overall mortality (Paluch et al., 2022) and various health conditions such as cancer, cardiovascular diseases, and dementia (Del Pozo Cruz, Ahmadi, et al., 2022; Del Pozo Cruz, Ahmadi, et al., 2022). Previous studies have also demonstrated an inverse correlation between the number of daily steps and disease severity in PwPD (Handlery et al., 2021; Skidmore et al., 2008).

Besides classical PD motor manifestations, non-motor symptoms are increasingly recognized as key features of the disease. Among these, cognitive dysfunction significantly impact quality of life in PwPD (Schapira et al., 2017). It encompasses deficits across various domains, including executive functions, attention, memory, and visuospatial abilities (Aarsland et al., 2021). Previous evidence reported an association between cognition, in particular executive and visuospatial functions, and different types of supervised gait and mobility tasks such as forward and backward walking and turning (Amboni et al., 2013; Correno et al., 2022; Mancini et al., 2015; Mirelman et al., 2014; Yogev-Seligmann et al., 2008). Indeed, mobility impairments in PD are not merely a consequence of motor symptoms and are closely linked to cognitive decline (Amboni et al., 2018; Morris, Martini, Smulders, et al., 2019). Executive functions (involving planning, decision-making, and task-switching abilities) play a crucial role in coordination and execution of complex motor tasks such as walking, especially under dual-task conditions and when more complex forms of gait are performed (e.g., turning, sideways and backward walking, etc.) (Gan et al., 2023; Maidan et al., 2017; Salazar et al., 2017). Previous studies have shown that PwPD who experience difficulties in executive functions are more prone to gait disturbances, such as freezing of gait (FOG) (Mc Ardle et al., 2022), and are at a higher risk of falls (Kataoka & Ueno, 2015).

This relationship suggests an interplay between cognitive and motor dysfunctions in PD, potentially sharing underlying neuropathological mechanisms. However, the association between cognitive functions and mobility was explored in a supervised setting (Gan et al., 2023; Maidan et al., 2017; Salazar et al., 2017) and very few evidence are available on unsupervised mobility (Mc Ardle et al., 2022).

To our knowledge no studies have investigated the contribution of cognition to both supervised and unsupervised mobility in PwPD. Indeed, previous studies have evaluated the association between cognitive function and each mobility state separately. Therefore, this study aimed to investigate the association between cognitive functions and both supervised and unsupervised mobility and the contribution of cognition to mobility in PwPD.

Material and Methods

Study design and ethics

This was a cross-sectional study aimed at investigating the association between cognitive functions, and both supervised and unsupervised mobility in PwPD. Participants meeting the inclusion and exclusion criteria were evaluated during their regular follow-up visits at the Neurology clinics of A.O.U. Sant'Andrea in Rome. Approval was granted by the local Ethical Committee of Sapienza, University of Rome (Ref. 0372/2022). This study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki of 1964 and subsequent amendments. Data collection and processing were carried out in compliance with current European data protection regulations.

Population

Participants were consecutively recruited from the Movement Disorders Centre at Sant'Andrea University Hospital (A.O.U. Sant'Andrea) in Rome between February 2023 and May 2024, in accordance to the following inclusion criteria: (i) diagnosis of idiopathic Parkinson's disease according to the Movement Disorders Society (MDS) criteria (Postuma et al., 2015); (ii) age 18 years or older; (iii) disease stage < 4 according to the modified Hoehn and Yahr scale (mHY) ("severe disability; still able to walk or stand unassisted") (Goetz et al., 2004); (v) ability to perform the experimental procedure. Exclusion criteria were defined as: (i) severe cognitive impairment as defined by a Montreal Cognitive Assessment (MoCA) score < 18 (Baek et al., 2024); (ii) orthopaedic, rheumatologic, or systemic conditions affecting mobility as judged by the assessor.

Experimental Procedure

This was a cross-sectional study aimed at investigating the association between cognitive functions, and both supervised and unsupervised mobility in PwPD. Participants meeting the inclusion and exclusion criteria were evaluated during their regular follow-up visits at the Neurology clinics of A.O.U. Sant'Andrea in Rome. Anthropometric (weight, height, BMI) and clinical-demographic data (age, sex, disease duration, levodopa equivalent daily dose [LEDD], mHY) were collected. Participants were evaluated through the following clinical scales: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III (MDS-UPDRS-III) (Goetz et al., 2008) was used to assess motor symptoms severity, Montreal cognitive assessment (MoCA) (Nasreddine et al., 2005) was used to evaluate global cognition. The time to complete the interference part of the word-color Stroop test (WCST) in seconds was used to evaluate executive functions (Scarpina & Tagini, 2017). Subsequently, participants were invited to perform two supervised mobility tasks while wearing a lower-back mounted research-grade inertial device for mobility analysis (BTS G-WALK, BTS Engineering Inc., Milan) (Vítečková et al., 2020): (i) a 20-meters Walking Test; and (ii) an instrumented Timed Up and Go (TUG) (Ortega-Bastidas et al., 2023). From these tasks, the following variables were computed in order to facilitate the comparison between the 2 supervised mobility tasks: forward walking speed (m/s) (FWS); mean angular velocity ($^{\circ}/s$) (MAV) of the intermediate 180-degree turn during the TUG. Additionally, a 3-meter Backward Walk Test (3MBWT) was performed according with previous validation studies (Barta et al., 2025; Kocer et al., 2023). PwPD were instructed to walk backward along a 3-meter walkway as quickly as possible while maintaining safety. An assessor followed each participant to ensure safety throughout the task. The test was repeated three times, and the completion time for each trial was recorded using a stopwatch. Backward walking speed (m/s) (BWS, m/s) was then calculated by dividing the distance (3 m) by the completion time, in order to harmonize it with other speed and velocity metrics. The average of the three trials was used for analysis. Garmin Vivosmart 4 smartwatch

(Garmin, Olathe, KS, USA, configured according to the manufacturer's specifications) by indicating the users' age, height, weight, was then worn on the wrist of the less affected side (i.e., left or right) (Bianchini et al., 2022) for 5 consecutive days, in line with previous findings showing that a minimum of 4 days of monitoring is needed to reliably estimate daily step count in PwPD (Bianchini et al., 2023). Participants were instructed to wear the smartwatch all time during day and night and remove it only when involved in water activities (e.g., bathing, showering, swimming, etc.). Participants were also asked to perform daily activities as usual. No additional reminder or instructions were provided to participants. During the monitoring period, participants could access information on the smartwatch screen, including the total number of steps, heart rate and sleep time. The device did not provide instructions, alerts or other messages to participants. The total daily steps recorded were extracted, and the average daily steps (AvDS) were computed (Bianchini, Rinaldi, et al., 2025; Bianchini et al., 2023). Compliance was assessed based on the participants' dashboard data. We could assess that the device was worn through heart rate and activity data. We considered all recording days with $\geq 80\%$ wear time while awake to be valid. We estimated the awake time as 24 hours minus the total sleep time as indicated by the device (Bianchini, Rinaldi, et al., 2025; Bianchini et al., 2023). Experimental procedure is summarized in fig. 9.1.

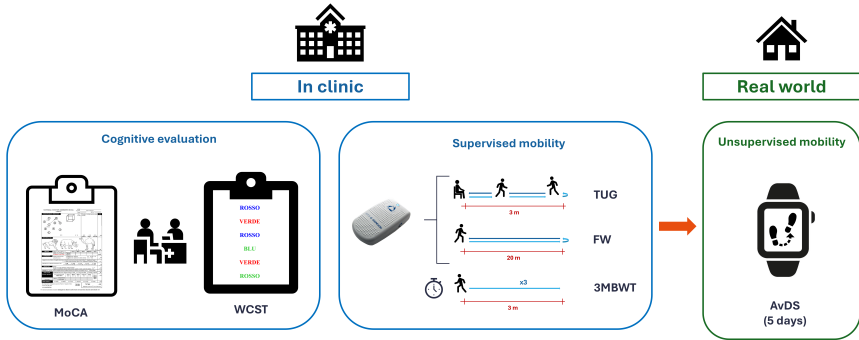


Figure 9.1. Schematic representation of study experimental procedure. 3MBWT: 3-meter backward walking test; AvDS: average daily steps; FW: forward walking; MoCA: Montreal Cognitive Assessment; TUG: Timed Up and Go; WCST: Word-Color Stroop test.

Statistical analyses

Statistical analyses were performed using JASP v0.18.3.0 (JASP Team, University of Amsterdam, The Netherlands), R v4.0.3, and R Studio v2023.12.0+369 for Windows (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were calculated for the considered variables and the normality was assessed by inspecting histograms and residual plots. Pearson's test was used to evaluate correlations between cognitive test scores and supervised and unsupervised mobility parameters. The cut-off points used for interpreting correlation coefficient values were as follows (Akoglu, 2018): < 0.1 : negligible; $0.1-0.2$: very weak; $0.2-0.4$: weak; $0.4-0.7$: moderate; $0.7-0.9$: strong; > 0.9 : very strong. Subsequently, to evaluate how much variance in supervised and unsupervised mobility parameters was explained by participants' cognitive performance, four separate multivariate linear regression models were constructed, with mobility-related variables as dependent variables and cognitive test scores as independent variables. A backward elimination method was used

to determine which independent variables were significant predictors of the model, with the elimination threshold set at $p \geq 0.1$. The adjusted R^2 value was calculated for each resulting model. Finally, we performed four additional multivariable analyses with backward elimination, including age, sex, disease duration, LEDD, and MDS-UPDRS III to account for other potentially relevant predictors of mobility in PD. For each model, the presence of influential points was assessed using Cook's distance, with values > 1 considered influential. For all analyses, the significance threshold was set at $\alpha < 0.05$. All data are reported as mean $\pm$ SD or median (Q1-Q3) for numerical variables and N (%) for categorical variables.

Results

Overview

A total of 105 PwPD who met the pre-specified inclusion and exclusion criteria were enrolled in the study. All participants were monitored through Garmin Vivosmart 4 at home for a period of 5 consecutive days. No participants or days were excluded based on the prespecified compliance criteria. The demographic, anthropometric, clinical and mobility features in supervised and unsupervised conditions are summarized in table 9.1.

Table 9.1. Demographic, anthropometric, clinical and mobility features of the study population.

PwPD (N=105)	
Age (years)	68.2 $\pm$ 8.7
Gender (female)	34 (32%)
Height (cm)	171 $\pm$ 8.7
Weight (kg)	76.0 $\pm$ 13.2
BMI	25.8 $\pm$ 3.4
Disease duration (years)	5.6 $\pm$ 3.8
LEDD (mg)	501 $\pm$ 237
mHY	2 (2-2.5)
MDS-UPDRS-III	26 (21-32)
MoCA	26 (25-28)
WCST (s)	41.6 $\pm$ 16.1
Supervised mobility parameters	
FWS (m/s)	1.19 $\pm$ 0.22
BWS (m/s)	0.60 $\pm$ 0.22
MAV (deg/s)	70.9 $\pm$ 17.9
Unsupervised mobility parameters	
AvDS (steps/day)	5979 $\pm$ 3037

AvDS: average daily steps; BWS: backward walking speed; FWS: forward walking speed; LEDD: levodopa equivalent daily dose; MAV: mean angular velocity; MDS-UPDRS-III: Movement Disorder Society Unified Parkinson's Disease Rating Scale part III; mHY: modified Hoehn and Yahr scale; MoCA: Montreal Cognitive Assessment; WCST: Word-Color Stroop test.

Correlations

Supervised mobility

Pearson's correlation test revealed a weak negative correlation between the WCST completion time and FWS ($R = -0.362$; $p < 0.001$), MAV ($R = -0.364$; $p < 0.001$), and BWS ($R = -0.379$; $p < 0.001$). There was also a weak positive correlation between the MoCA score and FWS ($R = 0.316$; $p = 0.001$), MAV ($R = 0.306$; $p = 0.002$), and BWS ($R = 0.328$; $p < 0.001$).

Unsupervised mobility

Pearson's correlation test revealed a weak negative correlation between the WCST completion time and AvDS ($R = -0.254$; $p = 0.009$). There was no significant correlation between the MoCA score and AvDS ($R = 0.114$; $p = 0.247$). Correlations are summarized in fig. 9.2.

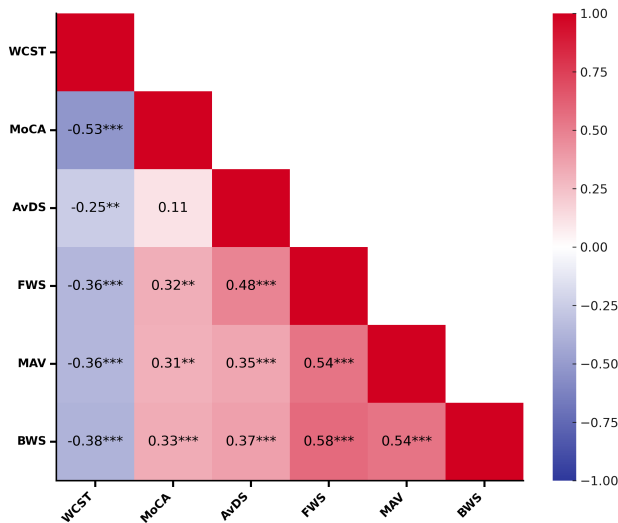


Figure 9.2. Heatmap showing correlations between variables. A color gradient was used to indicate the strength of positive (red) and negative (blue) associations. Pearson's correlation coefficient for each pair of variables is reported in each square. Significance of correlation is marked with asterisk as follows: * = $P < 0.05$; ** = $P < 0.01$; *** = $P < 0.001$. AvDS: average daily steps; BWS: backward walking speed; FWS: forward walking speed; MAV: mean angular velocity; MoCA: Montreal Cognitive Assessment; WCST: Word-Color Stroop test.

Linear Regression Analysis

Supervised mobility

For FWS, the linear regression model following backward elimination method, identified only the WCST completion time as a statistically significant predictor ($t = -3.947$; $p < 0.001$). The final regression model was statistically significant ($F = 15.581$; $\text{adj}R^2 = 0.123$; $p < 0.001$) (fig. 9.3A). For MAV during the TUG, the linear regression model also identified the WCST completion time as the only statistically significant predictor after backward elimination ($t = -3.967$; $p < 0.001$). The final regression model was statistically significant ($F = 15.738$; $\text{adj}R^2 = 0.124$; $p < 0.001$) (fig. 9.3B). For BWS, the linear regression model included both WCST completion time ($t = -2.682$; $p = 0.009$) and MoCA score ($t = 1.663$; $p = 0.099$) as predictors for the overall model but only WCST completion time reached the significance. The final regression model was statistically significant ($F = 10.168$; $\text{adj}R^2 = 0.150$; $p < 0.001$) (fig. 9.3C). Since the p-value of MoCA in the final model was very close to the threshold for inclusion, we also assessed the model without this variable. This model was statistically significant ($F = 17.273$; $R^2 = 0.144$; $p < 0.001$; WCST $t = -4.156$; $p < 0.001$). No influential points (Cook's distance > 1) were found in the models.

Unsupervised mobility

For AvDS, the linear regression model, after backward elimination, identified only the WCST completion time as a statistically significant predictor ($t = -2.660$; $p = 0.009$). The final regression model was statistically significant ($F = 7.077$; $R^2 = 0.055$; $p = 0.009$) (fig. 9.3D). No influential points (Cook's distance > 1) were found in the models.

Unsupervised mobility

For FWS, age, sex, MDS-UPDRS-III and LEDD were included in the regression model and all variables but LEDD were significant predictors. For MAV, WCST, MDS-UPDRS-III, sex, MoCA and LEDD were included in the regression model and only MDS-UPDRS-III was a significant predictor. For BWS, age, disease duration, MDS-UPDRS-III, sex and LEDD were included in the regression model and were a significant predictor. Finally, for AvDS, age, MDS-UPDRS-III, sex and LEDD were included in the regression model and all variables but sex were significant predictors. No influential points (Cook's distance > 1) were found in the models. Details of the multivariable regression models are shown in Table 2.

Table 9.2. Details of the multivariable regression models showing overall significance, adjusted R², predictors included in the model after backward elimination and their coefficients and p-values.

Variable	F-statistics	adj R ² (%)	p-value (model)	Predictors	Coefficients	p-value (coeff.)
FWS	13.628	32.7	< 0.001	(Intercept)	12.718	< 0.001***
				Age	-2.958	0.004**
				MDS-UPDRS III	-3.329	< 0.001**
				Sex (M)	2.845	0.005**
MAV	6.968	22.3	< 0.001	LEDD	-1.731	0.087
				(Intercept)	2.787	0.006**
				WCST	-1.844	0.068
				MDS-UPDRS III	-2.371	0.02*
BWS	18.590	45.8	< 0.001	Sex (M)	1.029	0.306
				MoCA	1.088	0.279
				LEDD	-1.731	0.087
				(Intercept)	11.522	< 0.001***
AVDS	11.893	29.5	< 0.001	Age	-5.448	< 0.001***
				Disease duration	2.184	0.031*
				MDS-UPDRS III	-3.306	0.001**
				Sex (M)	3.742	< 0.001***
AVDS	11.893	29.5	< 0.001	LEDD	-3.072	0.003**
				(Intercept)	7.437	< 0.001***
				Age	-2.652	0.009**
				MDS-UPDRS III	-3.136	0.002**
AVDS	11.893	29.5	< 0.001	Sex (M)	1.574	0.119
				LEDD	-2.315	0.023*
				(Intercept)	7.437	< 0.001***
				Age	-2.652	0.009**
				MDS-UPDRS III	-3.136	0.002**
				Sex (M)	1.574	0.119
				LEDD	-2.315	0.023*

AVDS: average daily steps; BWS: backward walking speed; FWS: forward walking speed; LEDD: levodopa equivalent daily dose; MAV: mean angular velocity; MDS-UPDRS-III: Movement Disorder Society Unified Parkinson's Disease Rating Scale part III; MoCA: Montreal Cognitive Assessment; WCST: Word-Colour Stroop test.

* p < 0.05; **p < 0.01; ***p < 0.001

Discussion

This study aimed to explore the association between cognitive functions and both supervised and unsupervised mobility and the contribution of cognition to mobility in PwPD. Our findings revealed significant associations between cognition, particularly executive functions, and mobility in supervised and unsupervised conditions, emphasizing the role of cognitive processes in maintaining mobility in PwPD. However, when considering other clinical and demographics metrics, cognitive predictors lost their significance.

Cognitive Functions and Supervised Mobility

Our results indicate that executive functions, as measured by the WCST, are a significant predictor of supervised mobility. Specifically, FWS, BWS and MAV were significantly associated with WCST performance. The WCST requires the prefrontal cortex to suppress automatic responses and engage in cognitive flexibility (Scarpina & Tagini, 2017). The frontal cortex and, particularly, the prefrontal areas, are heavily involved in planning, initiation, and execution of complex motor tasks, including walking (Corti et al., 2017). Imaging studies have shown activation of these areas during gait, supporting the notion that executive dysfunction can directly impact motor performance (Kotegawa & Teramoto, 2022; Maidan et al., 2017; Nóbrega-Sousa et al., 2020).

Impairments in these executive functions can lead to difficulties in adapting to changing environmental demands, which is essential for safe and efficient mobility. Our finding aligns with existing literature that highlights the critical role of frontal-executive functions in gait and motor control in both healthy elderly and PwPD (Amboni et al., 2013; Yogev-Seligmann et al., 2008). Previous studies in PwPD, indeed, highlighted how executive functions are linked to deterioration in spatiotemporal gait parameters, in particular regarding the domains of pace and rhythms (Amboni et al., 2018; Morris, Martini, Smulders, et al., 2019). Furthermore, executive functions have been associated with different types of mobility such as turning (Maidan et al., 2017) and backward walking (Peterson & Horak, 2016).

The association between gait and cognitive dysfunction could point toward a shared neurodegenerative basis. In particular, the basal ganglia are implicated in gait control and cognitive processes, particularly those related to executive functions. Thus, the degeneration of dopaminergic neurons in the substantia nigra, could disrupt the circuitry between basal ganglia and prefrontal cortex, leading to both motor and cognitive deficits (Peterson & Horak, 2016). This disruption could contribute to difficulties in initiating and maintaining gait in PwPD, particularly under conditions requiring cognitive engagement, such as navigating obstacles or multitasking (Nwogo et al., 2022). Furthermore, the interaction between cognitive decline and mobility in PD could be influenced by non-dopaminergic systems such as cholinergic (Morris, Martini, Madhyastha, et al., 2019), noradrenergic (Tosserams et al., 2023), GABA and glutamatergic neurotransmission dysfunction (O’Gorman Tuura et al., 2018). The complexity of these interactions underscores the need for comprehensive management strategies that address both cognitive and motor aspects of the disease.

Interestingly, in our study, global cognitive functions, as assessed by the MoCA, were included in the linear regression model only for BWS test, although with minimal contribution, and not for FWS or MAV and a slightly higher portion of variance was explained by cognition for BWS compared to FWS and MAV (15% vs 12.3% vs 12.4%, respectively). This result may suggest that backward walking, a more complex and less practiced motor task, places greater cognitive demands on PwPD (Koçer et al., 2023). The increased difficulty of the task, which lacks visual cues and requires higher levels of proprioceptive integration and motor planning, could explain the stronger association with global cognitive function (Correno et al., 2022). This finding underscores the importance of including varied mobility tasks in clinical assessments to capture the full spectrum of motor-cognitive interactions in PD.

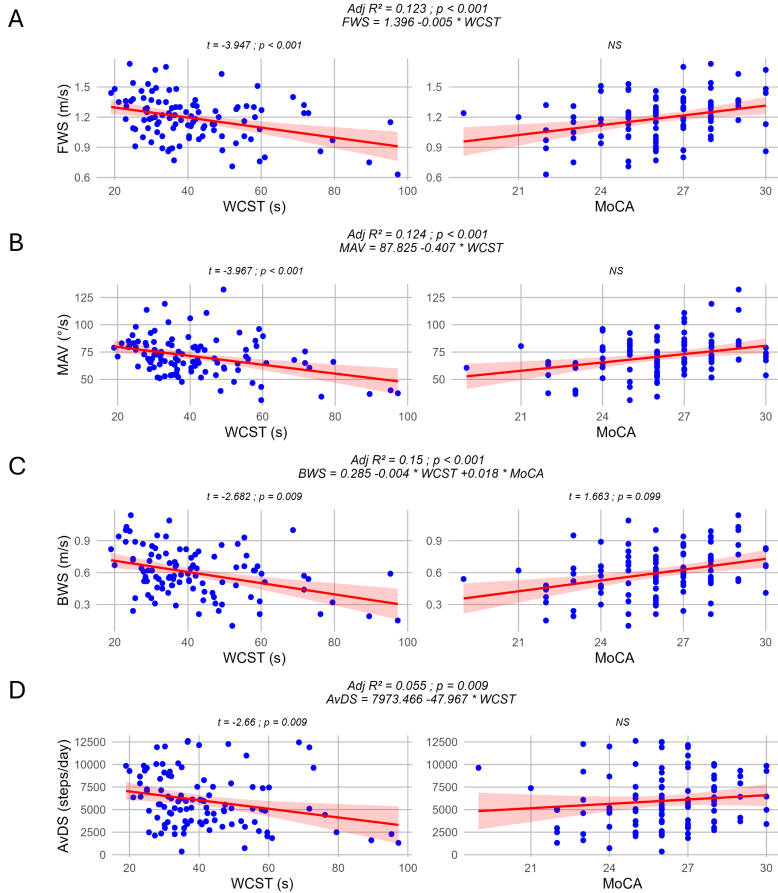


Figure 9.3. Linear regression models and scatterplot of paired independent and dependent variables. Panel A: Linear regression model for FWS. Panel B: Linear regression model for MAV. Panel C: Linear regression model for BWS. Panel D: Linear regression model for AvDS. For each graph, a linear regression line was added. The shaded area indicates the 95% confidence interval. Adjusted R^2 , p-values and regression equations of each model after backward elimination were added above each variable pair. T-statistics and p-value was also added on top of each significant predictor. NS was added for non-significant predictors. AvDS: average daily steps; BWS: backward walking speed; FWS: forward walking speed; MAV: mean angular velocity; MoCA: Montreal Cognitive Assessment; WCST: Word-Color Stroop test.

Cognitive Functions and Unsupervised Mobility

Differently from supervised mobility, unsupervised mobility, as measured by AvDS, displayed a weaker correlation with cognition. In fact, WCST performance explained only a modest proportion of the variance (5.5%) of AvDS. This might depend on the mobility measure adopted. Indeed, a very recent study by Burgos and colleagues (Burgos et al., 2025) reported that executive and visuospatial domains of cognition are associated with spatiotemporal gait parameters such as gait speed, stride length, and double support time in real-world conditions. Daily step count represents a global measure of mobility and physical activity, providing an estimate of how much an individual walks on average throughout the day. However, this measure does not capture subtle and detailed gait features or parameters. The development of validated real-world gait measures is currently a hot research topic, and several international consortia are actively working toward this goal (Micó-Amigo et al., 2023). To date, however, these efforts rely mainly on research-grade devices, thus limiting the advantages of commercial wearables in terms of scalability, accessibility, and ease of use. Nevertheless, previous studies underlined the association between daily steps and cognition in older adults (S.-T. Chen et al., 2020) and in different populations of people with neuropsychiatric disorders (L.-J. Chen et al., 2022; Ito et al., 2021). Our findings are in line with those of Mc Ardle and colleagues (Mc Ardle et al., 2022), reporting that frontal executive functions, as measured by the verbal fluency task, were a significant predictor of daily step count, measured by a research-grade, lower-back mounted, triaxial accelerometer for 7 days, in a population of 64 mild-to-moderate PwPD. We validate these findings in a larger PwPD population ($n=105$), using a consumer-grade instrument to collect AvDS. Moreover, we recently reported that the minimal clinically important difference (MCID) for AvDS, measured with the Garmin Vivosmart 4 in PwPD, was 1200 steps/day for clinical-related measures (Bianchini, Alborghetti, et al., 2025). Based on the present regression results, each 1-second change in the WCST interference part corresponds to a variation of 48 steps. Thus, a change of approximately 25 seconds would be required to reach a clinically meaningful difference in AvDS. Notably, this value falls within the reported MCID range for WCST interference in older adults at risk of falls (11.5 to 26.0 seconds) (Jehu et al., 2022), which provides additional clinical relevance to our findings.

The weaker association between cognition and unsupervised mobility could also reflect the influence of environmental, contextual and individual factors that affect free-living movements but are not captured in a controlled laboratory setting (Domingues et al., 2024). Indeed, previous evidence highlighted the discrepancy between capacity (what an individual can do) and performance (what an individual does do) (Giannouli et al., 2016; Lang et al., 2023; Zajac et al., 2022). In the real world, mobility is often influenced by a multitude of factors beyond cognitive ability, such as environmental barriers, weather, work and socioeconomic status, motivation, pain, fatigue, and physical health conditions (Suri et al., 2022). Thus, while cognitive functions are crucial for specific, controlled motor tasks, their influence on everyday mobility might be modulated and dampened by other external factors.

Multivariable regression

We found that after including clinical and demographic covariates (age, sex, disease duration, LEDD, and MDS-UPDRS III), WCST and MoCA were no longer retained in the regression models for FWS, BWS, and AvDS after backward elimination. Cognitive variables entered the regression model for MAV but did not emerge as significant predictors. The predominant effect of age is expected, given its well-established contribution to mobility and gait, with numerous studies demonstrating the impact of ageing on walking in both healthy adults (Schimpl et al., 2011) and PwPD (Zhou et al., 2023). This is also consistent with the recognized predictive value of gait speed for mortality in older adults (Studenski et al., 2011) and in healthy ageing in general (Furrer & Handschin, 2025). The strong and consistent predictive role of the MDS-UPDRS part III is likewise unsurprising, as gait and mobility are motor functions, and this aligns with previous findings (Allali et al., 2014;

Mirelman et al., 2019; Shearin et al., 2021). Similarly, the impact of disease duration is in line with its close association with neurodegeneration (Kordower et al., 2013) and disease severity (Holden et al., 2017), in this progressive disorder. The effect of LEDD also reflects prior evidence showing its influence on gait parameters deterioration over time (Wilson et al., 2020). While dopaminergic therapy remains the cornerstone of PD management (Poewe et al., 2017), the response to treatment of gait and mobility disturbances, as well as other axial symptoms, may hinder in advanced stages (Imbalzano et al., 2023). Nevertheless, walking parameters often retain some responsiveness to pharmacological treatment (Mirelman et al., 2019). Finally, sex differences in mobility outcomes have been reported in PwPD (Dallaire et al., 2024; Porta et al., 2019). This may explain why sex was a significant predictor of FWS and BWS in our models. In summary, our multivariable analysis indicates that although global and executive functions can affect mobility in PwPD, their influence is outweighed by stronger determinants such as clinical and demographic variables.

Implications for Clinical Practice

The association between executive dysfunction and impaired supervised mobility underscores the importance of incorporating cognitive rehabilitation strategies into PD management. Interventions targeting inhibitory control and selective attention may have the potential to improve motor performance and reduce risk of falls (Michels et al., 2022; Mirelman et al., 2011). Previous studies underlined the positive effect of training cognitive and motor functions together (motor-cognitive dual-task) on both supervised gait and cognitive abilities in PwPD (San Martín Valenzuela et al., 2020; Strouwen et al., 2017). Moreover, previous evidence demonstrated that cognitive training alone could lead to an improvement in motor symptoms (Michels et al., 2022) and vice versa (da Silva et al., 2018). Moreover, the significant association between global cognitive function and BWS emphasizes the value of including diverse mobility assessments in clinical evaluations. Backward walking tests might indeed serve as an indicator of both motor and cognitive impairments, facilitating early identification of people at higher risk of mobility decline (Correno et al., 2022; Hackney & Earhart, 2009). Additionally, Shen and Mak (Shen & Mak, 2012) reported that step training including backward training improved balance and mobility in PwPD, supporting the inclusion of such tasks in rehabilitation programs. Nevertheless, the modest correlation between cognitive function and unsupervised mobility, as well as the predominant role of clinical and demographic parameters in the multivariable analysis, highlights the need for comprehensive, multidimensional assessments that consider both cognitive, individual and environmental factors when planning interventions for PwPD.

Limitations and Future Directions

Despite the novel insights provided by this study, several limitations must be acknowledged. First, the cross-sectional design limits our ability to infer causality between cognitive functions and mobility outcomes. Longitudinal studies are needed to determine whether cognitive decline precedes or follows mobility impairments in PD and clarify this association. Additionally, while we focused on executive functions, other cognitive domains, such as visuospatial abilities, might also play a critical role in mobility (Amboni et al., 2013) and are commonly altered in PwPD (Aarsland et al., 2021). These should be explored in future research. We also included only PwPD with MoCA ≥ 18 . While this is a lower threshold, compared with other proposed MoCA cut-offs reported in literature, yet we did not investigate the entire spectrum of cognitive impairment in PD. Therefore, we could not draw information regarding the relationship between mobility and cognition in PwPD with severe cognitive impairment. Indeed, it is likely that in more advanced stages of the disease, severe cognitive deficits and dementia could have a detrimental effect on mobility, as reported previously (Bovonsunthonchai et al., 2022). However, we decided to focus on the PD population with sufficiently preserved cognitive functions and most likely to use consumer-

grade wearable devices. We only considered AvDS as unsupervised mobility parameter, in line with previous research (Zajac et al., 2022). A growing body of evidence highlighted the possibility of collecting, measuring and monitoring gait parameters in free-living real world settings (Kirk et al., 2024; Pilotto et al., 2023) and several international consortia are working on validating and refining this possibility (Hinchliffe et al., 2024; Micó-Amigo et al., 2023). Future studies are warranted to include more detailed analysis of real-world mobility in order to more accurately assess the association with cognition. Finally, the use of consumer-grade smartwatch for unsupervised mobility data collection may have reduced the accuracy and reliability in AvDS collection, particularly in people with more severe PD or those exhibiting tremor and dyskinesias. However, previous studies from ours and other groups highlighted the accuracy and reliability of AvDS estimation in mild-to-moderate PwPD (Bianchini, Rinaldi, et al., 2025; Bianchini et al., 2022, 2023; Ginis et al., 2023). In addition, because the device algorithm is not publicly available, we could not assess its potential impact on our results. For example, the Garmin Vivosmart 4 requires users to input age, weight, and height into their profile, and we followed these instructions to ensure that smartwatch use reflected typical real-world conditions. However, whether and how the device incorporates this information into its calculations remains unknown, as the algorithm is proprietary. Nevertheless, the use of commercially available device could facilitate the capillary collection of mobility measures in clinical practice, thus providing valuable insight in PwPD conditions in free-living, real-world settings. The possibility for participants to access their smartwatch data may have influenced their physical activity levels during the monitoring period. Previous studies, indeed, have reported that activity trackers can increase physical activity (Ferguson et al., 2022). However, we acknowledge this potential systematic bias in our study, as done in previous work from our group (Bianchini, Alborghetti, et al., 2025), as our aim was to implement smartwatch in a way that closely reflected real-world conditions and use. Restricting access to the data, indeed, would have deviated from typical usage by the general population. Finally, the use of consumer-grade smartwatches raises additional concerns, particularly regarding data security, privacy, and access to raw data. It should be noted, however, that the use of the device in our study adhered to the manufacturer's instructions, and data storage and processing were therefore compliant with European Union regulations. A further limitation lies in the fact that raw data from Garmin devices are not accessible or downloadable through the user dashboard, which may restrict the development of more advanced and standardized analytical pipelines. Nonetheless, this was beyond the scope of our study, as our aim was to employ the smartwatches in a way that closely reflected their common use in daily life.

Conclusions

Our findings highlight the role of executive functions in mobility among PwPD, particularly during more complex motor tasks such as backward walking. While cognitive functions significantly influence supervised mobility, their impact on unsupervised, real-world mobility appears less pronounced, likely reflecting the interplay of environmental and individual factors. Moreover, although global and executive functions can affect mobility, their contribution is outweighed by stronger determinants such as clinical and demographic variables. These results suggest that comprehensive PD management should integrate cognitive assessments alongside motor evaluations, emphasizing interventions that address both cognitive and environmental barriers to improve patient outcomes. Future research should further explore the interplay between cognition, mobility, and other non-motor symptoms in PD through longitudinal designs and advanced monitoring technologies, to better capture the multifaceted challenges faced by PwPD.

References

- Aarsland, D., Batzu, L., Halliday, G. M., Geurtsen, G. J., Ballard, C., Ray Chaudhuri, K., & Weintraub, D. (2021). Parkinson disease-associated cognitive impairment. *Nature Reviews. Disease Primers*, 7(1), 47. <https://doi.org/10.1038/s41572-021-00280-3>
- Akoglu, H. (2018). User's guide to correlation coefficients. *Turkish Journal of Emergency Medicine*, 18(3), 91–93. <https://doi.org/10.1016/j.tjem.2018.08.001>
- Allali, G., Verghese, J., & Mahoney, J. R. (2014). Contributions of mild parkinsonian signs to gait performance in the elderly. *Age (Dordrecht, Netherlands)*, 36(4), 9678. <https://doi.org/10.1007/s11357-014-9678-4>
- Amboni, M., Barone, P., & Hausdorff, J. M. (2013). Cognitive contributions to gait and falls: Evidence and implications. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(11), 1520–1533. <https://doi.org/10.1002/mds.25674>
- Amboni, M., Iuppariello, L., Iavarone, A., Fasano, A., Palladino, R., Rucco, R., Picillo, M., Lista, I., Varriale, P., Vitale, C., Cesarelli, M., Sorrentino, G., & Barone, P. (2018). Step length predicts executive dysfunction in Parkinson's disease: A 3-year prospective study. *Journal of Neurology*, 265(10), 2211–2220. <https://doi.org/10.1007/s00415-018-8973-x>
- Baek, K., Kim, Y. M., Na, H. K., Lee, J., Shin, D. H., Heo, S.-J., Chung, S. J., Kim, K., Lee, P. H., Sohn, Y. H., Yoon, J., & Kim, Y. J. (2024). Comparing Montreal Cognitive Assessment Performance in Parkinson's Disease Patients: Age- and Education-Adjusted Cutoffs vs. Machine Learning. *Journal of Movement Disorders*, 17(2), 171–180. <https://doi.org/10.14802/jmd.23271>
- Barta, K., Boddy, A. H., Flores, M., Perry, L., Sawyer, K., & Campbell, A. (2025). Psychometric properties of 3-meter backward walk test (3MBWT) in people with Parkinson disease. *Physiotherapy Theory and Practice*, 41(3), 656–663. <https://doi.org/10.1080/09593985.2024.2348034>
- Bianchini, E., Rinaldi, D., De Carolis, L., Galli, S., Alborghetti, M., Hansen, C., Suppa, A., Salvetti, M., Pontieri, F., & Vuillerme, N. (2025). Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study. *JMIR Formative Research*, 9. <https://doi.org/10.2196/63153>
Export Date: 14 April 2025; Cited By: 0.
- Bianchini, E., Alborghetti, M., Galli, S., Hansen, C., Zampogna, A., Suppa, A., Salvetti, M., Pontieri, F. E., Rinaldi, D., & Vuillerme, N. (2025). Minimal Clinically Important Difference of Average Daily Steps Measured Through a Consumer Smartwatch in People With Mild-to-Moderate Parkinson Disease: Cross-Sectional Study [Company: JMIR mHealth and uHealth Distributor: JMIR mHealth and uHealth Institution: JMIR mHealth and uHealth Label: JMIR mHealth and uHealth Publisher: JMIR Publications Inc., Toronto, Canada]. *JMIR mHealth and uHealth*, 13(1), e64213. <https://doi.org/10.2196/64213>
- Bianchini, E., Calì, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzler, W., & Pontieri, F. E. (2022). Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, 23(1), 214. <https://doi.org/10.3390/s23010214>
- Bianchini, E., Galli, S., Alborghetti, M., De Carolis, L., Zampogna, A., Hansen, C., Vuillerme, N., Suppa, A., & Pontieri, F. E. (2023). Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch [Number: 21 Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 23(21), 8971. <https://doi.org/10.3390/s23218971>
- Bianchini, E., & Maetzler, W. (2023, May). Wearable systems in movement disorders. In *International Review of Movement Disorders*. Academic Press. <https://doi.org/10.1016/bs.irmvd.2023.04.002>
- Bovonsunthonchai, S., Vachalathiti, R., Hiengkaew, V., Bryant, M. S., Richards, J., & Senanarong, V. (2022). Quantitative gait analysis in mild cognitive impairment, dementia, and cognitively intact individuals:

- A cross-sectional case-control study. *BMC Geriatrics*, 22(1), 767. <https://doi.org/10.1186/s12877-022-03405-9>
- Burgos, P. I., Silva-Batista, C., Ragothaman, A., Shah, V. V., Carlson-Kuhta, P., Horak, F. B., & Mancini, M. (2025). Cognition is associated with daily-life mobility in people with Parkinson's disease. *Clinical Parkinsonism & Related Disorders*, 13, 100393. <https://doi.org/10.1016/j.prdoa.2025.100393>
- Chen, L.-J., Stubbs, B., Chien, I.-C., Lan, T.-H., Chung, M.-S., Lee, H.-L., Hsu, W.-C., & Ku, P.-W. (2022). Associations between daily steps and cognitive function among inpatients with schizophrenia. *BMC Psychiatry*, 22(1), 87. <https://doi.org/10.1186/s12888-022-03736-2>
- Chen, S.-T., Stevinson, C., Tian, T., Chen, L.-J., & Ku, P.-W. (2020). Accelerometer-measured daily steps and subjective cognitive ability in older adults: A two-year follow-up study. *Experimental Gerontology*, 133, 110874. <https://doi.org/10.1016/j.exger.2020.110874>
- Correno, M. B., Hansen, C., Chardon, M., Milane, T., Bianchini, E., & Vuillerme, N. (2022). Association between Backward Walking and Cognition in Parkinson Disease: A Systematic Review. *International Journal of Environmental Research and Public Health*, 19(19), 12810. <https://doi.org/10.3390/ijerph191912810>
- Corti, E. J., Johnson, A. R., Riddle, H., Gasson, N., Kane, R., & Loftus, A. M. (2017). The relationship between executive function and fine motor control in young and older adults. *Human Movement Science*, 51, 41–50. <https://doi.org/10.1016/j.humov.2016.11.001>
- da Silva, F. C., Iop, R. d. R., de Oliveira, L. C., Boll, A. M., de Alvarenga, J. G. S., Gutierrez Filho, P. J. B., de Melo, L. M. A. B., Xavier, A. J., & da Silva, R. (2018). Effects of physical exercise programs on cognitive function in Parkinson's disease patients: A systematic review of randomized controlled trials of the last 10 years. *PLoS One*, 13(2), e0193113. <https://doi.org/10.1371/journal.pone.0193113>
- Dallaire, M., Houde-Thibeault, A., Bouchard-Tremblay, J., Wotto, E. A., Côté, S., Santos Oliveira, C., Ngomo, S., & da Silva, R. A. (2024). Impact of frailty and sex-related differences on postural control and gait in older adults with Parkinson's Disease. *Experimental Gerontology*, 186, 112360. <https://doi.org/10.1016/j.exger.2024.112360>
- Del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK. *JAMA neurology*, 79(10), 1059–1063. <https://doi.org/10.1001/jamaneurol.2022.2672>
- Del Pozo Cruz, B., Ahmadi, M. N., Lee, I.-M., & Stamatakis, E. (2022). Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. *JAMA internal medicine*. <https://doi.org/10.1001/jamainternmed.2022.4000>
- Domingues, V. L., Makhoul, M. P., de Freitas, T. B., Polese, J. C., Silva-Batista, C., Barbieri, F. A., & Torriani-Pasin, C. (2024). Factors Associated With Physical Activity and Sedentary Behavior in People With Parkinson Disease: A Systematic Review and Meta-Analysis. *Physical Therapy*, 104(12), pzae114. <https://doi.org/10.1093/ptj/pzae114>
- Ferguson, T., Olds, T., Curtis, R., Blake, H., Crozier, A. J., Dankiw, K., Dumuid, D., Kasai, D., O'Connor, E., Virgara, R., & Maher, C. (2022). Effectiveness of wearable activity trackers to increase physical activity and improve health: A systematic review of systematic reviews and meta-analyses. *The Lancet. Digital Health*, 4(8), e615–e626. [https://doi.org/10.1016/S2589-7500\(22\)00111-X](https://doi.org/10.1016/S2589-7500(22)00111-X)
- Furrer, R., & Handschin, C. (2025). Biomarkers of aging: Functional aspects still trump molecular parameters. *NPJ Aging*, 11(1), 15. <https://doi.org/10.1038/s41514-025-00207-2>
- Gan, Y., Xie, H., Qin, G., Wu, D., Shan, M., Hu, T., Yin, Z., An, Q., Ma, R., Wang, S., Zhang, Q., Zhu, G., & Zhang, J. (2023). Association between Cognitive Impairment and Freezing of Gait in Patients with Parkin-

- son's Disease. *Journal of Clinical Medicine*, 12(8), 2799. <https://doi.org/10.3390/jcm12082799>
- Giannouli, E., Bock, O., Mellone, S., & Zijlstra, W. (2016). Mobility in Old Age: Capacity Is Not Performance. *BioMed Research International*, 2016, 3261567. <https://doi.org/10.1155/2016/3261567>
- Ginis, P., Goris, M., De Groef, A., Blondeel, A., Gilat, M., Demeyer, H., Troosters, T., & Nieuwboer, A. (2023). Validation of Commercial Activity Trackers in Everyday Life of People with Parkinson's Disease. *Sensors*, 23(8). <https://doi.org/10.3390/s23084156>
Export Date: 14 April 2025; Cited By: 6.
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., Giladi, N., Holloway, R. G., Moore, C. G., Wenning, G. K., Yahr, M. D., Seidl, L., & Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 19(9), 1020–1028. <https://doi.org/10.1002/mds.20213>
- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Hackney, M. E., & Earhart, G. M. (2009). Backward walking in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 24(2), 218–223. <https://doi.org/10.1002/mds.22330>
- Handlery, R., Stewart, J. C., Pellegrini, C., Monroe, C., Hainline, G., Flach, A., Handlery, K., & Fritz, S. (2021). Physical Activity in De Novo Parkinson Disease: Daily Step Recommendation and Effects of Treadmill Exercise on Physical Activity. *Physical Therapy*, 101(10), pzab174. <https://doi.org/10.1093/ptj/pzab174>
- Hinchliffe, C., Rehman, R. Z. U., Pinaud, C., Branco, D., Jackson, D., Ahmaniemi, T., Guerreiro, T., Chatterjee, M., Manyakov, N. V., Pandis, I., Davies, K., Macrae, V., Aufenberg, S., Paulides, E., Hildesheim, H., Kudelka, J., Emmert, K., Van Gassen, G., Rochester, L., ... IDEA-FAST Consortium. (2024). Evaluation of walking activity and gait to identify physical and mental fatigue in neurodegenerative and immune disorders: Preliminary insights from the IDEA-FAST feasibility study. *Journal of Neuroengineering and Rehabilitation*, 21(1), 94. <https://doi.org/10.1186/s12984-024-01390-1>
- Holden, S. K., Finseth, T., Sillau, S. H., & Berman, B. D. (2017). Progression of MDS-UPDRS Scores Over Five Years in De Novo Parkinson Disease from the Parkinson's Progression Markers Initiative Cohort. *Movement Disorders Clinical Practice*, 5(1), 47–53. <https://doi.org/10.1002/mdc3.12553>
- Imbalzano, G., Rinaldi, D., Calandra-Buonaura, G., Contin, M., Amato, F., Giannini, G., Sambati, L., Ledda, C., Romagnolo, A., Olmo, G., Cortelli, P., Zibetti, M., Lopiano, L., & Artusi, C. A. (2023). How resistant are levodopa-resistant axial symptoms? Response of freezing, posture, and voice to increasing levodopa intestinal infusion rates in Parkinson disease. *European Journal of Neurology*, 30(1), 96–106. <https://doi.org/10.1111/ene.15558>
- Ito, D., Kawakami, M., Narita, Y., Yoshida, T., Mori, N., & Kondo, K. (2021). Cognitive Function is a Predictor of the Daily Step Count in Patients With Subacute Stroke With Independent Walking Ability: A Prospective Cohort Study. *Archives of Rehabilitation Research and Clinical Translation*, 3(3), 100132. <https://doi.org/10.1016/j.arrct.2021.100132>
- Jehu, D. A., Davis, J. C., Madden, K., Parmar, N., & Liu-Ambrose, T. (2022). Minimal Clinically Important Difference of Executive Function Performance in Older Adults Who Fall: A Secondary Analysis of a Randomized Controlled Trial. *Gerontology*, 68(7), 771–779. <https://doi.org/10.1159/000518939>

- Kataoka, H., & Ueno, S. (2015). Low FAB score as a predictor of future falling in patients with Parkinson's disease: A 2.5-year prospective study. *Journal of Neurology*, 262(9), 2049–2055. <https://doi.org/10.1007/s00415-015-7814-4>
- Kirk, C., Küderle, A., Micó-Amigo, M. E., Bonci, T., Paraschiv-Ionescu, A., Ullrich, M., Soltani, A., Gazit, E., Salis, F., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Brown, P., Buckley, E., Cantu, A., Carsin, A.-E., Caruso, M., Caulfield, B., ... Mobilise-D consortium. (2024). Mobilise-D insights to estimate real-world walking speed in multiple conditions with a wearable device. *Scientific Reports*, 14(1), 1754. <https://doi.org/10.1038/s41598-024-51766-5>
- Koçer, B., Gülşen, Ç., Söke, F., Özcan Gülşen, E., Ersoy, N., Tunca Yılmaz, Ö., & Çomoğlu, S. S. (2023). Comparison of dual-task costs during different types of walking in people with Parkinson's disease: A controlled study. *Acta Neurologica Belgica*, 123(6), 2221–2227. <https://doi.org/10.1007/s13760-023-02271-5>
- Kocer, B., Soke, F., Ataoglu, N. E. E., Ersoy, N., Gulsen, C., Gulsen, E. O., Yasa, M. E., Uysal, I., Comoglu, S. S., & Bora, H. A. T. (2023). The reliability and validity of the 3-m backward walk test in people with Parkinson's disease. *Irish Journal of Medical Science*. <https://doi.org/10.1007/s11845-023-03384-9>
- Kordower, J. H., Olanow, C. W., Dodiya, H. B., Chu, Y., Beach, T. G., Adler, C. H., Halliday, G. M., & Bartus, R. T. (2013). Disease duration and the integrity of the nigrostriatal system in Parkinson's disease. *Brain*, 136(8), 2419–2431. <https://doi.org/10.1093/brain/awt192>
- Kotegawa, K., & Teramoto, W. (2022). Association of executive function capacity with gait motor imagery ability and PFC activity: An fNIRS study. *Neuroscience Letters*, 766, 136350. <https://doi.org/10.1016/j.neulet.2021.136350>
- Lang, C. E., Holleran, C. L., Strube, M. J., Ellis, T. D., Newman, C. A., Fahey, M., DeAngelis, T. R., Nordahl, T. J., Reisman, D. S., Earhart, G. M., Lohse, K. R., & Bland, M. D. (2023). Improvement in the Capacity for Activity Versus Improvement in Performance of Activity in Daily Life During Out-patient Rehabilitation. *Journal of neurologic physical therapy: JNPT*, 47(1), 16–25. <https://doi.org/10.1097/NPT.0000000000000413>
- Maidan, I., Bernad-Elazari, H., Giladi, N., Hausdorff, J. M., & Mirelman, A. (2017). When is Higher Level Cognitive Control Needed for Locomotor Tasks Among Patients with Parkinson's Disease? *Brain Topography*, 30(4), 531–538. <https://doi.org/10.1007/s10548-017-0564-0>
- Mancini, M., El-Gohary, M., Pearson, S., McNames, J., Schlueter, H., Nutt, J. G., King, L. A., & Horak, F. B. (2015). Continuous monitoring of turning in Parkinson's disease: Rehabilitation potential. *NeuroRehabilitation*, 37(1), 3–10. <https://doi.org/10.3233/NRE-151236>
- Mc Ardle, R., Del Din, S., Morris, R., Alcock, L., Yarnall, A. J., Burn, D. J., Rochester, L., Lawson, R. A., & On Behalf Of The Icele-Pd Study Group, n. (2022). Factors Influencing Habitual Physical Activity in Parkinson's Disease: Considering the Psychosocial State and Wellbeing of People with Parkinson's and Their Carers. *Sensors (Basel, Switzerland)*, 22(3), 871. <https://doi.org/10.3390/s22030871>
- Michels, J., Werner, C. J., Schumann-Werner, B., Schulz, J. B., Costa, A. S., & Reetz, K. (2022). Why cognitive training is important for the health status in Parkinson's disease: Preliminary evidence from a clinical three-weeks multidisciplinary intervention. *Neurological Research and Practice*, 4(1), 47. <https://doi.org/10.1186/s42466-022-00210-y>
- Micó-Amigo, M. E., Bonci, T., Paraschiv-Ionescu, A., Ullrich, M., Kirk, C., Soltani, A., Küderle, A., Gazit, E., Salis, F., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Brown, P., Buckley, E., Cantu, A., Carsin, A.-E., Caruso, M., Caulfield, B., ... Mobilise-D consortium. (2023). Assessing real-world gait with digital technology? Validation, insights and recommendations from the Mobilise-D consortium. *Journal of Neuroengineering and Rehabilitation*, 20(1), 78. <https://doi.org/10.1186/s12984-023-01198-5>
- Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L.,

- Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)
- Mirelman, A., Maidan, I., Herman, T., Deutsch, J. E., Giladi, N., & Hausdorff, J. M. (2011). Virtual reality for gait training: Can it induce motor learning to enhance complex walking and reduce fall risk in patients with Parkinson's disease? *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 66(2), 234–240. <https://doi.org/10.1093/gerona/glq201>
- Mirelman, A., Weiss, A., Buchman, A. S., Bennett, D. A., Giladi, N., & Hausdorff, J. M. (2014). Association between performance on Timed Up and Go subtasks and mild cognitive impairment: Further insights into the links between cognitive and motor function. *Journal of the American Geriatrics Society*, 62(4), 673–678. <https://doi.org/10.1111/jgs.12734>
- Morris, R., Martini, D. N., Madhyastha, T., Kelly, V. E., Grabowski, T. J., Nutt, J., & Horak, F. (2019). Overview of the cholinergic contribution to gait, balance and falls in Parkinson's disease. *Parkinsonism & Related Disorders*, 63, 20–30. <https://doi.org/10.1016/j.parkreldis.2019.02.017>
- Morris, R., Martini, D. N., Smulders, K., Kelly, V. E., Zabetian, C. P., Poston, K., Hiller, A., Chung, K. A., Yang, L., Hu, S.-C., Edwards, K. L., Cholerton, B., Grabowski, T. J., Montine, T. J., Quinn, J. F., & Horak, F. (2019). Cognitive associations with comprehensive gait and static balance measures in Parkinson's disease. *Parkinsonism & Related Disorders*, 69, 104–110. <https://doi.org/10.1016/j.parkreldis.2019.06.014>
- Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>
- Nóbrega-Sousa, P., Gobbi, L. T. B., Orcioli-Silva, D., Conceição, N. R. d., Beretta, V. S., & Vitorio, R. (2020). Prefrontal Cortex Activity During Walking: Effects of Aging and Associations With Gait and Executive Function. *Neurorehabilitation and Neural Repair*, 34(10), 915–924. <https://doi.org/10.1177/1545968320953824>
- Nwogo, R. O., Kammermeier, S., & Singh, A. (2022). Abnormal neural oscillations during gait and dual-task in Parkinson's disease. *Frontiers in Systems Neuroscience*, 16, 995375. <https://doi.org/10.3389/fnsys.2022.995375>
- O'Gorman Tuura, R. L., Baumann, C. R., & Baumann-Vogel, H. (2018). Beyond Dopamine: GABA, Glutamate, and the Axial Symptoms of Parkinson Disease. *Frontiers in Neurology*, 9, 806. <https://doi.org/10.3389/fneur.2018.00806>
- Ortega-Bastidas, P., Gómez, B., Aqueveque, P., Luarte-Martínez, S., & Cano-de-la-Cuerda, R. (2023). Instrumented Timed Up and Go Test (iTUG)-More Than Assessing Time to Predict Falls: A Systematic Review. *Sensors (Basel, Switzerland)*, 23(7), 3426. <https://doi.org/10.3390/s23073426>
- Paluch, A. E., Bajpai, S., Bassett, D. R., Carnethon, M. R., Ekelund, U., Evenson, K. R., Galuska, D. A., Jefferis, B. J., Kraus, W. E., Lee, I.-M., Matthews, C. E., Omura, J. D., Patel, A. V., Pieper, C. F., Rees-Punia, E., Dallmeier, D., Klenk, J., Whincup, P. H., Dooley, E. E., ... Fulton, J. E. (2022). Daily steps and all-cause mortality: A meta-analysis of 15 international cohorts [Publisher: Elsevier]. *The Lancet Public Health*, 7(3), e219–e228. [https://doi.org/10.1016/S2468-2667\(21\)00302-9](https://doi.org/10.1016/S2468-2667(21)00302-9)
- Peterson, D. S., & Horak, F. B. (2016). Neural Control of Walking in People with Parkinsonism. *Physiology (Bethesda, Md.)*, 31(2), 95–107. <https://doi.org/10.1152/physiol.00034.2015>
- Pilotto, A., Rizzardi, A., Zatti, C., Hansen, C., Donini, A., Romijnders, R., Maetzler, W., & Padovani, A. (2023). Unsupervised but not supervised gait parameters are related to fatigue in Parkinson's disease: A pilot study. *Frontiers in Aging Neuroscience*, 15, 1279722. <https://doi.org/10.3389/fnagi.2023.1279722>
- Poewe, W., Seppi, K., Tanner, C. M., Halliday, G. M., Brundin, P., Volkman, J., Schrag, A.-E., & Lang, A. E. (2017).

- Parkinson disease. *Nature Reviews. Disease Primers*, 3, 17013. <https://doi.org/10.1038/nrdp.2017.13>
- Porta, M., Piloni, G., Aripa, F., Casula, C., Cossu, G., & Pau, M. (2019). Similarities and Differences of Gait Patterns in Women and Men With Parkinson Disease With Mild Disability. *Archives of Physical Medicine and Rehabilitation*, 100(11), 2039–2045. <https://doi.org/10.1016/j.apmr.2019.04.010>
- Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., Obeso, J., Marek, K., Litvan, I., Lang, A. E., Halliday, G., Goetz, C. G., Gasser, T., Dubois, B., Chan, P., Bloem, B. R., Adler, C. H., & Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 30(12), 1591–1601. <https://doi.org/10.1002/mds.26424>
- Salazar, R. D., Ren, X., Ellis, T. D., Toraif, N., Barthelemy, O. J., Nearing, S., & Cronin-Golomb, A. (2017). Dual tasking in Parkinson's disease: Cognitive consequences while walking. *Neuropsychology*, 31(6), 613–623. <https://doi.org/10.1037/neu0000331>
- San Martín Valenzuela, C., Moscardó, L. D., López-Pascual, J., Serra-Añó, P., & Tomás, J. M. (2020). Effects of Dual-Task Group Training on Gait, Cognitive Executive Function, and Quality of Life in People With Parkinson Disease: Results of Randomized Controlled DUALGAIT Trial. *Archives of Physical Medicine and Rehabilitation*, 101(11), 1849–1856.e1. <https://doi.org/10.1016/j.apmr.2020.07.008>
- Scarpina, F., & Tagini, S. (2017). The Stroop Color and Word Test. *Frontiers in Psychology*, 8, 557. <https://doi.org/10.3389/fpsyg.2017.00557>
- Schapira, A. H. V., Chaudhuri, K. R., & Jenner, P. (2017). Non-motor features of Parkinson disease. *Nature Reviews. Neuroscience*, 18(7), 435–450. <https://doi.org/10.1038/nrn.2017.62>
- Schimpl, M., Moore, C., Lederer, C., Neuhaus, A., Sambrook, J., Danesh, J., Ouwehand, W., & Daumer, M. (2011). Association between walking speed and age in healthy, free-living individuals using mobile accelerometry—a cross-sectional study. *PloS One*, 6(8), e23299. <https://doi.org/10.1371/journal.pone.0023299>
- Shearin, S., Medley, A., Trudelle-Jackson, E., Swank, C., & Querry, R. (2021). Differences in predictors for gait speed and gait endurance in Parkinson's disease. *Gait & Posture*, 87, 49–53. <https://doi.org/10.1016/j.gaitpost.2021.04.019>
- Shen, X., & Mak, M. K. Y. (2012). Repetitive step training with preparatory signals improves stability limits in patients with Parkinson's disease. *Journal of Rehabilitation Medicine*, 44(11), 944–949. <https://doi.org/10.2340/16501977-1056>
- Skidmore, F. M., Mackman, C. A., Pav, B., Shulman, L. M., Garvan, C., Macko, R. F., & Heilman, K. M. (2008). Daily ambulatory activity levels in idiopathic Parkinson disease. *Journal of Rehabilitation Research and Development*, 45(9), 1343–1348.
- Strouwen, C., Molenaar, E. A. L. M., Munks, L., Keus, S. H. J., Zijlmans, J. C. M., Vandenberghe, W., Bloem, B. R., & Nieuwboer, A. (2017). Training dual tasks together or apart in Parkinson's disease: Results from the DUALITY trial. *Movement Disorders: Official Journal of the Movement Disorder Society*, 32(8), 1201–1210. <https://doi.org/10.1002/mds.27014>
- Studenski, S., Perera, S., Patel, K., Rosano, C., Faulkner, K., Inzitari, M., Brach, J., Chandler, J., Cawthon, P., Connor, E. B., Nevitt, M., Visser, M., Kritchevsky, S., Badinelli, S., Harris, T., Newman, A. B., Cauley, J., Ferrucci, L., & Guralnik, J. (2011). Gait speed and survival in older adults. *JAMA*, 305(1), 50–58. <https://doi.org/10.1001/jama.2010.1923>
- Suri, A., VanSwearingen, J., Dunlap, P., Redfern, M. S., Rosso, A. L., & Sejdíć, E. (2022). Facilitators and barriers to real-life mobility in community-dwelling older adults: A narrative review of accelerometry- and global positioning system-based studies. *Aging Clinical and Experimental Research*, 34(8), 1733–1746. <https://doi.org/10.1007/s40520-022-02096-x>
- Tosserams, A., Bloem, B. R., Ehgoetz Martens, K. A., Helmich, R. C., Kessels, R. P. C., Shine, J. M., Taylor, N. L., Wain-

stein, G., Lewis, S. J. G., & Nonnekes, J. (2023). Modulating arousal to overcome gait impairments in Parkinson's disease: How the noradrenergic system may act as a double-edged sword. *Translational Neurodegeneration*, 12(1), 15. <https://doi.org/10.1186/s40035-023-00347-z>

Vítečková, S., Horáková, H., Poláková, K., Krupička, R., Růžicka, E., & Brožová, H. (2020). Agreement between the GAITRite® System and the Wearable Sensor BTS G-Walk® for measurement of gait parameters in healthy adults and Parkinson's disease patients. *PeerJ*, 8, e8835. <https://doi.org/10.7717/peerj.8835>

Wilson, J., Alcock, L., Yarnall, A. J., Lord, S., Lawson, R. A., Morris, R., Taylor, J.-P., Burn, D. J., Rochester, L., & Galna, B. (2020). Gait Progression Over 6 Years in Parkinson's Disease: Effects of Age, Medication, and Pathology. *Frontiers in Aging Neuroscience*, 12, 577435. <https://doi.org/10.3389/fnagi.2020.577435>

Yogev-Seligmann, G., Hausdorff, J. M., & Giladi, N. (2008). The role of executive function and attention in gait. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(3), 329–342, quiz 472. <https://doi.org/10.1002/mds.21720>

Zajac, J. A., Cavanaugh, J. T., Baker, T., Duncan, R. P., Fulford, D., Giris, J., LaValley, M., Nordahl, T., Porciuncula, F., Rawson, K. S., Saint-Hilaire, M., Thomas, C. A., Earhart, G. M., & Ellis, T. D. (2022). Does clinically measured walking capacity contribute to real-world walking performance in Parkinson's disease? *Parkinsonism & Related Disorders*, 105, 123–127. <https://doi.org/10.1016/j.parkreldis.2022.11.016>

Zhou, J., Cattaneo, G., Yu, W., Lo, O.-Y., Gouskova, N. A., Delgado-Gallén, S., Redondo-Camós, M., España-Irla, G., Solana-Sánchez, J., Tormos, J. M., Lipsitz, L. A., Bartrés-Faz, D., Pascual-Leone, A., & Manor, B. (2023). The age-related contribution of cognitive function to dual-task gait in middle-aged adults in Spain: Observations from a population-based study. *The lancet. Healthy longevity*, 4(3), e98–e106. [https://doi.org/10.1016/S2666-7568\(23\)00009-0](https://doi.org/10.1016/S2666-7568(23)00009-0)

Chapter 10

Contribution 7: Motor and non-motor symptoms impact on different domains of capacity- and performance-based mobility measures in Parkinson's disease.

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Abstract

Mobility impairment in Parkinson's disease (PD) arises from both motor symptoms (MS) and non-motor symptoms (NMS). While supervised mobility assessments capture capacity, wearable devices now allow evaluation of unsupervised real-world performance. The relative contributions of MS and NMS across these domains remain unclear.

We conducted a cross-sectional study including 105 mild-to-moderate PD individuals. Participants underwent standardized supervised assessments of forward walking (FW), backward walking (BW), and turning, as well as free-living monitoring with a consumer smart-watch to collect average daily steps (AvDS) for 5 consecutive days. MS burden was quantified using MDS-UPDRS subscores, and NMS were assessed with validated scales of cognition, mood, sleep, and fatigue. Robust multivariable linear regression was used to evaluate the variance explained by MS, NMS, and their combination.

MS and NMS explained a modest proportion of mobility variance, with stronger effects on capacity than performance. Complex tasks (BW, turning) were more strongly associated with symptoms than FW. TD and PIGD were the main MS predictors of supervised mobility, while AR predicted AvDS. Among NMS, executive dysfunction and fatigue were determinants of capacity, whereas executive dysfunction also predicted AvDS. Depression and sleep disturbances influenced mobility only in NMS-only models.

Mobility in PD reflects an interplay of motor and non-motor determinants. While MS remain key drivers, NMS, particularly executive dysfunction and fatigue, exert a significant impact. These findings highlight the importance of multidimensional mobility assessment and suggest that addressing both MS and NMS may optimize interventions to preserve independence in PD.

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the combination of motor symptoms (MS), such as bradykinesia, rigidity, tremor, and postural instability, and a wide spectrum of non-motor symptoms (NMS), including sleep disturbances, fatigue, depression, cognitive impairment, autonomic dysfunction, and pain, among others (Poewe et al., 2017; Schapira et al., 2017). While MS have traditionally been considered as the clinical hallmark of PD and remain central to its diagnosis and monitoring, NMS are now recognized as highly prevalent, often preceding the onset of motor manifestations, and contributing substantially to disability and reduced quality of life (Schapira et al., 2017). Importantly, the burden of NMS frequently exceeds that of MS as the disease progresses, highlighting the need to address both dimensions for comprehensive patient care (Barone et al., 2009). Mobility impairments are among the most disabling features of PD. Gait disturbances, reduced walking speed, shuffling steps, turning difficulties, and freezing of gait severely compromise independence and increase the risk of falls and institutionalization (Fasano et al., 2017; Hackney & Earhart, 2009; Mirelman et al., 2019). Traditionally, mobility has been assessed in clinical or laboratory settings, where patients perform standardized tasks under supervision. These supervised assessments provide measures of capacity, that is, the ability to execute a motor task under controlled conditions. However, with the advent of wearable technologies, it has become possible to quantify mobility also in free-living environments, reflecting performance, or what patients actually do in their daily lives (Maetzler et al., 2021). The distinction between capacity and performance is increasingly emphasized, as it is now evident that the two domains capture complementary but not interchangeable aspects of mobility (Atrsaie et al., 2021; Giannouli et al., 2016; Zajac et al., 2022). Indeed, performance could be modulated by a broader set of factors such as personal, psychosocial, or environmental factors (Organization, 2002; Roussos et al., 2022). When considering performance, average daily steps (AvDS) have gained attention as a simple yet powerful marker of unsupervised mobility. This metric can be obtained continuously and unobtrusively using wearable activity monitors, providing an estimate of habitual ambulatory activity in daily life (Bassett et al., 2017). While step count does not capture specific gait characteristics, lower AvDS values consistently reflect greater mobility limitations and poorer health outcomes. In older adults, reduced daily steps have been associated with higher all-cause mortality, as highlighted in a recent meta-analysis (Ding et al., 2025), as well as an increased risk of chronic conditions including cancer and cardiovascular disease (Del Pozo Cruz, Ahmadi, et al., 2022), depression (Bizzozero-Peroni et al., 2024), and dementia (Del Pozo Cruz, Ahmadi, et al., 2022). In the context of PD, lower step counts have been linked to more severe motor impairment and reduced levels of habitual physical activity (Christiansen et al., 2017; Nagaki et al., 2022), supporting the potential of AvDS as a clinically meaningful outcome measure (Bianchini, Alborghetti, et al., 2025) for disease monitoring and management. A growing body of literature has investigated the impact of both MS and NMS on mobility in PD. MS, particularly axial features such as postural instability and gait disorders (PIGD), are strongly associated with poor mobility outcomes, including impaired turning and backward walking, as well as reduced physical activity in daily life (Bryant et al., 2018; Herman et al., 2014; Pongmala et al., 2025). Similarly, NMS such as cognitive dysfunction, sleep problems, depression, and fatigue have emerged as independent contributors to mobility decline (Burgos et al., 2025; Lord, Galna, Coleman, et al., 2013; Pilotto et al., 2023; Yogev-Seligmann et al., 2008). Executive dysfunction is particularly relevant, as it impairs dual-tasking and planning during walking, and has been linked to falls and mobility impairment in terms of forward walking (FW), turning and backward walking (BW) (Burgos et al., 2025; Mancini et al., 2016; Yogev-Seligmann et al., 2008). Fatigue also exacerbates gait impairment and may reduce habitual activity levels (Garber & Friedman, 2003; Pilotto et al., 2023). Depression and apathy further contribute by limiting motivation and physical engagement, leading to sedentary behavior and impaired gait (Lord, Galna, Coleman, et al., 2013; Still et al., 2024). Despite these insights, most studies have either focused on single symptom domains (Burgos et al., 2025; Pilotto et al., 2023), restricted the assessment to supervised mobility (Lord, Galna,

Coleman, et al., 2013), often encompassing only straight FW (Dragašević-Mišković et al., 2021) and neglecting more complex tasks and real-world performance. Consequently, the relationship between MS, NMS, and mobility across multiple domains remains incompletely understood. In particular, it is still unclear to what extent NMS burden explains variance in complex supervised tasks (e.g., turning, BW) and unsupervised performance measures (e.g., average daily steps) beyond motor impairment. Addressing this gap is clinically relevant, as it may reveal modifiable determinants of mobility that are not captured by conventional motor assessments and may guide the development of personalized interventions targeting both MS and NMS. Therefore, the aim of the present study was to investigate the impact of motor and non-motor symptoms on different domains of mobility in mild-to-moderate PD, encompassing both supervised tasks (forward walking, backward walking, turning) and unsupervised daily step count. We hypothesized that, while MS (particularly bradykinesia, rigidity and axial symptoms) would strongly predict mobility outcomes, NMS would provide additional explanatory power, particularly for complex tasks and real-world performance, underscoring the need for integrated multidimensional assessments in PD.

Material and Methods

Study design and ethics

This was an analysis conducted on a cross-sectional dataset of 121 mild-to-moderate PwPD collected to validate wearable-based measures and investigate the interaction between mobility, MS and NMS in PwPD. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines. Approval was granted by the local Ethical Committee of Sapienza, University of Rome, Italy (Ref. 0372/2022). This study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki of 1964 and subsequent amendments. Data collection and processing were carried out in compliance with current European data protection regulations. All data were deidentified. Participants did not receive any form of compensation.

Population

Participants were consecutively recruited from the Movement Disorders Centre at Sant'Andrea University Hospital (A.O.U. Sant'Andrea) in Rome between February 2023 and May 2024. Inclusion criteria included: (i) diagnosis of idiopathic Parkinson's disease according to the MDS criteria (Postuma et al., 2015); (ii) age 18 years or older; (iii) disease stage < 4 according to the modified Hoehn and Yahr scale (mHY) ("severe disability; still able to walk or stand unassisted") (Goetz et al., 2004); (iv) ability to perform the experimental procedure; and (v) availability of data regarding NMS and mobility. Exclusion criteria were: (i) severe cognitive impairment as defined by a Montreal Cognitive Assessment (MoCA) score < 18 (Baek et al., 2024); and (ii) orthopedic, rheumatologic, or systemic conditions affecting mobility as judged by the assessor.

Experimental Procedure

Participants meeting the inclusion and exclusion criteria were evaluated during their regular follow-up visits at the Neurology clinics of A.O.U. Sant'Andrea in Rome. After collecting demographic (age, sex), anthropometric (weight, height, BMI) and clinical data (disease duration, levodopa equivalent daily dose [LEDD] Jost et al., 2023, mHY), the following clinical scales were used to evaluate MS and NMS:

The MDS-UPDRS (Goetz et al., 2008) part I was used to assess the global burden of NMSs. MDS-UPDRS part I is a self-reported scale composed of 12 items investigating

Non-Motor Aspects of Experiences of Daily Living. A higher score indicating worse NMS burden.

The MDS-UPDRS part II was used to assess the global burden of MS. MDS-UPDRS part II is a self-reported scale composed of 13 items investigating Motor Aspects of Experiences of Daily Living. A higher score indicating worse MS burden.

The MDS-UPDRS part III was used to assess MS severity. MDS-UPDRS part III is the Motor Examination section and one of the most used protocols to assess MS. A higher score indicating worse MS severity.

From MDS-UPDRS part II and III, the tremor dominant (TD) and postural instability and gait disorders (PIGD) subscores were calculated according to Stebbins et al. (Stebbins et al., 2013) and the akinetic-rigid (AR) subscore was calculated according to Adams et al. (Adams et al., 2023).

The Parkinson's disease sleep scale version 2 (PDSS-2) (Trenkwalder et al., 2011) was used to assess sleep disturbances severity. A higher score indicates worse sleep problems and a score ≥ 15 has been reported as cut-off to define clinically significant disturbances (Suzuki et al., 2015).

The Epworth Sleepiness Scale (ESS) (Johns, 1991) was used to rate daytime sleepiness. A higher score at ESS indicates worse sleepiness and a score ≥ 10 is generally accepted as cut-off to define the presence of excessive daytime sleepiness.

The Fatigue Severity Scale (FSS) (Siciliano et al., 2019) was used to assess daytime sleepiness. A higher score indicates more impactful fatigue. In Italian PwPD a cut-off of 4.67 was reported to identify clinically relevant fatigue in Italian PwPD (Siciliano et al., 2019).

The Beck Depression Inventory II (BDI-II) (Maggi et al., 2023) was used to assess the severity of depressive symptoms. BDI-II is a self-administered scale, and a higher score indicates more severe depressive symptoms.

The MoCA (Nasreddine et al., 2005) was used to evaluate global cognition. The MoCA is an extensively used screening tool to assess global cognition and the presence of cognitive impairment. The score ranges from 0 to 30 and a lower score indicates worse cognitive performance. A cut-off of 22 was suggested to identify MCI in Italian PwPD (Fiorenzato et al., 2024).

The time to complete the interference part of the word-color Stroop test (WCST) in seconds was used to evaluate executive functions. WCST is a cognitive test assessing working memory and inhibition (Scarpina & Tagini, 2017).

Participants were then asked to perform two supervised mobility tasks while wearing a lower-back mounted research-grade inertial device for mobility analysis (BTS G-WALK, BTS Engineering Inc., Milan) (Vítečková et al., 2020): (i) a 20-meter FW task; and (ii) an instrumented Timed Up and Go (iTUG) (Ortega-Bastidas et al., 2023). Additionally, a 3-meter Backward Walk Test (3MBWT) was performed according with previous validation studies (Barta et al., 2025; Kocer et al., 2023). From the FW, spatiotemporal gait parameters were measured, including FW speed (m/s), cadence (steps/min), stride length normalized to height (%), cycle duration (s), stance and swing phases duration expressed as % of gait cycle. These were classified in parameters of pace (FW speed, cadence and stride length) and rhythm (cycle duration, stance and swing) according to the framework proposed by Lord et al. (Lord, Galna, Verghese, et al., 2013). From the iTUG, total iTUG duration, mean and peak angular velocity ($^{\circ}/s$) (MAV and PAV, respectively) of the intermediate 180° turn as well as duration of the turning (s) were collected. iTUG variables were divided in turning-related parameters (turning duration, MAV and PAV) and global mobility (iTUG duration). For the 3MBWT, PwPD performed 3 trials. The average of the time

(s) to complete each trial was collected (Barta et al., 2025) and BW speed (m/s) (BWS) was computed. To collect data on free-living walking, participants were asked to wear the Garmin Vivosmart 4 smartwatch (Garmin, Olathe, KS, USA), configured according to the manufacturer’s specifications by indicating the users’ age, height, weight, and the wrist on which the smartwatch was worn (i.e., left or right), on the wrist of the less affected side, in line with previous research findings (Bianchini, Rinaldi, et al., 2025; Bianchini et al., 2022, 2023) for 5 consecutive days. We choose a 5-day period since we demonstrated previously that a minimum of 4 days of monitoring is needed to reliably estimate daily step count in PwPD (Bianchini et al., 2023) and that 5 days of monitoring led to acceptable reliability regardless of PD severity, stage and phenotype (Bianchini, Rinaldi, et al., 2025). Moreover, in a proof-of-concept experiment, we recently demonstrated that Garmin Vivosmart 4 was valid and decently accurate in estimating avDS in PD (Bianchini, Rinaldi, et al., 2025). Participants were instructed to wear the smartwatch all time during day and night and to remove it only when involved in water activities (e.g., bathing, showering, swimming, etc.). Participants were asked to perform daily activities as usual. No additional reminder or instructions were provided to participants during the monitoring period. During the monitoring period, participants could access information on the smartwatch screen, including the total number of steps, heart rate and sleep time. The device did not provide instructions, alerts or other messages to participants. The total daily steps recorded were extracted, and the average daily steps (AvDS) were calculated (Bianchini et al., 2023). Compliance was assessed based on the participants’ dashboard data. We could assess that the device was worn through heart rate and activity data. We considered all recording days with $\geq 80\%$ wear time while awake to be valid. We estimated the awake time as 24 hours minus the total sleep time as indicated by the device (Bianchini, Rinaldi, et al., 2025). Experimental procedure is summarized in fig. 10.1.

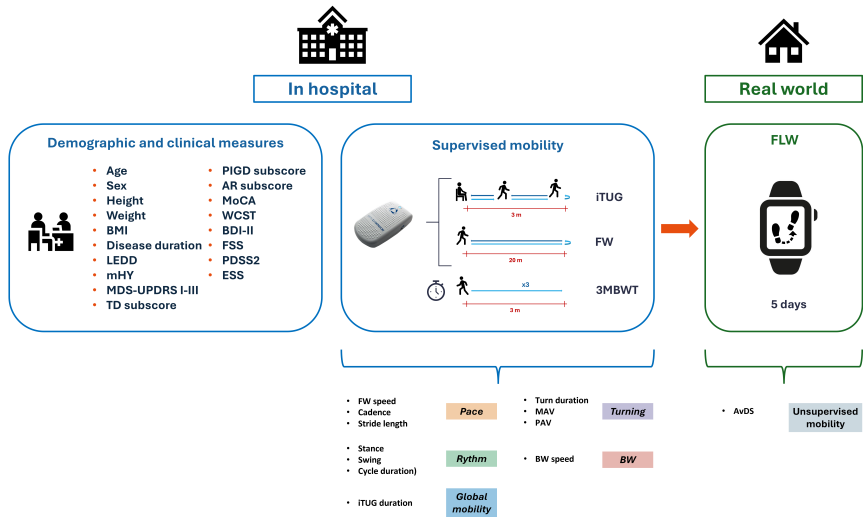


Figure 10.1. Schematic representation of study experimental procedure. 3MBWT: 3-meter backward walking test; AR: akinetic-rigid; AvDS: average daily steps; BDI-II: Beck depression inventory II; BMI: Body mass index; ESS: Epworth sleepiness scale; FLW: Free-living walking; FSS: Fatigue severity scale; FW: forward walking; iTUG: instrumented Timed Up and Go; LEDD: Levodopa equivalent daily dose; MDS-UPDRS: Movement Disorder Society unified Parkinson’s disease rating scale; mHY: Modified Hoehn and Yahr stage; MoCA: Montreal cognitive assessment; PDSS-2: Parkinson’s disease sleep scale 2; PIGD: postural instability and gait disorders; TD: tremor-dominant; WCST: Word-color Stroop test.

Statistical analyses

Statistical analyses were performed using JASP v0.19.3.0 (JASP Team, University of Amsterdam, The Netherlands), R v4.4.5 and RStudio v2025.05.0+496 for Windows (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were calculated for the variables under study, with continuous variables reported as mean (SD) or median (Q1-Q3), and categorical variables reported as N (%). Since certain assumptions of parametric multivariable linear regression were violated, robust multivariable linear regression models were used to evaluate the extent to which MS, NMS and NM+NMS explained the variance of capacity- and performance-related measures of mobility. Separate models were constructed for each mobility-related outcome variable, with MS, NMS and NM+NMS scores included as independent variables, respectively. Robust multivariable linear regression models were fitted using M-estimation with Huber weighting via the `rlm()` function from the MASS package in R (Venables & Ripley, 2002). Inference on the model coefficients was performed using robust standard errors computed using the sandwich estimator with the `vcovHC()` function from the sandwich package (Zeileis et al., 2020). Two-tailed p-values were derived using t-distribution-based Wald tests, computed with the `coefest()` function from the `lmtest` package (Zeileis & Hothorn, 2002) in order to adjust for finite sample size. A step-

wise variable selection approach based on Akaike Information Criterion (AIC) was applied using the `stepAIC()` function from the `MASS` package, to further reduce dimensionality and identify the most relevant covariates. This procedure used bidirectional elimination, iteratively adding or removing variables to minimize the AIC. Multicollinearity was tested using the `performance` package (Lüdtke et al., 2021). The R^2 was computed manually for each robust model as:

$$R^2 = 1 - \frac{SS_{\text{residuals}}}{SS_{\text{total}}}$$

where $SS_{\text{residuals}}$ is the sum of squared residuals and SS_{total} is the total sum of squares. The adjusted R^2 was calculated using the classical formula:

$$R^{*2} = 1 - \left(\frac{SS_{\text{residuals}}/(n - k - 1)}{SS_{\text{total}}/(n - 1)} \right)$$

Results

Overview

From the original cross-sectional dataset of 121 individuals, a total of 105 people with mild-to-moderate PD were included in the study, based on predefined inclusion and exclusion criteria. Specifically, 8 patients were excluded due to incomplete mobility data caused by technical issues, and another 8 were excluded due to missing data on MDS-UPDRS subitems, which made it impossible to compute the TD, PIGD, and AR subscores. The demographic, anthropometric, and clinical features are summarized in table 10.1. The characteristics of included PwPD in terms of mobility variables is reported in table 10.2. MDS-UPDRS part I and III were excluded from all models due to the collinearity above the predefined threshold.

Table 10.1. Demographic, anthropometric, basic clinical characteristics and NMS parameters of the enrolled population.

	PwPD (n=105)
Age (years)	69.2 (8.7)
Sex (F)	34 (32%)
Height (cm)	171 (8.7)
Weight (kg)	75.8 (13.1)
BMI (kg/m ²)	25.8 (3.4)
Disease duration (years)	5.73 (3.9)
LEDD (mg)	506 (245)
mHY	2 (2-2.5)
MDS-UPDRS part I	6 (4-9)
MDS-UPDRS part II	4 (2-7)
MDS-UPDRS part III	26 (21-32)
TD subscore	3 (0-6)
PIGD subscore	2 (1-5)
AR subscore	18 (14-22)
PDSS-2	9 (6-14)
ESS	6 (4-7)
FSS	3.23 (1.68)
BDI-II	7 (4-10)
MoCA	26 (25-28)
sVASI	41.7 (16.0)

AR: axial-rigid; BDI-II: Beck depression inventory II; BMI: Body mass index; ESS: Epworth sleepiness scale; FSS: Fatigue severity scale; LEDD: Levodopa equivalent daily dose; MDS-UPDRS: Movement Disorder Society unified Parkinson's disease rating scale; mHY: modified Hoehn and Yahr stage; MoCA: Montreal cognitive assessment; NMS: non-motor symptoms; PDSS-2: Parkinson's disease sleep scale 2; PIGD: postural instability and gait disorders; PwPD: people with Parkinson's disease; sVASI: small vessel disease; TD: tremor dominant; sVASI: Vascular aging score.

Table 10.2. Mobility parameters in the enrolled population.

Test	Domain	Outcome	Value
FLW	<i>Unsupervised mobility</i>	AvDS (steps/day)	5971 (3027)
FW	<i>Pace</i>	FW speed (m/s)	1.18 (0.23)
		Cadence (steps/min)	112.3 (8.4)
		Stride length% (%height)	73.9 (11.6)
	<i>Rhythm</i>	Stance (%cycle)	61.1 (2.2)
		Swing (%cycle)	38.9 (2.2)
		Cycle duration (s)	1.09 (0.09)
iTUG	<i>Global mobility</i>	iTUG duration (s)	12.0 (4.5)
	<i>Turning</i>	Turn duration (s)	2.68 (0.98)
		MAV (°/s)	70.6 (18.1)
		PAV (°/s)	140.9 (41.9)
3MBWT	<i>Backward walking</i>	BW speed (m/s)	0.59 (0.23)

3MBWT: 3-meter backward walking test; AvDS: average daily steps; BW: backward walking; FLW: free-living walking; FW: forward walking; iTUG: instrumented timed-up-and-go; MAV: mean angular velocity; PAV: peak angular velocity; PwPD: people with Parkinson's disease.

Motor symptoms

All robust linear regression models were statistically significant, excluding the one for cadence ($P = .091$), stance ($P = .112$) and swing duration ($P = .117$). Adjusted R^2 ranged from 0.053 to 0.313. Details of the models and predictors are summarized in table S10.1 and table S10.4, respectively. The adjusted R^2 for each mobility domain is graphically shown in fig. 10.2A.

Details of inclusion and significance of each MS predictor are shown in fig. 10.3A. In brief, TD, PIGD and AR subscores were the most relevant predictors of mobility parameters. In particular, TD was a significant predictor for turning, BW, FW in the pace domain and global mobility, as measured by the total iTUG duration. TD showed a negative relationship with all mobility parameters (the worse the score the better the mobility parameters). AR was a significant predictor of turning variables as well as iTUG duration and FW in the rhythm domain. Notably, AR subscore was the only MS predictor of unsupervised mobility. Finally, PIGD was a significant predictor only of BW speed and iTUG duration. Both AR and PIGD score showed a positive relationship with all mobility parameters (the better the score the better the mobility).

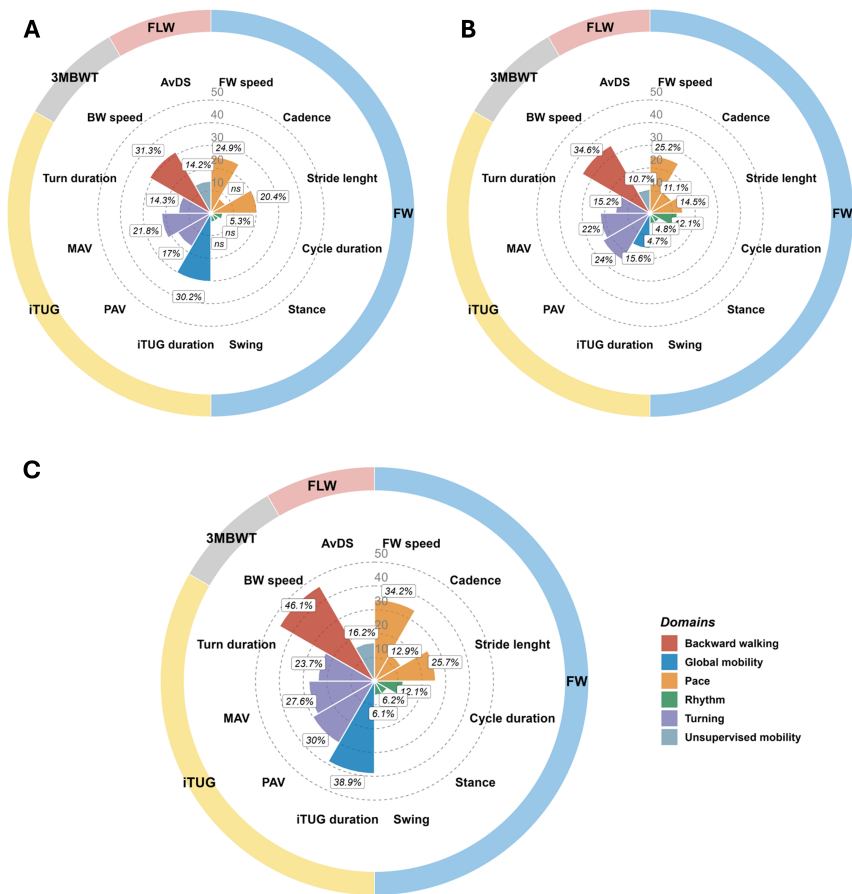


Figure 10.2. Radar plots showing the proportion of variance explained by MS (panel A), NMS (panel B) and MS+NMS (panel C) for each mobility measure in PwPD. The radius of each circular sector represents the adjusted R^2 value (expressed as a percentage), which is also shown as a label above each variable. The color of the circular sectors indicates the domain to which each variable belongs (see legend). The outer colored ring corresponds to the four tests used for mobility assessment. 3MBWT: 3-meter backward walking test; AvDS: average daily steps; BW: backward walking; FLW: free-living walking; FW: forward walking; iTUG: instrumented Timed Up and Go; MAV: mean angular velocity; NMS: non-motor symptoms; PAV: peak angular velocity; PwPD: people with Parkinson's disease.

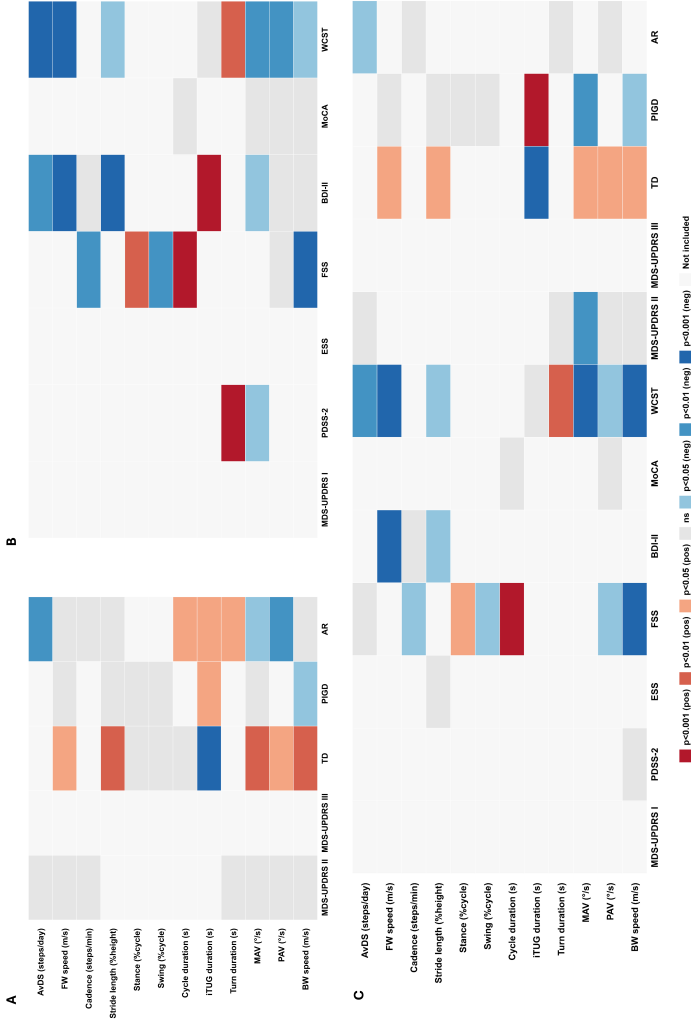


Figure 10.3. Heatmaps showing which MS (panel A), NMS (panel B) and MS+NMS (panel C) predictor is included in each model. Predictors not included are shown in light grey. Predictors which were included but non-significant are shown in darker grey. The level of significance and the direction of the association between variables are shown with different shades of color (see legend). AR: akinetic rigid; AvDS: average daily steps; BW: backward walking; FW: forward walking; iTUG: instrumented Timed Up and Go; MAV: mean angular velocity; MDS-UPDRS: Movement Disorder Society unified Parkinson's disease rating scale; NMS: non-motor symptoms; ns: non-significant; PAV: peak angular velocity; PIGD: postural instability and gait disorders; TD: tremor-dominant.

Non-motor symptoms

All robust linear regression models were statistically significant. Adjusted R² ranged from 0.047 to 0.346. Details of the models and predictors are summarized in table S10.2 and table S10.5, respectively. The adjusted R² for each mobility domain is graphically shown in fig. 10.2B. Details of inclusion and significance of each NMS predictor are shown in fig. 10.3B. In brief, executive functions, fatigue and depression were the most relevant predictors of mobility. In particular, executive functions and depression were significant predictors of turning, FW in the pace domain and unsupervised mobility. In addition executive functions significantly predicted BW whereas depression was a the only significant predictor of global mobility, as measured by iTUG duration. Fatigue, on the other hand, was a significant predictor of BW and FW, mainly in the rhythm domain. Interestingly, sleep problems were a significant predictor only of turning parameters. All NMS showed a positive relationship with mobility parameters (the better the score the better the mobility).

Combined MS and NMS

All robust linear regression models were statistically significant. Adjusted R² ranged from 0.061 to 0.461. Details of the models and predictors are summarized in table 10.3 and table S10.3, respectively. The adjusted R² for each mobility domain is graphically shown in fig. 10.2C. Details of inclusion and significance of each NMS predictor are shown in fig. 10.3C. In brief, regarding NMS, executive functions were confirmed as the most relevant predictor of mobility. In particular, they were significant predictor of BW, turning, FW in the pace domain and were the only non-motor predictor of unsupervised mobility. Fatigue was a significant predictor of BW and turning PAV and was confirmed as the only significant overall predictor of FW rhythm domain. Notably depression was confirmed to be a significant predictor only for FW pace domain and sleep problems were not a significant predictor for any mobility parameter. Regarding MS, TD score was confirmed as a significant predictor of turning, BW, FW in the pace domain and global mobility, as measured by the total iTUG duration. Interestingly, when considering both MS and NMS, AR was not a significant predictor of any mobility parameters except AvDS, for which it was the only motor predictor. PIGD, conversely, was confirmed to be a significant predictor of BW and global mobility but also showed a significant impact on turning MAV.

Table 10.3. Summary of the robust multivariate linear models for each dependent variable using MS+NMS as independent variables. For each model R^2 (in percentage), p-value, the included independent variables after backward elimination and the significant predictors are reported.

Test	Domain	Outcome	R^2	aR^2	p-value	Included predictors	Significant predictors
FLW	<i>Unsupervised mobility</i>	AvDS (steps/day)	19.4	16.2	< 0.001	MDS-UPDRS II, FSS, WCST, AR	WCST, AR
FW	<i>Pace</i>	FW speed (m/s)	36.7	34.2	< 0.001	WCST, BDI-II, TD, PIGD	WCST, BDI-II, TD
		Cadence (step-s/min)	15.4	12.9	0.005	FSS, BDI-II, AR	FSS
		Stride length (%)	29.3	25.7	< 0.001	ESS, WCST, BDI-II, TD, PIGD	WCST, BDI-II, TD
		Stride height (%)					
iTUG	<i>Rhythm</i>	Stance (%cycle)	8.0	6.2	0.015	FSS, PIGD	FSS
		Swing (%cycle)	7.9	6.1	0.016	FSS, PIGD	FSS
		Cycle duration (s)	13.8	12.1	< 0.001	FSS, MoCA	FSS
iTUG	<i>Global mobility</i>	iTUG duration (s)	40.7	38.9	< 0.001	WCST, TD, PIGD	TD, PIGD
	<i>Turning</i>	Turn duration (s)	25.9	23.7	< 0.001	MDS-UPDRS II, WCST, AR	WCST
		MAV ($^{\circ}$ /s)	30.4	27.6	< 0.001	MDS-UPDRS II, WCST, TD, PIGD	MDS-UPDRS II, WCST, TD, PIGD
		PAV ($^{\circ}$ /s)	34.0	30.0	< 0.001	MDS-UPDRS II, FSS, WCST, MoCA, TD, AR	FSS, WCST, TD
3MBWT	<i>Backward walking</i>	BW speed (m/s)	49.2	46.1	< 0.001	MDS-UPDRS II, PDSS-2, FSS, WCST, TD, PIGD	FSS, WCST, TD, PIGD

3MBWT: 3-meter backward walking test; AR: aknetic-rigid; AvDS: average daily steps; BDI-II: Beck depression inventory II; BW: backward walking; FLW: free-living walking; FSS: Fatigue severity scale; FW: forward walking; iTUG: instrumented timed-up-and-go; MAV: mean angular velocity; MoCA: Montreal cognitive assessment; PAV: peak angular velocity; PDSS-2: Parkinson's disease sleep scale 2; PIGD: postural instability and gait disorders; TD: tremor-dominant; WCST: Word-color Stroop test.

Discussion

Overview

The aim of this cross-sectional study was to investigate the impact of MS and NMS on supervised and unsupervised mobility in mild-to-moderate PD. In particular, we explored how different domains of NMS influenced specific supervised tasks, such as FW, BW and turning as well as FLW, assessed by AvDS. Our findings showed that: (i) the overall contribution of MS and NMS to mobility was modest; (ii) their impact was greater on supervised than unsupervised measures, and particularly evident in complex tasks such as BW and turning; (iii) TD and PIGD domains, together with executive function and fatigue, were the strongest predictors of supervised mobility; and (iv) AR symptoms and executive dysfunction best predicted unsupervised performance.

General effect of MS and NMS on mobility

MS and NMS explained only a modest share of variance in mobility, around one quarter on average, with stronger effects on capacity than performance. Within supervised assessments, complex tasks such as BW and turning were most affected, while FW showed weaker associations. These results underscore the multifactorial nature of mobility in PD, where demographics and lifestyle (age, fitness, education) (Lee et al., 2019; Schlachetzki et al., 2017); personal factors (motivation, mood, fear of falling) (Nemanich et al., 2013; Paker et al., 2015; Yang, 2025); comorbidities (obesity, malnutrition, pain, orthopedic issues) (Grande et al., 2019; Yilmaz et al., 2019); and external elements (medications, walking aids) (O'Donnell et al., 2025; Smulders et al., 2016) also play a role. Real-world performance is further shaped by environment, weather, work and socio-economic context (Roussos et al., 2022). Despite controlling some of these elements, capturing all determinants is unrealistic in routine practice and likely contributes to the modest variance explained, especially for AvDS. Moreover, our cohort of relatively high-functioning participants may also have used compensatory strategies (e.g., pacing, activity scheduling) that preserve daily step totals despite symptoms (Mirelman et al., 2019). The greater explanatory power for BW and turning is consistent with the observation that complex gait challenges axial control and cognitive-motor integration to a greater extent than FW. BW particularly showed the highest symptom-related variance and is known to be disproportionately impaired and linked to falls (Hackney & Earhart, 2009; Milane et al., 2025), likely due to higher postural, proprioceptive, and cognitive demands (Correno et al., 2022; Hackney & Earhart, 2009; Hulbert et al., 2015; Mancini et al., 2015, 2016; Milane et al., 2025).

MS and NMS impact on capacity

In MS-only models, all three motor subdomains related to capacity, with AR associated with faster turning and better overall mobility (shorter iTUG) and gait rhythmicity, in line with the global impact of bradykinesia/rigidity on timing and smoothness (Allali et al., 2014; Winogrodzka et al., 2005). TD showed an inverse association with impairment, consistent with the clinical observation of relatively milder disability in TD individuals (Aleksowski et al., 2018; Stebbins et al., 2013). When MS and NMS were combined, AR no longer predicted supervised mobility parameters, whereas TD retained its inverse association across several mobility metrics, while PIGD remained linked to BW and turning. This result is rather expected given the contribution of axial symptoms to mobility (Bryant et al., 2018; Pongmala et al., 2025; Prime et al., 2020). The attenuation of AR in combined models may reflect overlapping variance with NMS and stronger TD effects. However, as this is the first report on this topic, confirmation is warranted. Among NMS, executive dysfunction emerged as the most consistent predictor of supervised mobility, predicting poorer turning, BW, and slower FW pace, and it remained significant in combined models, aligning with

evidence that set-shifting, attention and dual-tasking deficits degrade complex gait (Salazar et al., 2017; Yogev-Seligmann et al., 2008). Fatigue also related to slower BW and altered FW rhythm and continued to influence turning when MS were included (Alix-Fages et al., 2023; Branscheidt et al., n.d.; Carvalho et al., 2020; Garber & Friedman, 2003; Huang et al., 2017). Depression affected FW pace and global iTUG in NMS-only models but lost significance when MS were added, suggesting indirect effects mediated by increasing motor severity or reducing physical activity and fitness (Dragašević-Mišković et al., 2021; Lord, Galna, Coleman, et al., 2013; Mayeli et al., 2024; Timblin et al., 2022). This is similarly observed for sleep problems which were associated with turning parameters in the NMS-only model but were not significant when MS were included. Indeed, poor sleep quality has been shown to worsen both motor and non-motor symptoms of PD (Yi et al., 2022). This interplay between NMS and MS in affecting mobility underscores the need for a global clinical approach since addressing NMS like cognitive dysfunction, depression, or fatigue might indirectly improve mobility by allowing patients to better utilize their motor capacity.

MS and NMS impact on performance

For unsupervised mobility, AR was the primary motor predictor of AvDS in MS-only and combined models. Worse AR related to fewer daily steps, consistent with bradykinesia and rigidity negatively impacting overall activity in PwPD (Christiansen et al., 2017; Galperin et al., 2019; Nagaki et al., 2022). TD did not predict AvDS, in line with clinical experience that tremor does not necessarily reduce habitual walking (Galperin et al., 2020; Safarpour et al., 2022). Notably, PIGD was not associated with AvDS, suggesting that even with gait/postural impairments, participants maintained daily walking volumes, consistent with the possibility of compensation in a mild-to-moderate cohort. Within NMS, depression and executive dysfunction predicted lower AvDS in NMS-only models. Previous evidence reported the negative impact of these symptoms on gait impairments. A recent large systematic review by Bizzozero-Peroni and colleagues recently showed that daily steps are inversely associated with the risk of depression in adults (Bizzozero-Peroni et al., 2024). Additionally, Burgos et al. reported that executive dysfunction negatively impacted gait in PwPD in real-world conditions (Burgos et al., 2025). However, in combined models, executive dysfunction and AR remained the only significant factors. This is consistent with previous evidence highlighting the impact of bradykinesia and executive functions on real-world activity (Burgos et al., 2025; Mc Ardle et al., 2022; Still et al., 2024). Depression, on the other hand, was not a significant predictor in the combined model, consistent with the findings on capacity-related metrics. This could be again attributable to an indirect effect. In fact, previous evidence indicated how depression could negatively impact executive functions and other symptoms in PwPD (Kummer et al., 2009; Uekermann et al., 2003). Fatigue did not independently relate to AvDS. This is in contrast with a previous study from Pilotto and colleagues (Pilotto et al., 2023), showing that fatigue impacts unsupervised walking but not supervised in a cohort of 42 early PwPD. However, in that study, authors examined spatiotemporal gait parameters and fatigue was associated with step metrics. Differently, we did not examine detailed walking parameters but rather the volume of walking during the day. It is, indeed, possible that our patients could compensate for fatigue by distributing their activity throughout the day and thus they might still achieve a certain number of steps, albeit with more pauses and at a slower pace. The dominance of AR and executive function as predictors in the combined model underscores the importance of considering both motor and non-motor factors in real-life mobility. A patient may have the physical ability to walk but still be limited by executive deficits that reduce navigation skills or confidence; conversely, preserved cognition cannot compensate for severe bradykinesia and rigidity. This dual influence highlights the need for integrated interventions, addressing motor symptoms (e.g., physiotherapy or medication) alongside cognitive and mood aspects. Cognitive rehabilitation or treatment of depression, for instance, may enhance patients' willingness and capacity to remain active, complementing motor improve-

ments. Evidence supports this interdependence, as treating NMS can improve functional motor status (Chaudhuri et al., 2024; Michels et al., 2022). and cognitive training has been shown to benefit motor symptoms in mild-to-moderate PD (Michels et al., 2022). While our study was not interventional, the observed associations reinforce these links.

Limitations, strengths and perspectives

We acknowledge that this study has limitations. First, the cross-sectional design prevents us from inferring causal relationships between variables. Second, the sample included individuals in mild-to-moderate PD stages, and those with more severe cognitive or motor impairments and unable to walk independently were excluded. This could limit the generalizability of our findings across disease severities. The mobility assessment was also limited: supervised mobility relied only on spatiotemporal gait and turning parameters, while unsupervised mobility relied only on AvDS. Although our evaluation was more extensive compared with several previous studies, incorporating a more comprehensive range of mobility indicators, especially under real-world conditions, could enhance our understanding of ecological mobility. Regarding NMS, we did not explore in detail all the different domains that are usually reported in PD. Specifically, we did not include specific assessment for autonomic dysfunction (including cardiovascular, sexual, gastrointestinal and urinary problems), anxiety and perceptual problems/hallucinations. However, we partially accounted for the lack of dedicated assessment for these domains by including part I of MDS-UPDRS (Non-Motor Aspects of Experiences of Daily Living), which include items regarding these domains, to capture the global impact of NMS. Regarding MS assessment, technological advancement allows now neurologists to collect quantitative data regarding motor symptoms such as bradykinesia and tremor by means of wearable devices, computer vision or other methods (Moreau et al., 2023; Pecoraro et al., 2025). The implementation of quantitative measures of MS could increase the level of informativeness of PwPD evaluation as well as granting the possibility to monitor patients at home, achieving a more comprehensive assessment of motor impairment. Allowing participants to view smartwatch feedback may have influenced their behavior, as step-count displays can encourage activity (Ferguson et al., 2022). We accepted this potential bias since our goal was to mirror real-world conditions of smartwatch usage. Using consumer-grade devices also raises concerns about data privacy and the opacity of proprietary algorithms. Although our procedures followed manufacturer instructions and EU data protection standards, we could not assess how demographic inputs (e.g., age, height, weight) or proprietary algorithms affected step counts. Moreover, raw data are not directly accessible, limiting independent analysis and advanced processing. Despite these limitations, our study presents notable strengths. One is the broad range of supervised mobility tasks assessed, including FW, BW, turning and global supervised mobility. Another key strength lies in the application of standardized and well-established motor subscores extraction. Furthermore, the application of robust linear regression made our analysis more resilient to deviations from classical linear model’s assumptions. Lastly, our findings emphasize the value of integrating both supervised and unsupervised mobility assessments to achieve a comprehensive evaluation of individuals with PD and stimulate further research to understand in greater detail how motor and non-motor components of PD interact.

Conclusions

In conclusion, we demonstrated that both motor and non-motor symptoms significantly contribute to different domains of supervised and unsupervised mobility in people with Parkinson’s disease. Our findings emphasize that mobility is a multidimensional construct influenced not only by motor impairments but also by the burden of non-motor symptoms, such as sleep disturbances, fatigue, depression, and cognitive deficits. Importantly, the differential impact of these symptoms across mobility domains suggests that no single mea-

sure can fully capture mobility limitations in Parkinson's disease. Instead, an integrated approach combining both supervised tasks and real-world performance should be preferred to comprehensively characterize patients' mobility. From a clinical perspective, these results reinforce the need for multidimensional assessments that go beyond motor symptoms alone, acknowledging the role of non-motor features as key determinants of mobility and daily functioning. This perspective may inform the design of tailored interventions aimed at addressing both motor and non-motor symptoms to improve mobility, independence, and quality of life in Parkinson's disease. Future longitudinal studies are warranted to clarify causal pathways and to determine whether targeted management of non-motor symptoms could mitigate mobility decline and enhance therapeutic outcomes.

Supplementary material

Table S10.1. Summary of the robust multivariate linear models for each dependent variable using MS as independent variables. For each model R^2 (in percentage), p-value, the included independent variables after backward elimination and the significant predictors are reported.

Test	Domain	Outcome	R^2	ΔR^2	p-value	Included tors	predic- tors	Significant predictors	pre-
FLW	Unsupervised bitility	mo- AVDS (steps/day)	15.9	14.2	< 0.001	MDS-UPDRS AR	II, AR		
FW	Pace	FW speed (m/s)	27.8	24.9	< 0.001	MDS-UPDRS TD, PIGD, AR	II, TD		
	Rhythm	Cadence s/min	9.3	7.5	0.091	MDS-UPDRS AR	II, TD, PIGD, AR		
	Rhythm	Stride length%	22.7	20.4	< 0.001	TD, PIGD, AR	TD		
	Rhythm	Stance (%cycle)	5.8	4.0	0.112	TD, PIGD	TD, PIGD		
	Rhythm	Swing (%cycle)	5.8	3.9	0.117	TD, PIGD	TD, PIGD		
	Rhythm	Cycle duration (s)	7.1	5.3	0.020	TD, AR	AR		
iTUG	Global mobility Turning	iTUG duration (s)	32.2	30.2	< 0.001	TD, PIGD, AR	TD, PIGD, AR		
	Global mobility Turning	Turn duration (s)	16.0	14.3	< 0.001	MDS-UPDRS AR	II, AR		
	Global mobility Turning	MAV (°/s)	24.8	21.8	< 0.001	MDS-UPDRS TD, PIGD, AR	II, TD, AR		
	Global mobility Turning	PAV (°/s)	19.3	17.0	< 0.001	MDS-UPDRS TD, AR	II, TD, AR		
3MBWT	Backward walking	BW speed (m/s)	33.9	31.3	< 0.001	MDS-UPDRS TD, PIGD, AR	II, TD, PIGD		

3MBWT: 3-meter backward walking test; AR: akinetic-rigid; AVDS: average daily steps; BW: backward walking; FLW: free-living walking; FW: forward walking; iTUG: instrumented timed-up-and-go; MAV: mean angular velocity; MDS-UPDRS: Movement Disorder Society unified Parkinson's disease rating scale; PAV: peak angular velocity; PIGD: postural instability and gait disorders; TD: tremor-dominant.

Table S10.2. Summary of the robust multivariate linear models for each dependent variable using NMS as independent variables. For each model R^2 (in percentage), p-value, the included independent variables after backward elimination and the significant predictors are reported.

Test	Domain	Outcome	R^2 (%)	a R^2 (%)	p-value	Included predictors	Significant predictors
FLW	<i>Unsupervised mobility</i>	AvDS (steps/day)	12.4	10.7	< 0.001	WCST, BDI-II	WCST, BDI-II
FW	<i>Pace</i>	FW speed (m/s)	26.7	25.2	< 0.001	WCST, BDI-II	WCST, BDI-II
		Cadence (steps/min)	12.8	11.1	< 0.001	FSS, BDI-II	FSS
		Stride length (%)	16.2	14.5	< 0.001	WCST, BDI-II	WCST, BDI-II
	<i>Rhythm</i>	Stance (%cycle)	5.7	4.8	0.003	FSS	FSS
		Swing (%cycle)	5.6	4.7	0.003	FSS	FSS
iTUG	<i>Global mobility</i>	Cycle duration (s)	13.8	12.1	< 0.001	FSS, MoCA	FSS
		iTUG duration (s)	17.2	15.6	< 0.001	WCST, BDI-II	BDI-II
		Turn duration (s)	16.8	15.2	< 0.001	PDSS-2, WCST	PDSS-2, WCST
		MAV ($^{\circ}$ /s)	25.0	22.0	< 0.001	PDSS-2, WCST, BDI-II, MoCA	PDSS-2, WCST, BDI-II
		PAV ($^{\circ}$ /s)	26.9	24.0	< 0.001	FSS, WCST, BDI-II, MoCA	FSS, WCST
3MBWT	<i>Backward walking</i>	BW speed (m/s)	37.1	34.6	< 0.001	FSS, WCST, BDI-II, MoCA	FSS, WCST

3MBWT: 3-meter backward walking test; AvDS: average daily steps; BDI-II: Beck depression inventory II; BW: backward walking; FLW: free-living walking; FSS: Fatigue severity scale; FW: forward walking; iTUG: instrumented timed-up-and-go; MAV: mean angular velocity; MoCA: Montreal cognitive assessment; PAV: peak angular velocity; PDSS-2: Parkinson's disease sleep scale 2; WCST: Word-color Stroop test.

Table S10.3. Summary of the MS+NMS predictors for each robust regression model. The intercept of the regression models is also shown for each dependent variable. For each predictor the estimated coefficient, p-value and level of significance are reported.

Outcome	Predictor	Estimate	p-value
AvDS (steps/day)	(Intercept)	10859.281	< 0.001***
	MDS-UPDRS II	-125.440	0.097
	FSS	-310.128	0.050
	WCST	-43.592	0.003**
	AR	-90.349	0.049*
FW speed (m/s)	(Intercept)	1.488	< 0.001***
	WCST	-0.005	< 0.001***
	BDI-II	-0.013	< 0.001***
	TD	0.009	0.018*
	PIGD	-0.022	0.138
Cadence (steps/min)	(Intercept)	121.022	< 0.001***
	FSS	-1.376	0.011*
	BDI-II	-0.195	0.319
	AR	-0.173	0.247
Stride length (%height)	(Intercept)	63.525	< 0.001***
	ESS	0.380	0.232
	WCST	-0.159	0.029*
	BDI-II	-0.500	0.012*
	TD	0.483	0.012*
	PIGD	-1.335	0.071
Stance (%cycle)	(Intercept)	59.851	< 0.001***
	FSS	0.283	0.011*
	PIGD	0.114	0.375
Swing (%cycle)	(Intercept)	40.147	< 0.001***
	FSS	-0.283	0.012*
	PIGD	-0.114	0.375
Cycle duration (s)	(Intercept)	1.202	< 0.001***
	FSS	0.018	< 0.001***
	MoCA	-0.007	0.076
iTUG duration (s)	(Intercept)	8.429	< 0.001***
	WCST	0.026	0.406
	TD	-0.207	< 0.001***
	PIGD	0.661	< 0.001***
Turn duration (s)	(Intercept)	1.283	< 0.001***
	MDS-UPDRS II	0.038	0.051
	WCST	0.015	0.008**
	AR	0.026	0.068
MAV (°/s)	(Intercept)	91.136	< 0.001***
	MDS-UPDRS II	-0.535	0.007**
	WCST	-0.334	< 0.001***
	TD	0.560	0.012*
	PIGD	-1.504	0.004**
PAV (°/s)	(Intercept)	121.770	0.008**
	MDS-UPDRS II	-1.114	0.147
	FSS	-3.390	0.044*
	WCST	-0.505	0.028*
	MoCA	2.334	0.071
	TD	1.288	0.091
	AR	-1.205	0.116
BW speed (m/s)	(Intercept)	0.976	< 0.001***
	MDS-UPDRS II	-0.011	0.056
	PDSS-2	0.006	0.152
	FSS	-0.046	< 0.001***
	WCST	-0.005	0.008**
	TD	0.008	0.023*
	PIGD	-0.027	0.042*

AR: akinetic-rigid; AvDS: average daily steps; BDI-II: Beck depression inventory II; BW: backward walking; FSS: Fatigue severity scale; FW: forward walking; iTUG: instrumented timed-up-and-go; MAV: mean angular velocity; MoCA: Montreal cognitive assessment; PAV: peak angular velocity; PDSS-2: Parkinson's disease sleep scale 2; PIGD: postural instability and gait disorders; TD: tremor-dominant; WCST: Word-color Stroop test.

Table S10.4. Summary of the MS predictors for each robust regression model. The intercept of the regression models is also shown for each dependent variable. For each predictor the estimated coefficient, p-value and level of significance are reported.

Outcome	Predictor	Estimate	p-value
AvDS (steps/day)	(Intercept)	9059.072	< 0.001***
	MDS-UPDRS II	-137.935	0.075
	AR	-138.130	0.005**
FW speed (m/s)	(Intercept)	1.376	< 0.001***
	MDS-UPDRS II	-0.006	0.416
	TD	0.011	0.013*
	PIGD	-0.016	0.439
	AR	-0.009	0.370
Cadence (steps/min)	(Intercept)	117.149	< 0.001***
	MDS-UPDRS II	-0.348	0.169
	AR	-0.181	0.254
Stride length (%height)	(Intercept)	80.707	< 0.001***
	TD	0.562	0.008**
	PIGD	-1.301	0.213
	AR	-0.301	0.279
Stance (%cycle)	(Intercept)	60.861	< 0.001***
	TD	-0.078	0.135
	PIGD	0.194	0.125
Swing (%cycle)	(Intercept)	39.140	< 0.001***
	TD	0.077	0.142
	PIGD	-0.193	0.127
Cycle duration (s)	(Intercept)	1.045	< 0.001***
	TD	-0.002	0.053
	AR	0.003	0.025*
iTUG duration (s)	(Intercept)	9.171	< 0.001***
	TD	-0.199	< 0.001***
	PIGD	0.535	0.010*
	AR	0.092	0.048*
Turn duration (s)	(Intercept)	1.751	< 0.001***
	MDS-UPDRS II	0.031	0.142
	AR	0.035	0.016*
MAV ($^{\circ}$ /s)	(Intercept)	84.510	< 0.001***
	MDS-UPDRS II	-0.582	0.161
	TD	0.688	0.003**
	PIGD	-1.184	0.120
	AR	-0.630	0.028*
PAV ($^{\circ}$ /s)	(Intercept)	177.343	< 0.001***
	MDS-UPDRS II	-0.953	0.234
	TD	1.412	0.018*
	AR	-2.252	0.002**
BW speed (m/s)	(Intercept)	0.959	< 0.001***
	MDS-UPDRS II	-0.008	0.202
	TD	0.011	0.007**
	PIGD	-0.026	0.011*
	AR	-0.008	0.071

AR: akinetic-rigid; AvDS: average daily steps; BW: backward walking; FW: forward walking; iTUG: instrumented timed-up-and-go; MAV: mean angular velocity; MDS-UPDRS: Movement Disorder Society unified Parkinson's disease rating scale; PAV: peak angular velocity; PIGD: postural instability and gait disorders; TD: tremor-dominant.

Table S10.5. Summary of the NMS predictors for each robust regression model. The intercept of the regression models is also shown for each dependent variable. For each predictor the estimated coefficient, p-value and level of significance are reported.

Outcome	Predictor	Estimate	p-value
AvDS (steps/day)	(Intercept)	9320.876	< 0.001***
	WCST	-54.667	< 0.001***
	BDI-II	-174.071	0.004**
FW speed (m/s)	(Intercept)	1.523	< 0.001***
	WCST	-0.005	< 0.001***
	BDI-II	-0.017	< 0.001***
Cadence (steps/min)	(Intercept)	118.541	< 0.001***
	FSS	-1.441	0.016*
	BDI-II	-0.229	0.239
Stride length (%height)	(Intercept)	87.075	< 0.001***
	WCST	-0.178	0.014*
	BDI-II	-0.692	< 0.001***
Stance (%cycle)	(Intercept)	60.017	< 0.001***
	FSS	0.319	0.002**
Swing (%cycle)	(Intercept)	39.971	< 0.001***
	FSS	-0.316	0.003**
Cycle duration (s)	(Intercept)	1.202	< 0.001***
	FSS	0.018	< 0.001***
	MoCA	-0.007	0.076
iTUG duration (s)	(Intercept)	7.164	< 0.001***
	WCST	0.060	0.063
	BDI-II	0.222	< 0.001***
Turn duration (s)	(Intercept)	1.411	< 0.001***
	PDSS-2	0.042	< 0.001***
	WCST	0.018	0.004**
MAV (°/s)	(Intercept)	78.294	< 0.001***
	PDSS-2	-0.542	0.015*
	WCST	-0.319	0.003**
	BDI-II	-0.652	0.012*
	MoCA	0.585	0.409
PAV (°/s)	(Intercept)	113.296	0.026*
	FSS	-4.470	0.073
	WCST	-0.672	0.006**
	BDI-II	-1.181	0.066
	MoCA	2.942	0.086
BW speed (m/s)	(Intercept)	0.638	0.050*
	FSS	-0.046	< 0.001***
	WCST	-0.004	0.038*
	BDI-II	-0.008	0.069
	MoCA	0.013	0.266

AvDS: average daily steps; BDI-II: Beck depression inventory II; BW: backward walking; FSS: Fatigue severity scale; FW: forward walking; iTUG: instrumented timed-up-and-go; MAV: mean angular velocity; MoCA: Montreal cognitive assessment; PAV: peak angular velocity; PDSS-2: Parkinson's disease sleep scale 2; WCST: Word-color Stroop test.

References

- Adams, C., Suescun, J., Haque, A., Block, K., Chandra, S., Ellmore, T. M., & Schiess, M. C. (2023). Updated Parkinson's disease motor subtypes classification and correlation to cerebrospinal homovanillic acid and 5-hydroxyindoleacetic acid levels. *Clinical Parkinsonism & Related Disorders*, 8, 100187. <https://doi.org/10.1016/j.prdoa.2023.100187>
- Aleksovski, D., Miljkovic, D., Bravi, D., & Antonini, A. (2018). Disease progression in Parkinson subtypes: The PPMI dataset. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 39(11), 1971–1976. <https://doi.org/10.1007/s10072-018-3522-z>
- Alix-Fages, C., Jiménez-Martínez, P., de Oliveira, D. S., Möck, S., Balsalobre-Fernández, C., & Del Vecchio, A. (2023). Mental fatigue impairs physical performance but not the neural drive to the muscle: A preliminary analysis. *European Journal of Applied Physiology*, 123(8), 1671–1684. <https://doi.org/10.1007/s00421-023-05189-1>
- Allali, G., Verghese, J., & Mahoney, J. R. (2014). Contributions of mild parkinsonian signs to gait performance in the elderly. *Age (Dordrecht, Netherlands)*, 36(4), 9678. <https://doi.org/10.1007/s11357-014-9678-4>
- Atsraei, A., Corrà, M. F., Dadashi, F., Vila-Chã, N., Maia, L., Mariani, B., Maetzel, W., & Aminian, K. (2021). Gait speed in clinical and daily living assessments in Parkinson's disease patients: Performance versus capacity. *NPJ Parkinson's disease*, 7(1), 24. <https://doi.org/10.1038/s41531-021-00171-0>
- Baek, K., Kim, Y. M., Na, H. K., Lee, J., Shin, D. H., Heo, S.-J., Chung, S. J., Kim, K., Lee, P. H., Sohn, Y. H., Yoon, J., & Kim, Y. J. (2024). Comparing Montreal Cognitive Assessment Performance in Parkinson's Disease Patients: Age- and Education-Adjusted Cutoffs vs. Machine Learning. *Journal of Movement Disorders*, 17(2), 171–180. <https://doi.org/10.14802/jmd.23271>
- Barone, P., Antonini, A., Colosimo, C., Marconi, R., Morgante, L., Avarello, T. P., Bot-tacchi, E., Cannas, A., Ceravolo, G., Ceravolo, R., Cicarelli, G., Gaglio, R. M., Giglia, R. M., Iemolo, F., Manfredi, M., Meco, G., Nicoletti, A., Pederzoli, M., Petrone, A., ... PRIAMO study group. (2009). The PRIAMO study: A multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 24(11), 1641–1649. <https://doi.org/10.1002/mds.22643>
- Barta, K., Boddy, A. H., Flores, M., Perry, L., Sawyer, K., & Campbell, A. (2025). Psychometric properties of 3-meter backward walk test (3MBWT) in people with Parkinson disease. *Physiotherapy Theory and Practice*, 41(3), 656–663. <https://doi.org/10.1080/09593985.2024.2348034>
- Bassett, D. R., Toth, L. P., LaMunion, S. R., & Crouter, S. E. (2017). Step Counting: A Review of Measurement Considerations and Health-Related Applications. *Sports Medicine (Auckland, N.Z.)*, 47(7), 1303–1315. <https://doi.org/10.1007/s40279-016-0663-1>
- Bianchini, E., Rinaldi, D., De Carolis, L., Galli, S., Alborghetti, M., Hansen, C., Suppa, A., Salvetti, M., Pontieri, F., & Vuillerme, N. (2025). Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study. *JMIR Formative Research*, 9. <https://doi.org/10.2196/63153>
Export Date: 14 April 2025; Cited By: 0.
- Bianchini, E., Alborghetti, M., Galli, S., Hansen, C., Zampogna, A., Suppa, A., Salvetti, M., Pontieri, F. E., Rinaldi, D., & Vuillerme, N. (2025). Minimal Clinically Important Difference of Average Daily Steps Measured Through a Consumer Smartwatch in People With Mild-to-Moderate Parkinson Disease: Cross-Sectional Study [Company: JMIR mHealth and uHealth Distributor: JMIR mHealth and uHealth Institution: JMIR mHealth and uHealth Label: JMIR mHealth and uHealth Publisher: JMIR Publications Inc., Toronto, Canada]. *JMIR mHealth and uHealth*, 13(1), e64213. <https://doi.org/10.2196/64213>
- Bianchini, E., Calì, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzel, W., & Pontieri, F. E. (2022). Step-

- Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, 23(1), 214. <https://doi.org/10.3390/s23010214>
- Bianchini, E., Galli, S., Alborghetti, M., De Carolis, L., Zampogna, A., Hansen, C., Vuillerme, N., Suppa, A., & Pontieri, F. E. (2023). Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch [Number: 21 Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 23(21), 8971. <https://doi.org/10.3390/s23218971>
- Bizzozero-Peroni, B., Díaz-Goñi, V., Jiménez-López, E., Rodríguez-Gutiérrez, E., Sequí-Domínguez, I., Núñez de Arenas-Arroyo, S., López-Gil, J. F., Martínez-Vizcaíno, V., & Mesas, A. E. (2024). Daily Step Count and Depression in Adults: A Systematic Review and Meta-Analysis. *JAMA network open*, 7(12), e2451208. <https://doi.org/10.1001/jamanetworkopen.2024.51208>
- Branscheidt, M., Kassavetis, P., Anaya, M., Rogers, D., Huang, H. D., Lindquist, M. A., & Celnik, P. (n.d.). Fatigue induces long-lasting detrimental changes in motor-skill learning. *eLife*, 8, e40578. <https://doi.org/10.7554/eLife.40578>
- Bryant, M. S., Hou, J.-G. G., Workman, C. D., & Protas, E. J. (2018). Predictive ability of functional tests for postural instability and gait difficulty in Parkinson's disease. *European Geriatric Medicine*, 9(1), 83–88. <https://doi.org/10.1007/s41999-017-0021-3>
- Burgos, P. I., Silva-Batista, C., Ragothaman, A., Shah, V. V., Carlson-Kuhta, P., Horak, F. B., & Mancini, M. (2025). Cognition is associated with daily-life mobility in people with Parkinson's disease. *Clinical Parkinsonism & Related Disorders*, 13, 100393. <https://doi.org/10.1016/j.prdoa.2025.100393>
- Carvalho, D. V., Santos, R. M. S., Magalhães, H. C. d., Souza, M. S. d., Christo, P. P., Almeida-Leite, C. M. d., & Scalzo, P. L. (2020). Can fatigue predict walking capacity of patients with Parkinson's disease? *Arquivos De Neuro-Psiquiatria*, 78(2), 70–75. <https://doi.org/10.1590/0004-282X20190136>
- Chaudhuri, K. R., Facheris, M. F., Bergmans, B., Bergquist, F., Criswell, S. R., Jia, J., Kukreja, P., Mukai, Y., Spiegel, A. M., Gupta, R., Bergmann, L., & Pahwa, R. (2024). Improved Sleep Correlates with Improved Quality of Life and Motor Symptoms with Foslevodopa/Foscarbidopa. *Movement Disorders Clinical Practice*, 11(7), 861–866. <https://doi.org/10.1002/mdc3.14018>
- Christiansen, C., Moore, C., Schenkman, M., Kluger, B., Kohrt, W., Delitto, A., Berman, B., Hall, D., Josbeno, D., Poon, C., Robichaud, J., Wellington, T., Jain, S., Comella, C., Corcos, D., & Melanson, E. (2017). Factors Associated With Ambulatory Activity in De Novo Parkinson Disease. *Journal of neurologic physical therapy: JNPT*, 41(2), 93–100. <https://doi.org/10.1097/NPT.0000000000000169>
- Correno, M. B., Hansen, C., Chardon, M., Milane, T., Bianchini, E., & Vuillerme, N. (2022). Association between Backward Walking and Cognition in Parkinson Disease: A Systematic Review. *International Journal of Environmental Research and Public Health*, 19(19), 12810. <https://doi.org/10.3390/ijerph191912810>
- Del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK. *JAMA neurology*, 79(10), 1059–1063. <https://doi.org/10.1001/jamaneurol.2022.2672>
- Del Pozo Cruz, B., Ahmadi, M. N., Lee, I.-M., & Stamatakis, E. (2022). Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. *JAMA internal medicine*. <https://doi.org/10.1001/jamainternmed.2022.4000>
- Ding, D., Nguyen, B., Nau, T., Luo, M., Del Pozo Cruz, B., Dempsey, P. C., Munn, Z., Jefferis, B. J., Sherrington, C., Calleja, E. A., Hau Chong, K., Davis, R., Francois, M. E., Tiedemann, A., Biddle, S. J. H., Okely, A., Bauman, A., Ekelund, U., Clare, P., & Owen, K. (2025). Daily steps and

- health outcomes in adults: A systematic review and dose-response meta-analysis. *The Lancet. Public Health*, 10(8), e668–e681. [https://doi.org/10.1016/S2468-2667\(25\)00164-1](https://doi.org/10.1016/S2468-2667(25)00164-1)
- Dragašević-Mišković, N. T., Bobić, V., Kostić, M., Stanković, I., Radovanović, S., Dimitrijević, K., Svetel, M., Petrović, I., & Đurić-Jovičić, M. (2021). Impact of depression on gait variability in Parkinson's disease. *Clinical Neurology and Neurosurgery*, 200, 106324. <https://doi.org/10.1016/j.clineuro.2020.106324>
- Fasano, A., Canning, C. G., Hausdorff, J. M., Lord, S., & Rochester, L. (2017). Falls in Parkinson's disease: A complex and evolving picture. *Movement Disorders: Official Journal of the Movement Disorder Society*, 32(11), 1524–1536. <https://doi.org/10.1002/mds.27195>
- Ferguson, T., Olds, T., Curtis, R., Blake, H., Crozier, A. J., Dankiw, K., Dumuid, D., Kasai, D., O'Connor, E., Virgara, R., & Maher, C. (2022). Effectiveness of wearable activity trackers to increase physical activity and improve health: A systematic review of systematic reviews and meta-analyses. *The Lancet. Digital Health*, 4(8), e615–e626. [https://doi.org/10.1016/S2589-7500\(22\)00111-X](https://doi.org/10.1016/S2589-7500(22)00111-X)
- Fiorenzato, E., Cauzzo, S., Weis, L., Garon, M., Pistonesi, F., Ciani, V., Nasi, M. L., Vianello, F., Zecchinelli, A. L., Pezzoli, G., Reali, E., Pozzi, B., Isaias, I. U., Siri, C., Santangelo, G., Cuoco, S., Barone, P., Antonini, A., & Biundo, R. (2024). Optimal MMSE and MoCA cutoffs for cognitive diagnoses in Parkinson's disease: A data-driven decision tree model. *Journal of the Neurological Sciences*, 466, 123283. <https://doi.org/10.1016/j.jns.2024.123283>
- Galperin, I., Herman, T., Assad, M., Ganz, N., Mirelman, A., Giladi, N., & Hausdorff, J. M. (2020). Sensor-Based and Patient-Based Assessment of Daily-Living Physical Activity in People with Parkinson's Disease: Do Motor Subtypes Play a Role? [Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 20(24), 7015. <https://doi.org/10.3390/s20247015>
- Galperin, I., Hillel, I., Del Din, S., Bekkers, E. M. J., Nieuwboer, A., Abbruzzese, G., Avanzino, L., Nieuwhof, F., Bloem, B. R., Rochester, L., Della Croce, U., Cereatti, A., Giladi, N., Mirelman, A., & Hausdorff, J. M. (2019). Associations between daily-living physical activity and laboratory-based assessments of motor severity in patients with falls and Parkinson's disease. *Parkinsonism & Related Disorders*, 62, 85–90. <https://doi.org/10.1016/j.parkreldis.2019.01.022>
- Garber, C. E., & Friedman, J. H. (2003). Effects of fatigue on physical activity and function in patients with Parkinson's disease. *Neurology*, 60(7), 1119–1124. <https://doi.org/10.1212/01.wnl.0000055868.06222.ab>
- Giannouli, E., Bock, O., Mellone, S., & Zijlstra, W. (2016). Mobility in Old Age: Capacity Is Not Performance. *BioMed Research International*, 2016, 3261567. <https://doi.org/10.1155/2016/3261567>
- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Grande, G., Triolo, F., Nuara, A., Welmer, A.-K., Fratiglioni, L., & Vetrano, D. L. (2019). Measuring gait speed to better identify prodromal dementia. *Experimental Gerontology*, 124, 110625. <https://doi.org/10.1016/j.exger.2019.05.014>
- Hackney, M. E., & Earhart, G. M. (2009). Backward walking in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 24(2), 218–223. <https://doi.org/10.1002/mds.22330>
- Herman, T., Weiss, A., Brozgol, M., Giladi, N., & Hausdorff, J. (2014). Gait and balance in Parkinson's disease subtypes: Objective measures and classification considerations. *Journal of Neurology*, 261(12), 2401–2410. <https://doi.org/10.1007/s00415-014-7513-6>

- Huang, Y.-Z., Chang, F.-Y., Liu, W.-C., Chuang, Y.-F., Chuang, L.-L., & Chang, Y.-J. (2017). Fatigue and Muscle Strength Involving Walking Speed in Parkinson's Disease: Insights for Developing Rehabilitation Strategy for PD. *Neural Plasticity*, 2017, 1941980. <https://doi.org/10.1155/2017/1941980>
- Hulbert, S., Ashburn, A., Robert, L., & Verheyden, G. (2015). A narrative review of turning deficits in people with Parkinson's disease. *Disability and Rehabilitation*, 37(15), 1382–1389. <https://doi.org/10.3109/09638288.2014.961661>
- Johns, M. W. (1991). A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep*, 14(6), 540–545. <https://doi.org/10.1093/sleep/14.6.540>
- Jost, S. T., Kaldenbach, M.-A., Antonini, A., Martinez-Martin, P., Timmermann, L., Odin, P., Katzenschlager, R., Borgohain, R., Fasano, A., Stocchi, F., Hattori, N., Kukkle, P. L., Rodríguez-Violante, M., Falup-Pecurariu, C., Schade, S., Petry-Schmelzer, J. N., Metta, V., Weintraub, D., Deuschl, G., ... International Parkinson and Movement Disorders Society Non-Motor Parkinson Disease Study Group. (2023). Levodopa Dose Equivalency in Parkinson's Disease: Updated Systematic Review and Proposals. *Movement Disorders: Official Journal of the Movement Disorder Society*, 38(7), 1236–1252. <https://doi.org/10.1002/mds.29410>
- Kocer, B., Soke, F., Ataoglu, N. E. E., Ersoy, N., Gulsen, C., Gulsen, E. O., Yasa, M. E., Uysal, I., Comoglu, S. S., & Bora, H. A. T. (2023). The reliability and validity of the 3-m backward walk test in people with Parkinson's disease. *Irish Journal of Medical Science*. <https://doi.org/10.1007/s11845-023-03384-9>
- Kummer, A., Harsányi, E., Dias, F. M. V., Cardoso, F., Caramelli, P., & Teixeira, A. L. (2009). Depression impairs executive functioning in Parkinson disease patients with low educational level. *Cognitive and Behavioral Neurology: Official Journal of the Society for Behavioral and Cognitive Neurology*, 22(3), 167–172. <https://doi.org/10.1097/WNN.0b013e3181b278f9>
- Lee, P.-C., Artaud, F., Cormier-Dequaire, F., Rascol, O., Durif, F., Derkinderen, P., Marques, A.-R., Bourdain, F., Brandel, J.-P., Pico, F., Lacomblez, L., Bonnet, C., Brefel-Courbon, C., Ory-Magne, F., Grabli, D., Klebe, S., Mangone, G., You, H., Mesnage, V., ... DIGPD Study Group. (2019). Examining the Reserve Hypothesis in Parkinson's Disease: A Longitudinal Study. *Movement Disorders: Official Journal of the Movement Disorder Society*, 34(11), 1663–1671. <https://doi.org/10.1002/mds.27854>
- Lord, S., Galna, B., Coleman, S., Burn, D., & Rochester, L. (2013). Mild depressive symptoms are associated with gait impairment in early Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(5), 634–639. <https://doi.org/10.1002/mds.25338>
- Lord, S., Galna, B., Verghese, J., Coleman, S., Burn, D., & Rochester, L. (2013). Independent domains of gait in older adults and associated motor and nonmotor attributes: Validation of a factor analysis approach. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 68(7), 820–827. <https://doi.org/10.1093/geronagls255>
- Lüdecke, D., Ben-Shachar, M. S., Patil, I., Waggoner, P., & Makowski, D. (2021). Performance: An R Package for Assessment, Comparison and Testing of Statistical Models. *Journal of Open Source Software*, 6(60), 3139. <https://doi.org/10.21105/joss.03139>
- Maetzler, W., Rochester, L., Bhidayasiri, R., Espay, A. J., Sánchez-Ferro, A., & van Uem, J. M. (2021). Modernizing Daily Function Assessment in Parkinson's Disease Using Capacity, Perception, and Performance Measures [eprint: <https://onlinelibrary.wiley.com/doi/pdf/10.1002/mds.28377>]. *Movement Disorders*, 36(1), 76–82. <https://doi.org/10.1002/mds.28377>
- Maggi, G., D'Iorio, A., Aiello, E. N., Poletti, B., Ticozzi, N., Silani, V., Amboni, M., Vitale, C., & Santangelo, G. (2023). Psychometrics and diagnostics of the Italian version of the Beck Depression Inventory-II (BDI-II) in Parkinson's disease. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of*

- Clinical Neurophysiology*, 44(5), 1607–1612. <https://doi.org/10.1007/s10072-023-06619-w>
- Mancini, M., El-Gohary, M., Pearson, S., McNames, J., Schlueter, H., Nutt, J. G., King, L. A., & Horak, F. B. (2015). Continuous monitoring of turning in Parkinson's disease: Rehabilitation potential. *NeuroRehabilitation*, 37(1), 3–10. <https://doi.org/10.3233/NRE-151236>
- Mancini, M., Schlueter, H., El-Gohary, M., Mattek, N., Duncan, C., Kaye, J., & Horak, F. B. (2016). Continuous Monitoring of Turning Mobility and Its Association to Falls and Cognitive Function: A Pilot Study. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 71(8), 1102–1108. <https://doi.org/10.1093/gerona/glw019>
- Mayeli, M., Shafie, M., Shiravi, M., Adl Parvar, T., Mirsepassi, Z., Rahiminejad, F., Sattarpour, R., & Aghamollai, V. (2024). Depression is associated with the nonmotor symptoms of Parkinson's disease: A comparative analysis. *Health Science Reports*, 7(5), e2106. <https://doi.org/10.1002/hsr.2.2106>
- Mc Ardle, R., Del Din, S., Morris, R., Alcock, L., Yarnall, A. J., Burn, D. J., Rochester, L., Lawson, R. A., & On Behalf Of The Icicle-Pd Study Group, n. (2022). Factors Influencing Habitual Physical Activity in Parkinson's Disease: Considering the Psychosocial State and Wellbeing of People with Parkinson's and Their Carers. *Sensors (Basel, Switzerland)*, 22(3), 871. <https://doi.org/10.3390/s22030871>
- Michels, J., Werner, C. J., Schumann-Werner, B., Schulz, J. B., Costa, A. S., & Rietz, K. (2022). Why cognitive training is important for the health status in Parkinson's disease: Preliminary evidence from a clinical three-weeks multidisciplinary intervention. *Neurological Research and Practice*, 4(1), 47. <https://doi.org/10.1186/s42466-022-00210-y>
- Milane, T., Vuillerme, N., Petit, P., Warmerdam, E., Romijnders, R., Bianchini, E., Maetzler, W., & Hansen, C. (2025). Impact of forward and backward walking on gait parameters across parkinson's disease stages and severity: A prospective observational study. *BMC Neurology*, 25(1), 379. <https://doi.org/10.1186/s12883-025-04321-2>
- Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L., Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)
- Moreau, C., Rouaud, T., Grabli, D., Benatru, I., Remy, P., Marques, A.-R., Drapier, S., Mariani, L.-L., Roze, E., Devos, D., Dupont, G., Bereau, M., & Fabbri, M. (2023). Overview on wearable sensors for the management of Parkinson's disease. *NPJ Parkinson's disease*, 9(1), 153. <https://doi.org/10.1038/s41531-023-00585-y>
- Nagaki, K., Fujioka, S., Sasai, H., Yamaguchi, Y., & Tsuboi, Y. (2022). Physical Activity and Its Diurnal Fluctuations Vary by Non-Motor Symptoms in Patients with Parkinson's Disease: An Exploratory Study. *Healthcare (Basel, Switzerland)*, 10(4), 749. <https://doi.org/10.3390/healthcare10040749>
- Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>
- Nemanich, S. T., Duncan, R. P., Dibble, L. E., Cavanaugh, J. T., Ellis, T. D., Ford, M. P., Foreman, K. B., & Earhart, G. M. (2013). Predictors of Gait Speeds and the Relationship of Gait Speeds to Falls in Men and Women with Parkinson Disease. *Parkinson's Disease*, 2013, 141720. <https://doi.org/10.1155/2013/141720>
- O' Donnell, D., Moriarty, F., Lavan, A., Kenny, R. A., & Briggs, R. (2025). The Association Between Psychotropic Medication Use and Gait and Mobility Impairment in Community-Dwelling Older People: Data From The Irish Longitudinal Study on Ageing (TILDA). *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 80(5), glae263. <https://doi.org/10.1093/gerona/glae263>

- Organization, W. H. (2002). Towards a common language for functioning, disability, and health : ICF [Publisher: World Health Organization]. *The International Classification of Functioning, Disability and Health*. Retrieved May 30, 2025, from <https://cir.nii.ac.jp/crid/1573668925447490176>
- Ortega-Bastidas, P., Gómez, B., Aqueveque, P., Luarte-Martínez, S., & Cano-de-la-Cuerda, R. (2023). Instrumented Timed Up and Go Test (iTUG)-More Than Assessing Time to Predict Falls: A Systematic Review. *Sensors (Basel, Switzerland)*, 23(7), 3426. <https://doi.org/10.3390/s23073426>
- Paker, N., Bugdayci, D., Goksenoglu, G., Demircioğlu, D. T., Kesiktaş, N., & Ince, N. (2015). Gait speed and related factors in Parkinson's disease. *Journal of Physical Therapy Science*, 27(12), 3675–3679. <https://doi.org/10.1589/jpts.27.3675>
- Pecoraro, P. M., Marsili, L., Espay, A. J., Bologna, M., & di Biase, L. (2025). Computer Vision Technologies in Movement Disorders: A Systematic Review. *Movement Disorders Clinical Practice*. <https://doi.org/10.1002/mdc3.70123>
- Pilotto, A., Rizzardi, A., Zatti, C., Hansen, C., Donini, A., Romijnders, R., Maetzler, W., & Padovani, A. (2023). Unsupervised but not supervised gait parameters are related to fatigue in Parkinson's disease: A pilot study. *Frontiers in Aging Neuroscience*, 15, 1279722. <https://doi.org/10.3389/fnagi.2023.1279722>
- Poewe, W., Seppi, K., Tanner, C. M., Halliday, G. M., Brundin, P., Volkman, J., Schrag, A.-E., & Lang, A. E. (2017). Parkinson disease. *Nature Reviews. Disease Primers*, 3, 17013. <https://doi.org/10.1038/nrdp.2017.13>
- Pongmala, C., Stonsaovapak, C., van Emde Boas, M., & Bohnen, N. I. (2025). Differential associations between retro walking versus forward walking, axial motor features and body composition in Parkinson's disease. *Parkinsonism & Related Disorders*, 137, 107924. <https://doi.org/10.1016/j.parkreldis.2025.107924>
- Prime, M., McKay, J. L., Bay, A., Hart, A., Kim, C., Abraham, A., & Hackney, M. E. (2020). Differentiating Parkinson Disease Subtypes Using Clinical Balance Measures. *Journal of neurologic physical therapy : JNPT*, 44(1), 34–41. <https://doi.org/10.1097/NPT.0000000000000297>
- Roussos, G., Herrero, T. R., Hill, D. L., Dowling, A. V., L T M Müller, M., Evers, L. J. W., Burton, J., Derungs, A., Fisher, K., Kilambi, K. P., Mehrotra, N., Bhatnagar, R., Sardar, S., Stephenson, D., Adams, J. L., Ray Dorsey, E., & Cosman, J. (2022). Identifying and characterising sources of variability in digital outcome measures in Parkinson's disease. *NPJ digital medicine*, 5(1), 93. <https://doi.org/10.1038/s41746-022-00643-4>
- Safarpour, D., Dale, M. L., Shah, V. V., Talman, L., Carlson-Kuhta, P., Horak, F. B., & Mancini, M. (2022). Surrogates for rigidity and PIGD MDS-UPDRS subscores using wearable sensors. *Gait & Posture*, 91, 186–191. <https://doi.org/10.1016/j.gaitpost.2021.10.029>
- Salazar, R. D., Ren, X., Ellis, T. D., Toraif, N., Barthelemy, O. J., Neargarder, S., & Cronin-Golomb, A. (2017). Dual tasking in Parkinson's disease: Cognitive consequences while walking. *Neuropsychology*, 31(6), 613–623. <https://doi.org/10.1037/neu0000331>
- Scarpina, F., & Tagini, S. (2017). The Stroop Color and Word Test. *Frontiers in Psychology*, 8, 557. <https://doi.org/10.3389/fpsyg.2017.00557>
- Schapira, A. H. V., Chaudhuri, K. R., & Jenner, P. (2017). Non-motor features of Parkinson disease. *Nature Reviews. Neuroscience*, 18(7), 435–450. <https://doi.org/10.1038/nrn.2017.62>
- Schlachetzki, J. C. M., Barth, J., Marxreiter, F., Gossler, J., Kohl, Z., Reinfelder, S., Gassner, H., Aminian, K., Eskofier, B. M., Winkler, J., & Klucken, J. (2017). Wearable sensors objectively measure gait parameters in Parkinson's disease. *PLoS One*, 12(10), e0183989. <https://doi.org/10.1371/journal.pone.0183989>
- Siciliano, M., Chiorri, C., De Micco, R., Russo, A., Tedeschi, G., Trojano, L., & Tesitore, A. (2019). Fatigue in Parkinson's disease: Italian validation of the Parkinson Fatigue Scale and the Fatigue Severity Scale using a Rasch analysis approach. *Parkinson-*

- ism & Related Disorders*, 65, 105–110. <https://doi.org/10.1016/j.parkreldis.2019.05.028>
- Smulders, K., Dale, M. L., Carlson-Kuhta, P., Nutt, J. G., & Horak, F. B. (2016). Pharmacological treatment in Parkinson's disease: Effects on gait. *Parkinsonism & related disorders*, 31, 3–13. <https://doi.org/10.1016/j.parkreldis.2016.07.006>
- Stebbins, G. T., Goetz, C. G., Burn, D. J., Jankovic, J., Khoo, T. K., & Tilley, B. C. (2013). How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: Comparison with the unified Parkinson's disease rating scale. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(5), 668–670. <https://doi.org/10.1002/mds.25383>
- Still, A., Hale, L., Alam, S., Morris, M. E., & Jayakaran, P. (2024). Relationships between physical activities performed under free-living conditions and non-motor symptoms in people with Parkinson's: A systematic review and meta-analysis. *Clinical Rehabilitation*, 38(11), 1534–1551. <https://doi.org/10.1177/02692155241272967>
- Suzuki, K., Miyamoto, T., Miyamoto, M., Suzuki, S., Numao, A., Watanabe, Y., Tatsumoto, M., Sakuta, H., Watanabe, Y., Fujita, H., Iwanami, M., Sada, T., Kadowaki, T., Hashimoto, K., Trenkwalder, C., & Hirata, K. (2015). Evaluation of cutoff scores for the Parkinson's disease sleep scale-2. *Acta Neurologica Scandinavica*, 131(6), 426–430. <https://doi.org/10.1111/ane.12347>
- Timblin, H., Rahmani, E., Ryczek, C. A., Hill, C. R., & Jones, J. D. (2022). Physical Inactivity Links Depressive Symptoms and Cognitive Functioning among Individuals with Parkinson's Disease. *Neuropsychology*, 36(6), 505–512. <https://doi.org/10.1037/neu0000837>
- Trenkwalder, C., Kohnen, R., Högl, B., Metta, V., Sixel-Döring, F., Frauscher, B., Hülsmann, J., Martinez-Martin, P., & Chaudhuri, K. R. (2011). Parkinson's disease sleep scale-validation of the revised version PDSS-2. *Movement Disorders: Official Journal of the Movement Disorder Society*, 26(4), 644–652. <https://doi.org/10.1002/mds.23476>
- Uekermann, J., Daum, I., Peters, S., Wiebel, B., Przuntek, H., & Müller, T. (2003). Depressed mood and executive dysfunction in early Parkinson's disease. *Acta Neurologica Scandinavica*, 107(5), 341–348. <https://doi.org/10.1034/j.1600-0404.2003.02155.x>
- Venables, W. N., & Ripley, B. D. (2002, August). *Modern Applied Statistics with S* (4th edition). Springer.
- Vítečková, S., Horáková, H., Poláková, K., Krupička, R., Růžicka, E., & Brožová, H. (2020). Agreement between the GAITRite® System and the Wearable Sensor BTS G-Walk® for measurement of gait parameters in healthy adults and Parkinson's disease patients. *PeerJ*, 8, e8835. <https://doi.org/10.7717/peerj.8835>
- Winogrodzka, A., Wagenaar, R. C., Booij, J., & Wolters, E. C. (2005). Rigidity and bradykinesia reduce interlimb coordination in Parkinsonian gait [Publisher: Elsevier]. *Archives of Physical Medicine and Rehabilitation*, 86(2), 183–189. <https://doi.org/10.1016/j.apmr.2004.09.010>
- Yang, F. (2025). What determines gait speed in community-living older adults? A relative weight analysis. *European Geriatric Medicine*, 16(3), 1045–1054. <https://doi.org/10.1007/s41999-025-01208-w>
- Yi, Q., Yu-Peng, C., Jiang-Ting, L., Jing-Yi, L., Qi-Xiong, Q., Dan-Lei, W., Jing-Wei, Z., Zhi-Juan, M., Yong-Jie, X., Zhe, M., & Zheng, X. (2022). Worse Sleep Quality Aggravates the Motor and Non-Motor Symptoms in Parkinson's Disease. *Frontiers in Aging Neuroscience*, 14, 887094. <https://doi.org/10.3389/fnagi.2022.887094>
- Yilmaz, N. H., Saricaoglu, M., Eser, H. Y., Düz, Ö. A., Polat, B., & Özer, F. F. (2019). The Relationship Between Pain, and Freezing of Gait and Falls in Parkinson's Disease. *Archives of Neuropsychiatry*, 57(1), 56–60. <https://doi.org/10.29399/npa.24716>
- Yogev-Seligmann, G., Hausdorff, J. M., & Giladi, N. (2008). The role of executive function and attention in gait. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(3), 329–342, quiz 472. <https://doi.org/10.1002/mds.21720>
- Zajac, J. A., Cavanaugh, J. T., Baker, T., Duncan, R. P., Fulford, D., Giris, J., LaVal-

ley, M., Nordahl, T., Porciuncula, F., Rawson, K. S., Saint-Hilaire, M., Thomas, C. A., Earhart, G. M., & Ellis, T. D. (2022). Does clinically measured walking capacity contribute to real-world walking performance in Parkinson's disease? *Parkinsonism & Related Disorders*, 105, 123–127. <https://doi.org/10.1016/j.parkreldis.2022.11.016>

Zeileis, A., & Hothorn, T. (2002). Diagnostic Checking in Regression Relationships. *R News*, 2(3), 7–10. <https://CRAN.R-project.org/doc/Rnews>

Zeileis, A., Köll, S., & Graham, N. (2020). Various Versatile Variances: An Object-Oriented Implementation of Clustered Covariances in R. *Journal of Statistical Software*, 95, 1–36. <https://doi.org/10.18637/jss.v095.i01>

BEYOND DAYTIME MOBILITY

Chapter 11

Contribution 8: The impact of nocturnal hypokinesia on supervised and unsupervised mobility in people with Parkinson's disease

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npj Parkinson disease.

Submitted.

Abstract

Nocturnal hypokinesia (NH) is a disabling and underrecognized symptom of Parkinson's disease (PD), affecting nighttime movements and sleep quality. However, its impact on daytime mobility remains unclear. This study investigated supervised and unsupervised mobility in propensity score-matched mild-to-moderate PD patients with (PD NH+) and without NH (PD NH-). Eighty-eight participants (44 PD NH+ and 44 PD NH-) underwent clinical assessments, mobility tests (i.e., 20-metre forward walking, instrumented Timed-Up-and-Go and 3-metre backward walking test), and 5-day monitoring of average daily steps (avDS) through a commercial activity tracker (Garmin Vivosmart 4). PD NH+ demonstrated worse functional mobility, reduced turning velocity, slower backward walking, and fewer avDS than PD NH-. Furthermore, NH severity correlated negatively with most supervised measures and with avDS. These findings suggest that NH is associated with impaired daytime mobility and worse motor function. This highlights the importance of targeted interventions to address both nocturnal and diurnal mobility impairments in PD.

Introduction

Parkinson's disease (PD) is a neurodegenerative disease increasingly affecting people worldwide (GBD 2016 Parkinson's Disease Collaborators, 2018). The classical PD motor symptoms are bradykinesia, tremor, and rigidity (Postuma et al., 2015). With disease progression, more drug-resistant symptoms such as balance, posture and gait impairments could occur, leading to reduced functional independence and quality of life (Poewe et al., 2017). Besides motor manifestations, a number of non-motor symptoms (NMS), such as sleep problems, cognitive impairment, autonomic dysfunction, hallucinations, mood disturbances, urinary and gastrointestinal dysfunction have been described in PD, contributing to deterioration in quality of life (Schapira et al., 2017). Sleep disturbances are highly common NMS, affecting over 70% of people with PD (PwPD) (Dodet et al., 2024). These include insomnia/sleep fragmentation, restless leg syndrome, sleep breathing disorders, periodic limb movements syndrome, REM sleep behavior disorder (RBD) and excessive daytime sleepiness (EDS) (Dodet et al., 2024). Nocturnal hypokinesia (NH) is considered a disorder that lies at the interface between motor and non-motor symptoms (Bhidayasiri & Trenkwalder, 2018). This is characterized by reduced mobility during nighttime with static position during sleep, reduced postural transitions, difficulty in turning and getting out of bed (Bhidayasiri & Trenkwalder, 2018; Li et al., 2023; Mirelman et al., 2020; Sringean et al., 2024). The reduced bed mobility could result in poor sleep quality and increased daytime sleepiness with reduced daytime functioning (Louter et al., 2012; Sringean et al., 2024). However, NH remains an under-investigated symptom, mainly due to the challenge of assessing it. In fact, most of the assessments rely on patients-reported questionnaires, suffering from recall bias and with the risk of selecting people with more severe symptoms. Conversely, wearable digital technology allow to evaluate bed movements in a quantitative and objective way (Zampogna et al., 2020). Although some sensor-based studies granted us a better understanding of NH features and prevalence (Bhidayasiri, Sringean, Anan, et al., 2016; Bhidayasiri, Sringean, Chaiwong, et al., 2017; Bhidayasiri, Sringean, & Thanawattano, 2016, 2017; Mirelman et al., 2020), the implementation of these instruments to assess treatment response is still sparse. NH is generally considered a form of nighttime wearing-off (WO). Thus, reduced bed movements could be present even during early stages of the disease and could represent an early sign of a fluctuating disease (Bhidayasiri, Sringean, & Thanawattano, 2016; Dijkstra et al., 2008; Mirelman et al., 2020; Sringean et al., 2024). Accordingly, it is reasonable to think that in a progressing disease, signs of fluctuations appear first during nighttime as the effect of L-DOPA fade away, since almost all PD medications are taken during daytime. Based on this assumption, treatments for NH include controlled/delayed-release L-DOPA, long-acting Dopamine-Agonists and continuous dopaminergic delivery therapies (e.g. apomorphine infusion, levodopa-carbidopa intestinal gel) (Bhidayasiri, Sringean, Anan, et al., 2016; Bhidayasiri, Sringean, Chaiwong, et al., 2017; Sringean et al., 2024). Nevertheless, a recent study from Taniguchi et al. (Taniguchi et al., 2022) reported a positive association between hip adductors torque and bed movements velocity. This result supported the potential of rehabilitative approaches to treat NH (Souza et al., 2023) and set the rationale to assess an association between NH and other daily mobility impairments. Indeed, mobility problems are a common feature of people with PD (PwPD), with increasing prevalence along disease course and progression (Adams et al., 2024; Mirelman et al., 2019, 2024). Mobility could be assessed in both supervised (in the hospital or laboratory) and unsupervised, free-living conditions (in real world). A number of evidence highlighted that these two modalities of mobility assessment could capture different aspects of PwPD ability to move (Corrà et al., 2021; Zajac et al., 2022). In supervised conditions, previous evidence in PwPD demonstrated altered gait parameters in forward walking (FW) (e.g., reduced gait speed and automaticity, shortened step length, among others) (Mirelman et al., 2019), impaired turning abilities (reduced angular velocity and disrupted body segments reorientation sequence Bianchini, Warmerdam, et al., 2023) and altered backward walking (Hackney & Earhart, 2009). In unsupervised conditions, PwPD displayed altered turning (Mancini et al., 2015; Morgan et al., 2022), gait parameters (Adams et al., 2024; Mirelman et al., 2024) and reduced walking performance with

lower physical activity and average number of daily steps (Ginis et al., 2023; Shokouhi et al., 2022). To the best of our knowledge, no study assessed the relationship between NH and supervised and unsupervised mobility PwPD. Therefore, this study aimed to: (i) investigate differences in both supervised and unsupervised mobility between propensity score-matched mild-to-moderate PwPD with (PD NH+) and without NH (PD NH-); (ii) evaluate the association between mobility parameters and NH severity; (iii) evaluate the difference in clinical scores between PD NH+ and PD NH-.

Material and Methods

Study design and ethics

This was a propensity score-matched analysis conducted on a cross-sectional dataset of 121 mild-to-moderate PwPD collected to validate wearable-based measures and investigate the interaction between mobility, motor and non-motor symptoms in PwPD. Approval was granted by the local Ethical Committee of Sapienza, University of Rome (Ref. 0372/2022). This study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki of 1964 and subsequent amendments. Data collection and processing were carried out in compliance with current European data protection regulations. All data were deidentified. Participants did not receive any form of compensation.

Population

Participants were consecutively recruited from the Movement Disorders Centre at Sant'Andrea University Hospital (A.O.U. Sant'Andrea) in Rome between February 2023 and May 2024. Inclusion criteria included: (i) diagnosis of idiopathic PD according to the MDS criteria (Postuma et al., 2015); (ii) age 18 years or older; (iii) disease stage < 4 according to the modified Hoehn and Yahr scale (mHY) ("severe disability; still able to walk or stand unassisted") (Goetz et al., 2004); (iv) ability to walk independently without walking aids; and (v) ability to perform the experimental procedure. Exclusion criteria were: (i) severe cognitive impairment as defined by a Montreal Cognitive Assessment (MoCA) score < 18 ; and (ii) orthopedic, rheumatologic, or systemic conditions affecting mobility as judged by the assessor.

Experimental Procedure

Participants meeting the inclusion and exclusion criteria were evaluated during their regular neurological follow-up visits. After collecting demographic (age, sex), anthropometric (weight, height, BMI) and clinical data (disease duration, levodopa equivalent daily dose [LEDD], mHY), participants were clinically evaluated with different clinical scales to assess mobility, motor and non-motor symptoms. In particular, data regarding the following clinical scores were included in this analysis: the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) parts I-IV (Goetz et al., 2008) were used to assess global symptoms severity. The score of item 2.9 of MDS-UPDRS part II was used to evaluate the presence and severity of NH. A score ≥ 1 was used to define the presence of NH. From parts II and III of MDS-UPDRS, the postural instability and gait disorder (PIGD) and the tremor dominant (TD) scores were calculated (Stebbins et al., 2013). The MoCA (Nasreddine et al., 2005) was used to evaluate global cognition. The time to complete the interference part of the word-color Stroop test (WCST) in seconds was used to evaluate executive functions (Scarpina & Tagini, 2017). The Short Physical Performance Battery (Guralnik et al., 1994) was used to assess lower limb functions and general mobility. The Parkinson's Disease Questionnaire 39-items (PDQ-39) (Jenkinson et al., 1997) and the Functional Motor Composite Score (FMCS) (Hanff et al., 2023) was used to assess quality

of life and functional mobility. Parkinson's Disease Sleep Scale 2 (PDSS-2) (Trenkwalder et al., 2011), Epworth Sleepiness Scale (ESS) (Johns, 1991), Fatigue Severity Scale (FSS) (Siciliano et al., 2019) and Beck Depression Inventory II (BDI-II) (Maggi et al., 2023) were used to assess sleep problems, EDS, fatigue and depressive symptoms, respectively. Finally, the Wearing-Off Questionnaire 19-items (WOQ-19) (Abbruzzese et al., 2012) was used to investigate WO. The presence of Freezing of Gait (FOG) was defined using a cut-off of ≥ 1 score at item 2.13 of MDS-UPDRS-II. Subsequently, participants were invited to perform three supervised mobility tasks while wearing a lower-back mounted research-grade inertial device for mobility analysis (BTS G-WALK, BTS Engineering Inc., Milan) (Vítečková et al., 2020): (i) a 20-meter FW task; (ii) an instrumented Timed Up and Go (TUG) (Ortega-Bastidas et al., 2023), and (iii) a 3-meter Backward Walking Test (3MBWT) (Barta et al., 2025). From the FW, spatiotemporal gait parameters were measured, including speed (m/s), cadence (steps/min), stride length normalized to height (%), stance and swing phases duration expressed as % of gait cycle. For the TUG, total duration and mean and peak angular velocity (MAV and PAV, respectively) of the intermediate 180° turn were computed. For the 3MBWT, backward walking speed was measured. Participants were then asked to wear the Garmin Vivosmart 4 smartwatch (Garmin, Olathe, KS, USA), configured according to the manufacturer's specifications by indicating the users' age, height, weight, and the wrist on which the smartwatch was worn (i.e., left or right). The device was worn on the wrist of the less affected side, in line with previous research findings (Bianchini et al., 2025; Bianchini, Galli, et al., 2023; Bianchini et al., 2022) for 5 consecutive days. We chose a 5-day period since we demonstrated previously that a minimum of 4 days of monitoring is needed to reliably estimate daily step count in PwPD (Bianchini, Galli, et al., 2023) and that 5 days of monitoring led to acceptable reliability regardless of PD severity, stage and phenotype (Bianchini et al., 2025). Moreover, in a proof-of-concept experiment, we recently demonstrated that Garmin Vivosmart 4 was valid and decently accurate in estimating avDS in PD (Bianchini et al., 2025). Participants were instructed to wear the smartwatch all time during day and night and remove it only when involved in water activities (e.g., bathing, showering, swimming, etc.). Participants were also asked to perform daily activities as usual. No additional reminder or instructions were provided to participants during the monitoring period. During the monitoring period, participants could access information on the smartwatch screen, including the total number of steps, heart rate and sleep time. The device did not provide instructions, alerts or other messages to participants. The total daily steps recorded were extracted, and the average daily steps (AvDS) were calculated[48]. Compliance was assessed based on the participants' dashboard data. We could assess that the device was worn through heart rate and activity data. We considered all recording days with $\geq 80\%$ wear time while awake to be valid. We estimated the awake time as 24 hours minus the total sleep time as indicated by the device (Bianchini et al., 2025). Experimental procedure is summarized in fig. 11.1.

Statistical analyses

Statistical analyses were performed using JASP v0.18.3.0 (JASP Team, University of Amsterdam, The Netherlands), R v4.0.3, and R Studio v2023.12.0+369 for Windows (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were calculated for the study variables. The normality of the variables was assessed through histograms and residual plots inspection. From the total PwPD dataset, a nearest neighbour propensity score matching for age, sex and disease duration, with a 1:1 ratio between PD NH+ and PD NH- was performed using a custom script and the "MatchIt" package in R. We used the Mann-Whitney and Chi square test, to check the lack of significant differences between the matching variables. Mann-Whitney test was also used to compare variables between PD NH+ and PD NH-. Chi-square test was used to compare categorical variables between the two groups. Spearman's test was used to evaluate correlations between mobility and clinical variables and MDS-UPDRS 2.9 score. The cut-off points used for interpreting correlation coefficient values were as follows (Akoglu, 2018): < 0.1 : negligible; $0.1-0.2$: very weak;

0.2-0.4: weak; 0.4-0.7: moderate; 0.7-0.9: strong; > 0.9: very strong. The Kruskal-Wallis test was used to assess the difference in supervised and unsupervised mobility parameters across NH severity, as indicated by MDS-UPDRS item 2.9 score. Dunn's post-hoc test with Holm-Bonferroni correction was used for pairwise comparisons in case of overall significance. For all analyses, the significance threshold was set at $\alpha < 0.05$. FDR correction with a predefined FDR of 0.05 was applied to p-values to control error inflation due to multiple testing. All data are reported as mean $\pm$ SD or median (Q1-Q3) for numerical variables and N (%) for categorical variables.

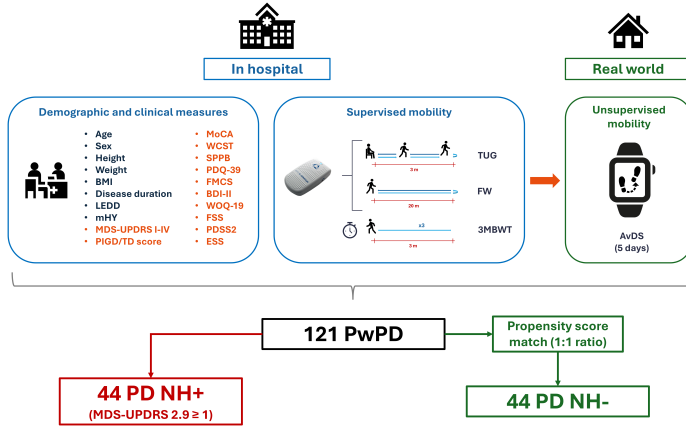


Figure 11.1. Schematic representation of study experimental procedure. 3MBWT: 3-meter backward walking test; AvDS: average daily steps; BDI-II: Beck depression inventory; BMI: Body mass index; ESS: Epworth sleepiness scale; FES-I: Falls Efficacy Scale International; FMCS: Functional mobility composite score; FOG: Freezing of gait; FSS: Fatigue severity scale; FW: forward walking; LEDD: Levodopa equivalent daily dose; MAV: Mean angular velocity; MDS-UPDRS: Movement Disorder Society Unified Parkinson's disease rating scale; mHY: Modified Hoehn and Yahr stage; MoCA: Montreal cognitive assessment; PAV: Peak angular velocity; PDQ-39: Parkinson's disease questionnaire 39; PDSS-2: Parkinson's disease sleep scale; PIGD: Postural instability and gait disorders; TD: Tremor dominant; TUG: Timed Up and Go; WCST: Word-color Stroop test; WO: Wearing-off; WOQ-19: Wearing-off questionnaire 19.

Results

Overview

Of the total 121 PwPD included in the cross-sectional dataset, 44 PD NH+ and 44 matched PD NH- were included for a total of 88 participants. Globally, participants demonstrated a median score at MDS-UPDRS item 2.9 of 1 (0 - 1; range 0 - 2). Demographic, clinical and mobility characteristics of the enrolled population are presented in table 11.1, table 11.2 and table 11.3, respectively.

Table 11.1. Demographic, anthropometric and basic clinical characteristics of the overall population, PD NH+ and PD NH-. The FDR adjusted p-value of the Mann-Whitney test are reported. Significance of the difference is shown as follows: * = $P < .05$; ** = $P < .01$; *** = $P < .001$.

	PwPD (N=88)	PD NH+ (N=44)	PD NH- (N=44)	Adj p
Age (years)	68.6 $\pm$ 9.0	68.7 $\pm$ 7.9	68.5 $\pm$ 10.1	0.997
Sex (female)	24 (27%)	13 (30%)	11 (25%)	1
Height (cm)	171 $\pm$ 8.7	170 $\pm$ 8.2	172 $\pm$ 9.2	0.410
Weight (kg)	76.4 $\pm$ 12.2	78.0 $\pm$ 12.0	74.7 $\pm$ 12.4	0.338
BMI (kg/m ²)	25.9 $\pm$ 3.3	26.7 $\pm$ 3.1	25.1 $\pm$ 3.4	0.068
Disease duration (years)	6.49 $\pm$ 4.04	6.89 $\pm$ 4.07	6.09 $\pm$ 4.02	0.338
LEDD (mg)	558 $\pm$ 269	659 $\pm$ 268	457 $\pm$ 252	<0.001***
mHY	2 (2–2.5)	2 (2–2.5)	2 (2–2.5)	0.188

BMI: Body mass index; mHY: Modified Hoehn and Yahr stage; LEDD: Levodopa equivalent daily dose.

Differences in mobility parameters between PD NH+ and PD NH-

Concerning supervised mobility, PD NH+ showed a significantly longer TUG duration ($P=0.035$), lower MAV ($P=0.031$), PAV ($P=0.035$) and 3MBWT speed ($P=0.031$). Regarding unsupervised mobility, PD NH+ took significantly less steps/day compared with PD NH- ($P=0.034$). Differences in supervised and unsupervised mobility between the two groups are summarized in table 11.3.

Correlation between NH severity and mobility parameters

Regarding supervised mobility, NH severity as measured as MDS-UPDRS item 2.9 showed a weak negative correlation with FW speed ($= -0.242$; $p=0.033$), normalized stride length ($= -0.268$; $p=0.019$), TUG duration ($= -0.337$; $p=0.004$), MAV ($= -0.331$; $p=0.004$), PAV ($= -0.322$; $p=0.004$) and 3MBWT speed ($= -0.325$; $p=0.004$). No significant correlations were found between MDS-UPDRS item 2.9 and FW cadence ($= -0.065$; $p=0.688$), FW swing ($= 0.009$; $p=0.936$) and FW stance ($= 0.009$; $p=0.936$). Considering unsupervised mobility, MDS-UPDRS item 2.9 showed a weak negative correlation with AvDS ($= -0.336$; $p=0.004$).

Differences in mobility parameters across NH scores

In terms of supervised mobility, Kruskal-Wallis test showed a significant difference across MDS-UPDRS item 2.9 scores in FW speed ($P=0.004$), FW stride length normalized ($P=0.003$), TUG duration ($P=0.003$), MAV ($P=0.004$), PAV ($P=0.004$) and 3MBWT speed ($P=0.006$). Dunn's test showed a significant difference between score 0 and 2 in all variables (fig. 11.2). Moreover, significant differences between scores 1 and 2 were found in FW speed (Figure 2A), FW stride length normalized (Figure 2B), TUG duration (Figure 2F) and PAV (Figure 2H). Regarding unsupervised mobility, a significant difference across NH severity was found for AvDS ($P=0.004$). Dunn's test showed a significant difference both between score 0 and 2 and between 1 and 2 (Figure 3). Details of the Kruskal-Wallis test and Dunn's pairwise comparisons are summarized in fig. 11.3.

Table 11.2. Clinical characteristics of the overall population, PD NH+ and PD NH-. The FDR adjusted p-value of the Mann-Whitney test are reported. Significance of the difference is shown as follows: * = $P < .05$; ** = $P < .01$; *** = $P < .001$.

	PwPD (N=88)	PD NH+ (N=44)	PD NH- (N=44)	Adj p
MDS-UPDRS I	7 (5–11)	8 (5–11)	6 (3–8)	0.031*
MDS-UPDRS II	5 (3–10)	8 (5–12)	4 (2–6)	<0.001***
MDS-UPDRS III	29 (23–33)	31 (25–34)	27 (22–32)	0.083
MDS-UPDRS IV	0 (0–2)	0 (0–2)	0 (0–0)	0.028*
MDS-UPDRS TOT	43 (34–51)	48 (42–56)	37 (30–44)	<0.001***
MDS-UPDRS 2.9	1 (0–1)	1 (1–1)	0 (0–0)	–
0	44 (50%)			
1	33 (37%)			
2	11 (13%)			
TD subscore	2 (0–5)	2 (0–4)	2.5 (0–5)	0.123
PIGD subscore	3 (1–5)	3.5 (2–5)	3 (1–4)	0.083
PDSS	4.3 ± 3.6	3.5 ± 1.7	1.2 ± 10.1	0.020*
FMCS	84.9 ± 15.1	79.1 ± 15.9	90.6 ± 11.9	<0.001***
WOQ-19	0 (0–2)	1 (0–3)	0 (0–1)	0.028*
PDSS2	10 (7–15)	11.5 (9–17)	8.5 (5–13)	0.021*
ESS	6 (4–8)	6 (6–8)	6 (4–8)	0.391
FSS	3.25 ± 1.66	3.70 ± 1.50	3.21 ± 1.79	0.127
FES I	22 (18–27)	25.5 (21–29)	20 (17–25)	0.007**
BDI II	7 (5–10)	8 (6–11)	6 (5–9)	0.031*
SPPB	10 (8–11)	10 (9–11)	11 (9–12)	0.182
MoCA	26 (25–27)	26 (25–27)	26 (24–28)	0.464
WCST	42.1 ± 15.9	43.3 ± 16.5	40.8 ± 15.3	0.464
FOG	15 (17%)	8 (18%)	7 (16%)	1
WO	32 (36%)	23 (52%)	9 (21%)	0.012*

BDI-II: Beck depression inventory; ESS: Epworth sleepiness scale; FES-I: Falls Efficacy Scale International; FMCS: Functional mobility composite score; FOG: Freezing of gait; FSS: Fatigue severity scale; MDS-UPDRS: Movement Disorder Society Unified Parkinson's disease rating scale; MoCA: Montreal cognitive assessment; PDQ-39: Parkinson's disease questionnaire 39; PDSS: PD Parkinson's disease sleep scale; PIGD: Postural instability and gait disorder; TD: tremor-dominant; WCST: Word-color Stroop test; WO: Wearing-off; WOQ-19: Wearing-off questionnaire 19.

Differences in clinical variables between PD NH+ and PD NH-

PD NH+ showed a significant higher LEDD ($P < 0.001$). No other differences were found in terms of anthropometric or demographic data (Table 1). PD NH+ demonstrated a significantly higher score at MDS-UPDRS part I ($P = 0.031$), part II ($P < 0.001$), part IV ($P = 0.028$) and total score ($P < 0.001$). PD NH+ also showed significantly higher scores in PDQ-39 ($P = 0.020$), WOQ-19 ($P = 0.028$), PDSS-2 ($P = 0.021$), FES-I ($P = 0.007$), BDI-II ($P = 0.031$), and lower FMCS ($P < 0.001$). Finally, in PD NH+, WO was significantly more prevalent than in PD NH- ($P = 0.026$). No difference was found in FOG prevalence. Differences in clinical variables between the two groups are summarized in table 11.2.

Table 11.3. Clinical characteristics of the overall population, PD NH+ and PD NH-. The FDR adjusted p-value of the Mann-Whitney test are reported. Significance of the difference is shown as follows: * = $P < .05$; ** = $P < .01$; *** = $P < .001$.

	PwPD (N=88)	PD NH+ (N=44)	PD NH- (N=44)	Adj p
FW Speed (m/s)	1.18 $\pm$ 0.23	1.14 $\pm$ 0.24	1.23 $\pm$ 0.22	0.274
FW Cadence (steps/min)	110.9 $\pm$ 12.7	109.7 $\pm$ 15.7	112.1 $\pm$ 8.7	0.804
FW Stride length norm (%)	74.0 $\pm$ 11.4	71.6 $\pm$ 11.5	76.4 $\pm$ 11.0	0.203
FW Swing (%)	61.2 $\pm$ 2.2	61.3 $\pm$ 2.4	61.0 $\pm$ 1.9	0.397
FW Swing (s)	38.7 $\pm$ 2.9	38.8 $\pm$ 2.4	38.6 $\pm$ 3.4	0.930
TUG duration (s)	12.0 $\pm$ 4.0	12.6 $\pm$ 3.5	11.5 $\pm$ 4.4	0.035*
MAV ($^{\circ}$ /s)	70.0 $\pm$ 18.9	65.6 $\pm$ 18.5	74.4 $\pm$ 18.4	0.031*
PAV ($^{\circ}$ /s)	138 $\pm$ 39.9	128 $\pm$ 31.2	147 $\pm$ 45.3	0.035*
3MWBt speed (m/s)	0.58 $\pm$ 0.22	0.52 $\pm$ 0.20	0.64 $\pm$ 0.22	0.031*
AvDS (steps/day)	5846 $\pm$ 3059	5126 $\pm$ 3095	6566 $\pm$ 2880	0.034*

AvDS: Average daily steps; 3MWBt: 3-meter backward walking test; FW: Forward walking; MAV: Mean angular velocity; PAV: Peak angular velocity; TUG: Timed Up and Go.

Table 11.4. Kruskal-Wallis test results across MDS-UPDRS item 2.9 scores for supervised and unsupervised mobility parameters. For Kruskal-Wallis test, The Chi-squared statistics and the FDR-adjusted p-values are reported. For variables showing a significant difference at the overall test, p-values of Dunn's pairwise comparisons with Holm-Bonferroni correction are also reported. Significance of the difference is shown as follows: * = $P < .05$; ** = $P < .01$; *** = $P < .001$.

	Statistics	Adj p	Pairwise	Dunn's p
FW Speed (m/s)	13.800	0.003**	0-1 0-2 1-2	0.910 0.002** 0.002**
FW Cadence (steps/min)	0.996	0.893	0-1 0-2 1-2	– – –
FW stride length norm (%)	15.819	0.003**	0-1 0-2 1-2	0.582 0.001*** <0.001***
FW Stance avg (%)	0.062	0.969	0-1 0-2 1-2	– – –
FW Swing avg (%)	0.077	0.969	0-1 0-2 1-2	– – –
TUG dur (s)	13.864	0.003**	0-1 0-2 1-2	0.242 <0.001*** 0.009**
MAV ($^{\circ}$ /s)	11.201	0.006**	0-1 0-2 1-2	0.116 0.003** 0.065
PAV ($^{\circ}$ /s)	11.285	0.006**	0-1 0-2 1-2	0.171 0.003** 0.040*
3MBWT speed (m/s)	10.471	0.008**	0-1 0-2 1-2	0.104 0.005** 0.096
AvDS	12.961	0.004**	0-1 0-2 1-2	0.193 <0.001*** 0.018*

AvDS: Average daily steps; 3MBWT: 3-meter backward walking test; FW: Forward walking; MAV: Mean angular velocity; PAV: Peak angular velocity; TUG: Timed Up and Go.

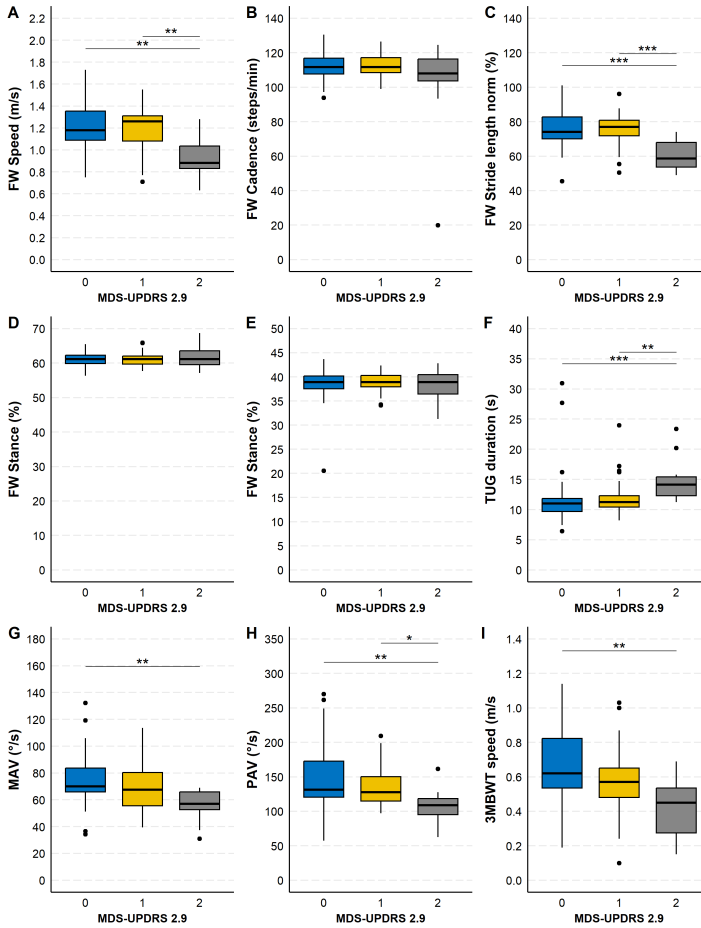


Figure 11.2. Comparisons of supervised mobility across NH severity. MDS-UPDRS item 2.9 scores are displayed on the x-axis. Supervised mobility parameters are reported on the y-axis. Significance of Dunn's pairwise comparisons are indicated with horizontal lines and marked with asterisks as follows: * = $P < .05$; ** = $P < .01$; *** = $P < .001$. 3MBWT: 3-meter backward walking test; FW: Forward walking; MAV: Mean angular velocity; MDS-UPDRS: Movement Disorder Society Unified Parkinson's disease rating scale; PAV: Peak angular velocity; TUG: Timed Up and Go.

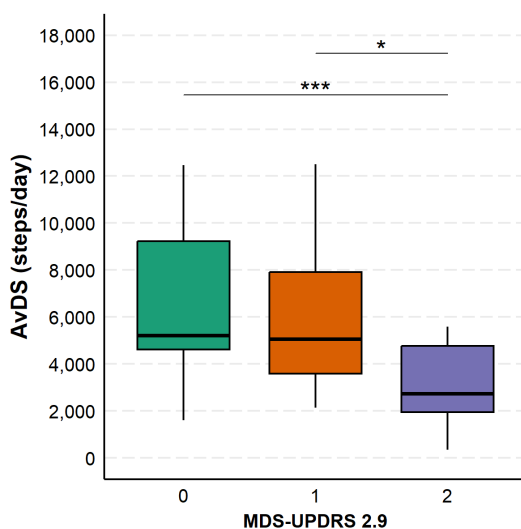


Figure 11.3. Comparison of unsupervised mobility across NH severity. MDS-UPDRS item 2.9 scores are displayed on the x-axis. AvDS are reported on the y-axis. Significance of Dunn's pairwise comparisons are indicated with horizontal lines and marked with asterisks as follows: * = $P < .05$; ** = $P < .01$; *** = $P < .001$. AvDS: Average daily steps; MDS-UPDRS: Movement Disorder Society Unified Parkinson's disease rating scale.

Discussion

This study had three objectives: (i) to examine differences in supervised and unsupervised mobility between propensity score-matched mild-to-moderate PwPD with and without NH; (ii) to evaluate the association between mobility parameters and NH severity; and (iii) to compare clinical scores between the two groups. Our findings revealed that: (i) PD NH+ exhibited worse supervised and unsupervised mobility parameters compared with PD NH- and significant differences were found in supervised and unsupervised mobility across NH severity scores; (ii) NH severity negatively correlated with FW speed, normalized stride length, TUG duration, MAV, PAV, 3MBWT speed, and AvDS; (iii) PD NH+ exhibited more severe clinical scores. To the best of our knowledge, this is the first study to assess supervised and unsupervised mobility in PD NH+.

NH and supervised mobility

Compared to PD NH-, PD NH+ demonstrated significantly longer TUG duration, reduced MAV and PAV, and slower 3MBWT speed. These findings suggest that PD NH+ experience significant impairments in supervised mobility, characterized by slower, less fluid, and weaker movements. Furthermore, NH severity was negatively correlated with FW speed, normalized stride length, TUG duration, MAV, PAV, and 3MBWT speed, suggesting that NH magnitude parallels the deterioration in supervised mobility parameters. These findings are reinforced by significant differences in these measures observed across NH scores. Taken together, our findings suggest that NH and daytime mobility impairments could share common underlying mechanisms. An alternative explanation could be that the severity of NH may contribute to sleep impairment that contribute to daytime mobility dysfunction. PD motor symptoms, in particular axial bradykinesia and rigidity, could lead to both impaired bed and supervised mobility (Amara et al., 2017). Axial motor symptoms include difficulties with balance, posture, speech, swallowing, and locomotion with freezing of gait, that typically have a poor response to dopaminergic therapy (O’Gorman Tuura et al., 2018). Evidence showed that difficulty turning in bed for PwPD is primarily due to impaired axial rotation[6], with previous studies reporting a significant positive association between axial impairment and turning in bed difficulty (Steiger et al., 1996). Nocturnal movements parameters, including turning duration, velocity, and magnitude, were reduced even in early stages of PD, and were associated with severe bradykinesia, rigidity, and PIGD scores, that could reflect axial symptoms severity (Mirelman et al., 2020). Moreover, previous studies have suggested that axial rigidity and reduced angular velocity could contribute to both difficulties in turning in bed and the postural and gait scores (Mirelman et al., 2020). A study by Xue et al. (Xue et al., 2018) found that nocturnal movements in PwPD were negatively correlated with UPDRS axial scores, suggesting that difficulties in axial movement lead to reduced, slower and smaller turning movements both during daytime and nighttime. Accordingly, in our study, PD NH+ had higher MDS-UPDRS total scores suggesting that they experience more severe global symptoms, strengthening the notion that symptoms severity is a relevant contributor to NH. Conversely, we did not find a significant difference between PD NH+ and PD NH- in MDS-UPDRS part III as well as in PIGD subscore. This could be explained by the adopted matching methodology, accounting for disease duration. In fact, previous studies have examined the relationship between bed mobility, disease duration, and mHY stages in PD. Mirelman et al. reported a significant positive association between impaired bed mobility, disease duration and mHY stages (Mirelman et al., 2020). Furthermore, as the disease progress the number and velocity of turns decreased, while turning duration increased (Mirelman et al., 2020). Similarly, in other studies, PwPD with impaired bed mobility symptoms were typically older, had longer disease duration, and displayed a more advanced disease stages (Sommerauer et al., 2015; Sringean et al., 2020). Furthermore, a study by Choi et al. found that the severity of NH increases with advancing disease duration and mHY stages (Choi et al., 2021). In our study, we matched the two groups by disease duration, therefore the difference in motor symptoms as assessed by the

part III of MDS-UPDRS could have been dampened. However, the methodology hereby used could have allowed us to better capture the impact of NH irrespective of other variables such as disease duration and age. Muscle weakness and low torque output in specific muscle groups could also contribute to difficulties in bed mobility and getting out of bed in PD (Taniguchi et al., 2022). Indeed, PwPD showed significantly weaker hip, knee and ankle flexors as well as hip abductors and adductors compared with healthy controls. Hip adductor torque on the more affected side was positively associated with slower movement time, greater arm rigidity on both sides, and higher akinesia scores (Taniguchi et al., 2022). PwPD demonstrated a movement pattern involving lateral trunk flexion without rotation, along with increased hand use while turning. This reliance on the upper limbs highlights their important role in bed mobility, while arm rigidity likely contributes to the slowness of getting out of bed (Taniguchi et al., 2022). Interestingly, we found lower MAV and PAV in PD NH+ compared with PD NH-. This result could suggest that an ineffective rotational strategy could contribute to both mobility and turning ability when lying and walking. This is likely due to a combination of factors (e.g., axial rigidity, reduced torque, weakness in hip muscles and disorganization of the fine-tuned body segments realignment during turning). As previously mentioned, the association between supervised mobility and bed mobility could be mediated also by the disruption of sleep. PwPD often spend prolonged periods in a supine position due to difficulties in turning and getting out of bed (Sommerauer et al., 2015; Sringean et al., 2020), which can cause pressure sores and sleep disordered breathing. This can further exacerbate health risks particularly in the advanced stages of PD by negatively impacting functional outcomes and increasing mortality (Matsumoto et al., 2014; Sommerauer et al., 2015). In our study, PD NH+ had higher PDSS-2 scores suggesting that those individuals had overall more disrupted sleep. Previous studies reported that impaired bed mobility is positively correlated with the severity of symptoms such as disease duration, dyskinesia and decreased sleep quality in patients with PD (Li et al., 2023; Xue et al., 2018). Indeed, PwPD with impaired bed mobility had reduced sleep efficiency (Louter et al., 2013), worse sleep quality (Louter et al., 2012), and altered waking up the following morning (Rizos et al., 2014). Poor sleep quality in PD is associated with more severe motor and non-motor symptoms (Yi et al., 2022). This is also supported by our findings of worse depressive symptoms in PD NH+. Therefore, on one side bradykinesia, rigidity and axial symptoms could contribute to NH and worse supervised mobility (Bhidayasiri, Sringean, & Thanawattano, 2016). NH, on the other side, could disrupt sleep quality and negatively affect motor and non-motor symptoms, leading to a reciprocal detrimental relationship.

NH and unsupervised mobility

Consistent with impaired supervised mobility outcomes, PD NH+ took fewer daily steps than PD NH- and a significant difference in AvDS was found across NH scores. Moreover, NH severity negatively correlates with daily step count. This suggest that as NH worsens, the number of step per day decreases. A study by Christiansen et al. (Christiansen et al., 2017) found that the absence fear of falling was associated with higher step counts in de novo PD. In our study, PD NH+ had higher FES-I scores, indicating greater fear of falling, those patients took less daily steps. Indeed, the fear of falling may led them to limit their mobility to avoid falling and causing injuries. Additionally, PD NH+ had higher MDS-UPDRS part II and FMCS scores suggesting that they experience more severe motor impairment and greater functional disability which can affect physical and ambulatory activity. Nagaki et al. (Nagaki et al., 2022) found that PwPD accumulating < 4200 steps/day had worse MDS-UPDRS total scores, underscoring the relationship between severe symptoms burden and physical activity. Similarly, Uchino et al. (Uchino et al., 2017) found that number of turnover movements in bed was negatively correlated with MDS-UPDRS part III and total score, mHY stage, while positively correlated with the Barthel index score. This suggests that fewer nocturnal turnover movements are associated with worse motor symptoms, disease severity and greater daytime immobility. PwPD with reduced motor

function, as measured by these scales, tended to spend more time in bed, longer time in a supine position, and longer interval between turnover movements (Uchino et al., 2017). Furthermore, when untreated, nocturnal impairments can greatly reduce quality of life of PwPD, leading to disrupted sleep and frequent awakenings, which could increase daytime sleepiness and impair daytime functioning (Sringean et al., 2024). This is reflected also by our findings of a reduced PDQ-39 score in PD NH+ indicating worse quality of life in PwPD with impaired bed mobility. These findings confirm the importance of considering nocturnal impairments in the management strategy of PD symptoms.

NH and other clinical measures

Finally, we found that PD NH+ exhibited a significantly higher LEDD than PD NH-. Similar to our findings, Mirelman et al. (Mirelman et al., 2020) also reported that nocturnal movements were negatively associated with LEDD. Accordingly to the concept of NH as a form of nocturnal WO, our results showed a higher WOQ-19 and MDS-UPDRS part IV score in PD NH+ and a higher prevalence of WO. This could explain the higher LEDD observed in PwPD with reduced bed mobility, since pharmacological therapy optimization is the primary strategy to address motor fluctuations. Indeed, previous evidence suggested that nighttime apomorphine (Bhidayasiri, Sringean, Anan, et al., 2016), rotigotine (Bhidayasiri, Sringean, Chaiwong, et al., 2017) and L-DOPA administration (Sringean et al., 2024) could improve NH severity. However, our findings showed that, despite higher LEDD, PD NH+ had worse functional outcomes as well as motor and non-motor impairments, suggesting that the increased doses may not be sufficient. This is consistent with the association between NH and axial symptoms (Mirelman et al., 2020), that are known to be less responsive to dopaminergic medications (Fabbri et al., 2016) and led us to speculate that other drug administration route and strategies could be more effective. Thus, Sringean and collaborators showed that bed mobility worsen as night duration progresses, further strengthening the notion that the progressing lack of dopaminergic stimulation is a key element and supporting the use of continuous nighttime dopaminergic drug delivery (Sringean et al., 2020). Moreover, the effectiveness of continuous dopaminergic stimulation to improve dopa-resistant symptoms has been reported before (Imbalzano et al., 2023).

Limitations, strengths and perspectives

We acknowledge that this study has several limitations. First, the study used a cross-sectional design, which limits us from establishing causal relationships between NH and mobility outcomes. In addition, the sample was restricted to participants with mild-to-moderate PD stages, excluding those with severe cognitive or mobility impairments, which prevented the generalization of the results to more advanced PD stages. Furthermore, the sample size was relatively small to perform multivariate analysis. Future studies including a larger sample size involving participants with more advanced disease stages are hence needed. In this study, the mobility assessment was also limited: supervised mobility was evaluated according to a limited set of parameters and unsupervised mobility evaluated solely with daily step count. Thus, implementing more detailed mobility parameters particularly in unsupervised conditions could provide a better understanding of real-world mobility. Moreover, NH severity was assessed using MDS-UPDRS item 2.9, and in our population the score range was only from 0 to 2, limiting the applicability of the results to PwPD with more severe NH (scores 3–4). Future studies using wearable digital technologies to assess bed mobility are needed, as they may provide objective continuous assessment of nocturnal mobility, thus helping to further exploring the relationship between daytime and nighttime mobility impairments in PD. Finally, we did not systematically test the effectiveness of propensity matching but assessed only the lack of significant differences in the matching variables between the two groups. However, we were not interested in using the propensity score to retrospectively compare an intervention/exposure but only to match PD

NH+ and PD NH- in a robust, less biased way. Despite these limitations, this study offers several strengths. One of the key strengths is its novel findings. Notably, this study provides new insights into the relationship between NH and both supervised and unsupervised mobility in PD. Additionally, the propensity score-matched design of the analysis helped control for potential confounding factors (i.e., disease duration, sex and age). Finally, the findings provide insights for clinical application, potential therapeutical and rehabilitative strategies that target both nocturnal and daytime mobility impairments to improve overall function in PD.

Conclusions

NH was associated with worse supervised and real-world mobility in PD. In particular, PD NH+ demonstrated worse functional mobility, reduced turning velocity, slower backward walking, and decreased daily step counts compared with PD NH- participants. Furthermore, NH severity was correlated with greater functional impairments across both supervised and unsupervised mobility parameters. Finally, PD NH+ showed worse motor and non-motor symptoms, despite higher LEDD. These findings underscore the importance of evaluating NH as it impacts both nocturnal and daytime functions. Finally, our results emphasize the need to develop targeted interventions that address nighttime mobility or daytime mobility impairments, aiming to improve overall functional mobility in PwPD.

References

- Abbruzzese, G., Antonini, A., Barone, P., Stocchi, F., Tamburini, T., Bernardi, L., Amboni, M., Vacca, L., Posocco, V., & Colombo, D. (2012). Linguistic, psychometric validation and diagnostic ability assessment of an Italian version of a 19-item wearing-off questionnaire for wearing-off detection in Parkinson's disease. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 33(6), 1319–1327. <https://doi.org/10.1007/s10072-012-0943-y>
- Adams, J. L., Kangaroo, T., Gong, Y., Khachadourian, V., Tracey, B., Volfson, D., Latzman, R. D., Cosman, J., Edgerton, J., Anderson, D., Best, A., Kostrzebski, M. A., Auinger, P., Wilmot, P., Pohlson, Y., Jensen-Roberts, S., Müller, M. L. T. M., Stephenson, D., Dorsey, E. R., & Parkinson Study Group Watch-PD Study Investigators and Collaborators. (2024). Using a smartwatch and smartphone to assess early Parkinson's disease in the WATCH-PD study over 12 months. *NPJ Parkinson's disease*, 10(1), 112. <https://doi.org/10.1038/s41531-024-00721-2>
- Akoglu, H. (2018). User's guide to correlation coefficients. *Turkish Journal of Emergency Medicine*, 18(3), 91–93. <https://doi.org/10.1016/j.tjem.2018.08.001>
- Amara, A. W., Chahine, L. M., & Videnovic, A. (2017). Treatment of Sleep Dysfunction in Parkinson's Disease. *Current Treatment Options in Neurology*, 19(7), 26. <https://doi.org/10.1007/s11940-017-0461-6>
- Barta, K., Boddy, A. H., Flores, M., Perry, L., Sawyer, K., & Campbell, A. (2025). Psychometric properties of 3-meter backward walk test (3MBWT) in people with Parkinson disease. *Physiotherapy Theory and Practice*, 41(3), 656–663. <https://doi.org/10.1080/09593985.2024.2348034>
- Bhidayasiri, R., Sringean, J., Anan, C., Boonpang, K., Thanawattano, C., & Ray Chaudhuri, K. (2016). Quantitative demonstration of the efficacy of night-time apomorphine infusion to treat nocturnal hypokinesia in Parkinson's disease using wearable sensors. *Parkinsonism & Related Disorders*, 33 Suppl 1, S36–S41. <https://doi.org/10.1016/j.parkreldis.2016.11.016>
- Bhidayasiri, R., Sringean, J., Chaiwong, S., Anan, C., Penkeaw, N., Leaknok, A., Boonpang, K., Saksornchai, K., Rattanachaisit, W., Thanawattano, C., & Jagota, P. (2017). Rotigotine for nocturnal hypokinesia in Parkinson's disease: Quantitative analysis of efficacy from a randomized, placebo-controlled trial using an axial inertial sensor. *Parkinsonism & Related Disorders*, 44, 124–128. <https://doi.org/10.1016/j.parkreldis.2017.08.010>
- Bhidayasiri, R., Sringean, J., & Thanawattano, C. (2016). Sensor-based evaluation and treatment of nocturnal hypokinesia in Parkinson's disease: An evidence-based review. *Parkinsonism & Related Disorders*, 22 Suppl 1, S127–133. <https://doi.org/10.1016/j.parkreldis.2015.09.049>
- Bhidayasiri, R., Sringean, J., & Thanawattano, C. (2017). Impaired bed mobility: Quantitative torque analysis with axial inertial sensors. *Neurodegenerative Disease Management*, 7(4), 235–243. <https://doi.org/10.2217/nmt-2017-0016>
- Bhidayasiri, R., & Trenkwalder, C. (2018). Getting a good night sleep? The importance of recognizing and treating nocturnal hypokinesia in Parkinson's disease. *Parkinsonism & Related Disorders*, 50, 10–18. <https://doi.org/10.1016/j.parkreldis.2018.01.008>
- Bianchini, E., Rinaldi, D., De Carolis, L., Galli, S., Alborghetti, M., Hansen, C., Suppa, A., Salvetti, M., Pontieri, F., & Vuillerme, N. (2025). Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study. *JMIR Formative Research*, 9. <https://doi.org/10.2196/63153>
- Export Date: 14 April 2025; Cited By: 0.
- Bianchini, E., Calì, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzler, W., & Pontieri, F. E. (2022). Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, 23(1), 214. <https://doi.org/10.3390/s23010214>
- Bianchini, E., Galli, S., Alborghetti, M., De Carolis, L., Zampogna, A., Hansen, C.,

- Vuillermé, N., Suppa, A., & Pontieri, F. E. (2023). Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch [Number: 21 Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 23(21), 8971. <https://doi.org/10.3390/s23218971>
- Bianchini, E., Warmerdam, E., Romijnders, R., Stürner, K. H., Baron, R., Heinzel, S., Pontieri, F. E., Hansen, C., & Maetzler, W. (2023). Turning When Using Smartphone in Persons With and Those Without Neurologic Conditions: Observational Study. *Journal of Medical Internet Research*, 25, e41082. <https://doi.org/10.2196/41082>
- Choi, J.-H., Lee, J.-Y., Shin, C., Yoo, D., Im, J. H., Woo, K. A., Kim, H.-J., Ahn, T.-B., Kim, J.-M., & Jeon, B. (2021). Investigation of Nocturnal Hypokinesia and Health-Related Quality of Life in Parkinsonian Patients with the Korean Version of the Nocturnal Hypokinesia Questionnaire. *Journal of Movement Disorders*, 14(3), 221–225. <https://doi.org/10.14802/jmd.20172>
- Christiansen, C., Moore, C., Schenkman, M., Kluger, B., Kohrt, W., Delitto, A., Berman, B., Hall, D., Josbeno, D., Poon, C., Robichaud, J., Wellington, T., Jain, S., Comella, C., Corcos, D., & Melanson, E. (2017). Factors Associated With Ambulatory Activity in De Novo Parkinson Disease. *Journal of neurologic physical therapy: JNPT*, 41(2), 93–100. <https://doi.org/10.1097/NPT.0000000000000169>
- Corrà, M. F., Atrsaee, A., Sardoreira, A., Hansen, C., Aminian, K., Correia, M., Vila-Chã, N., Maetzler, W., & Maia, L. (2021). Comparison of Laboratory and Daily-Life Gait Speed Assessment during ON and OFF States in Parkinson's Disease. *Sensors (Basel, Switzerland)*, 21(12), 3974. <https://doi.org/10.3390/s21123974>
- Dijkstra, B., Zijlstra, W., Scherder, E., & Kamsma, Y. (2008). Detection of walking periods and number of steps in older adults and patients with Parkinson's disease: Accuracy of a pedometer and an accelerometry-based method. *Age and Ageing*, 37(4), 436–441. <https://doi.org/10.1093/ageing/afn097> Export Date: 14 April 2025; Cited By: 98.
- Dodet, P., Houot, M., Leu-Semenescu, S., Corvol, J.-C., Lehéry, S., Mangone, G., Vidailhet, M., Roze, E., & Arnulf, I. (2024). Sleep disorders in Parkinson's disease, an early and multiple problem. *NPJ Parkinson's Disease*, 10, 46. <https://doi.org/10.1038/s41531-024-00642-0>
- Fabbri, M., Coelho, M., Abreu, D., Guedes, L. C., Rosa, M. M., Costa, N., Antonini, A., & Ferreira, J. J. (2016). Do patients with late-stage Parkinson's disease still respond to levodopa? *Parkinsonism & Related Disorders*, 26, 10–16. <https://doi.org/10.1016/j.parkreldis.2016.02.021>
- GBD 2016 Parkinson's Disease Collaborators. (2018). Global, regional, and national burden of Parkinson's disease, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *The Lancet. Neurology*, 17(11), 939–953. [https://doi.org/10.1016/S1474-4422\(18\)30295-3](https://doi.org/10.1016/S1474-4422(18)30295-3)
- Ginis, P., Goris, M., De Groef, A., Blondeel, A., Gilat, M., Demeyer, H., Troosters, T., & Nieuwboer, A. (2023). Validation of Commercial Activity Trackers in Everyday Life of People with Parkinson's Disease. *Sensors*, 23(8). <https://doi.org/10.3390/s23084156> Export Date: 14 April 2025; Cited By: 6.
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., Giladi, N., Holloway, R. G., Moore, C. G., Wenning, G. K., Yahr, M. D., Seidl, L., & Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 19(9), 1020–1028. <https://doi.org/10.1002/mds.20213>
- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement*

- Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Guralnik, J. M., Simonsick, E. M., Ferrucci, L., Glynn, R. J., Berkman, L. F., Blazer, D. G., Scherr, P. A., & Wallace, R. B. (1994). A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *Journal of Gerontology*, 49(2), M85–94. <https://doi.org/10.1093/geronj/49.2.m85>
- Hackney, M. E., & Earhart, G. M. (2009). Backward walking in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 24(2), 218–223. <https://doi.org/10.1002/mds.22330>
- Hanff, A.-M., McCrum, C., Rauschenberger, A., Aguayo, G. A., Zeegers, M. P., Leist, A. K., Krüger, R., & NCER-PD. (2023). Validation of a Parkinson's disease questionnaire-39-based functional mobility composite score (FMCS) in people with Parkinson's disease. *Parkinsonism & Related Disorders*, 112, 105442. <https://doi.org/10.1016/j.parkreldis.2023.105442>
- Imbalzano, G., Rinaldi, D., Calandra-Buonaura, G., Contin, M., Amato, F., Giannini, G., Sambati, L., Ledda, C., Romagnolo, A., Olmo, G., Cortelli, P., Zibetti, M., Lopian, L., & Artusi, C. A. (2023). How resistant are levodopa-resistant axial symptoms? Response of freezing, posture, and voice to increasing levodopa intestinal infusion rates in Parkinson disease. *European Journal of Neurology*, 30(1), 96–106. <https://doi.org/10.1111/ene.15558>
- Jenkinson, C., Fitzpatrick, R., Peto, V., Greenhall, R., & Hyman, N. (1997). The Parkinson's Disease Questionnaire (PDQ-39): Development and validation of a Parkinson's disease summary index score. *Age and Ageing*, 26(5), 353–357. <https://doi.org/10.1093/ageing/26.5.353>
- Johns, M. W. (1991). A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep*, 14(6), 540–545. <https://doi.org/10.1093/sleep/14.6.540>
- Li, S., Lin, Q., Bao, Y., Feng, Y., Li, D., & Zhang, C. (2023). Impaired night-time mobility in patients with Parkinson's disease: A systematic review. *Frontiers in Aging Neuroscience*, 15, 1264143. <https://doi.org/10.3389/fnagi.2023.1264143>
- Louter, M., Munneke, M., Bloem, B. R., & Overeem, S. (2012). Nocturnal hypokinesia and sleep quality in Parkinson's disease. *Journal of the American Geriatrics Society*, 60(6), 1104–1108. <https://doi.org/10.1111/j.1532-5415.2012.03966.x>
- Louter, M., van Sloun, R. J. G., Pevernagie, D. A. A., Arends, J. B. A. M., Cluitmans, P. J., Bloem, B. R., & Overeem, S. (2013). Subjectively impaired bed mobility in Parkinson disease affects sleep efficiency. *Sleep Medicine*, 14(7), 668–674. <https://doi.org/10.1016/j.sleep.2013.03.010>
- Maggi, G., D'Iorio, A., Aiello, E. N., Poletti, B., Ticozzi, N., Silani, V., Amboni, M., Vitale, C., & Santangelo, G. (2023). Psychometrics and diagnostics of the Italian version of the Beck Depression Inventory-II (BDI-II) in Parkinson's disease. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 44(5), 1607–1612. <https://doi.org/10.1007/s10072-023-06619-w>
- Mancini, M., El-Gohary, M., Pearson, S., McNames, J., Schlueter, H., Nutt, J. G., King, L. A., & Horak, F. B. (2015). Continuous monitoring of turning in Parkinson's disease: Rehabilitation potential. *NeuroRehabilitation*, 37(1), 3–10. <https://doi.org/10.3233/NRE-151236>
- Matsumoto, H., Sengoku, R., Saito, Y., Kakuta, Y., Murayama, S., & Imafuku, I. (2014). Sudden death in Parkinson's disease: A retrospective autopsy study. *Journal of the Neurological Sciences*, 343(1-2), 149–152. <https://doi.org/10.1016/j.jns.2014.05.060>
- Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L., Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)
- Mirelman, A., Hillel, I., Rochester, L., Del Din, S., Bloem, B. R., Avanzino, L., Nieuwboer, A., Maidan, I., Herman, T., Thaler,

- A., Gurevich, T., Kestenbaum, M., Orr-Urtreger, A., Brys, M., Cedarbaum, J. M., Giladi, N., & Hausdorff, J. M. (2020). Tossing and Turning in Bed: Nocturnal Movements in Parkinson's Disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 35(6), 959–968. <https://doi.org/10.1002/mds.28006>
- Mirelman, A., Volkov, J., Salomon, A., Gazit, E., Nieuwboer, A., Rochester, L., Del Din, S., Avanzino, L., Pelosin, E., Bloem, B. R., Della Croce, U., Cereatti, A., Thaler, A., Roggen, D., Mazza, C., Shirvan, J., Cedarbaum, J. M., Giladi, N., & Hausdorff, J. M. (2024). Digital Mobility Measures: A Window into Real-World Severity and Progression of Parkinson's Disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 39(2), 328–338. <https://doi.org/10.1002/mds.29689>
- Morgan, C., Jameson, J., Craddock, I., Tonkin, E. L., Oikonomou, G., Isotalus, H. K., Heidarinvinch, F., McConville, R., Tourte, G. J. L., Kinnunen, K. M., & Whone, A. (2022). Understanding how people with Parkinson's disease turn in gait from a real-world in-home dataset. *Parkinsonism & Related Disorders*, 105, 114–122. <https://doi.org/10.1016/j.parkreldis.2022.11.007>
- Nagaki, K., Fujioka, S., Sasai, H., Yamaguchi, Y., & Tsuboi, Y. (2022). Physical Activity and Its Diurnal Fluctuations Vary by Non-Motor Symptoms in Patients with Parkinson's Disease: An Exploratory Study. *Healthcare (Basel, Switzerland)*, 10(4), 749. <https://doi.org/10.3390/healthcare10040749>
- Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>
- O'Gorman Tuura, R. L., Baumann, C. R., & Baumann-Vogel, H. (2018). Beyond Dopamine: GABA, Glutamate, and the Axial Symptoms of Parkinson Disease. *Frontiers in Neurology*, 9, 806. <https://doi.org/10.3389/fneur.2018.00806>
- Ortega-Bastidas, P., Gómez, B., Aqueveque, P., Luarte-Martínez, S., & Cano-de-la-Cuerda, R. (2023). Instrumented Timed Up and Go Test (iTUG)-More Than Assessing Time to Predict Falls: A Systematic Review. *Sensors (Basel, Switzerland)*, 23(7), 3426. <https://doi.org/10.3390/s23073426>
- Poewe, W., Seppi, K., Tanner, C. M., Halliday, G. M., Brundin, P., Volkman, J., Schrag, A.-E., & Lang, A. E. (2017). Parkinson disease. *Nature Reviews. Disease Primers*, 3, 17013. <https://doi.org/10.1038/nrdp.2017.13>
- Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., Obeso, J., Marek, K., Litvan, I., Lang, A. E., Halliday, G., Goetz, C. G., Gasser, T., Dubois, B., Chan, P., Bloem, B. R., Adler, C. H., & Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 30(12), 1591–1601. <https://doi.org/10.1002/mds.26424>
- Rizos, A., Martinez-Martin, P., Odin, P., Antonini, A., Kessel, B., Kozul, T. K., Todorova, A., Douiri, A., Martin, A., Stocchi, F., Dietrichs, E., Chaudhuri, K. R., & EUROPAR and the IPDMDS non-Motor PD Study Group. (2014). Characterizing motor and non-motor aspects of early-morning off periods in Parkinson's disease: An international multicenter study. *Parkinsonism & Related Disorders*, 20(11), 1231–1235. <https://doi.org/10.1016/j.parkreldis.2014.09.013>
- Scarpina, F., & Tagini, S. (2017). The Stroop Color and Word Test. *Frontiers in Psychology*, 8, 557. <https://doi.org/10.3389/fpsyg.2017.00557>
- Schapira, A. H. V., Chaudhuri, K. R., & Jenner, P. (2017). Non-motor features of Parkinson disease. *Nature Reviews. Neuroscience*, 18(7), 435–450. <https://doi.org/10.1038/nrn.2017.62>
- Shokouhi, N., Khodakarami, H., Fernando, C., Osborn, S., & Horne, M. (2022). Accuracy of Step Count Estimations in Parkinson's Disease Can Be Predicted Using Ambulatory Monitoring. *Frontiers in Aging Neuroscience*, 14, 904895. <https://doi.org/10.3389/fnagi.2022.904895>

- Siciliano, M., Chiorri, C., De Micco, R., Russo, A., Tedeschi, G., Trojano, L., & Tesitore, A. (2019). Fatigue in Parkinson's disease: Italian validation of the Parkinson Fatigue Scale and the Fatigue Severity Scale using a Rasch analysis approach. *Parkinsonism & Related Disorders*, 65, 105–110. <https://doi.org/10.1016/j.parkreldis.2019.05.028>
- Sommerauer, M., Werth, E., Poryazova, R., Gavrilov, Y. V., Hauser, S., & Valko, P. O. (2015). Bound to supine sleep: Parkinson's disease and the impact of nocturnal immobility. *Parkinsonism & Related Disorders*, 21(10), 1269–1272. <https://doi.org/10.1016/j.parkreldis.2015.08.010>
- Souza, R. J. d., Shigaki, I. A. d. A., Terra, M. B., Barboza, N. M., Bueno, M. E. B., Mesas, A. E., & Smaili, S. M. (2023). Effectiveness of Neurofunctional Physical Therapy on the Quality of Sleep of Individuals with Parkinson's Disease: Case Series. *Sleep Science*, 16(2), 206–215. <https://doi.org/10.1055/s-0043-1770801>
- Sringeana, J., Anan, C., & Bhidayasiri, R. (2020). Impaired ability to turn in bed in parkinson's disease as a potential rare cause of positional asphyxia: A sensor-based analysis. *Clinical Neurology and Neurosurgery*, 192, 105713. <https://doi.org/10.1016/j.clineuro.2020.105713>
- Sringeana, J., Udomsirithamrong, O., & Bhidayasiri, R. (2024). Too little or too much nocturnal movements in Parkinson's disease: A practical guide to managing the unseen. *Clinical Parkinsonism & Related Disorders*, 10, 100258. <https://doi.org/10.1016/j.prdoa.2024.100258>
- Stebbins, G. T., Goetz, C. G., Burn, D. J., Jankovic, J., Khoo, T. K., & Tilley, B. C. (2013). How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: Comparison with the unified Parkinson's disease rating scale. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(5), 668–670. <https://doi.org/10.1002/mds.25383>
- Steiger, M. J., Thompson, P. D., & Marsden, C. D. (1996). Disordered axial movement in Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, 61(6), 645–648. <https://doi.org/10.1136/jnnp.61.6.645>
- Taniguchi, S., D'cruz, N., Nakagoshi, M., Osaki, T., & Nieuwboer, A. (2022). Determinants of impaired bed mobility in Parkinson's disease: Impact of hip muscle strength and motor symptoms. *NeuroRehabilitation*, 50(4), 445–452. <https://doi.org/10.3233/NRE-210301>
- Trenkwalder, C., Kohnen, R., Högl, B., Metta, V., Sixel-Döring, F., Frauscher, B., Hüllsmann, J., Martinez-Martin, P., & Chaudhuri, K. R. (2011). Parkinson's disease sleep scale-validation of the revised version PDSS-2. *Movement Disorders: Official Journal of the Movement Disorder Society*, 26(4), 644–652. <https://doi.org/10.1002/mds.23476>
- Uchino, K., Shiraishi, M., Tanaka, K., Akamatsu, M., & Hasegawa, Y. (2017). Impact of inability to turn in bed assessed by a wearable three-axis accelerometer on patients with Parkinson's disease. *PloS One*, 12(11), e0187616. <https://doi.org/10.1371/journal.pone.0187616>
- Vítečková, S., Horáková, H., Poláková, K., Krupička, R., Růžicka, E., & Brožová, H. (2020). Agreement between the GAITRite® System and the Wearable Sensor BTS G-Walk® for measurement of gait parameters in healthy adults and Parkinson's disease patients. *PeerJ*, 8, e8835. <https://doi.org/10.7717/peerj.8835>
- Xue, F., Wang, F.-Y., Mao, C.-J., Guo, S.-P., Chen, J., Li, J., Wang, Q.-J., Bei, H.-Z., Yu, Q., & Liu, C.-F. (2018). Analysis of nocturnal hypokinesia and sleep quality in Parkinson's disease. *Journal of Clinical Neuroscience: Official Journal of the Neurosurgical Society of Australasia*, 54, 96–101. <https://doi.org/10.1016/j.jocn.2018.06.016>
- Yi, Q., Yu-Peng, C., Jiang-Ting, L., Jing-Yi, L., Qi-Xiong, Q., Dan-Lei, W., Jing-Wei, Z., Zhi-Juan, M., Yong-Jie, X., Zhe, M., & Zheng, X. (2022). Worse Sleep Quality Aggravates the Motor and Non-Motor Symptoms in Parkinson's Disease. *Frontiers in Aging Neuroscience*, 14, 887094. <https://doi.org/10.3389/fnagi.2022.887094>
- Zajac, J. A., Cavanaugh, J. T., Baker, T., Duncan, R. P., Fulford, D., Gernis, J., LaVal-

ley, M., Nordahl, T., Porciuncula, F., Rawson, K. S., Saint-Hilaire, M., Thomas, C. A., Earhart, G. M., & Ellis, T. D. (2022). Does clinically measured walking capacity contribute to real-world walking performance in Parkinson's disease? *Parkinsonism & Related Disorders*, 105, 123–127. <https://doi.org/10.1016/j.parkreldis.2022.11.016>

Zampogna, A., Manoni, A., Asci, F., Liguori, C., Irrera, F., & Suppa, A. (2020). Shedding Light on Nocturnal Movements in Parkinson's Disease: Evidence from Wearable Technologies. *Sensors (Basel, Switzerland)*, 20(18). <https://doi.org/10.3390/s20185171>

Chapter 12

Contribution 9: Assessing night-time symptoms severity and response to treatment in Parkinson's disease: preliminary results

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Abstract

Impaired nocturnal mobility (i.e., nocturnal hypokinesia, NH) is frequent in fluctuating people with Parkinson's disease (PwPD). Wearable sensors could enable clinicians to detect this symptom and guide its management. However, only a few studies have objectively assessed the treatment response of NH in PwPD. Ambulating PwPD without dementia and with an indication to initiate treatment with either Opicapone (OPC) or foslevodopa/foscarbidopa (fLD/fCD) subcutaneous infusion for motor fluctuations were recruited. Participants underwent a clinical baseline evaluation (T0) including the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Parkinson's Disease Sleep Scale 2 (PDSS-2), Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), and the Nocturnal Hypokinesia Questionnaire (NHQ). Participants were also instructed to wear a lower-back-mounted inertial sensor (McRoberts MoveMonitor, The Hague, The Netherlands) for seven consecutive nights at home to assess nocturnal mobility. A follow-up evaluation was performed 4 weeks after treatment stabilization (T1). Sixteen PwPD were enrolled, and nine completed the follow-up evaluation (4 OPC; 5 fLD/fCD). PDSS-2 scores showed a statistically and clinically significant improvement between T0 and T1. However, no significant changes were observed in the objective mobility parameters. PwPD exhibited marked impairments in bed mobility. Treatment with OPC or fLD/fCD led to a clinically meaningful improvement in perceived sleep quality but did not significantly alter objective measures of nocturnal mobility. These findings support the hypothesis that dopaminergic therapies may enhance sleep quality through broader neurophysiological mechanisms beyond the mere improvement of nocturnal mobility.

Introduction

Nocturnal symptoms represent a significant burden for patients with Parkinson's disease (PD), substantially impacting quality of life and functional independence. Among these, nocturnal hypokinesia - defined as the inability to move freely during the night - emerges as one of the most disabling symptoms, affecting bed mobility, position changes, and the ability to get out of bed (Bhidayasiri & Trenkwalder, 2018). Sleep disturbances in PD encompass a complex spectrum of motor and non-motor symptoms that evolve throughout disease progression. While prodromal sleep disorders such as REM sleep behavior disorder (RBD) and excessive daytime sleepiness may precede motor symptoms by years, nocturnal hypokinesia typically manifests in complicated, more advanced disease stages as dopaminergic therapy effectiveness diminishes overnight (Dodet et al., 2024; Iranzo et al., 2024). The pathophysiology of nocturnal hypokinesia is primarily attributed to reduced dopamine availability during nighttime hours when antiparkinsonian medications are typically withheld. This dopaminergic depletion results in bradykinesia, rigidity, and akinesia that severely compromise nocturnal mobility, forcing patients to adopt specific sleeping positions, predominantly supine, which may exacerbate upper airway collapse and contribute to obstructive sleep apnea (Sommerauer et al., 2015; Sringean et al., 2020). Previous studies have linked the severity of nocturnal hypokinesia correlates with disease duration, age, Hoehn and Yahr staging as well as specific motor subdomains such as axial symptoms or bradykinesia and rigidity (Bhidayasiri & Trenkwalder, 2018; Louter et al., 2012; Mirelman et al., 2020). Traditionally, assessment relied exclusively on subjective clinical scales, presenting limitations due to recall bias and potential cognitive impairment complications in PD patients (Bhidayasiri et al., 2019). Recent advances in wearable inertial sensors have revolutionized objective assessment of nocturnal mobility. These devices, incorporating accelerometers and gyroscopes, enable quantitative analysis of movement intensity, frequency, and quality in home environments, providing insights beyond traditional clinical evaluations (Bhidayasiri et al., 2016; Mirelman et al., 2020; Sringean et al., 2016). Previous studies using wearable sensors demonstrated that PD patients exhibit reduced, less intense, and more fragmented nocturnal movements compared to healthy subjects as shown in previous studies (Bhidayasiri et al., 2016; Mirelman et al., 2020; Sringean et al., 2017; Zampogna et al., 2020) and summarized in a recent review by Zampogna et al. (Zampogna et al., 2020). Therapeutic strategies targeting nocturnal hypokinesia focus on achieving stable dopaminergic stimulation throughout the night. Extended-release formulations of levodopa, dopamine agonists such as rotigotina patches, and continuous apomorphine infusions have shown efficacy in improving nocturnal mobility (Bhidayasiri et al., 2016, 2017; Sringean et al., 2024). Recently introduced therapies include opicapone (OPC), a COMT inhibitor with once-daily evening administration that may extend dopaminergic coverage into nighttime hours (Ferreira et al., 2016, 2025; R. A. Hauser et al., 2024), and subcutaneous foslevodopa/foscarbidopa (fLD/fCD), enabling continuous 24-hour levodopa delivery with potential benefits for nocturnal symptoms (R. Hauser et al., 2024; Malaty et al., 2025). Despite the theoretical rationale supporting these treatments' efficacy on nocturnal mobility, specific objective evidence remains limited. This preliminary study aimed to objectively assess nocturnal mobility in complicated PD patients using wearable sensors and evaluate changes following treatment with OPC or subcutaneous fLD/fCD.

Material and Methods

Study design and ethics

This cross-sectional study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Approval was granted by the local Ethical Committee of Sapienza, University of Rome, Italy (0372/2022). Data collection and processing followed the current European regulations for data protection. All participants provided written informed consent before the beginning of measurements. All data were deidentified. Participants did not receive any form of compensation.

Population

Patients were recruited from the Movement Disorders Center of Sant'Andrea University Hospital between November 2024 and May 2025. Inclusion criteria were: idiopathic PD diagnosis according to MDS criteria; Hoehn and Yahr stage 1-3 (Goetz et al., 2004); independent walking ability without aids; willingness to participate; clinical indication for OPC or subcutaneous fLD/fCD initiation. Exclusion criteria included: severe cognitive impairment (MoCA <18) (Baek et al., 2024); orthopedic, rheumatologic, or postural conditions potentially affecting assessment.

Experimental Procedure

Patients underwent comprehensive clinical assessment during routine follow-up visits, including anthropometric and demographic data collection, followed by validated clinical scale administration:

Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III (Goetz et al., 2008); Wearing Off Questionnaire 19 (WOQ19) (Mantese et al., 2020); Parkinson's Disease Sleep Scale version 2 (PDSS2) (Trenkwalder et al., 2011); Epworth Sleepiness Scale (ESS) (Vignatelli et al., 2003); Insomnia Severity Index (ISI) (Castronovo et al., 2016); Nocturnal Hypokinesia Questionnaire (NHQ) (Bhidayasiri et al., 2019).

Subsequently, patients wore the MoveMonitor device (McRoberts, The Hague, Netherlands), a validated triaxial accelerometer (Mazzà et al., 2021; Micó-Amigo et al., 2023) positioned at the lumbar region (L5-S1) using a velcro belt for at least five consecutive days and nights. Participants received instructions to wear the device continuously except during water immersion. The complete assessment was performed one week before treatment modification with OPC or fLD/fCD initiation (T0) and repeated at least 4 weeks after achieving treatment stability (T1) (fig. 12.1).

The following nocturnal mobility parameters were extracted from MoveMonitor reports: times out of bed, percentage time in supine, prone, left, and right lateral positions; frequency, mean velocity, and duration of rotational movements classified as small, medium, large, and extra-large transitions (Mirelman et al., 2020).

Statistical analyses

Because no prior studies had examined the specific aspects explored here, this work was conceived as an exploratory pilot study; consequently, a formal sample-size calculation was not performed. Statistical analyses were carried out with JASP v0.19.3 (JASP Team, University of Amsterdam). Descriptive statistics and frequency tables were generated for all variables. To evaluate the effects of OPC or LD/CD SC treatment between T0 and T1 on nocturnal-mobility parameters and clinical variables, the Wilcoxon signed-rank test

for repeated measures was applied. The type-I error threshold was set at < 0.05 . Data are reported as mean $\pm$ SD (min – max) or median (Q1 – Q3; min – max) for quantitative variables and as N (%) for categorical variables.

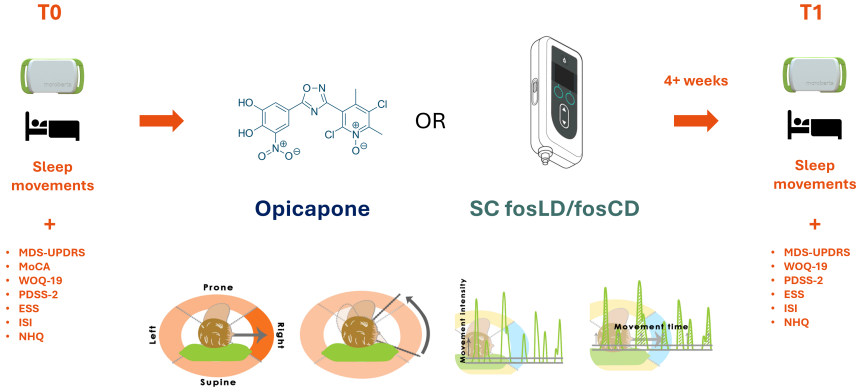


Figure 12.1. Schematic representation of study experimental procedure. ESS: Epworth sleepiness scale; ISI: Insomnia severity index; MDS-UPDRS: Movement Disorder Society unified Parkinson’s disease rating scale; MoCA: Montreal cognitive assessment; NHQ: Nocturnal hypokinesia questionnaire; PDSS-2: Parkinson’s disease sleep scale 2; WOQ-19: Wearing-off questionnaire 19.

Results

Overview

Sixteen PD patients and 11 healthy subjects were enrolled based on inclusion/exclusion criteria. Of 16 patients evaluated at T0 table 12.1, 9 completed T1 assessment. table 12.2 shows baseline clinical characteristics of enrolled PwPD.

For the 9 PD patients completing T1 evaluation (4 OPC; 5 fLD/fCD), Wilcoxon tests showed no statistically significant differences in nocturnal mobility parameters between T0 and T1 (all $p > 0.05$) fig. 12.2. Regarding clinical variables, only PDSS2 showed significant improvement between T0 and T1 ($p = 0.025$) fig. 12.3, with median scores decreasing from 16 to 10. table 12.3 and table 12.4 show nocturnal mobility and clinical variables, respectively, in PwPD at T0 and T1.

Table 12.1. Demographic, anthropometric and basic clinical characteristics of PwPD

PwPD (N=16)	
Age (years)	68.2 (7.4)
Sex (female)	6 (38%)
Height (cm)	173 (11.7)
Weight (kg)	77.2 (14.3)
BMI (kg/m ²)	25.7 (3.2)
Disease duration (years)	7 (5–9.5)
LEDD (mg)	–
mHY	2.5 (2–2.5)
MDS UPDRS III	31 (21–42)
WOQ19	5 (2–6)
PDSS2	16 (11–23)
ESS	5 (4–7)
ISI	8 (4–11)
NHQ	4 (3–5)
MoCA	24 (22–26)

BMI: Body mass index; ESS: Epworth Sleepiness Scale; HC: Healthy controls; ISI: Insomnia Severity Index; LEDD: Levodopa equivalent daily dose; MDS UPDRS III: Movement Disorder Society Unified Parkinson's Disease Rating Scale part III; mHY: modified Hoehn and Yahr scale; MoCA: Montreal Cognitive Assessment; NHQ: Nocturnal Hypokinesia Questionnaire; PDSS2: Parkinson's Disease Sleep Scale 2; PwPD: People with Parkinson's Disease; WOQ19: Wearing-Off Questionnaire 19.

Table 12.2. Baseline nocturnal movement parameters in PwPD. P-values and significance levels of Mann-Whitney test are also shown.

PwPD (N=16)	
Times out of bed (n)	1.69 (0.84)
Left (%)	34.07 (24.64)
Right (%)	28.68 (20.38)
Prone (%)	1.95 (4.57)
Supine (%)	31.30 (19.72)
Small transitions (n)	18.20 (10.32)
Medium transitions (n)	1.26 (3.03)
Large transitions (n)	0.93 (1.46)
ExtraLarge transitions (n)	0.15 (0.20)
Total transitions (n)	30.61 (12.88)
Frequency of transitions (n/h)	4.11 (1.90)
Velocity of transitions (°/s)	6.86 (1.32)
Duration of transitions (s)	6.85 (1.76)

PwPD: People with Parkinson's Disease.

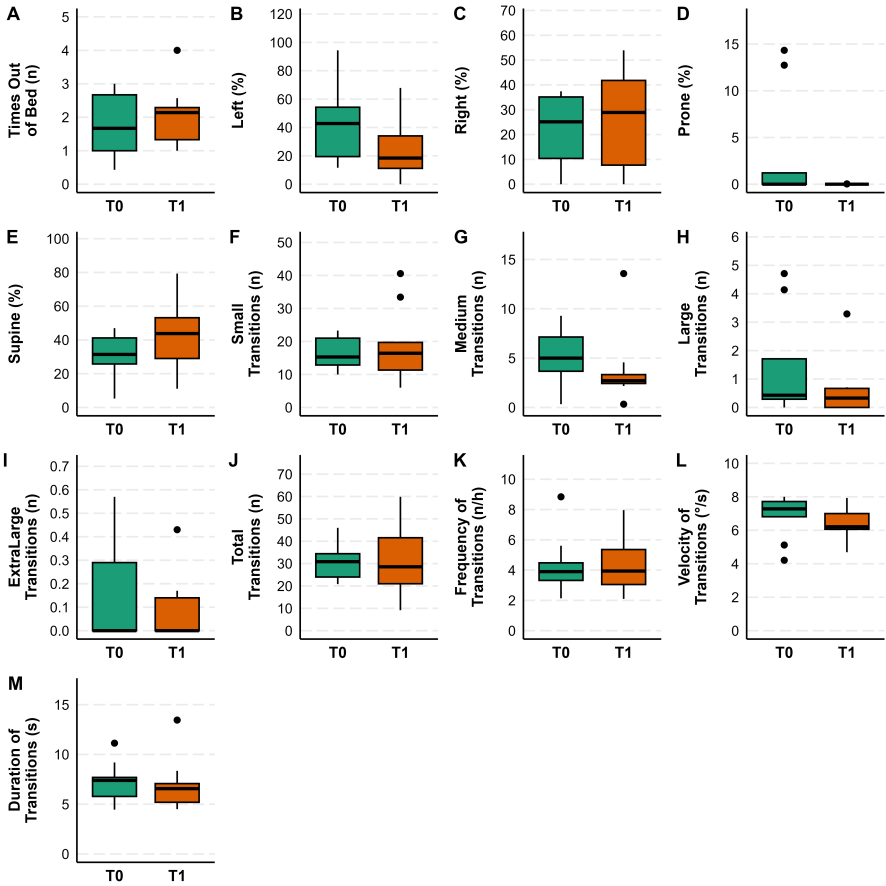


Figure 12.2. Comparisons of nocturnal mobility between T0 and T1 in PwPD. Significance of Wilcoxon test is indicated with horizontal lines and marked with asterisks as follows: * = $P < .05$; ** = $P < .01$; *** = $P < .001$.

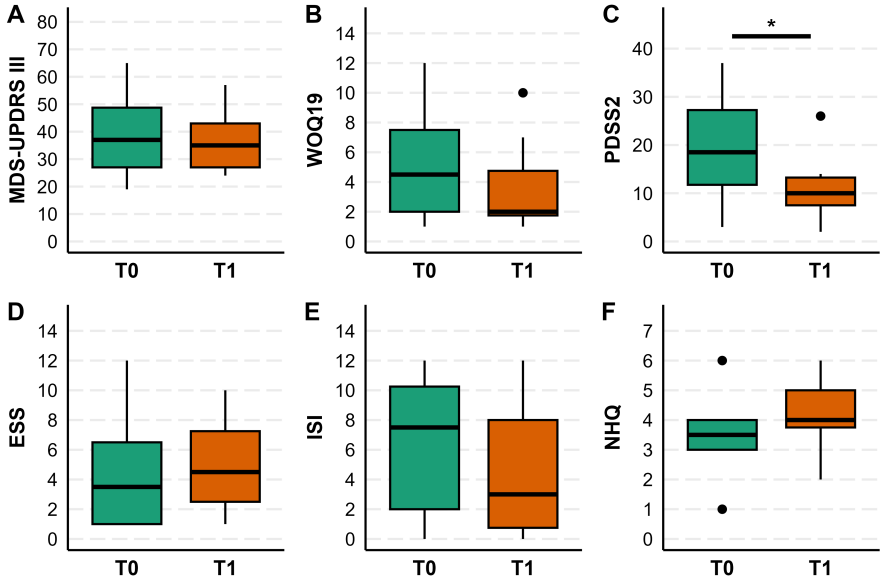


Figure 12.3. Comparisons of clinical variables between T0 and T1 in PwPD. Significance of Wilcoxon test is indicated with horizontal lines and marked with asterisks as follows: * = $P < .05$; ** = $P < .01$; *** = $P < .001$.

Table 12.3. Nocturnal movement parameters at T0 and T1 in PwPD who completed both evaluations (N=9). P-values and significance levels of Wilcoxon test are also shown.

	T0	T1	p-value
Mean movement intensity (g)	0.78 (2.19)	0.04 (0.01)	0.178
Total movement duration (s)	1.45 (0.76)	1.72 (0.73)	0.426
Times out of bed (n)	1.75 (0.96)	2.05 (0.92)	0.910
Left (%)	40.72 (26.58)	24.21 (21.46)	0.203
Right (%)	22.30 (15.16)	25.79 (19.52)	0.426
Prone (%)	3.14 (5.92)	0.01 (0.01)	0.279
Supine (%)	30.97 (13.20)	43.63 (22.16)	0.055
Small transitions (n)	16.81 (4.93)	18.31 (11.52)	0.910
Medium transitions (n)	5.36 (2.95)	3.85 (3.81)	0.359
Large transitions (n)	1.40 (1.80)	0.62 (1.04)	0.359
ExtraLarge transitions (n)	0.16 (0.22)	0.10 (0.14)	0.598
Total transitions (n)	7.51 (4.00)	8.44 (6.13)	0.624
Frequency of transitions (n/h)	31.24 (8.42)	31.33 (16.01)	0.820
Velocity of transitions ($^{\circ}$ /s)	4.22 (2.03)	4.30 (1.88)	0.734
Duration of transitions (s)	6.86 (1.32)	6.33 (0.94)	0.129
Mean movement intensity (g)	7.23 (2.06)	7.05 (2.70)	0.734

Table 12.4. Clinical variables at T0 and T1 in PwPD who completed both evaluations (N=9). P-values and significance levels of Mann-Whitney test are also shown.

	T0	T1	p-value
MDS-UPDRS III	31 (21–42)	35 (27–43)	0.799
WOQ19	5 (2–6)	2 (2–5)	0.139
PDSS2	16 (11–23)	10 (8–13)	0.025*
ESS	5 (4–7)	5 (3–7)	0.932
ISI	8 (4–11)	3 (1–8)	0.073
NHQ	4 (3–5)	4 (4–5)	0.168

ESS: Epworth Sleepiness Scale; ISI: Insomnia Severity Index; MDS-UPDRS III: Movement Disorder Society Unified Parkinson's Disease Rating Scale part III; NHQ: Nocturnal Hypokinesia Questionnaire; PDSS2: Parkinson's Disease Sleep Scale 2; WOQ19: Wearing-Off Questionnaire 19.

Discussion

This was a preliminary study to objectively assess nocturnal mobility in fluctuating PwPD patients using wearable sensors and to evaluate changes following treatment with OPC or subcutaneous fLD/fCD. This is the first study to investigate this topic. We found that: (i) PwPD exhibit significantly reduced nocturnal mobility compared to HS and (ii) nocturnal mobility parameters did not significantly improve after treatment with OPC of fLD/fCD despite a significant improvement in self-reported sleep quality.

In the present paper we found no statistically significant changes in objective nocturnal mobility parameters following OPC or subcutaneous fLD/fCD treatment. This contrasts with previous studies demonstrating efficacy of nocturnal dopaminergic treatments. Bhidayasiri et al. showed improved nocturnal mobility with night-time subcutaneous apomorphine infusion and rotigotine patches (Bhidayasiri et al., 2016, 2017). However, these studies included larger patient cohorts with more severe baseline nocturnal symptoms and different therapeutic interventions. The limited sample size in our study (9 patients completing both assessments) likely represents the primary limitation preventing detection of nocturnal mobility improvements. Additionally, our inclusion criteria may have selected patients with less severe nocturnal symptoms compared to previous studies that specifically required impactful nocturnal hypokinesia to be included. Interestingly, while objective nocturnal mobility parameters remained unchanged, PDSS2 scores significantly improved, indicating better subjective sleep quality. This dissociation between objective mobility measures and subjective sleep quality suggests that sleep improvement mechanisms extend beyond simple nocturnal mobility. The complex spectrum of PD sleep disorders includes insomnia, restless legs syndrome, excessive daytime sleepiness, RBD, and obstructive sleep apnea (Iranzo et al., 2024), many involving non-dopaminergic systems. In previous studies, both clinical and sensor-based measures of sleep improved following the pharmacological treatment with rotigotine (Bhidayasiri et al., 2017) and subcutaneous apomorphine (Bhidayasiri et al., 2016). However, it must be noted that in both paper, the improvement of clinical variables was larger than sensor-based ones. Our findings support the hypothesis that OPC and subcutaneous fLD/fCD improve sleep quality through mechanisms beyond motor symptom control, potentially involving non-motor symptoms improvement and non-motor fluctuations reduction. Although not statistically significanttm likely due to small sample size, the reduction of WOQ-19 scores (motor and non-motor fluctuations) support this hypothesis.

Limitations

This preliminary study has several limitations: small sample size limiting statistical power and generalizability; exclusion of most impaired patients in terms of cognitive and motor symptoms; evaluation of only two therapeutic interventions; and observational design limiting causal inference.

Conclusions

In conclusion, this preliminary study demonstrates significant nocturnal mobility impairment in PwPD and suggests that treatment with OPC or subcutaneous fLD/fCD improves sleep quality through mechanisms potentially independent of nocturnal mobility enhancement. Future studies with larger cohorts may reveal more subtle treatment effects on objective nocturnal mobility parameters. The dissociation between subjective sleep quality improvement and objective mobility measures warrants further investigation to better understand the complex relationship between dopaminergic treatment response and nocturnal symptom management in PD.

References

- Baek, K., Kim, Y. M., Na, H. K., Lee, J., Shin, D. H., Heo, S.-J., Chung, S. J., Kim, K., Lee, P. H., Sohn, Y. H., Yoon, J., & Kim, Y. J. (2024). Comparing Montreal Cognitive Assessment Performance in Parkinson's Disease Patients: Age- and Education-Adjusted Cutoffs vs. Machine Learning. *Journal of Movement Disorders*, 17(2), 171–180. <https://doi.org/10.14802/jmd.23271>
- Bhidayasiri, R., Phokaewvarangkul, O., Sringean, J., Martinez-Martin, P., Anan, C., Kantachavanich, N., Chaudhuri, K. R., & Hattori, N. (2019). Evaluation of nocturnal hypokinesia in Parkinson's disease using a novel patient/proxy questionnaire and correlations with objective monitoring. *Parkinsonism & Related Disorders*, 61, 219–223. <https://doi.org/10.1016/j.parkreldis.2018.09.023>
- Bhidayasiri, R., Sringean, J., Anan, C., Boonpang, K., Thanawattano, C., & Ray Chaudhuri, K. (2016). Quantitative demonstration of the efficacy of night-time apomorphine infusion to treat nocturnal hypokinesia in Parkinson's disease using wearable sensors. *Parkinsonism & Related Disorders*, 33 Suppl 1, S36–S41. <https://doi.org/10.1016/j.parkreldis.2016.11.016>
- Bhidayasiri, R., Sringean, J., Chaiwong, S., Anan, C., Penkeaw, N., Leaknok, A., Boonpang, K., Saksornchai, K., Rattanachaisit, W., Thanawattano, C., & Jagota, P. (2017). Rotigotine for nocturnal hypokinesia in Parkinson's disease: Quantitative analysis of efficacy from a randomized, placebo-controlled trial using an axial inertial sensor. *Parkinsonism & Related Disorders*, 44, 124–128. <https://doi.org/10.1016/j.parkreldis.2017.08.010>
- Bhidayasiri, R., & Trenkwalder, C. (2018). Getting a good night sleep? The importance of recognizing and treating nocturnal hypokinesia in Parkinson's disease. *Parkinsonism & Related Disorders*, 50, 10–18. <https://doi.org/10.1016/j.parkreldis.2018.01.008>
- Castronovo, V., Galbiati, A., Marelli, S., Brombin, C., Cugnata, F., Giarolli, L., Anelli, M. M., Rinaldi, F., & Ferini-Strambi, L. (2016). Validation study of the Italian version of the Insomnia Severity Index (ISI). *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 37(9), 1517–1524. <https://doi.org/10.1007/s10072-016-2620-z>
- Dodet, P., Houot, M., Leu-Semenescu, S., Corvol, J.-C., Lehericy, S., Mangone, G., Vidailhet, M., Roze, E., & Arnulf, I. (2024). Sleep disorders in Parkinson's disease, an early and multiple problem. *NPJ Parkinson's Disease*, 10, 46. <https://doi.org/10.1038/s41531-024-00642-0>
- Ferreira, J. J., Gago, M. F., Costa, R., Fonseca, M. M., Almeida, J., Rocha, J. F., Holenz, J., & Trenkwalder, C. (2025). Opicapone for Parkinson's disease-related sleep disturbances: The OASIS clinical trial. *Jour-*

nal of Parkinson's Disease, 15(1), 87–96. <https://doi.org/10.1177/1877718X241306711>

Ferreira, J. J., Lees, A., Rocha, J.-F., Poewe, W., Rascol, O., Soares-da-Silva, P., & Bi-Park 1 investigators. (2016). Opicapone as an adjunct to levodopa in patients with Parkinson's disease and end-of-dose motor fluctuations: A randomised, double-blind, controlled trial. *The Lancet. Neurology*, 15(2), 154–165. [https://doi.org/10.1016/S1474-4422\(15\)00336-1](https://doi.org/10.1016/S1474-4422(15)00336-1)

Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., Giladi, N., Holloway, R. G., Moore, C. G., Wenning, G. K., Yahr, M. D., Seidl, L., & Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 19(9), 1020–1028. <https://doi.org/10.1002/mds.20213>

Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>

Hauser, R., Bergmans, B., Malaty, I., Cobb, D., Homola, J., Bergmann, L., Gupta, R., Jia, J., Shah, M., & Chaudhuri, K. R. (2024). Effects of Continuous Subcutaneous Infusion of Foslevodopa/Foscarbidopa on Sleep Dysfunction in People With Parkinson's [Publisher: Elsevier]. *Parkinsonism & Related Disorders*, 122. <https://doi.org/10.1016/j.parkreldis.2024.106567>

Hauser, R. A., Videnovic, A., Soares-da-Silva, P., Liang, G. S., Olson, K., Jen, E., Rocha, J.-F., & Klepitskaya, O. (2024). OFF-times before, during, and after nighttime sleep periods in Parkinson's disease pa-

tients with motor fluctuations and the effects of opicapone: A post hoc analysis of diary data from BIPARK-1 and -2. *Parkinsonism & Related Disorders*, 123, 106971. <https://doi.org/10.1016/j.parkreldis.2024.106971>

Iranzo, A., Cochen De Cock, V., Fantini, M. L., Pérez-Carbonell, L., & Trotti, L. M. (2024). Sleep and sleep disorders in people with Parkinson's disease. *The Lancet. Neurology*, 23(9), 925–937. [https://doi.org/10.1016/S1474-4422\(24\)00170-4](https://doi.org/10.1016/S1474-4422(24)00170-4)

Louter, M., Munneke, M., Bloem, B. R., & Overeem, S. (2012). Nocturnal hypokinesia and sleep quality in Parkinson's disease. *Journal of the American Geriatrics Society*, 60(6), 1104–1108. <https://doi.org/10.1111/j.1532-5415.2012.03966.x>

Malaty, I., Vaou, E. O., Hauser, R. A., Bergmans, B., Odin, P., Shah, M., Bergmann, L., Harmer, L., Gupta, R., & Chaudhuri, K. R. (2025). Correlation between sleep and quality of life in people with Parkinson's disease treated with continuous subcutaneous infusion of foslevodopa/foscarbidopa. *Parkinsonism & Related Disorders*, 134, 107599. <https://doi.org/10.1016/j.parkreldis.2025.107599>

Mantese, C. E., Medeiros, M., Schumacher-Schuh, A., & Rieder, C. R. d. M. (2020). Validation of 19-items wearing-off (WOQ-19) questionnaire to Portuguese. *Arquivos De Neuro-Psiquiatria*, 78(10), 624–628. <https://doi.org/10.1590/0004-282X20200045>

Mazzà, C., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Bonci, T., Brown, P., Brozgol, M., Buckley, E., Carsin, A.-E., Caruso, M., Caulfield, B., Cereatti, A., Chiari, L., Chynkiamis, N., Ciravegna, F., Del Din, S., Eskofier, B., Evers, J., ... Rochester, L. (2021). Technical validation of real-world monitoring of gait: A multicentric observational study. *BMJ open*, 11(12), e050785. <https://doi.org/10.1136/bmjopen-2021-050785>

Micó-Amigo, M. E., Bonci, T., Paraschiv-Ionescu, A., Ullrich, M., Kirk, C., Soltani, A., Küderle, A., Gazit, E., Salis, F., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Brown, P., Buckley, E., Cantu, A., Carsin, A.-E., Caruso, M., Caulfield, B., ... Mobilise-D consortium. (2023). Assessing real-world gait with digital technology? Val-

- idation, insights and recommendations from the Mobilise-D consortium. *Journal of Neuroengineering and Rehabilitation*, 20(1), 78. <https://doi.org/10.1186/s12984-023-01198-5>
- Mirelman, A., Hillel, I., Rochester, L., Del Din, S., Bloem, B. R., Avanzino, L., Nieuwboer, A., Maidan, I., Herman, T., Thaler, A., Gurevich, T., Kestenbaum, M., Orr-Urtreger, A., Brys, M., Cedarbaum, J. M., Giladi, N., & Hausdorff, J. M. (2020). Tossing and Turning in Bed: Nocturnal Movements in Parkinson's Disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 35(6), 959–968. <https://doi.org/10.1002/mds.28006>
- Sommerauer, M., Werth, E., Poryazova, R., Gavrilov, Y. V., Hauser, S., & Valko, P. O. (2015). Bound to supine sleep: Parkinson's disease and the impact of nocturnal immobility. *Parkinsonism & Related Disorders*, 21(10), 1269–1272. <https://doi.org/10.1016/j.parkreldis.2015.08.010>
- Sringean, J., Anan, C., & Bhidayasiri, R. (2020). Impaired ability to turn in bed in parkinson's disease as a potential rare cause of positional asphyxia: A sensor-based analysis. *Clinical Neurology and Neurosurgery*, 192, 105713. <https://doi.org/10.1016/j.clineuro.2020.105713>
- Sringean, J., Anan, C., Thanawattano, C., & Bhidayasiri, R. (2017). Time for a strategy in night-time dopaminergic therapy? An objective sensor-based analysis of nocturnal hypokinesia and sleeping positions in Parkinson's disease. *Journal of the Neurological Sciences*, 373, 244–248. <https://doi.org/10.1016/j.jns.2016.12.045>
- Sringean, J., Taechalertpaisarn, P., Thanawattano, C., & Bhidayasiri, R. (2016). How well do Parkinson's disease patients turn in bed? Quantitative analysis of nocturnal hypokinesia using multisite wearable inertial sensors. *Parkinsonism & Related Disorders*, 23, 10–16. <https://doi.org/10.1016/j.parkreldis.2015.11.003>
- Sringean, J., Udomsirithamrong, O., & Bhidayasiri, R. (2024). Too little or too much nocturnal movements in Parkinson's disease: A practical guide to managing the unseen. *Clinical Parkinsonism & Related Disorders*, 10, 100258. <https://doi.org/10.1016/j.prdoa.2024.100258>
- Trenkwalder, C., Kohnen, R., Högl, B., Metta, V., Sixel-Döring, F., Frauscher, B., Hüllsmann, J., Martinez-Martin, P., & Chaudhuri, K. R. (2011). Parkinson's disease sleep scale—validation of the revised version PDSS-2. *Movement Disorders: Official Journal of the Movement Disorder Society*, 26(4), 644–652. <https://doi.org/10.1002/mds.23476>
- Vignatelli, L., Plazzi, G., Barbato, A., Ferini-Strambi, L., Manni, R., Pompei, F., D'Alessandro, R., & GINSEN (Gruppo Italiano Narcolessia Studio Epidemiologico Nazionale. (2003). Italian version of the Epworth sleepiness scale: External validity. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 23(6), 295–300. <https://doi.org/10.1007/s100720300004>
- Zampogna, A., Manoni, A., Asci, F., Liguori, C., Irrera, F., & Suppa, A. (2020). Shedding Light on Nocturnal Movements in Parkinson's Disease: Evidence from Wearable Technologies. *Sensors (Basel, Switzerland)*, 20(18). <https://doi.org/10.3390/s20185171>

Chapter 13

General discussion

This doctoral thesis investigated mobility in PD through an integrative and ecologically oriented framework, conceptualizing mobility as a multidimensional behavior shaped by motor, non motor, and environmental factors. Moving beyond traditional laboratory assessments, mobility was explored as a continuum across supervised and unsupervised setting and extended over the full 24-hour cycle. The work was articulated into three complementary parts:

- The first focused on the metrology of digital mobility measures, validating smartwatch-derived step count as an accurate and reliable outcome in PD, and defining the MCID for AvDS.
- The second examined the determinants of mobility, investigating how supervised (capacity) and unsupervised (performance) mobility interact and are influenced by motor and non-motor symptoms through.
- The third extended the analysis to the 24-hour continuum, exploring nocturnal mobility as an integral component of PD motor dysfunction and its relationship with daytime mobility and dopaminergic treatment.

Together, these studies delineate a coherent progression from technological validation to mechanistic understanding and clinical translation and are discussed in the following sections.

Cohort

Regarding the characteristics of our cohort, these are broadly comparable to those described in recent large studies using wearable sensors in PD (Table 1) (Adams et al., 2023; Mirelman et al., 2024; Oyama et al., 2023; Powers et al., 2021; Rosenfeldt et al., 2024; Schalkamp et al., 2024; Silva de Lima et al., 2017). The sample size, which exceeds one hundred participants, places it among the most numerically robust single-center datasets in this field. The age distribution reflects a typical PD population, largely composed of older adults, while the proportion of male participants aligns with the well-documented sex imbalance of the disease and is consistent with previous cohorts (Adams et al., 2023; Mirelman et al., 2024; Powers et al., 2021; Silva de Lima et al., 2017). Disease severity corresponds to mild-to-moderate stages, as indicated by Hoehn and Yahr classification and motor scores, positioning the cohort close to those investigated in multicenter studies (Adams et al., 2023; Mirelman et al., 2024; Silva de Lima et al., 2017). Indeed, stages above 3 are rarely suitable for wearable-based mobility assessment, as they typically correspond to patients requiring walking aids (stage 4), with consequent alterations in gait pattern and data validity (Kooner et al., 2024), or to individuals in stage 5 who are wheelchair-bound or bedridden, in whom mobility evaluation is not feasible or of limited clinical meaning. In terms of cognitive functions, these were globally preserved, although this result is partly influenced by the inclusion criterion of MoCA ≥ 18 . This clinical profile depicts a population that is both ecologically representative and technically compatible with continuous digital assessment. The balance between sample size, disease stage, and functional integrity ensures comparability with other real-world mobility studies, while providing one of the few comprehensive cohorts integrating both supervised and unsupervised mobility measures, thus offering a valuable bridge between experimental and clinical applications of DMOs collected with both research-grade and commercial wearables in PD.

Table 13.1. Comparisons of the main demographic and clinical features of our cohort with other relevant cohorts in which wearable devices were used to collect data in PD in the last 10 years.

Study	N	Age (years)	Sex (males)	Disease duration (years)	H&Y	MDS-UPDRS-III	MDS-UPDRS	MoCA	Wearable	Setting
Our cohort	121	69.7 ± 9.7	83 (68%)	6.1 ± 4.3	2 (2–2.5)	27 (21–32)	39 (28–49)	26 (25–28)	BTS G-Walk + Garmin Vivosmart 4 + McRoberts MoveMonitor	Supervised + unsupervised (mobility)
Mirelman et al., 2024 (Mirelman et al., 2024)	587	68.0 ± 8.5	356 (61%)	6.4 ± 5.7	I: 85 (15%) II: 342 (59%) III: 155 (26%) IV: 5 (<1%)	26.5 ± 13.0	±	24.4 ± 3.6	Activity AX3/AX6	Unsuper-vised (mobility)
Adams et al., 2023 (Adams et al., 2023)	82	63.3 ± 9.4	46 (56%)	0.8 ± 0.6	I: 19 (23%) II: 62 (76%) III-V: 1 (<1%)	24.1 ± 10.2	± 35.2 ± 12.4	27.6 ± 1.4	APDM + Smartwatch + smart-phone	Supervised + unsupervised (mobility/-motor symp-toms)
Oyama et al., 2023 (Oyama et al., 2023)	96	62.3 ± 8.5	44 (46%)	12.5 ± 5.8	2.8 ± 0.9	46.1 ± 21.4	± 88.9 ± 23.2	–	Verily Study Watch	Supervised + unsuper-vised (motor symptoms)
Powers et al., 2021 (pilot) (Powers et al., 2021)	118	68.1 ± 9.0	82 (69%)	6.5 ± 5.6	–	–	–	–	Apple Watch	Supervised + unsuper-vised (motor symptoms)
Powers et al., 2021 (longitudi-nal) (Powers et al., 2021)	225	71.4 ± 8.9	156 (69%)	10.3 ± 6.5	–	–	–	–	Apple Watch	Unsuper-vised (motor symptoms)
Silva de Lima et al., 2017 (Silva de Lima et al., 2017)	805	<50: 130 (17%) 50–69: 517 (66%) >69: 134 (17%)	454 (56%)	–	I: 308 (43%) II: 261 (36%) III: 132 (18%) IV-V: 19 (3%)	–	52.5 (35–69)	–	Smartwatch + smart-phone	Unsuper-vised (motor symptoms)
Schalkamp et al., 2024 (Schalkamp et al., 2024)	149	67.7 ± 7.5	–	6.8 ± 2.1	–	–	–	–	Verily Study Watch (PPMI cohort)	Unsuper-vised (mobility)
Rosenfeldt et al., 2025 (Rosenfeldt et al., 2024)	119	65 ± 8	79 (66%)	4.9 ± 4.2	I: 16 (14%) II: 80 (67%) III: 23 (19%);	28 ± 13	–	–	Garmin VivoFit 4 (ankle)	Unsuper-vised (mobility)

H&Y: Hoehn and Yahr stage; MDS-UPDRS: Movement Disorder Society-Unified Parkinson's Disease Rating Scale; MoCA: Montreal Cognitive Assessment; PPMI: Parkinson's Progression Markers Initiative.

Metrology of digital mobility outcomes in Parkinson's disease: building a bridge between numbers and patients

Key Messages

- Validation of smartwatch-based metrics, including **accuracy**, **reliability** and **clinical meaningfulness**, lays the foundation for their use as **digital mobility outcomes** both in clinical trials and real-world monitoring.
- Consumer-grade smartwatches can provide **valid**, **reliable**, and **clinically interpretable** estimates of **daily steps** in people with PD.
- Further steps toward **harmonization**, **integration** with clinical endpoints, and **validation** across phenotypes, disease stages, and ecological contexts are essential to bridge the gap between digital numbers and patient-centered outcomes.

The progressive diffusion of wearable sensors has transformed how mobility can be quantified in people with PD (Giansanti et al., 2008; Kirk et al., 2025; Maetzler et al., 2013, 2021; Moreau et al., 2023). Kirk et al. (Kirk et al., 2025) systematically reviewed real-world studies on gait-related DMOs, demonstrating that wearable devices can accurately capture parameters such as walking speed, stride length, and variability in daily life, thereby distinguishing PD from controls and supervised from unsupervised conditions. However, they emphasized the wide methodological heterogeneity across studies, from sensor placement to data aggregation, and the need for harmonized protocols to improve comparability and clinical use. Therefore, translating raw sensor data into clinically meaningful and actionable indicators requires a rigorous metrological validation comparable to that applied to conventional clinical instruments (Mokkink et al., 2010). This was done previously using different commercial wearables with general positive results as indicated by recent systematic reviews on the topic (Feehan et al., 2018; Fuller et al., 2020). Earlier, Godinho et al. (Godinho et al., 2016) had already classified more than seventy monitoring technologies for PD according to their clinimetric robustness, identifying a small subset of wearable systems, such as APDM Mobility Lab, Physilog®, StepWatch, and DynaPort, as “recommended” based on evidence of reliability, validity, and sensitivity to change, thereby laying the groundwork for subsequent validation efforts. Accordingly, the four studies included in this section collectively outlined such a pathway, moving from the analytical accuracy of step detection in supervised settings to the reliability of daily monitoring in real-world conditions and, ultimately, to the clinical interpretability of measurable change. This evolution reflects a broader paradigm shift in digital health, with the ultimate goal of bridging the gap between digital metrics and clinically relevant endpoints for people with neurological disorders (Espay et al., 2019).

The first step in this process was to establish the conditions under which consumer devices can accurately measure walking activity in PD. Wrist-worn consumer-grade devices, while accessible and user-friendly, are not designed for specific disease populations and are particularly sensitive to PD-related motor alterations such as tremor, bradykinesia, movement fragmentation, and asymmetry (Kim et al., 2019; Wendel et al., 2018). Nonetheless, the wrist remains a common and practical location (Sun et al., 2025) for long-term monitoring due to its comfort and low intrusiveness (Taylor et al., 2025). Moreover, the widespread availability of commercial smartwatches facilitates large-scale data collection and real-world deployment, making this position a pragmatic compromise between ecological validity and

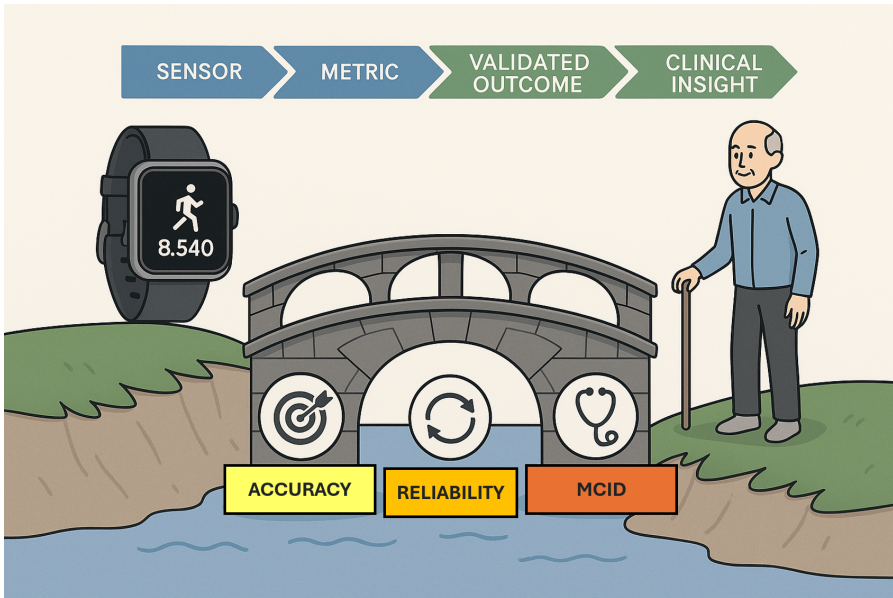


Figure 13.1. Metrological pillars supporting the translation from wearable-derived metrics to clinically interpretable outcomes.

signal specificity. Our work demonstrated that, in PwPD, accuracy depends on both pharmacological state and wearing side, highlighting how disease expression interacts with device algorithms. These findings reinforce a key principle of digital metrology: validity is context-dependent, and measures must be verified within the populations and conditions in which they are intended to be used as indicated by the V3 framework (Goldsack et al., 2020) which delineates a structured pathway for digital endpoint development through Verification (device performance under controlled conditions), Analytical Validation (algorithmic accuracy), and Clinical Validation (association with meaningful clinical outcomes). However, accuracy alone does not ensure clinical usability (Mokkink et al., 2010). The subsequent studies extended the validation to reliability, emphasizing measurement stability across multiple days and patient subgroups. We demonstrated that average daily steps (AvDS) are globally reliable in PwPD, including across phenotypes and disease severities. This is particularly relevant in PD, where intraday and interday fluctuations in mobility reflect both disease-specific variability and environmental influences that is known to modulate real-world mobility (Ryder-Burbidge et al., 2022). Nonetheless, reliability appeared slightly reduced in individuals with tremor and in less advanced disease stages, confirming the dynamic interaction between PD symptoms and device's performance. Such information is essential for researchers and clinicians, allowing an informed and critical use of these metrics in clinical and research contexts. The finding that reliable estimates can be achieved within four consecutive monitoring days represents a concrete step toward making digital mobility assessment both scientifically sound and feasible in everyday settings. Reliability allows repeated measurements to be trusted, but not necessarily to be understood. The next metrological milestone is interpretability: defining how much change represents a meaningful difference for clinicians and, more importantly, for patients. In this regard,

we strongly believe that identifying and reporting the MCID (Bloom et al., 2023) of AvDS represents a key advancement. By anchoring step-count changes to both objective clinical scales and patient-reported outcomes, the measure acquires interpretive value beyond statistical variability. This approach (Motl et al., 2013) acknowledges that meaningful change may differ depending on whether it is viewed through the lens of motor performance, global health, or subjective perception, and provides a flexible framework adaptable to different clinical endpoints. Importantly, the convergence between MCID estimates and the MDC that we reported in our reliability studies supports internal consistency within the measurement framework. The resulting range, spanning approximately 10% to 25% of AvDS, offers a solid benchmark for interpreting longitudinal data and for designing clinical trials that use digital mobility outcomes as endpoints. This transition transforms smartwatch-derived AvDS from a descriptive metric confined to exploratory research into a quantitative, clinically interpretable indicator, supporting its potential qualification as a digital biomarker. Beyond the specific findings, these studies illustrate how consumer-grade devices can gain scientific and clinical credibility when subjected to a structured validation process. This progression mirrors the conceptual framework proposed for clinical endpoint development, addressing successive layers of measurement uncertainty and aligning with international standards such as the COSMIN validation framework (Mokkink et al., 2010). In this context, accuracy ensures that the device measures what it is intended to measure, reliability guarantees consistency over time and across conditions, and the MCID connects quantitative measurement to clinical meaning (Mokkink et al., 2010). This framework also reflects a methodological approach that places patients at the center of digital measurement. By enabling continuous, real-world monitoring, wearable-based assessments can enhance patients' awareness of their own condition, promote engagement in self-management, and a sense of empowerment in the care process (Hansen et al., 2018; Ma et al., 2025). Nevertheless, without clinical interpretability, such data remain disconnected from clinical decision-making. By defining reliability and clinically meaningful thresholds, these studies allow the translation of raw, real-world data into patient-relevant insights. This is particularly pertinent for PD, a condition characterized by fluctuating symptoms (Poewe et al., 2017), where traditional clinic-based assessments often fail to capture real-world functioning. Limitations and open challenges

Limitations and open challenges

Despite substantial progress, several limitations remain. Indeed, the studies focused on individuals with mild-to-moderate PD, limiting generalizability to advanced stages or to patients with cognitive impairment, who may show lower adherence and altered movement patterns. Tremor interference remains an intrinsic limitation of wrist-worn sensors, requiring algorithmic refinements or multimodal sensor fusion to differentiate physiological motion from artifacts when higher metrological validity is required (Kim et al., 2019). Furthermore, the cross-sectional design of most analyses precludes the evaluation of longitudinal responsiveness and long-term stability. Establishing whether observed changes in daily steps correspond to therapeutic effects or disease progression will require prospective validation. Another major limitation concerns the “black-box” nature of commercial algorithms. While leveraging consumer devices enhances scalability, it also restricts transparency and reproducibility. We strongly believe that open data pipelines, shared calibration standards, and algorithmic documentation are crucial to ensure interoperability and regulatory acceptance. This challenge is exacerbated by the rapid turnover of the consumer electronics market, where frequent hardware updates and discontinuation of models may hinder longitudinal comparability. Finally, step count, although intuitive, explainable and useful, captures only one dimension of mobility. Future research should aim to integrate complementary metrics such as spatiotemporal parameters (Kirk et al., 2025), turning dynamics (Mancini et al., 2015), postural transitions (Romijnders et al., 2025) and sleep-related mobility (Zampogna et al., 2020) to obtain the entire “movie” of individuals' mobility rather than just a snapshot.

From metrology to clinical translation

The metrological validation of smartwatch-derived mobility measures provided the methodological groundwork for translating digital data into clinical understanding. Demonstrating accuracy, reliability, and clinical interpretability was essential to ensure that these metrics genuinely reflect patients' real-world mobility rather than technological artifacts. This process transformed consumer devices into clinically sound instruments, establishing the conditions under which digital mobility outcomes can serve as robust indicators of functional health in PD. On this foundation, the next phase of research moved from how mobility can be measured to what mobility reveals about PD. The validated DMOs enabled the exploration of how motor and non-motor symptoms jointly determine movement, and to what extent and how the gap between supervised capacity and real-world performance reflects the functional impact of PD in daily life. This transition from metrology to clinical translation sets the stage for the following section, dedicated to disentangling the complex relationship between mobility patterns and the symptom architecture of PD.

Disentangling the connection between mobility and Parkinson's disease symptoms

Key Messages

- **Capacity-based** metrics explained only a **modest** component of **performance-based** ones, highlighting how these measures capture **complementary but distinct** dimensions of movement in Parkinson's disease.
- **Motor predictors** mainly influence **supervised mobility**, with a stronger impact on **complex tasks** such as turning and backward walking. Phenotypic differences emerge, with **TD and PIGD** profiles associated with **capacity** and **AR** with **performance**.
- Among NMS, **executive functions** and, to a lesser extent, **fatigue** are the most relevant contributors to mobility. **Depression and sleep disturbances** influenced mobility but only when motor symptoms are not considered, suggesting an **indirect effect**.

Our research demonstrated that supervised mobility measures explained only one quarter of variability in AvDS. These findings confirm and expand previous evidence for a structural gap between laboratory and real-world mobility in PD (Atrsaei et al., 2021; Corrà et al., 2021; Del Din et al., 2016; Toosizadeh et al., 2015; Zajac et al., 2022), even when multiple tasks covering forward, backward, and turning components are included, and are further reinforced by a recent systematic review by Kirk et al. (Kirk et al., 2025). This review comprehensively examined studies comparing DMOs collected in supervised versus real-world conditions, revealing that gait parameters are consistently and significantly lower when assessed in daily-life environments. Across the included studies, people with PD showed slower walking speeds, shorter step and stride lengths, and greater variability during free-living walking compared to structured clinical assessments. These discrepancies were interpreted as reflecting contextual and behavioral influences that are minimized or absent in laboratory conditions (Kirk et al., 2025). The authors concluded that the ecological context profoundly shapes gait behavior and that real-world monitoring provides unique insights into functional mobility and daily-life limitations that cannot be inferred from supervised tests alone (Kirk et al., 2025). This confirms that supervised mobility represents a necessary but not sufficient condition for daily walking performance, echoing the distinction between capacity and performance defined by the ICF framework (Organization, 2002). A large proportion of variability in AvDS remains unexplained by capacity-related parameters, suggesting the contribution of behavioral, contextual, and symptomatic factors beyond physical ability alone (Giannouli et al., 2016; Mate & Mayo, 2020; Roussos et al., 2022). The additional two studies analyzed combined motor and non-motor predictors and revealed that motor variables contribute more strongly to supervised than to unsupervised mobility. Complex tasks, especially backward walking and turning, were the most sensitive to motor symptom severity, consistent with their higher cognitive, postural, and planning demands (Correno et al., 2022; Hackney & Earhart, 2009; Hulbert et al., 2015). Motor phenotype also modulated results. Indeed, TD and PIGD subtypes were associated with supervised mobility metrics, whereas the AR phenotype was linked to lower AvDS. This pattern highlights that gait components requiring anticipatory postural adjustments and axial control are particularly vulnerable to PD-related motor impairment. Their impact is most evident under standardized testing, where external cues and motivation are maxi-

mized. In contrast, the translation of these deficits into real-world activity appears partly mediated by other personal and contextual factors. Overall, the data indicate that motor determinants define the potential limit of achievable capacity, whereas the degree to which this capacity is expressed in daily life mainly depends on additional modulating domains. Our research confirmed the role of executive functions as consistent predictors of supervised mobility in PD (Amboni et al., 2018; Nóbrega-Sousa et al., 2020; Yogev-Seligmann et al., 2008). In particular, executive control is more relevant when tasks require planning and adaptation, conditions typical of standardized supervised tasks, while its influence on spontaneous walking behavior could be comparatively weaker. Indeed, when considering clinical and demographic variables such as age, disease duration, and LEDD, cognitive predictors lost statistical significance, indicating that their contribution is not independent from global disease burden and several other factors come into play in shaping mobility in PD (Roussos et al., 2022). However, it must be noted that executive functions were confirmed to be the most influential NMS and represented the only one that retained its role as a significant predictor of both supervised and unsupervised mobility even when considering other motor and non-motor determinants. In addition to executive functions, fatigue emerged as an additional predictor for supervised outcomes, consistent with previous evidence (Carvalho et al., 2020; Pilotto et al., 2023), whereas depression and sleep disturbances appeared only in NMS-only models, suggesting indirect or context-dependent effects. Together, these results delineate a selective non-motor signature of mobility in PD. Executive dysfunction and fatigue predominantly affect controlled, laboratory-based mobility tasks, whereas their translation into everyday performance is modulated by broader clinical and contextual factors. The three studies provide a coherent interpretation of mobility in PD. From a clinical perspective, our results suggest that in mild-to-moderate PD, mobility evaluation should incorporate both metrics of supervised and unsupervised mobility to capture a comprehensive snapshot of patients' conditions. Furthermore, these findings urge the need to include both capacity- and performance-related outcomes in research and clinical trials. In fact, improvement in performance is the aim in the management of PD, and an improvement in supervised mobility metrics could reflect only to a limited degree an actual improvement in patients' real-world experience (Lang et al., 2023). Additionally, our results support a multidimensional assessment of PwPD. Indeed, mobility emerged as a multidimensional construct influenced not only by motor impairments, but also by the burden of non-motor symptoms. For instance, executive dysfunction can impair planning and adaptation of gait to environmental demands (Yogev-Seligmann et al., 2008), fatigue may reduce overall walking activity (Pilotto et al., 2023), and depressive symptoms can diminish motivation and engagement in daily activities (Zhang et al., 2022), all ultimately leading to reduced real-world mobility. Importantly, the differential impact of these symptoms across mobility domains suggests that no single measure can accurately capture mobility limitations in PD. This integrated approach can inform individualized rehabilitation strategies, combining motor-oriented interventions targeting gait and balance as well as cognitive or fatigue-management components when indicated by patient profiles.

Limitations and perspectives

Methodologically, all three studies share limitations. Their cross-sectional design precludes causal inference and prevents the identification of temporal dynamics linking symptom progression and mobility decline. Samples mainly included mild-to-moderate PD, reducing generalizability to advanced stages. Furthermore, step count remains a unidimensional index of performance, while supervised tasks, though diversified, cannot capture all facets of mobility. Longitudinal and multimodal designs integrating contextual variables, qualitative real-world gait metrics, and patient-reported outcomes are needed to clarify how capacity translates into performance over time. Given the clinical and prognostic relevance of falls in PD (Fasano et al., 2017), future studies should also focus on the detection (Silva de Lima et al., 2020) and characterization of fall events and near-falls (Huang et al., 2023), integrating them into digital mobility frameworks to better capture real-world risk and its relationship with motor and non-motor fluctuations.

Integrating diurnal and nocturnal mobility

Together, these results underscore the need to interpret mobility as a continuous process that extends beyond daytime activity. The interplay between capacity, performance, and their motor and non-motor determinants reflects only one side of the 24-hour spectrum. The upcoming section will expand this perspective to the night, exploring how motor limitations persist during sleep and how nocturnal hypomobility interacts with daytime mobility and dopaminergic treatment. Understanding mobility as a continuous phenomenon will complete the picture of movement behavior in PD, bridging daytime and nocturnal domains and further advancing the ecological and patient-centered approach that underpins this doctoral work.

Shedding a light on nocturnal mobility

Key Messages

- **Nocturnal mobility impairment** is a common occurrence in PwPD with high impact on **quality of life** and **sleep quality**. Monitoring night-time mobility can provide unique insight into the persistence of motor limitations across sleep–wake cycles.
- **Nocturnal hypokinesia** reflects diurnal mobility impairment and overall functional independence supporting the hypothesis that mobility alterations in PD extend across the **entire 24-hour cycle**.
- **Subjective sleep disturbances** may **improve** with dopaminergic treatment even when **objective nocturnal mobility** parameters remain **unchanged**.

Mobility in PD extends beyond daytime walking and postural control, encompassing a wide range of motor and non-motor phenomena that persist throughout the 24-hour cycle (Dodet et al., 2024; Iranzo et al., 2024). Nocturnal hypokinesia (NH), the reduction of movement during sleep and nighttime wakefulness, represents a particularly disabling yet often overlooked manifestation of PD (Bhidayasiri & Trenkwalder, 2018; Mirelman et al., 2020; Sringean et al., 2024). Building on the conceptual framework established in the previous sections, the studies included in this last part aimed to explore nocturnal mobility as an integral component of the mobility continuum, linking night-time motor behaviour with daytime function (Yoneyama et al., 2013) and assessing its response to dopaminergic therapy (fig. 13.2).

The first study compared clinical variables as well as supervised and unsupervised mobility parameters between PwPD with and without NH. The results revealed an association between impaired nocturnal mobility and reduced daytime capacity and performance. In particular, participants who displayed worse NH also walked fewer steps per day and performed worse in turning, forward and backward walking tasks. This finding supports the notion that nocturnal mobility reflects a global motor impairment rather than an isolated nocturnal symptom, bridging day and night as parts of a continuous motor spectrum (Mirelman et al., 2020; Sringean et al., 2017). Moreover, NH was more pronounced in patients with higher disease stage, longer disease duration, and more severe axial symptoms. These relationships are consistent with earlier reports describing how rigidity and bradykinesia during the night are driven by dopaminergic wearing-off and axial involvement (Bhidayasiri, Sringean, & Thanawattano, 2017; Mirelman et al., 2020; Taniguchi et al., 2022). The second study explored the effects of dopaminergic therapy on nocturnal mobility and sleep quality in a subgroup of patients starting either Opicapone or subcutaneous foslevodopa/foscarbidopa (fLD/fCD), two treatments with a favorable profile in improving nighttime symptoms (Chaudhuri et al., 2024; Ferreira et al., 2025; R. Hauser et al., 2024; R. A. Hauser et al., 2024). The introduction of treatment improved subjective sleep quality as measured by the PDSS-2 but did not significantly change objective nocturnal mobility metrics over the observational period. These findings suggest that sleep improvement mechanisms following dopaminergic treatment extend beyond nocturnal mobility. Indeed, the complex spectrum of PD sleep disorders includes insomnia, restless legs syndrome, excessive daytime sleepiness, RBD, and obstructive sleep apnea, many involving non-dopaminergic systems (Dodet et al., 2024; Iranzo et al., 2024). Nevertheless, previous studies demonstrated the effectiveness

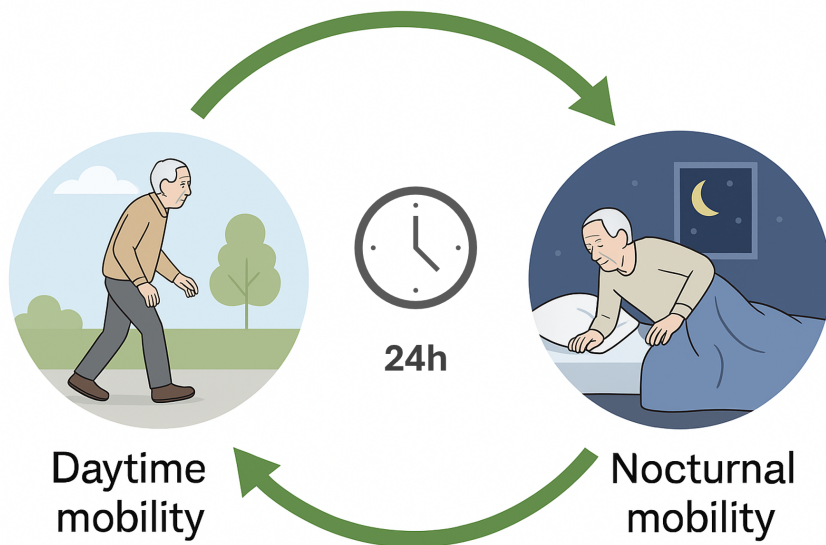


Figure 13.2. The proposed framework considers mobility as a 24h continuum with a bidirectional interaction between diurnal and nocturnal mobility.

of nocturnal dopaminergic stimulation in improving NH in PwPD (Bhidayasiri, Sringean, Chaiwong, et al., 2017; Bhidayasiri et al., 2016), therefore more studies are needed to confirm and expand the preliminary findings from our study. From a clinical perspective, these findings highlight the need to systematically consider night-time mobility when evaluating functional status in PD. Quantifying nocturnal movements provides a window into aspects of the disease that are poorly captured by traditional assessments but highly relevant to quality of life (Choi et al., 2021). Difficulties turning in bed or rising from a supine position not only disturb sleep but also contribute to morning akinesia, pain, and increased fall risk during nocturnal awakenings (Bhidayasiri & Trenkwalder, 2018). Continuous objective monitoring of nocturnal mobility could therefore support a more complete evaluation of disease burden and treatment response. Furthermore, nocturnal mobility metrics could serve as complementary digital endpoints in clinical trials. Their integration with diurnal mobility data allows for the assessment of treatment efficacy across the full circadian cycle, particularly for therapies with extended-release or continuous dopaminergic delivery systems. In the context of personalized care, detecting worsening nocturnal mobility might inform medication timing or prompt the use of nighttime dopaminergic supplementation. Collectively, results obtained in the two studies demonstrate that nocturnal mobility is a clinically relevant and quantifiable marker reflecting the persistence of motor impairment across the 24-hour cycle. Its association with daytime mobility reinforces the concept of PD as a continuously fluctuating disorder in which motor limitations are not confined to wakefulness but permeate rest periods as well. Furthermore, additional studies are needed to better understand the complex relationship between dopaminergic treatment response

and nocturnal symptom management in PD.

Limitations and future directions Both studies share limitations. Sample sizes were modest, and observation periods were short, restricting the power to detect subtle changes in nocturnal metrics and limiting longitudinal inference. The absence of healthy control groups precluded comparison with normative night-time movement patterns. Moreover, while IMU-based measures provide a proxy of nocturnal movement quantity, they cannot differentiate between voluntary movement, tremor-related motion, or sleep-stage-specific motor phenomena such as RBD. Combining inertial data with polysomnographic or electromyographic recordings in future work would allow a more granular understanding of nocturnal motor activity. Future studies should aim to validate nocturnal mobility metrics as standardized digital endpoints, defining their clinimetric properties, minimal detectable change, and relationship with patient-reported outcomes. Integrating day–night mobility profiles into multimodal frameworks combining wearables, sleep questionnaires, and chronobiological markers could clarify the interaction between motor, circadian, and sleep-related mechanisms in PD. These developments will be included in the continuation of this work, following the same methodological framework and analytical pipeline validated in Part 1 and Part 2 of this thesis.

Conclusion Nocturnal mobility embodies the final piece of the 24-hour mobility continuum in PD. The persistence of hypokinesia during sleep reflects the continuity of motor dysfunction across behavioural states and its partial independence from subjective sleep quality or dopaminergic modulation. By quantifying movements that occur at night, objective nocturnal monitoring enriches our understanding of how PD affects daily life beyond waking hours. This approach not only complements the assessment of diurnal capacity and performance, but also closes the conceptual circle of this thesis, paving the way toward an integrated, round-the-clock model of mobility that truly reflects the lived experience of people with PD.

Chapter 14

Conclusions

This doctoral thesis advanced a comprehensive understanding of mobility in PD (PD) through an integrative and ecologically grounded framework. By combining wearable-based metrics, clinical assessments, and symptom characterization, the work conceptualized mobility as a multidimensional behaviour shaped by the continuous interaction of motor, non-motor, and environmental factors. Together, the three sections of the thesis traced a coherent trajectory, from measurement validation to mechanistic interpretation and clinical translation, and finally to the 24-hour representation of movement in PD.

The first section established the metrological foundation for digital daily mobility assessment. Consumer-grade smartwatches were shown to provide accurate and reliable estimates of step count in mild-to-moderate PD when validated under disease-specific conditions. By defining the MCID for average daily steps, the work transformed raw step data into clinically interpretable outcomes, enabling their use as standardized digital mobility endpoints. These studies demonstrated that digital measures can achieve the same level of methodological rigour as traditional clinical instruments, provided that their accuracy, reliability, and interpretability are systematically established.

The second section expanded the focus from how mobility is measured to why mobility is altered. By examining the relationship between supervised and real-world mobility, it revealed that capacity and performance represent related, but distinct, domains, with in-clinic measures explaining only a fraction of daily walking activity as already reported in other populations. This finding underscores the limitations of relying exclusively on laboratory testing and highlights the role of behavioural, motivational, and environmental factors in shaping real-world function. Multivariate analyses further demonstrated that while motor symptoms largely determine mobility capacity, non-motor symptoms, especially executive dysfunction and fatigue, play a major role in translating capacity into performance. These insights advocate for multidomain assessment strategies and for therapeutic approaches targeting both motor and cognitive-affective determinants of mobility.

The third section extended the analysis beyond the waking day, revealing that mobility impairment persists during sleep as nocturnal hypomobility. Nocturnal movement metrics correlated with daytime mobility and disease severity, confirming that PD-related motor dysfunction spans the entire 24-hour cycle. Importantly, dopaminergic therapy improved subjective sleep quality without significantly changing objective nocturnal mobility, suggesting that more complex, non-dopaminergic mechanisms contribute to nighttime symptoms. Together, these findings emphasize the need for continuous, ecologically valid monitoring that captures fluctuations across the entire day.

Ultimately, this doctoral thesis illustrates how digital technology can bridge the gap between DMOs and the lived experience of patients. By validating wearable-derived

metrics, identifying multidimensional determinants, and extending analysis to the nocturnal domain, it contributes to redefining mobility as a dynamic indicator of health, function, and quality of life. The integration of wearables-based continuous measures with clinical and patient-reported data fosters a truly patient-centred understanding of PD. Clinically, it supports a shift from snapshots to movie, offering new tools for individualized treatment optimization and remote care. Finally, it lays the foundation for future research linking digital biomarkers with disease mechanisms, predicting clinical trajectories, and personalizing interventions, moving from measuring movement to understanding the moving individual.

Bibliography

Aarsland, D., Batzu, L., Halliday, G. M., Geurtsen, G. J., Ballard, C., Ray Chaudhuri, K., & Weintraub, D. (2021). Parkinson disease-associated cognitive impairment. *Nature Reviews. Disease Primers*, 7(1), 47. <https://doi.org/10.1038/s41572-021-00280-3>

Abbruzzese, G., Antonini, A., Barone, P., Stocchi, F., Tamburini, T., Bernardi, L., Amboni, M., Vacca, L., Posocco, V., & Colombo, D. (2012). Linguistic, psychometric validation and diagnostic ability assessment of an Italian version of a 19-item wearing-off questionnaire for wearing-off detection in Parkinson's disease. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 33(6), 1319–1327. <https://doi.org/10.1007/s10072-012-0943-y>

Adams, C., Suescun, J., Haque, A., Block, K., Chandra, S., Ellmore, T. M., & Schiess, M. C. (2023). Updated Parkinson's disease motor subtypes classification and correlation to cerebrospinal homovanillic acid and 5-hydroxyindoleacetic acid levels. *Clinical Parkinsonism & Related Disorders*, 8, 100187. <https://doi.org/10.1016/j.prdoa.2023.100187>

Adams, J. L., Kangarloo, T., Gong, Y., Khachadourian, V., Tracey, B., Volfson, D., Latzman, R. D., Cosman, J., Edgerton, J., Anderson, D., Best, A., Kostrzebski, M. A., Auinger, P., Wilmot, P., Pohlson, Y., Jensen-Roberts, S., Müller, M. L. T. M., Stephenson, D., Dorsey, E. R., & Parkinson Study Group Watch-PD Study Investigators and Collaborators. (2024). Using a smartwatch and smartphone to assess early Parkinson's disease in the WATCH-PD study over 12 months. *NPJ Parkinson's disease*, 10(1), 112. <https://doi.org/10.1038/s41531-024-00721-2>

Adams, J. L., Kangarloo, T., Tracey, B., O'Donnell, P., Volfson, D., Latzman, R. D., Zach, N., Alexander, R., Bergethon, P., Cosman, J., Anderson, D., Best, A., Severson, J., Kostrzebski, M. A., Auinger, P., Wilmot, P., Pohlson, Y., Waddell, E., Jensen-Roberts, S., ... Parkinson Study Group Watch-PD Study Investigators and Collaborators. (2023). Using a smartwatch

and smartphone to assess early Parkinson's disease in the WATCH-PD study. *NPJ Parkinson's disease*, 9(1), 64. <https://doi.org/10.1038/s41531-023-00497-x>

Adler, C. H., Beach, T. G., Zhang, N., Shill, H. A., Driver-Dunckley, E., Mehta, S. H., Atri, A., Caviness, J. N., Serrano, G., Shprecher, D. R., Sue, L. I., & Belden, C. M. (2021). Clinical Diagnostic Accuracy of Early/Advanced Parkinson Disease: An Updated Clinicopathologic Study. *Neurology. Clinical Practice*, 11(4), e414–e421. <https://doi.org/10.1212/CPJ.0000000000001016>

Akoglu, H. (2018). User's guide to correlation coefficients. *Turkish Journal of Emergency Medicine*, 18(3), 91–93. <https://doi.org/10.1016/j.tjem.2018.08.001>

Aleksovski, D., Miljkovic, D., Bravi, D., & Antonini, A. (2018). Disease progression in Parkinson subtypes: The PPMI dataset. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 39(11), 1971–1976. <https://doi.org/10.1007/s10072-018-3522-z>

Alix-Fages, C., Jiménez-Martínez, P., de Oliveira, D. S., Möck, S., Balsalobre-Fernández, C., & Del Vecchio, A. (2023). Mental fatigue impairs physical performance but not the neural drive to the muscle: A preliminary analysis. *European Journal of Applied Physiology*, 123(8), 1671–1684. <https://doi.org/10.1007/s00421-023-05189-1>

Allali, G., Verghese, J., & Mahoney, J. R. (2014). Contributions of mild parkinsonian signs to gait performance in the elderly. *Age (Dordrecht, Netherlands)*, 36(4), 9678. <https://doi.org/10.1007/s11357-014-9678-4>

Almeida, G. J. M., Wasko, M. C. M., Jeong, K., Moore, C. G., & Piva, S. R. (2011). Physical activity measured by the SenseWear Armband in women with rheumatoid arthritis. *Physical Therapy*, 91(9), 1367–1376. <https://doi.org/10.2522/ptj.20100291>

Alves, G., Larsen, J. P., Emre, M., Wentzel-Larsen, T., & Aarsland, D. (2006). Changes in motor subtype and risk for incident dementia in Parkinson's disease. *Movement Disorders: Official Journal of the Movement*

- Disorder Society*, 21(8), 1123–1130. <https://doi.org/10.1002/mds.20897>
- Amara, A. W., Chahine, L. M., & Videnovic, A. (2017). Treatment of Sleep Dysfunction in Parkinson's Disease. *Current Treatment Options in Neurology*, 19(7), 26. <https://doi.org/10.1007/s11940-017-0461-6>
- Amboni, M., Barone, P., & Hausdorff, J. M. (2013). Cognitive contributions to gait and falls: Evidence and implications. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(11), 1520–1533. <https://doi.org/10.1002/mds.25674>
- Amboni, M., Ippariello, L., Iavarone, A., Fasano, A., Palladino, R., Rucco, R., Picillo, M., Lista, I., Varriale, P., Vitale, C., Cesarelli, M., Sorrentino, G., & Barone, P. (2018). Step length predicts executive dysfunction in Parkinson's disease: A 3-year prospective study. *Journal of Neurology*, 265(10), 2211–2220. <https://doi.org/10.1007/s00415-018-8973-x>
- Andrić, R. B., Papić, E., & Vuletić, V. (2025). Comparison of the effects of levodopa/carbidopa and foslevodopa/foscarbidopa pump on the quality of life and sleep in Parkinson's disease patients. *Parkinsonism & Related Disorders*, 134, 107619. <https://doi.org/10.1016/j.parkreldis.2025.107619>
- Armstrong, M. J., & Okun, M. S. (2020). Diagnosis and Treatment of Parkinson Disease: A Review. *JAMA*, 323(6), 548–560. <https://doi.org/10.1001/jama.2019.22360>
- Artese, A. L., Rawat, R., & Sung, A. D. (2023). The use of commercial wrist-worn technology to track physiological outcomes in behavioral interventions. *Current Opinion in Clinical Nutrition and Metabolic Care*. <https://doi.org/10.1097/MCO.0000000000000970>
- Assogna, F., Pellicano, C., Cravello, L., Savini, C., Pierantozzi, M., Mercuri, B., Caltagirone, C., Pontieri, F. E., Spalletta, G., & Stefani, A. (2018). Psychiatric profile of motor subtypes of de novo drug-naïve Parkinson's disease patients. *Brain and Behavior*, 8(10), e01094. <https://doi.org/10.1002/brb3.1094>
- Atrsaei, A., Corrà, M. F., Dadashi, F., Vila-Chã, N., Maia, L., Mariani, B., Maetzel, W., & Aminian, K. (2021). Gait speed in clinical and daily living assessments in Parkinson's disease patients: Performance versus capacity. *NPJ Parkinson's disease*, 7(1), 24. <https://doi.org/10.1038/s41531-021-00171-0>
- Atrsaei, A., Hansen, C., Elshehabi, M., Solbrig, S., Berg, D., Liepelt-Scarfone, I., Maetzel, W., & Aminian, K. (2021). Effect of Fear of Falling on Mobility Measured During Lab and Daily Activity Assessments in Parkinson's Disease. *Frontiers in Aging Neuroscience*, 13, 722830. <https://doi.org/10.3389/fnagi.2021.722830>
- Austin, P. C., & Hux, J. E. (2002). A brief note on overlapping confidence intervals. *Journal of Vascular Surgery*, 36(1), 194–195. <https://doi.org/10.1067/mva.2002.125015>
- Ba, F., Obaid, M., Wieler, M., Camicioli, R., & Martin, W. R. W. (2016). Parkinson Disease: The Relationship Between Non-motor Symptoms and Motor Phenotype. *The Canadian Journal of Neurological Sciences. Le Journal Canadien Des Sciences Neurologiques*, 43(2), 261–267. <https://doi.org/10.1017/cjn.2015.328>
- Baek, K., Kim, Y. M., Na, H. K., Lee, J., Shin, D. H., Heo, S.-J., Chung, S. J., Kim, K., Lee, P. H., Sohn, Y. H., Yoon, J., & Kim, Y. J. (2024). Comparing Montreal Cognitive Assessment Performance in Parkinson's Disease Patients: Age- and Education-Adjusted Cutoffs vs. Machine Learning. *Journal of Movement Disorders*, 17(2), 171–180. <https://doi.org/10.14802/jmd.23271>
- Balaguier, R., Madeleine, P., & Vuillerme, N. (2016). Intra-session absolute and relative reliability of pressure pain thresholds in the low back region of vine-workers: Effect of the number of trials. *BMC musculoskeletal disorders*, 17(1), 350. <https://doi.org/10.1186/s12891-016-1212-7>
- Banach, M., Lewek, J., Surma, S., Penson, P. E., Sahebkar, A., Martin, S. S., Bajraktari, G., Henein, M. Y., Reiner, Ž., Bielecka-Dąbrowa, A., & Bytyçi, I. (2023). The association between daily step count and all-cause and cardiovascular mortality: A meta-analysis. *European Journal of Preventive Cardiology*, 30(18), 1975–1985. <https://doi.org/10.1093/eurjpc/zwad229>

- Barone, P., Antonini, A., Colosimo, C., Marconi, R., Morgante, L., Avarello, T. P., Bot-tacchi, E., Cannas, A., Ceravolo, G., Ceravolo, R., Cicarelli, G., Gaglio, R. M., Giglia, R. M., Iemolo, F., Manfredi, M., Meco, G., Nicoletti, A., Pederzoli, M., Petrone, A., ... PRIAMO study group. (2009). The PRIAMO study: A multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 24(11), 1641–1649. <https://doi.org/10.1002/mds.22643>
- Barta, K., Boddy, A. H., Flores, M., Perry, L., Sawyer, K., & Campbell, A. (2025). Psychometric properties of 3-meter backward walk test (3MBWT) in people with Parkinson disease. *Physiotherapy Theory and Practice*, 41(3), 656–663. <https://doi.org/10.1080/09593985.2024.2348034>
- Bassett, D. R., Toth, L. P., LaMunion, S. R., & Crouter, S. E. (2017). Step Counting: A Review of Measurement Considerations and Health-Related Applications. *Sports Medicine (Auckland, N.Z.)*, 47(7), 1303–1315. <https://doi.org/10.1007/s40279-016-0663-1>
- Bate, G. L., Kirk, C., Rehman, R. Z. U., Guan, Y., Yarnall, A. J., Del Din, S., & Lawson, R. A. (2023). The Role of Wearable Sensors to Monitor Physical Activity and Sleep Patterns in Older Adult Inpatients: A Structured Review. *Sensors (Basel, Switzerland)*, 23(10), 4881. <https://doi.org/10.3390/s23104881>
- Baumann, C. R. (2012). Epidemiology, diagnosis and differential diagnosis in Parkinson's disease tremor. *Parkinsonism & Related Disorders*, 18 Suppl 1, S90–92. [https://doi.org/10.1016/S1353-8020\(11\)70029-3](https://doi.org/10.1016/S1353-8020(11)70029-3)
- Benka Wallén, M., Franzén, E., Nero, H., & Hagströmer, M. (2015). Levels and Patterns of Physical Activity and Sedentary Behavior in Elderly People With Mild to Moderate Parkinson Disease. *Physical Therapy*, 95(8), 1135–1141. <https://doi.org/10.2522/ptj.20140374>
- Berg, D., Borghammer, P., Ferestehnejad, S.-M., Heinzel, S., Horsager, J., Schaeffer, E., & Postuma, R. B. (2021). Prodromal Parkinson disease subtypes - key to understanding heterogeneity. *Nature Reviews. Neurology*, 17(6), 349–361. <https://doi.org/10.1038/s41582-021-00486-9>
- Bhidayasiri, R., Phokaewvarangkul, O., Sringean, J., Martinez-Martin, P., Anan, C., Kantachadvanich, N., Chaudhuri, K. R., & Hattori, N. (2019). Evaluation of nocturnal hypokinesia in Parkinson's disease using a novel patient/proxy questionnaire and correlations with objective monitoring. *Parkinsonism & Related Disorders*, 61, 219–223. <https://doi.org/10.1016/j.parkreldis.2018.09.023>
- Bhidayasiri, R., Sringean, J., Anan, C., Boonpang, K., Thanawattano, C., & Ray Chaudhuri, K. (2016). Quantitative demonstration of the efficacy of night-time apomorphine infusion to treat nocturnal hypokinesia in Parkinson's disease using wearable sensors. *Parkinsonism & Related Disorders*, 33 Suppl 1, S36–S41. <https://doi.org/10.1016/j.parkreldis.2016.11.016>
- Bhidayasiri, R., Sringean, J., Chaiwong, S., Anan, C., Penkeaw, N., Leaknok, A., Boonpang, K., Saksornchai, K., Rattana-chaisit, W., Thanawattano, C., & Jagota, P. (2017). Rotigotine for nocturnal hypokinesia in Parkinson's disease: Quantitative analysis of efficacy from a randomized, placebo-controlled trial using an axial inertial sensor. *Parkinsonism & Related Disorders*, 44, 124–128. <https://doi.org/10.1016/j.parkreldis.2017.08.010>
- Bhidayasiri, R., Sringean, J., & Thanawattano, C. (2016). Sensor-based evaluation and treatment of nocturnal hypokinesia in Parkinson's disease: An evidence-based review. *Parkinsonism & Related Disorders*, 22 Suppl 1, S127–133. <https://doi.org/10.1016/j.parkreldis.2015.09.049>
- Bhidayasiri, R., Sringean, J., & Thanawattano, C. (2017). Impaired bed mobility: Quantitative torque analysis with axial inertial sensors. *Neurodegenerative Disease Management*, 7(4), 235–243. <https://doi.org/10.2217/nmt-2017-0016>
- Bhidayasiri, R., & Trenkwalder, C. (2018). Getting a good night sleep? The importance of recognizing and treating nocturnal hypokinesia in Parkinson's disease. *Parkinsonism & Related Disorders*, 50, 10–18. <https://doi.org/10.1016/j.parkreldis.2018.01.008>

- Bianchini, E., Rinaldi, D., De Carolis, L., Galli, S., Alborghetti, M., Hansen, C., Suppa, A., Salvetti, M., Pontieri, F., & Vuillerme, N. (2025). Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study. *JMIR Formative Research*, 9. <https://doi.org/10.2196/63153>
Export Date: 14 April 2025; Cited By: 0.
- Bianchini, E., Alborghetti, M., Galli, S., Hansen, C., Zampogna, A., Suppa, A., Salvetti, M., Pontieri, F. E., Rinaldi, D., & Vuillerme, N. (2025). Minimal Clinically Important Difference of Average Daily Steps Measured Through a Consumer Smartwatch in People With Mild-to-Moderate Parkinson Disease: Cross-Sectional Study [Company: JMIR mHealth and uHealth Distributor: JMIR mHealth and uHealth Institution: JMIR mHealth and uHealth Label: JMIR mHealth and uHealth Publisher: JMIR Publications Inc., Toronto, Canada]. *JMIR mHealth and uHealth*, 13(1), e64213. <https://doi.org/10.2196/64213>
- Bianchini, E., Calì, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzler, W., & Pontieri, F. E. (2022). Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, 23(1), 214. <https://doi.org/10.3390/s23010214>
- Bianchini, E., Galli, S., Alborghetti, M., De Carolis, L., Zampogna, A., Hansen, C., Vuillerme, N., Suppa, A., & Pontieri, F. E. (2023). Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch [Number: 21 Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 23(21), 8971. <https://doi.org/10.3390/s23218971>
- Bianchini, E., & Maetzler, W. (2023, May). Wearable systems in movement disorders. In *International Review of Movement Disorders*. Academic Press. <https://doi.org/10.1016/bs.irmvd.2023.04.002>
- Bianchini, E., Rinaldi, D., De Carolis, L., Galli, S., Alborghetti, M., Hansen, C., Suppa, A., Salvetti, M., Pontieri, F. E., & Vuillerme, N. (2025). Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study. *JMIR Form Res*, 9, e63153. <https://doi.org/10.2196/63153>
- Bianchini, E., Warmerdam, E., Romijnders, R., Stürner, K. H., Baron, R., Heinzel, S., Pontieri, F. E., Hansen, C., & Maetzler, W. (2023). Turning When Using Smartphone in Persons With and Those Without Neurologic Conditions: Observational Study. *Journal of Medical Internet Research*, 25, e41082. <https://doi.org/10.2196/41082>
- Bizzozero-Peroni, B., Díaz-Goñi, V., Jiménez-López, E., Rodríguez-Gutiérrez, E., Sequí-Domínguez, I., Núñez de Arenas-Arroyo, S., López-Gil, J. F., Martínez-Vizcaíno, V., & Mesas, A. E. (2024). Daily Step Count and Depression in Adults: A Systematic Review and Meta-Analysis. *JAMA network open*, 7(12), e2451208. <https://doi.org/10.1001/jamanetworkopen.2024.51208>
- Bloom, D. A., Kaplan, D. J., Mojica, E., Strauss, E. J., Gonzalez-Lomas, G., Campbell, K. A., Alaia, M. J., & Jazrawi, L. M. (2023). The Minimal Clinically Important Difference: A Review of Clinical Significance. *The American Journal of Sports Medicine*, 51(2), 520–524. <https://doi.org/10.1177/03635465211053869>
- Bohnen, N. I., & Albin, R. L. (2011). The cholinergic system and Parkinson disease. *Behavioural Brain Research*, 221(2), 564–573. <https://doi.org/10.1016/j.bbr.2009.12.048>
- Bovonsunthonchai, S., Vachalathiti, R., Hiengkaew, V., Bryant, M. S., Richards, J., & Senanarong, V. (2022). Quantitative gait analysis in mild cognitive impairment, dementia, and cognitively intact individuals: A cross-sectional case-control study. *BMC Geriatrics*, 22(1), 767. <https://doi.org/10.1186/s12877-022-03405-9>
- Branscheidt, M., Kassavetis, P., Anaya, M., Rogers, D., Huang, H. D., Lindquist, M. A., & Celnik, P. (n.d.). Fatigue induces long-lasting detrimental changes in motor-skill learning. *eLife*, 8, e40578. <https://doi.org/10.7554/eLife.40578>

- Brewer, W., Swanson, B. T., & Ortiz, A. (2017). Validity of Fitbit's active minutes as compared with a research-grade accelerometer and self-reported measures. *BMJ open sport & exercise medicine*, 3(1), e000254. <https://doi.org/10.1136/bmjsem-2017-000254>
- Bryant, M. S., Hou, J.-G. G., Workman, C. D., & Protas, E. J. (2018). Predictive ability of functional tests for postural instability and gait difficulty in Parkinson's disease. *European Geriatric Medicine*, 9(1), 83–88. <https://doi.org/10.1007/s41999-017-0021-3>
- Burgos, P. I., Silva-Batista, C., Ragothaman, A., Shah, V. V., Carlson-Kuhta, P., Horak, F. B., & Mancini, M. (2025). Cognition is associated with daily-life mobility in people with Parkinson's disease. *Clinical Parkinsonism & Related Disorders*, 13, 100393. <https://doi.org/10.1016/j.prdoa.2025.100393>
- Byrom, B., Breedon, P., Tulkki-Wilke, R., & Platko, J. V. (2020). Meaningful change: Defining the interpretability of changes in endpoints derived from interactive and mHealth technologies in healthcare and clinical research. *Journal of Rehabilitation and Assistive Technologies Engineering*, 7, 2055668319892778. <https://doi.org/10.1177/2055668319892778>
- Cardoso, F., Goetz, C. G., Mestre, T. A., Sampaio, C., Adler, C. H., Berg, D., Bloem, B. R., Burn, D. J., Fitts, M. S., Gasser, T., Klein, C., de Tijssen, M. A. J., Lang, A. E., Lim, S.-Y., Litvan, I., Meissner, W. G., Mollenhauer, B., Okubadejo, N., Okun, M. S., ... Trenkwalder, C. (2024). A Statement of the MDS on Biological Definition, Staging, and Classification of Parkinson's Disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 39(2), 259–266. <https://doi.org/10.1002/mds.29683>
- Carvalho, D. V., Santos, R. M. S., Magalhães, H. C. d., Souza, M. S. d., Christo, P. P., Almeida-Leite, C. M. d., & Scalzo, P. L. (2020). Can fatigue predict walking capacity of patients with Parkinson's disease? *Arquivos De Neuro-Psiquiatria*, 78(2), 70–75. <https://doi.org/10.1590/0004-282X20190136>
- Castronovo, V., Galbiati, A., Marelli, S., Brombin, C., Cugnata, F., Giarolli, L., Anelli, M. M., Rinaldi, F., & Ferini-Strambi, L. (2016). Validation study of the Italian version of the Insomnia Severity Index (ISI). *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 37(9), 1517–1524. <https://doi.org/10.1007/s10072-016-2620-z>
- Cavanaugh, J. T., Ellis, T. D., Earhart, G. M., Ford, M. P., Foreman, K. B., & Dibble, L. E. (2012). Capturing ambulatory activity decline in Parkinson's disease. *Journal of neurologic physical therapy: JNPT*, 36(2), 51–57. <https://doi.org/10.1097/NPT.0b013e318254ba7a>
- Cederberg, K. L. J., Jeng, B., Sasaki, J. E., Lai, B., Bamman, M., & Motl, R. W. (2021). Accuracy and precision of wrist-worn actigraphy for measuring steps taken during overground and treadmill walking in adults with Parkinson's disease. *Parkinsonism & Related Disorders*, 88, 102–107. <https://doi.org/10.1016/j.parkreldis.2021.06.009>
- Chandrabhatla, A. S., Pomeranec, I. J., & Ksendzovsky, A. (2022). Co-evolution of machine learning and digital technologies to improve monitoring of Parkinson's disease motor symptoms. *NPJ digital medicine*, 5(1), 32. <https://doi.org/10.1038/s41746-022-00568-y>
- Chaudhuri, K. R., Facheris, M. F., Bergmans, B., Bergquist, F., Criswell, S. R., Jia, J., Kukreja, P., Mukai, Y., Spiegel, A. M., Gupta, R., Bergmann, L., & Pahwa, R. (2024). Improved Sleep Correlates with Improved Quality of Life and Motor Symptoms with Foslevodopa/Foscarbidopa. *Movement Disorders Clinical Practice*, 11(7), 861–866. <https://doi.org/10.1002/mdc3.14018>
- Che, N., Ou, R., Li, C., Zhang, L., Wei, Q., Wang, S., Jiang, Q., Yang, T., Xiao, Y., Lin, J., Zhao, B., Chen, X., & Shang, H. (2024). Plasma GFAP as a prognostic biomarker of motor subtype in early Parkinson's disease. *NPJ Parkinson's disease*, 10(1), 48. <https://doi.org/10.1038/s41531-024-00664-8>
- Chen, L.-J., Stubbs, B., Chien, I.-C., Lan, T.-H., Chung, M.-S., Lee, H.-L., Hsu, W.-C., & Ku, P.-W. (2022). Associations between daily steps and cognitive function among inpatients with schizophrenia. *BMC Psychiatry*

- try, 22(1), 87. <https://doi.org/10.1186/s12888-022-03736-2>
- Chen, M.-D., Kuo, C.-C., Pellegrini, C. A., & Hsu, M.-J. (2016). Accuracy of Wristband Activity Monitors during Ambulation and Activities. *Medicine and Science in Sports and Exercise*, 48(10), 1942–1949. <https://doi.org/10.1249/MSS.0000000000000984>
- Chen, S.-T., Stevinson, C., Tian, T., Chen, L.-J., & Ku, P.-W. (2020). Accelerometer-measured daily steps and subjective cognitive ability in older adults: A two-year follow-up study. *Experimental Gerontology*, 133, 110874. <https://doi.org/10.1016/j.exger.2020.110874>
- Chevance, G., Golaszewski, N. M., Tip-ton, E., Hekler, E. B., Buman, M., Welk, G. J., Patrick, K., & Godino, J. G. (2022). Accuracy and Precision of Energy Expenditure, Heart Rate, and Steps Measured by Combined-Sensing Fitbits Against Reference Measures: Systematic Review and Meta-analysis. *JMIR mHealth and uHealth*, 10(4), e35626. <https://doi.org/10.2196/35626>
- Chien, J. H., Post, J., & Siu, K.-C. (2018). Effects of Aging on the Obstacle Negotiation Strategy while Stepping over Multiple Obstacles [Publisher: Nature Publishing Group]. *Scientific Reports*, 8(1), 8576. <https://doi.org/10.1038/s41598-018-26807-5>
- Cho, J., Seo, D. M., & Uh, Y. (2020). Clinical Application of Overlapping Confidence Intervals for Monitoring Changes in Serial Clinical Chemistry Test Results. *Annals of Laboratory Medicine*, 40(3), 201–208. <https://doi.org/10.3343/alm.2020.40.3.201>
- Choi, J.-H., Lee, J.-Y., Shin, C., Yoo, D., Im, J. H., Woo, K. A., Kim, H.-J., Ahn, T.-B., Kim, J.-M., & Jeon, B. (2021). Investigation of Nocturnal Hypokinesia and Health-Related Quality of Life in Parkinsonian Patients with the Korean Version of the Nocturnal Hypokinesia Questionnaire. *Journal of Movement Disorders*, 14(3), 221–225. <https://doi.org/10.14802/jmd.20172>
- Chow, J. J., Thom, J. M., Weweg, M. A., Ward, R. E., & Parmenter, B. J. (2017). Accuracy of step count measured by physical activity monitors: The effect of gait speed and anatomical placement site. *Gait & Posture*, 57, 199–203. <https://doi.org/10.1016/j.gaitpost.2017.06.012>
- Christiansen, C., Moore, C., Schenkman, M., Kluger, B., Kohrt, W., Delitto, A., Berman, B., Hall, D., Josbeno, D., Poon, C., Robichaud, J., Wellington, T., Jain, S., Comella, C., Corcos, D., & Melanson, E. (2017). Factors Associated With Ambulatory Activity in De Novo Parkinson Disease. *Journal of neurologic physical therapy: JNPT*, 41(2), 93–100. <https://doi.org/10.1097/NPT.0000000000000169>
- Christopher, A., Kraft, E., Olenick, H., Kiesling, R., & Doty, A. (2021). The reliability and validity of the Timed Up and Go as a clinical tool in individuals with and without disabilities across a lifespan: A systematic review. *Disability and Rehabilitation*, 43(13), 1799–1813. <https://doi.org/10.1080/09638288.2019.1682066>
- Clemes, S. A., & Griffiths, P. L. (2008). How many days of pedometer monitoring predict monthly ambulatory activity in adults? *Medicine and Science in Sports and Exercise*, 40(9), 1589–1595. <https://doi.org/10.1249/MSS.0b013e318177eb96>
- Cohen, J. A., & Verghese, J. (2019). Gait and dementia. *Handbook of Clinical Neurology*, 167, 419–427. <https://doi.org/10.1016/B978-0-12-804766-8.00022-4>
- Corrà, M. F., Atrsaeci, A., Sardoreira, A., Hansen, C., Aminian, K., Correia, M., Vila-Chã, N., Maetzler, W., & Maia, L. (2021). Comparison of Laboratory and Daily-Life Gait Speed Assessment during ON and OFF States in Parkinson's Disease. *Sensors (Basel, Switzerland)*, 21(12), 3974. <https://doi.org/10.3390/s21123974>
- Correno, M. B., Hansen, C., Chardon, M., Milane, T., Bianchini, E., & Vuillerme, N. (2022). Association between Backward Walking and Cognition in Parkinson Disease: A Systematic Review. *International Journal of Environmental Research and Public Health*, 19(19), 12810. <https://doi.org/10.3390/ijerph191912810>
- Corti, E. J., Johnson, A. R., Riddle, H., Gasson, N., Kane, R., & Loftus, A. M. (2017). The relationship between executive function and fine motor control in young and older adults. *Human Movement Science*, 51, 41–

50. <https://doi.org/10.1016/j.humov.2016.11.001>
- Creaby, M. W., & Cole, M. H. (2018). Gait characteristics and falls in Parkinson's disease: A systematic review and meta-analysis. *Parkinsonism & Related Disorders*, 57, 1–8. <https://doi.org/10.1016/j.parkreldis.2018.07.008>
- Cristini, J., Weiss, M., De Las Heras, B., Medina-Rincón, A., Dagher, A., Postuma, R. B., Huber, R., Doyon, J., Rosa-Neto, P., Carrier, J., Amara, A. W., & Roig, M. (2021). The effects of exercise on sleep quality in persons with Parkinson's disease: A systematic review with meta-analysis. *Sleep Medicine Reviews*, 55, 101384. <https://doi.org/10.1016/j.smrv.2020.101384>
- CTA/ANSI. (2016). CTA 2056-2016 (ANSI) - Physical Activity Monitoring for Fitness Wearables: Step Counting. Retrieved October 19, 2022, from <https://webstore.ansi.org/Standards/ANSI/cta20562016ansi>
- da Silva, F. C., Iop, R. d. R., de Oliveira, L. C., Boll, A. M., de Alvarenga, J. G. S., Gutierrez Filho, P. J. B., de Melo, L. M. A. B., Xavier, A. J., & da Silva, R. (2018). Effects of physical exercise programs on cognitive function in Parkinson's disease patients: A systematic review of randomized controlled trials of the last 10 years. *PloS One*, 13(2), e0193113. <https://doi.org/10.1371/journal.pone.0193113>
- Dallaire, M., Houde-Thibeault, A., Bouchard-Tremblay, J., Wotto, E. A., Côté, S., Santos Oliveira, C., Ngomo, S., & da Silva, R. A. (2024). Impact of frailty and sex-related differences on postural control and gait in older adults with Parkinson's Disease. *Experimental Gerontology*, 186, 112360. <https://doi.org/10.1016/j.exger.2024.112360>
- Danks, K. A., Pohlig, R. T., Roos, M., Wright, T. R., & Reisman, D. S. (2016). The Relationship Between Walking Capacity, Biopsychosocial Factors, Self-Efficacy and Walking Activity in Individuals Post Stroke. *Journal of neurologic physical therapy : JNPT*, 40(4), 232–238. <https://doi.org/10.1097/NPT.0000000000000143>
- de Roos, P., Bloem, B. R., Kelley, T. A., Antonini, A., Dodel, R., Hagell, P., Maras, C., Martinez-Martin, P., Mehta, S. H., Odin, P., Chaudhuri, K. R., Weintraub, D., Wilson, B., & Utti, R. J. (2017). A Consensus Set of Outcomes for Parkinson's Disease from the International Consortium for Health Outcomes Measurement. *Journal of Parkinson's disease*, 7(3), 533–543. <https://doi.org/10.3233/JPD-161055>
- De Carolis, L., Galli, S., Bianchini, E., Rinaldi, D., Raju, M., Calì, B., Alborghetti, M., & Pontieri, F. E. (2023). Age at Onset Influences Progression of Motor and Non-Motor Symptoms during the Early Stage of Parkinson's Disease: A Monocentric Retrospective Study. *Brain Sciences*, 13(2), 157. <https://doi.org/10.3390/brainsci13020157>
- Degroote, L., De Bourdeaudhuij, I., Verloigne, M., Poppe, L., & Crombez, G. (2018). The Accuracy of Smart Devices for Measuring Physical Activity in Daily Life: Validation Study. *JMIR mHealth and uHealth*, 6(12), e10972. <https://doi.org/10.2196/10972>
- Del Din, S., Godfrey, A., Galna, B., Lord, S., & Rochester, L. (2016). Free-living gait characteristics in ageing and Parkinson's disease: Impact of environment and ambulatory bout length. *Journal of NeuroEngineering and Rehabilitation*, 13, 46. <https://doi.org/10.1186/s12984-016-0154-5>
- Del Pozo Cruz, B., Ahmadi, M., Naismith, S. L., & Stamatakis, E. (2022). Association of Daily Step Count and Intensity With Incident Dementia in 78 430 Adults Living in the UK. *JAMA neurology*, 79(10), 1059–1063. <https://doi.org/10.1001/jamaneurol.2022.2672>
- Del Pozo Cruz, B., Ahmadi, M. N., Lee, I.-M., & Stamatakis, E. (2022). Prospective Associations of Daily Step Counts and Intensity With Cancer and Cardiovascular Disease Incidence and Mortality and All-Cause Mortality. *JAMA internal medicine*. <https://doi.org/10.1001/jamainternmed.2022.4000>
- Dijkstra, B., Zijlstra, W., Scherder, E., & Kamsma, Y. (2008). Detection of walking periods and number of steps in older adults and patients with Parkinson's disease: Accuracy of a pedometer and an accelerometry-based method. *Age and Ageing*, 37(4), 436–

441. <https://doi.org/10.1093/ageing/afn097>
Export Date: 14 April 2025; Cited By: 98.
- Ding, D., Nguyen, B., Nau, T., Luo, M., Del Pozo Cruz, B., Dempsey, P. C., Munn, Z., Jefferis, B. J., Sherrington, C., Calleja, E. A., Hau Chong, K., Davis, R., Francois, M. E., Tiedemann, A., Biddle, S. J. H., Okely, A., Bauman, A., Ekelund, U., Clare, P., & Owen, K. (2025). Daily steps and health outcomes in adults: A systematic review and dose-response meta-analysis. *The Lancet. Public Health*, 10(8), e668–e681. [https://doi.org/10.1016/S2468-2667\(25\)00164-1](https://doi.org/10.1016/S2468-2667(25)00164-1)
- Dodet, P., Houot, M., Leu-Semenescu, S., Corvol, J.-C., Lehericy, S., Mangone, G., Vidailhet, M., Roze, E., & Arnulf, I. (2024). Sleep disorders in Parkinson's disease, an early and multiple problem. *NPJ Parkinson's Disease*, 10, 46. <https://doi.org/10.1038/s41531-024-00642-0>
- Domingues, V. L., Makhoul, M. P., de Freitas, T. B., Polese, J. C., Silva-Batista, C., Barbieri, F. A., & Torriani-Pasin, C. (2024). Factors Associated With Physical Activity and Sedentary Behavior in People With Parkinson Disease: A Systematic Review and Meta-Analysis. *Physical Therapy*, 104(12), pzae114. <https://doi.org/10.1093/ptj/pzae114>
- Dorsey, E. R., Sherer, T., Okun, M. S., & Bloem, B. R. (2018). The Emerging Evidence of the Parkinson Pandemic. *Journal of Parkinson's Disease*, 8(s1), S3–S8. <https://doi.org/10.3233/JPD-181474>
- Dragašević-Mišković, N. T., Bobić, V., Kostić, M., Stanković, I., Radovanović, S., Dimitrijević, K., Svetel, M., Petrović, I., & Đurić-Jovičić, M. (2021). Impact of depression on gait variability in Parkinson's disease. *Clinical Neurology and Neurosurgery*, 200, 106324. <https://doi.org/10.1016/j.clineuro.2020.106324>
- Ellis, T. D., Cavanaugh, J. T., DeAngelis, T., Hendron, K., Thomas, C. A., Saint-Hilaire, M., Pencina, K., & Latham, N. K. (2019). Comparative Effectiveness of mHealth-Supported Exercise Compared With Exercise Alone for People With Parkinson Disease: Randomized Controlled Pilot Study. *Physical Therapy*, 99(2), 203–216. <https://doi.org/10.1093/ptj/pzy131>
- Erro, R., Vitale, C., Amboni, M., Picillo, M., Moccia, M., Longo, K., Santangelo, G., De Rosa, A., Allocca, R., Giordano, F., Orefice, G., De Michele, G., Santoro, L., Pellecchia, M. T., & Barone, P. (2013). The heterogeneity of early Parkinson's disease: A cluster analysis on newly diagnosed untreated patients. *PLoS One*, 8(8), e70244. <https://doi.org/10.1371/journal.pone.0070244>
- Espay, A. J., Bonato, P., Nahab, F. B., Maetzler, W., Dean, J. M., Klucken, J., Eskofier, B. M., Merola, A., Horak, F., Lang, A. E., Reilmann, R., Giuffrida, J., Nieuwboer, A., Horne, M., Little, M. A., Litvan, I., Simuni, T., Dorsey, E. R., Burack, M. A., ... Movement Disorders Society Task Force on Technology. (2016). Technology in Parkinson's disease: Challenges and opportunities. *Movement Disorders: Official Journal of the Movement Disorder Society*, 31(9), 1272–1282. <https://doi.org/10.1002/mds.26642>
- Espay, A. J., Hausdorff, J. M., Sánchez-Ferro, Á., Klucken, J., Merola, A., Bonato, P., Paul, S. S., Horak, F. B., Vizcarra, J. A., Mestre, T. A., Reilmann, R., Nieuwboer, A., Dorsey, E. R., Rochester, L., Bloem, B. R., Maetzler, W., & Movement Disorder Society Task Force on Technology. (2019). A roadmap for implementation of patient-centered digital outcome measures in Parkinson's disease obtained using mobile health technologies. *Movement Disorders: Official Journal of the Movement Disorder Society*, 34(5), 657–663. <https://doi.org/10.1002/mds.27671>
- Evenson, K. R., & Spade, C. L. (2020). Review of Validity and Reliability of Garmin Activity Trackers. *Journal for the Measurement of Physical Behaviour*, 3(2), 170–185. <https://doi.org/10.1123/jmpb.2019-0035>
- Evenson, K. R., Wen, F., Metzger, J. S., & Herring, A. H. (2015). Physical activity and sedentary behavior patterns using accelerometry from a national sample of United States adults. *The International Journal of Behavioral Nutrition and Physical Activity*, 12, 20. <https://doi.org/10.1186/s12966-015-0183-7>
- Fabbri, M., Coelho, M., Abreu, D., Guedes, L. C., Rosa, M. M., Costa, N., Antonini, A., & Ferreira, J. J. (2016). Do patients with late-stage Parkinson's disease still respond to levodopa? *Parkinsonism & Related Dis-*

- orders, 26, 10–16. <https://doi.org/10.1016/j.parkreldis.2016.02.021>
- Fasano, A., Canning, C. G., Hausdorff, J. M., Lord, S., & Rochester, L. (2017). Falls in Parkinson's disease: A complex and evolving picture. *Movement Disorders: Official Journal of the Movement Disorder Society*, 32(11), 1524–1536. <https://doi.org/10.1002/mds.27195>
- Fasano, A., Fung, V. S. C., Lopiano, L., Elibol, B., Smolentseva, I. G., Seppi, K., Takáts, A., Onuk, K., Parra, J. C., Bergmann, L., Sail, K., Jalundhwa, Y., & Pirtosek, Z. (2019). Characterizing advanced Parkinson's disease: OBSERVE-PD observational study results of 2615 patients. *BMC neurology*, 19(1), 50. <https://doi.org/10.1186/s12883-019-1276-8>
- Feehan, L. M., Geldman, J., Sayre, E. C., Park, C., Ezzat, A. M., Yoo, J. Y., Hamilton, C. B., & Li, L. C. (2018). Accuracy of Fitbit Devices: Systematic Review and Narrative Syntheses of Quantitative Data. *JMIR mHealth and uHealth*, 6(8), e10527. <https://doi.org/10.2196/10527>
- Ferguson, T., Olds, T., Curtis, R., Blake, H., Crozier, A. J., Dankiw, K., Dumuid, D., Kasai, D., O'Connor, E., Virgara, R., & Maher, C. (2022). Effectiveness of wearable activity trackers to increase physical activity and improve health: A systematic review of systematic reviews and meta-analyses. *The Lancet. Digital Health*, 4(8), e615–e626. [https://doi.org/10.1016/S2589-7500\(22\)00111-X](https://doi.org/10.1016/S2589-7500(22)00111-X)
- Ferreira, J. J., Gago, M. F., Costa, R., Fonseca, M. M., Almeida, J., Rocha, J. F., Holenz, J., & Trenkwalder, C. (2025). Opicapone for Parkinson's disease-related sleep disturbances: The OASIS clinical trial. *Journal of Parkinson's Disease*, 15(1), 87–96. <https://doi.org/10.1177/1877718X241306711>
- Ferreira, J. J., Lees, A., Rocha, J.-F., Poewe, W., Rascol, O., Soares-da-Silva, P., & Bi-Park 1 investigators. (2016). Opicapone as an adjunct to levodopa in patients with Parkinson's disease and end-of-dose motor fluctuations: A randomised, double-blind, controlled trial. *The Lancet. Neurology*, 15(2), 154–165. [https://doi.org/10.1016/S1474-4422\(15\)00336-1](https://doi.org/10.1016/S1474-4422(15)00336-1)
- Finì, N. A., Burge, A. T., Bernhardt, J., & Holland, A. E. (2019). Two Days of Measurement Provides Reliable Estimates of Physical Activity Poststroke: An Observational Study. *Archives of Physical Medicine and Rehabilitation*, 100(5), 883–890. <https://doi.org/10.1016/j.apmr.2018.10.006>
- Fiorenzato, E., Cauzzo, S., Weis, L., Garon, M., Pistonesi, F., Cianci, V., Nasi, M. L., Vianello, F., Zecchinelli, A. L., Pezzoli, G., Reali, E., Pozzi, B., Isaias, I. U., Siri, C., Santangelo, G., Cuoco, S., Barone, P., Antonini, A., & Biundo, R. (2024). Optimal MMSE and MoCA cutoffs for cognitive diagnoses in Parkinson's disease: A data-driven decision tree model. *Journal of the Neurological Sciences*, 466, 123283. <https://doi.org/10.1016/j.jns.2024.123283>
- Fokkema, T., Kooiman, T. J. M., Krijnen, W. P., VAN DER Schans, C. P., & DE Groot, M. (2017). Reliability and Validity of Ten Consumer Activity Trackers Depend on Walking Speed. *Medicine and Science in Sports and Exercise*, 49(4), 793–800. <https://doi.org/10.1249/MSS.0000000000001146>
- Franceschini, M., Boffa, A., Pignotti, E., Andriolo, L., Zaffagnini, S., & Filardo, G. (2023). The Minimal Clinically Important Difference Changes Greatly Based on the Different Calculation Methods. *The American Journal of Sports Medicine*, 51(4), 1067–1073. <https://doi.org/10.1177/03635465231152484>
- Fuller, D., Colwell, E., Low, J., Orychock, K., Tobin, M. A., Simango, B., Buote, R., Van Heerden, D., Luan, H., Cullen, K., Slade, L., & Taylor, N. G. A. (2020). Reliability and Validity of Commercially Available Wearable Devices for Measuring Steps, Energy Expenditure, and Heart Rate: Systematic Review. *JMIR mHealth and uHealth*, 8(9), e18694. <https://doi.org/10.2196/18694>
- Furrer, R., & Handschin, C. (2025). Biomarkers of aging: Functional aspects still trump molecular parameters. *NPJ Aging*, 11(1), 15. <https://doi.org/10.1038/s41514-025-00207-2>
- Gallea, C., Ewencyk, C., Degos, B., Welter, M.-L., Grabli, D., Leu-Semenescu, S., Valabregue, R., Berroir, P., Yahia-Cherif, L., Bertasi, E., Fernandez-Vidal, S., Bar-

- dinet, E., Roze, E., Benali, H., Poupon, C., François, C., Arnulf, I., Lehericy, S., & Vidailhet, M. (2017). Pedunculopontine network dysfunction in Parkinson's disease with postural control and sleep disorders. *Movement Disorders: Official Journal of the Movement Disorder Society*, 32(5), 693–704. <https://doi.org/10.1002/mds.26923>
- Galperin, I., Herman, T., Assad, M., Ganz, N., Mirelman, A., Giladi, N., & Hausdorff, J. M. (2020). Sensor-Based and Patient-Based Assessment of Daily-Living Physical Activity in People with Parkinson's Disease: Do Motor Subtypes Play a Role? [Publisher: Multidisciplinary Digital Publishing Institute]. *Sensors*, 20(24), 7015. <https://doi.org/10.3390/s20247015>
- Galperin, I., Hillel, I., Del Din, S., Bekkers, E. M. J., Nieuwboer, A., Abbruzzese, G., Avanzino, L., Nieuwhof, F., Bloem, B. R., Rochester, L., Della Croce, U., Cereatti, A., Giladi, N., Mirelman, A., & Hausdorff, J. M. (2019). Associations between daily-living physical activity and laboratory-based assessments of motor severity in patients with falls and Parkinson's disease. *Parkinsonism & Related Disorders*, 62, 85–90. <https://doi.org/10.1016/j.parkreldis.2019.01.022>
- Gan, Y., Xie, H., Qin, G., Wu, D., Shan, M., Hu, T., Yin, Z., An, Q., Ma, R., Wang, S., Zhang, Q., Zhu, G., & Zhang, J. (2023). Association between Cognitive Impairment and Freezing of Gait in Patients with Parkinson's Disease. *Journal of Clinical Medicine*, 12(8), 2799. <https://doi.org/10.3390/jcm12082799>
- Garber, C. E., & Friedman, J. H. (2003). Effects of fatigue on physical activity and function in patients with Parkinson's disease. *Neurology*, 60(7), 1119–1124. <https://doi.org/10.1212/01.wnl.0000055868.06222.ab>
- García-Bustillo, Á., Valiñas-Sieiro, F., Allende-Río, M., González-Santos, J., Cubo, E., & and the Multidisciplinary Telemedicine Group. (2022). Assistive Devices for Personal Mobility in Parkinson's Disease: A Systematic Review of the Literature. *Movement Disorders Clinical Practice*, 9(8), 1040–1046. <https://doi.org/10.1002/mdc3.13568>
- Garmin. (n.d.). Vivosmart 4 - Introduction. Retrieved September 13, 2023, from <https://www8.garmin.com/manuals/webhelp/vivosmart4/EN-US/GUID-8B9070D6-C0EA-45EE-8F62-1602492BF264.html>
- GBD 2016 Parkinson's Disease Collaborators. (2018). Global, regional, and national burden of Parkinson's disease, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *The Lancet. Neurology*, 17(11), 939–953. [https://doi.org/10.1016/S1474-4422\(18\)30295-3](https://doi.org/10.1016/S1474-4422(18)30295-3)
- Geritz, J., Welzel, J., Hansen, C., Maetzel, C., Hobert, M. A., Elshehabi, M., Sobczak, A., Kudelka, J., Stiel, C., Hieke, J., Alpes, A., Bunzeck, N., & Maetzel, W. (2022). Does Executive Function Influence Walking in Acutely Hospitalized Patients With Advanced Parkinson's Disease: A Quantitative Analysis. [Place: Switzerland]. *Frontiers in neurology*, 13, 852725. <https://doi.org/10.3389/fneur.2022.852725>
- Germini, F., Noronha, N., Borg Debono, V., Abraham Philip, B., Pete, D., Navarro, T., Keepanasseril, A., Parpia, S., de Wit, K., & Iorio, A. (2022). Accuracy and Acceptability of Wrist-Wearable Activity-Tracking Devices: Systematic Review of the Literature. *Journal of Medical Internet Research*, 24(1), e30791. <https://doi.org/10.2196/30791>
- Giannouli, E., Bock, O., Mellone, S., & Zijlstra, W. (2016). Mobility in Old Age: Capacity Is Not Performance. *BioMed Research International*, 2016, 3261567. <https://doi.org/10.1155/2016/3261567>
- Giansanti, D., Macellari, V., & Maccioni, G. (2008). Telemonitoring and telerehabilitation of patients with Parkinson's disease: Health technology assessment of a novel wearable step counter. *Telemedicine and e-Health*, 14(1), 76–83. <https://doi.org/10.1089/tmj.2007.0019>
- Export Date: 14 April 2025; Cited By: 44.
- Gilmore, G., Gouelle, A., Adamson, M. B., Pieterman, M., & Jog, M. (2019). Forward and backward walking in Parkinson disease: A factor analysis. *Gait & Posture*, 74, 14–19. <https://doi.org/10.1016/j.gaitpost.2019.08.005>
- Ginis, P., Goris, M., De Groef, A., Blondeel, A., Gilat, M., Demeyer, H., Troosters, T.,

- & Nieuwboer, A. (2023). Validation of Commercial Activity Trackers in Everyday Life of People with Parkinson's Disease. *Sensors*, 23(8). <https://doi.org/10.3390/s23084156> Export Date: 14 April 2025; Cited By: 6.
- Godfrey, A., Morris, R., Hickey, A., & Del Din, S. (2016). Beyond the front end: Investigating a thigh worn accelerometer device for step count and bout detection in Parkinson's disease. *Medical Engineering and Physics*, 38(12), 1524–1529. <https://doi.org/10.1016/j.medengphy.2016.09.023> Export Date: 14 April 2025; Cited By: 14.
- Godinho, C., Domingos, J., Cunha, G., Santos, A. T., Fernandes, R. M., Abreu, D., Gonçalves, N., Matthews, H., Isaacs, T., Duffen, J., Al-Jawad, A., Larsen, F., Serano, A., Weber, P., Thoms, A., Sollinger, S., Graessner, H., Maetzler, W., & Ferreira, J. J. (2016). A systematic review of the characteristics and validity of monitoring technologies to assess Parkinson's disease. *Journal of Neuroengineering and Rehabilitation*, 13, 24. <https://doi.org/10.1186/s12984-016-0136-7>
- Goetz, C. G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G. T., Counsell, C., Giladi, N., Holloway, R. G., Moore, C. G., Wenning, G. K., Yahr, M. D., Seidl, L., & Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. (2004). Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: Status and recommendations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 19(9), 1020–1028. <https://doi.org/10.1002/mds.20213>
- Goetz, C. G., Tilley, B. C., Shaftman, S. R., Stebbins, G. T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M. B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A. E., Lees, A., Leurgans, S., LeWitt, P. A., Nyenhuis, D., ... Movement Disorder Society UPDRS Revision Task Force. (2008). Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale presentation and clinimetric testing results. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(15), 2129–2170. <https://doi.org/10.1002/mds.22340>
- Goldsack, J. C., Coravos, A., Bakker, J. P., Bent, B., Dowling, A. V., Fitzer-Attas, C., Godfrey, A., Godino, J. G., Gujar, N., Izmailova, E., Manta, C., Peterson, B., Vandenriessche, B., Wood, W. A., Wang, K. W., & Dunn, J. (2020). Verification, analytical validation, and clinical validation (V3): The foundation of determining fit-for-purpose for Biometric Monitoring Technologies (BioMeTs). *NPJ digital medicine*, 3, 55. <https://doi.org/10.1038/s41746-020-0260-4>
- Grande, G., Triolo, F., Nuara, A., Welmer, A.-K., Fratiglioni, L., & Vetrano, D. L. (2019). Measuring gait speed to better identify prodromal dementia. *Experimental Gerontology*, 124, 110625. <https://doi.org/10.1016/j.exger.2019.05.014>
- Guralnik, J. M., Simonsick, E. M., Ferrucci, L., Glynn, R. J., Berkman, L. F., Blazer, D. G., Scherr, P. A., & Wallace, R. B. (1994). A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *Journal of Gerontology*, 49(2), M85–94. <https://doi.org/10.1093/geronj/49.2.m85>
- Hackney, M. E., & Earhart, G. M. (2009). Backward walking in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 24(2), 218–223. <https://doi.org/10.1002/mds.22330>
- Haertner, L., Elshehabi, M., Zaunbrecher, L., Pham, M. H., Maetzler, C., van Uem, J. M. T., Hobert, M. A., Hucker, S., Nussbaum, S., Berg, D., Liepelt-Scarfone, I., & Maetzler, W. (2018). Effect of Fear of Falling on Turning Performance in Parkinson's Disease in the Lab and at Home. *Frontiers in Aging Neuroscience*, 10, 78. <https://doi.org/10.3389/fnagi.2018.00078>
- Handlery, R., Stewart, J. C., Pellegrini, C., Monroe, C., Hainline, G., Flach, A., Handlery, K., & Fritz, S. (2021). Physical Activity in De Novo Parkinson Disease: Daily Step Recommendation and Effects of Treadmill Exercise on Physical Activity. *Physical Therapy*, 101(10), pzab174. <https://doi.org/10.1093/ptj/pzab174>
- Hanff, A.-M., McCrum, C., Rauschenberger, A., Aguayo, G. A., Zeegers, M. P., Leist, A. K., Krüger, R., & NCER-PD.

- (2023). Validation of a Parkinson's disease questionnaire-39-based functional mobility composite score (FMCS) in people with Parkinson's disease. *Parkinsonism & Related Disorders*, 112, 105442. <https://doi.org/10.1016/j.parkreldis.2023.105442>
- Hansen, C., Ortlieb, C., Romijnders, R., Warmerdam, E., Welzel, J., Geritz, J., & Maetzler, W. (2022). Reliability of IMU-Derived Temporal Gait Parameters in Neurological Diseases. *Sensors (Basel, Switzerland)*, 22(6), 2304. <https://doi.org/10.3390/s22062304>
- Hansen, C., Sanchez-Ferro, A., & Maetzler, W. (2018). How Mobile Health Technology and Electronic Health Records Will Change Care of Patients with Parkinson's Disease. *Journal of Parkinson's Disease*, 8(s1), S41–S45. <https://doi.org/10.3233/JPD-181498>
- Hart, T. L., Swartz, A. M., Cashin, S. E., & Strath, S. J. (2011). How many days of monitoring predict physical activity and sedentary behaviour in older adults? *The International Journal of Behavioral Nutrition and Physical Activity*, 8, 62. <https://doi.org/10.1186/1479-5868-8-62>
- Hauser, R., Bergmans, B., Malaty, I., Cobb, D., Homola, J., Bergmann, L., Gupta, R., Jia, J., Shah, M., & Chaudhuri, K. R. (2024). Effects of Continuous Subcutaneous Infusion of Foslevodopa/Foscarbidopa on Sleep Dysfunction in People With Parkinson's [Publisher: Elsevier]. *Parkinsonism & Related Disorders*, 122. <https://doi.org/10.1016/j.parkreldis.2024.106567>
- Hauser, R. A., Videnovic, A., Soares-da-Silva, P., Liang, G. S., Olson, K., Jen, E., Rocha, J.-F., & Klepitskaya, O. (2024). OFF-times before, during, and after nighttime sleep periods in Parkinson's disease patients with motor fluctuations and the effects of opicapone: A post hoc analysis of diary data from BIPARK-1 and -2. *Parkinsonism & Related Disorders*, 123, 106971. <https://doi.org/10.1016/j.parkreldis.2024.106971>
- Heinzel, S., Berg, D., Gasser, T., Chen, H., Yao, C., Postuma, R. B., & MDS Task Force on the Definition of Parkinson's Disease. (2019). Update of the MDS research criteria for prodromal Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 34(10), 1464–1470. <https://doi.org/10.1002/mds.27802>
- Heremans, E., Nieuwboer, A., Spildooren, J., Vandenbossche, J., Deroost, N., Soetens, E., Kerckhofs, E., & Vercruyse, S. (2013). Cognitive aspects of freezing of gait in Parkinson's disease: A challenge for rehabilitation. *Journal of Neural Transmission (Vienna, Austria: 1996)*, 120(4), 543–557. <https://doi.org/10.1007/s00702-012-0964-y>
- Hergenroeder, A. L., Barone Gibbs, B., Kotlarczyk, M. P., Kowalsky, R. J., Perera, S., & Brach, J. S. (2018). Accuracy of Objective Physical Activity Monitors in Measuring Steps in Older Adults. *Gerontology & Geriatric Medicine*, 4, 2333721418781126. <https://doi.org/10.1177/2333721418781126>
- Herman, T., Weiss, A., Brozgol, M., Giladi, N., & Hausdorff, J. (2014). Gait and balance in Parkinson's disease subtypes: Objective measures and classification considerations. *Journal of Neurology*, 261(12), 2401–2410. <https://doi.org/10.1007/s00415-014-7513-6> Export Date: 14 April 2025; Cited By: 84.
- Hillel, I., Gazit, E., Nieuwboer, A., Avanzino, L., Rochester, L., Cereatti, A., Croce, U. D., Rikkert, M. O., Bloem, B. R., Pelosin, E., Del Din, S., Ginis, P., Giladi, N., Mirelman, A., & Hausdorff, J. M. (2019). 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. *European Review of Aging and Physical Activity: Official Journal of the European Group for Research into Elderly and Physical Activity*, 16, 6. <https://doi.org/10.1186/s11556-019-0214-5>
- Hinchliffe, C., Rehman, R. Z. U., Pinaud, C., Branco, D., Jackson, D., Ahmaniemi, T., Guerreiro, T., Chatterjee, M., Manyakov, N. V., Pandis, I., Davies, K., Macrae, V., Aufenberg, S., Paulides, E., Hildesheim, H., Kudelka, J., Emmert, K., Van Gassen, G., Rochester, L., ... IDEA-FAST Consortium. (2024). Evaluation of walking activity and gait to identify physical and mental fatigue in neurodegenerative and immune disorders: Preliminary insights from the IDEA-FAST feasibility study. *Journal of Neuroengineering and Rehabilitation*, 21(1), 94. <https://doi.org/10.1186/s12984-024-01390-1>

- Hobert, M. A., Nussbaum, S., Heger, T., Berg, D., Maetzler, W., & Heinzel, S. (2019). Progressive Gait Deficits in Parkinson's Disease: A Wearable-Based Biannual 5-Year Prospective Study. *Frontiers in Aging Neuroscience*, 11, 22. <https://doi.org/10.3389/fnagi.2019.00022>
- Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: Onset, progression and mortality. *Neurology*, 17(5), 427–442. <https://doi.org/10.1212/wnl.17.5.427>
- Höglinger, G. U., Adler, C. H., Berg, D., Klein, C., Outeiro, T. F., Poewe, W., Postuma, R., Stoessl, A. J., & Lang, A. E. (2024). A biological classification of Parkinson's disease: The SynNeurGe research diagnostic criteria. *The Lancet. Neurology*, 23(2), 191–204. [https://doi.org/10.1016/S1474-4422\(23\)00404-0](https://doi.org/10.1016/S1474-4422(23)00404-0)
- Holden, S. K., Finseth, T., Sillau, S. H., & Berman, B. D. (2017). Progression of MDS-UPDRS Scores Over Five Years in De Novo Parkinson Disease from the Parkinson's Progression Markers Initiative Cohort. *Movement Disorders Clinical Practice*, 5(1), 47–53. <https://doi.org/10.1002/mdc3.12553>
- Horsager, J., & Borghammer, P. (2024). Brain-first vs. body-first Parkinson's disease: An update on recent evidence. *Parkinsonism & Related Disorders*, 106101. <https://doi.org/10.1016/j.parkreldis.2024.106101>
- Horváth, K., Aschermann, Z., Ács, P., Deli, G., Janszky, J., Komoly, S., Balázs, É., Takács, K., Karádi, K., & Kovács, N. (2015). Minimal clinically important difference on the Motor Examination part of MDS-UPDRS. *Parkinsonism & Related Disorders*, 21(12), 1421–1426. <https://doi.org/10.1016/j.parkreldis.2015.10.006>
- Huang, T., Li, M., & Huang, J. (2023). Recent trends in wearable device used to detect freezing of gait and falls in people with Parkinson's disease: A systematic review. *Frontiers in Aging Neuroscience*, 15, 1119956. <https://doi.org/10.3389/fnagi.2023.1119956>
- Huang, X., Ng, S. Y.-E., Chia, N. S.-Y., Setiawan, F., Tay, K.-Y., Au, W.-L., Tan, E.-K., & Tan, L. C.-S. (2019). Non-motor symptoms in early Parkinson's disease with different motor subtypes and their associations with quality of life. *European Journal of Neurology*, 26(3), 400–406. <https://doi.org/10.1111/ene.13803>
- Huang, Y.-Z., Chang, F.-Y., Liu, W.-C., Chuang, Y.-F., Chuang, L.-L., & Chang, Y.-J. (2017). Fatigue and Muscle Strength Involving Walking Speed in Parkinson's Disease: Insights for Developing Rehabilitation Strategy for PD. *Neural Plasticity*, 2017, 1941980. <https://doi.org/10.1155/2017/1941980>
- Hulbert, S., Ashburn, A., Robert, L., & Verheyden, G. (2015). A narrative review of turning deficits in people with Parkinson's disease. *Disability and Rehabilitation*, 37(15), 1382–1389. <https://doi.org/10.3109/09638288.2014.961661>
- Ibanez, A., Melloni, L., Świeboda, P., Hynes, W., Ikiz, B., Ayadi, R., Thioye, M., Walss-Bass, C., Güntekin, B., Mishra, J., Salama, M., Dunlop, S., Duran-Aniotz, C., & Eyre, H. A. (2024). Neuroecological links of the exposome and One Health. *Neuron*, 112(12), 1905–1910. <https://doi.org/10.1016/j.neuron.2024.04.016>
- Imbalzano, G., Rinaldi, D., Calandra-Buonaura, G., Contin, M., Amato, F., Giannini, G., Sambati, L., Ledda, C., Romagnolo, A., Olmo, G., Cortelli, P., Zibetti, M., Lopiano, L., & Artusi, C. A. (2023). How resistant are levodopa-resistant axial symptoms? Response of freezing, posture, and voice to increasing levodopa intestinal infusion rates in Parkinson disease. *European Journal of Neurology*, 30(1), 96–106. <https://doi.org/10.1111/ene.15558>
- Inoue, K., Tsugawa, Y., Mayeda, E. R., & Ritz, B. (2023). Association of Daily Step Patterns With Mortality in US Adults. *JAMA network open*, 6(3), e235174. <https://doi.org/10.1001/jamanetworkopen.2023.5174>
- Iranzo, A., Cohen De Cock, V., Fantini, M. L., Pérez-Carbonell, L., & Trotti, L. M. (2024). Sleep and sleep disorders in people with Parkinson's disease. *The Lancet. Neurology*, 23(9), 925–937. [https://doi.org/10.1016/S1474-4422\(24\)00170-4](https://doi.org/10.1016/S1474-4422(24)00170-4)
- Ito, D., Kawakami, M., Narita, Y., Yoshida, T., Mori, N., & Kondo, K. (2021). Cognitive Function is a Predictor of the Daily

- Step Count in Patients With Subacute Stroke With Independent Walking Ability: A Prospective Cohort Study. *Archives of Rehabilitation Research and Clinical Translation*, 3(3), 100132. <https://doi.org/10.1016/j.arct.2021.100132>
- Jankovic, J., McDermott, M., Carter, J., Gauthier, S., Goetz, C., Golbe, L., Huber, S., Koller, W., Olanow, C., & Shoulson, I. (1990). Variable expression of Parkinson's disease: A base-line analysis of the DATATOP cohort. The Parkinson Study Group. *Neurology*, 40(10), 1529–1534. <https://doi.org/10.1212/wnl.40.10.1529>
- Jankovic, J. (2005). Motor fluctuations and dyskinesias in Parkinson's disease: Clinical manifestations. *Movement Disorders: Official Journal of the Movement Disorder Society*, 20 Suppl 11, S11–16. <https://doi.org/10.1002/mds.20458>
- Jehu, D. A., Davis, J. C., Madden, K., Parmar, N., & Liu-Ambrose, T. (2022). Minimal Clinically Important Difference of Executive Function Performance in Older Adults Who Fall: A Secondary Analysis of a Randomized Controlled Trial. *Gerontology*, 68(7), 771–779. <https://doi.org/10.1159/000518939>
- Jenkinson, C., Fitzpatrick, R., Peto, V., Greenhall, R., & Hyman, N. (1997). The Parkinson's Disease Questionnaire (PDQ-39): Development and validation of a Parkinson's disease summary index score. *Age and Ageing*, 26(5), 353–357. <https://doi.org/10.1093/ageing/26.5.353>
- Johansson, H., Ekman, U., Rennie, L., Petersson, D. S., Leavy, B., & Franzén, E. (2021). Dual-Task Effects During a Motor-Cognitive Task in Parkinson's Disease: Patterns of Prioritization and the Influence of Cognitive Status. *Neurorehabilitation and Neural Repair*, 35(4), 356–366. <https://doi.org/10.1177/1545968321999053>
- Johansson, H., Folkerts, A.-K., Hammarström, I., Kalbe, E., & Leavy, B. (2023). Effects of motor-cognitive training on dual-task performance in people with Parkinson's disease: A systematic review and meta-analysis. *Journal of Neurology*, 270(6), 2890–2907. <https://doi.org/10.1007/s00415-023-11610-8>
- Johns, M. W. (1991). A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep*, 14(6), 540–545. <https://doi.org/10.1093/sleep/14.6.540>
- Johnston, W., Judice, P. B., Molina García, P., Mühlen, J. M., Lykke Skovgaard, E., Stang, J., Schumann, M., Cheng, S., Bloch, W., Brønd, J. C., Ekelund, U., Grøntved, A., Caulfield, B., Ortega, F. B., & Sardinha, L. B. (2021). Recommendations for determining the validity of consumer wearable and smartphone step count: Expert statement and checklist of the INTERLIVE network. *British Journal of Sports Medicine*, 55(14), 780–793. <https://doi.org/10.1136/bjsports-2020-103147>
- Jost, S. T., Kaldenbach, M.-A., Antonini, A., Martinez-Martin, P., Timmermann, L., Odin, P., Katzenschlager, R., Borgohain, R., Fasano, A., Stocchi, F., Hattori, N., Kukkle, P. L., Rodríguez-Violante, M., Falup-Pecurariu, C., Schade, S., Petry-Schmelzer, J. N., Metta, V., Weintraub, D., Deusch, G., ... International Parkinson and Movement Disorders Society Non-Motor Parkinson Disease Study Group. (2023). Levodopa Dose Equivalency in Parkinson's Disease: Updated Systematic Review and Proposals. *Movement Disorders: Official Journal of the Movement Disorder Society*, 38(7), 1236–1252. <https://doi.org/10.1002/mds.29410>
- Kang, M., Bassett, D. R., Barreira, T. V., Tudor-Locke, C., Ainsworth, B., Reis, J. P., Strath, S., & Swartz, A. (2009). How many days are enough? A study of 365 days of pedometer monitoring. *Research Quarterly for Exercise and Sport*, 80(3), 445–453. <https://doi.org/10.1080/02701367.2009.10599582>
- Kataoka, H., & Ueno, S. (2015). Low FAB score as a predictor of future falling in patients with Parkinson's disease: A 2.5-year prospective study. *Journal of Neurology*, 262(9), 2049–2055. <https://doi.org/10.1007/s00415-015-7814-4>
- Keith, R. A., Granger, C. V., Hamilton, B. B., & Sherwin, F. S. (1987). The functional independence measure: A new tool for rehabilitation. *Advances in Clinical Rehabilitation*, 1, 6–18.
- Kelly, V. E., Eusterbrock, A. J., & Shumway-Cook, A. (2012). A review of dual-

- task walking deficits in people with Parkinson's disease: Motor and cognitive contributions, mechanisms, and clinical implications. *Parkinson's Disease*, 2012, 918719. <https://doi.org/10.1155/2012/918719>
- Kim, D. W., Hassett, L. M., Nguy, V., & Allen, N. E. (2019). A Comparison of Activity Monitor Data from Devices Worn on the Wrist and the Waist in People with Parkinson's Disease. [Place: United States]. *Movement disorders clinical practice*, 6(8), 693–699. <https://doi.org/10.1002/mdc3.12850>
- Kirk, C., Küderle, A., Micó-Amigo, M. E., Bonci, T., Paraschiv-Ionescu, A., Ullrich, M., Soltani, A., Gazit, E., Salis, F., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Brown, P., Buckley, E., Cantu, A., Carsin, A.-E., Caruso, M., Caulfield, B., ... Mobilise-D consortium. (2024). Mobilise-D insights to estimate real-world walking speed in multiple conditions with a wearable device. *Scientific Reports*, 14(1), 1754. <https://doi.org/10.1038/s41598-024-51766-5>
- Kirk, C., Packer, E., Polhemus, A., MacLean, M. K., Bailey, H., Kluge, F., Gaßner, H., Rochester, L., Del Din, S., & Yarnall, A. J. (2025). A systematic review of real-world gait-related digital mobility outcomes in Parkinson's disease [Publisher: Nature Publishing Group]. *npj Digital Medicine*, 8(1), 585. <https://doi.org/10.1038/s41746-025-01938-y>
- Knol, M. J., Pestman, W. R., & Grobbee, D. E. (2011). The (mis)use of overlap of confidence intervals to assess effect modification. *European Journal of Epidemiology*, 26(4), 253–254. <https://doi.org/10.1007/s10654-011-9563-8>
- Koçer, B., Gülşen, Ç., Söke, F., Özcan Gülşen, E., Ersoy, N., Tunca Yılmaz, Ö., & Çomoğlu, S. S. (2023). Comparison of dual-task costs during different types of walking in people with Parkinson's disease: A controlled study. *Acta Neurologica Belgica*, 123(6), 2221–2227. <https://doi.org/10.1007/s13760-023-02271-5>
- Kocer, B., Soke, F., Ataoglu, N. E. E., Ersoy, N., Gulsen, C., Gulsen, E. O., Yasa, M. E., Uysal, I., Comoglu, S. S., & Bora, H. A. T. (2023). The reliability and validity of the 3-m backward walk test in people with Parkinson's disease. *Irish Journal of Medical Science*. <https://doi.org/10.1007/s11845-023-03384-9>
- Koerts, J., König, M., Tucha, L., & Tucha, O. (2016). Working capacity of patients with Parkinson's disease - A systematic review. *Parkinsonism & Related Disorders*, 27, 9–24. <https://doi.org/10.1016/j.parkreldis.2016.03.017>
- Koo, T. K., & Li, M. Y. (2016). A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *Journal of Chiropractic Medicine*, 15(2), 155–163. <https://doi.org/10.1016/j.jcm.2016.02.012>
- Kooner, P., Baskaran, S., Gibbs, V., Wein, S., Dimentberg, R., & Albers, A. (2024). Commercially available activity monitors such as the fitbit charge and apple watch show poor validity in patients with gait aids after total knee arthroplasty. *Journal of Orthopaedic Surgery and Research*, 19(1), 404. <https://doi.org/10.1186/s13018-024-04892-9>
- Kordower, J. H., Olanow, C. W., Dodiya, H. B., Chu, Y., Beach, T. G., Adler, C. H., Halliday, G. M., & Bartus, R. T. (2013). Disease duration and the integrity of the nigrostriatal system in Parkinson's disease. *Brain*, 136(8), 2419–2431. <https://doi.org/10.1093/brain/awt192>
- Kotegawa, K., & Teramoto, W. (2022). Association of executive function capacity with gait motor imagery ability and PFC activity: An fNIRS study. *Neuroscience Letters*, 766, 136350. <https://doi.org/10.1016/j.neulet.2021.136350>
- Kummer, A., Harsányi, E., Dias, F. M. V., Cardoso, F., Caramelli, P., & Teixeira, A. L. (2009). Depression impairs executive functioning in Parkinson disease patients with low educational level. *Cognitive and Behavioral Neurology: Official Journal of the Society for Behavioral and Cognitive Neurology*, 22(3), 167–172. <https://doi.org/10.1097/WNN.0b013e3181b278f9>
- Lai, B., Sasaki, J. E., Jeng, B., Cederberg, K. L., Bamman, M. M., & Motl, R. W. (2020). Accuracy and Precision of Three Consumer-Grade Motion Sensors During Overground and Treadmill Walking in People With Parkinson Disease: Cross-

- Sectional Comparative Study. *JMIR rehabilitation and assistive technologies*, 7(1), e14059. <https://doi.org/10.2196/14059>
- Lamont, R. M., Daniel, H. L., Payne, C. L., & Brauer, S. G. (2018). Accuracy of wearable physical activity trackers in people with Parkinson's disease. [Place: England]. *Gait & posture*, 63, 104–108. <https://doi.org/10.1016/j.gaitpost.2018.04.034>
- Lang, C. E., Holleran, C. L., Strube, M. J., Ellis, T. D., Newman, C. A., Fahey, M., DeAngelis, T. R., Nordahl, T. J., Reisman, D. S., Earhart, G. M., Lohse, K. R., & Bland, M. D. (2023). Improvement in the Capacity for Activity Versus Improvement in Performance of Activity in Daily Life During Outpatient Rehabilitation. *Journal of neurologic physical therapy: JNPT*, 47(1), 16–25. <https://doi.org/10.1097/NPT.0000000000000413>
- Lee, I.-M., Shiroma, E. J., Kamada, M., Bassett, D. R., Matthews, C. E., & Buring, J. E. (2019). Association of Step Volume and Intensity With All-Cause Mortality in Older Women. *JAMA internal medicine*, 179(8), 1105–1112. <https://doi.org/10.1001/jamainternmed.2019.0899>
- Lee, J. A., & Laurson, K. R. (2015). Validity of the SenseWear armband step count measure during controlled and free-living conditions. *Journal of Exercise Science and Fitness*, 13(1), 16–23. <https://doi.org/10.1016/j.jesf.2014.11.002>
- Lee, M., Noh, Y., Youm, C., Kim, S., Park, H., Noh, B., Kim, B., Choi, H., & Yoon, H. (2021). Estimating Health-Related Quality of Life Based on Demographic Characteristics, Questionnaires, Gait Ability, and Physical Fitness in Korean Elderly Adults. *International Journal of Environmental Research and Public Health*, 18(22), 11816. <https://doi.org/10.3390/ijerph182211816>
- Lee, P.-C., Artaud, F., Cormier-Dequaire, F., Rascol, O., Durif, F., Derkinderen, P., Marques, A.-R., Bourdain, F., Brandel, J.-P., Pico, F., Lacomblez, L., Bonnet, C., Brefel-Courbon, C., Ory-Magne, F., Grabli, D., Klebe, S., Mangone, G., You, H., Mesnage, V., ... DIGPD Study Group. (2019). Examining the Reserve Hypothesis in Parkinson's Disease: A Longitudinal Study. *Movement Disorders: Official Journal of the Movement Disorder Society*, 34(11), 1663–1671. <https://doi.org/10.1002/mds.27854>
- Leone, C., Feys, P., Moumdjian, L., D'Amico, E., Zappia, M., & Patti, F. (2017). Cognitive-motor dual-task interference: A systematic review of neural correlates. *Neuroscience and Biobehavioral Reviews*, 75, 348–360. <https://doi.org/10.1016/j.neubiorev.2017.01.010>
- Lexell, J. E., & Downham, D. Y. (2005). How to assess the reliability of measurements in rehabilitation. *American Journal of Physical Medicine & Rehabilitation*, 84(9), 719–723. <https://doi.org/10.1097/01.phm.0000176452.17771.20>
- Li, D., Zhou, L., Cao, Z., Wang, J., Yang, H., Lyu, M., Zhang, Y., Yang, R., Wang, J., Bian, Y., Xu, W., & Wang, Y. (2024). Associations of environmental factors with neurodegeneration: An exposome-wide Mendelian randomization investigation. *Ageing Research Reviews*, 95, 102254. <https://doi.org/10.1016/j.arr.2024.102254>
- Li, S., Lin, Q., Bao, Y., Feng, Y., Li, D., & Zhang, C. (2023). Impaired night-time mobility in patients with Parkinson's disease: A systematic review. *Frontiers in Aging Neuroscience*, 15, 1264143. <https://doi.org/10.3389/fnagi.2023.1264143>
- Lim, S. E. R., Dodds, R., Bacon, D., Sayer, A. A., & Roberts, H. C. (2018). Physical activity among hospitalised older people: Insights from upper and lower limb accelerometry. *Aging Clinical and Experimental Research*, 30(11), 1363–1369. <https://doi.org/10.1007/s40520-018-0930-0>
- Liu, M., Gan, X., Ye, Z., Zhang, Y., He, P., Zhou, C., Yang, S., Zhang, Y., & Qin, X. (2023). Association of accelerometer-measured physical activity intensity, sedentary time, and exercise time with incident Parkinson's disease. *NPJ digital medicine*, 6(1), 224. <https://doi.org/10.1038/s41746-023-00969-7>
- Löhle, M., Timpka, J., Bremer, A., Khodakarami, H., Gandor, F., Horne, M., Ebersbach, G., Odin, P., & Storch, A. (2023). Application of single wrist-wearable accelerometry for objective motor diary assessment in fluctuating Parkinson's disease. *NPJ digital*

- medicine*, 6(1), 194. <https://doi.org/10.1038/s41746-023-00937-1>
- Lord, S., Godfrey, A., Galna, B., Mhiripiri, D., Burn, D., & Rochester, L. (2013a). Ambulatory activity in incident Parkinson's: More than meets the eye? *Journal of Neurology*, 260(12), 2964–2972. <https://doi.org/10.1007/s00415-013-7037-5>
Export Date: 14 April 2025; Cited By: 135.
- Lord, S., Galna, B., Coleman, S., Burn, D., & Rochester, L. (2013). Mild depressive symptoms are associated with gait impairment in early Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(5), 634–639. <https://doi.org/10.1002/mds.25338>
- Lord, S., Galna, B., Verghese, J., Coleman, S., Burn, D., & Rochester, L. (2013). Independent domains of gait in older adults and associated motor and nonmotor attributes: Validation of a factor analysis approach. *The Journals of Gerontology: Series A, Biological Sciences and Medical Sciences*, 68(7), 820–827. <https://doi.org/10.1093/gerona/gls255>
- Lord, S., Godfrey, A., Galna, B., Mhiripiri, D., Burn, D., & Rochester, L. (2013b). Ambulatory activity in incident Parkinson's: More than meets the eye? *Journal of Neurology*, 260(12), 2964–2972. <https://doi.org/10.1007/s00415-013-7037-5>
- Louter, M., Munneke, M., Bloem, B. R., & Overeem, S. (2012). Nocturnal hypokinesia and sleep quality in Parkinson's disease. *Journal of the American Geriatrics Society*, 60(6), 1104–1108. <https://doi.org/10.1111/j.1532-5415.2012.03966.x>
- Louter, M., van Sloun, R. J. G., Pevernagie, D. A. A., Arends, J. B. A. M., Cluitmans, P. J., Bloem, B. R., & Overeem, S. (2013). Subjectively impaired bed mobility in Parkinson disease affects sleep efficiency. *Sleep Medicine*, 14(7), 668–674. <https://doi.org/10.1016/j.sleep.2013.03.010>
- Lüdecke, D., Ben-Shachar, M. S., Patil, I., Waggoner, P., & Makowski, D. (2021). Performance: An R Package for Assessment, Comparison and Testing of Statistical Models. *Journal of Open Source Software*, 6(60), 3139. <https://doi.org/10.21105/joss.03139>
- Ma, Y., Zhang, Y., Li, R., Cheng, W., & Wu, F. (2025). The experience and perception of wearable devices in Parkinson's disease patients: A systematic review and meta-synthesis of qualitative studies. *Journal of Neurology*, 272(5), 350. <https://doi.org/10.1007/s00415-025-13085-1>
- MacKinnon, C. D. (2018). Sensorimotor anatomy of gait, balance, and falls. *Handbook of Clinical Neurology*, 159, 3–26. <https://doi.org/10.1016/B978-0-444-63916-5.00001-X>
- Maetzler, W., Domingos, J., Srulijes, K., Ferreira, J. J., & Bloem, B. R. (2013). Quantitative wearable sensors for objective assessment of Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(12), 1628–1637. <https://doi.org/10.1002/mds.25628>
- Maetzler, W., Rochester, L., Bhidayasiri, R., Espay, A. J., Sánchez-Ferro, A., & van Uem, J. M. (2021). Modernizing Daily Function Assessment in Parkinson's Disease Using Capacity, Perception, and Performance Measures [eprint: <https://onlinelibrary.wiley.com/doi/pdf/10.1002/mds.28377>]. *Movement Disorders*, 36(1), 76–82. <https://doi.org/10.1002/mds.28377>
- Maggi, G., D'Iorio, A., Aiello, E. N., Poletti, B., Ticozzi, N., Silani, V., Amboni, M., Vitale, C., & Santangelo, G. (2023). Psychometrics and diagnostics of the Italian version of the Beck Depression Inventory-II (BDI-II) in Parkinson's disease. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 44(5), 1607–1612. <https://doi.org/10.1007/s10072-023-06619-w>
- Maggioni, M. A., Veicsteinas, A., Rampichini, S., Cè, E., Nemni, R., Riboldazzi, G., & Merati, G. (2012). Energy cost of spontaneous walking in Parkinson's disease patients. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 33(4), 779–784. <https://doi.org/10.1007/s10072-011-0827-6>
- Maidan, I., Bernad-Elazari, H., Giladi, N., Hausdorff, J. M., & Mirelman, A. (2017). When is Higher Level Cognitive Control

- Needed for Locomotor Tasks Among Patients with Parkinson's Disease? *Brain Topography*, 30(4), 531–538. <https://doi.org/10.1007/s10548-017-0564-0>
- Malaty, I., Vaou, E. O., Hauser, R. A., Bergmans, B., Odin, P., Shah, M., Bergmann, L., Harmer, L., Gupta, R., & Chaudhuri, K. R. (2025). Correlation between sleep and quality of life in people with Parkinson's disease treated with continuous subcutaneous infusion of foslevodopa/foscarbidopa. *Parkinsonism & Related Disorders*, 134, 107599. <https://doi.org/10.1016/j.parkreldis.2025.107599>
- Mancini, M., El-Gohary, M., Pearson, S., McNames, J., Schlueter, H., Nutt, J. G., King, L. A., & Horak, F. B. (2015). Continuous monitoring of turning in Parkinson's disease: Rehabilitation potential. *NeuroRehabilitation*, 37(1), 3–10. <https://doi.org/10.3233/NRE-151236>
- Mancini, M., Hausdorff, J. M., Pelosin, E., Bonato, P., Camicioli, R., Ellis, T. D., Klucken, J., Gifford, L., Fasano, A., Nieuwboer, A., Kopil, C., Klapper, K., Kirsch, L., Dexter, D. T., Fuest, R., Miller, V., Asis, A., Müller, M. L., Stephenson, D., & Mirelman, A. (2025). A framework to standardize gait study protocols in Parkinson's disease. *Journal of Parkinson's Disease*, 15(1), 129–139. <https://doi.org/10.1177/1877718X241305626>
- Mancini, M., McKay, J. L., Cockx, H., D'Cruz, N., Esper, C. D., Filtjens, B., Heimler, B., MacKinnon, C. D., Palmerini, L., Roerdink, M., Young, W. R., Hausdorff, J. M., & ICFOG Investigators. (2025). Technology for measuring freezing of gait: Current state of the art and recommendations. *Journal of Parkinson's Disease*, 15(1), 19–40. <https://doi.org/10.1177/1877718X241301065>
- Mancini, M., Schlueter, H., El-Gohary, M., Mattek, N., Duncan, C., Kaye, J., & Horak, F. B. (2016). Continuous Monitoring of Turning Mobility and Its Association to Falls and Cognitive Function: A Pilot Study. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 71(8), 1102–1108. <https://doi.org/10.1093/gerona/glw019>
- Mantese, C. E., Schumacher-Schuh, A., & Rieder, C. R. M. (2018). Clinimetrics of the 9- and 19-Item Wearing-Off Questionnaire: A Systematic Review. *Parkinson's Disease*, 2018, 5308491. <https://doi.org/10.1155/2018/5308491>
- Mantese, C. E., Medeiros, M., Schumacher-Schuh, A., & Rieder, C. R. d. M. (2020). Validation of 19-items wearing-off (WOQ-19) questionnaire to Portuguese. *Arquivos De Neuro-Psiquiatria*, 78(10), 624–628. <https://doi.org/10.1590/0004-282X20200045>
- Mantri, S., Wood, S., Duda, J., & Morley, J. (2019). Comparing self-reported and objective monitoring of physical activity in Parkinson disease. *Parkinsonism and Related Disorders*, 67, 56–59. <https://doi.org/10.1016/j.parkreldis.2019.09.004>
Export Date: 14 April 2025; Cited By: 36.
- Martikainen, K. K., Luukkaala, T. H., & Marttila, R. J. (2006). Parkinson's disease and working capacity. *Movement Disorders: Official Journal of the Movement Disorder Society*, 21(12), 2187–2191. <https://doi.org/10.1002/mds.21171>
- Martinez-Martin, P., Rodriguez-Blazquez, C., & Frades-Payo, B. (2008). Specific patient-reported outcome measures for Parkinson's disease: Analysis and applications. *Expert Review of Pharmacoeconomics & Outcomes Research*, 8(4), 401–418. <https://doi.org/10.1586/14737167.8.4.401>
- Martínez-Martín, P., Rodríguez-Blázquez, C., Mario Alvarez, n., Arakaki, T., Arillo, V. C., Chaná, P., Fernández, W., Garretto, N., Martínez-Castrillo, J. C., Rodríguez-Violante, M., Serrano-Dueñas, M., Ballesteros, D., Rojo-Abuin, J. M., Chaudhuri, K. R., & Merello, M. (2015). Parkinson's disease severity levels and MDS-Unified Parkinson's Disease Rating Scale. *Parkinsonism & Related Disorders*, 21(1), 50–54. <https://doi.org/10.1016/j.parkreldis.2014.10.026>
- Master, H., Annis, J., Huang, S., Beckman, J. A., Ratsimbazafy, F., Marginean, K., Carroll, R., Natarajan, K., Harrell, F. E., Roden, D. M., Harris, P., & Brittain, E. L. (2022). Association of step counts over time with the risk of chronic disease in the All of Us Research Program. *Nature Medicine*, 28(11), 2301–2308. <https://doi.org/10.1038/s41591-022-02012-w>

- Mate, K. K., & Mayo, N. E. (2020). Clinically Assessed Walking Capacity Versus Real-World Walking Performance in People with Multiple Sclerosis. *International Journal of MS Care*, 22(3), 143–150. <https://doi.org/10.7224/1537-2073.2019-047>
- Matsumoto, H., Sengoku, R., Saito, Y., Kakuta, Y., Murayama, S., & Imafuku, I. (2014). Sudden death in Parkinson's disease: A retrospective autopsy study. *Journal of the Neurological Sciences*, 343(1-2), 149–152. <https://doi.org/10.1016/j.jns.2014.05.060>
- Matthews, C. E., Ainsworth, B. E., Thompson, R. W., & Bassett, D. R. (2002). Sources of variance in daily physical activity levels as measured by an accelerometer. *Medicine and Science in Sports and Exercise*, 34(8), 1376–1381. <https://doi.org/10.1097/00005768-200208000-00021>
- Mattison, G., Canfell, O., Forrester, D., Dobbins, C., Smith, D., Töyräs, J., & Sullivan, C. (2022). The Influence of Wearables on Health Care Outcomes in Chronic Disease: Systematic Review. *Journal of Medical Internet Research*, 24(7), e36690. <https://doi.org/10.2196/36690>
- Mayeli, M., Shafie, M., Shiravi, M., Adl Parvar, T., Mirsepassi, Z., Rahiminejad, F., Sattarpour, R., & Aghamollaii, V. (2024). Depression is associated with the nonmotor symptoms of Parkinson's disease: A comparative analysis. *Health Science Reports*, 7(5), e2106. <https://doi.org/10.1002/hsr.2.2106>
- Mayo, N. E., & Mate, K. K. V. (2022). Quantifying Mobility in Quality of Life. In K. Wac & S. Wulfovich (Eds.), *Quantifying Quality of Life: Incorporating Daily Life into Medicine* (pp. 119–136). Springer International Publishing. https://doi.org/10.1007/978-3-030-94212-0_5
- Mazzà, C., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Bonci, T., Brown, P., Brozgol, M., Buckley, E., Carsin, A.-E., Caruso, M., Caulfield, B., Cereatti, A., Chiari, L., Chynkiamis, N., Ciravegna, F., Del Din, S., Eskofier, B., Evers, J., ... Rochester, L. (2021). Technical validation of real-world monitoring of gait: A multicentric observational study. *BMJ open*, 11(12), e050785. <https://doi.org/10.1136/bmjopen-2021-050785>
- Mc Ardle, R., Del Din, S., Morris, R., Alcock, L., Yarnall, A. J., Burn, D. J., Rochester, L., Lawson, R. A., & On Behalf Of The Icicle-Pd Study Group, n. (2022). Factors Influencing Habitual Physical Activity in Parkinson's Disease: Considering the Psychosocial State and Wellbeing of People with Parkinson's and Their Carers. *Sensors (Basel, Switzerland)*, 22(3), 871. <https://doi.org/10.3390/s22030871>
- McLeod, L. D., Coon, C. D., Martin, S. A., Fehnel, S. E., & Hays, R. D. (2011). Interpreting patient-reported outcome results: US FDA guidance and emerging methods. *Expert Review of Pharmacoeconomics & Outcomes Research*, 11(2), 163–169. <https://doi.org/10.1586/erp.11.12>
- Mehdizadeh, M., Martinez-Martin, P., Habibi, S.-A., Fereshtehnejad, S.-M., Abasi, A., Niazi Khatoun, J., Saneii, S. H., & Taghizadeh, G. (2019). Reliability and Validity of Fall Efficacy Scale-International in People with Parkinson's Disease during On- and Off-Drug Phases. *Parkinson's Disease*, 2019, 6505232. <https://doi.org/10.1155/2019/6505232>
- Michels, J., Werner, C. J., Schumann-Werner, B., Schulz, J. B., Costa, A. S., & Reetz, K. (2022). Why cognitive training is important for the health status in Parkinson's disease: Preliminary evidence from a clinical three-weeks multidisciplinary intervention. *Neurological Research and Practice*, 4(1), 47. <https://doi.org/10.1186/s42466-022-00210-y>
- Micó-Amigo, M. E., Bonci, T., Paraschiv-Ionescu, A., Ullrich, M., Kirk, C., Soltani, A., Küderle, A., Gazit, E., Salis, F., Alcock, L., Aminian, K., Becker, C., Bertuletti, S., Brown, P., Buckley, E., Cantu, A., Carsin, A.-E., Caruso, M., Caulfield, B., ... Mobilise-D consortium. (2023). Assessing real-world gait with digital technology? Validation, insights and recommendations from the Mobilise-D consortium. *Journal of Neuroengineering and Rehabilitation*, 20(1), 78. <https://doi.org/10.1186/s12984-023-01198-5>
- Mikolaizak, A. S., Rochester, L., Maetzler, W., Sharrack, B., Demeyer, H., Mazzà, C., Caulfield, B., Garcia-Aymerich, J., Vereijken, B., Arnera, V., Miller, R., Piraino, P., Ammour, N., Gordon, M. F., Troost-

- ers, T., Yarnall, A. J., Alcock, L., Gaßner, H., Winkler, J., ... clinical validation study (WP4) on behalf of Mobilise-D consortium. (2022). Connecting real-world digital mobility assessment to clinical outcomes for regulatory and clinical endorsement—the Mobilise-D study protocol. *PloS One*, 17(10), e0269615. <https://doi.org/10.1371/journal.pone.0269615>
- Milane, T., Hansen, C., Chardon, M., Bianchini, E., & Vuillerme, N. (2023). Comparing Backward Walking Performance in Parkinson's Disease with and without Freezing of Gait-A Systematic Review. *International Journal of Environmental Research and Public Health*, 20(2), 953. <https://doi.org/10.3390/ijerph20020953>
- Milane, T., Hansen, C., Correno, M. B., Chardon, M., Barbieri, F. A., Bianchini, E., & Vuillerme, N. (2024a). Comparison of sleep characteristics between Parkinson's disease with and without freezing of gait: A systematic review. *Sleep Medicine*, 114, 24–41. <https://doi.org/10.1016/j.sleep.2023.11.021>
- Milane, T., Hansen, C., Correno, M. B., Chardon, M., Barbieri, F. A., Bianchini, E., & Vuillerme, N. (2024b). Comparison of number of people with freezing of gait in Parkinson's disease with and without sleep disturbances: A systematic review. *Sleep Medicine*, 121, 32–41. <https://doi.org/10.1016/j.sleep.2024.06.001>
- Milane, T., Vuillerme, N., Petit, P., Warmerdam, E., Romijnders, R., Bianchini, E., Maetzler, W., & Hansen, C. (2025). Impact of forward and backward walking on gait parameters across parkinson's disease stages and severity: A prospective observational study. *BMC Neurology*, 25(1), 379. <https://doi.org/10.1186/s12883-025-04321-2>
- Miller-Patterson, C., Buesa, R., McLaughlin, N., Jones, R., Akbar, U., & Friedman, J. H. (2018). Motor asymmetry over time in Parkinson's disease. *Journal of the Neurological Sciences*, 393, 14–17. <https://doi.org/10.1016/j.jns.2018.08.001>
- Mirelman, A., Bonato, P., Camicioli, R., Ellis, T. D., Giladi, N., Hamilton, J. L., Hass, C. J., Hausdorff, J. M., Pelosin, E., & Almeida, Q. J. (2019). Gait impairments in Parkinson's disease. *The Lancet. Neurology*, 18(7), 697–708. [https://doi.org/10.1016/S1474-4422\(19\)30044-4](https://doi.org/10.1016/S1474-4422(19)30044-4)
- Mirelman, A., Hillel, I., Rochester, L., Del Din, S., Bloem, B. R., Avanzino, L., Nieuwboer, A., Maidan, I., Herman, T., Thaler, A., Gurevich, T., Kestenbaum, M., Orr-Urtreger, A., Brys, M., Cedarbaum, J. M., Giladi, N., & Hausdorff, J. M. (2020). Tossing and Turning in Bed: Nocturnal Movements in Parkinson's Disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 35(6), 959–968. <https://doi.org/10.1002/mds.28006>
- Mirelman, A., Maidan, I., Herman, T., Deutsch, J. E., Giladi, N., & Hausdorff, J. M. (2011). Virtual reality for gait training: Can it induce motor learning to enhance complex walking and reduce fall risk in patients with Parkinson's disease? *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 66(2), 234–240. <https://doi.org/10.1093/gerona/glq201>
- Mirelman, A., Volkov, J., Salomon, A., Gazit, E., Nieuwboer, A., Rochester, L., Del Din, S., Avanzino, L., Pelosin, E., Bloem, B. R., Della Croce, U., Cereatti, A., Thaler, A., Roggen, D., Mazza, C., Shirvan, J., Cedarbaum, J. M., Giladi, N., & Hausdorff, J. M. (2024). Digital Mobility Measures: A Window into Real-World Severity and Progression of Parkinson's Disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 39(2), 328–338. <https://doi.org/10.1002/mds.29689>
- Mirelman, A., Weiss, A., Buchman, A. S., Bennett, D. A., Giladi, N., & Hausdorff, J. M. (2014). Association between performance on Timed Up and Go subtasks and mild cognitive impairment: Further insights into the links between cognitive and motor function. *Journal of the American Geriatrics Society*, 62(4), 673–678. <https://doi.org/10.1111/jgs.12734>
- Mokkink, L. B., Terwee, C. B., Patrick, D. L., Alonso, J., Stratford, P. W., Knol, D. L., Bouter, L. M., & de Vet, H. C. W. (2010). The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: An international Delphi study. *Quality of Life Research: An International Journal of Quality of Life As-*

- pects of Treatment, Care and Rehabilitation*, 19(4), 539–549. <https://doi.org/10.1007/s11136-010-9606-8>
- Moreau, C., Rouaud, T., Grabli, D., Benatru, I., Remy, P., Marques, A.-R., Drapier, S., Mariani, L.-L., Roze, E., Devos, D., Dupont, G., Bereau, M., & Fabbri, M. (2023). Overview on wearable sensors for the management of Parkinson's disease. *NPJ Parkinson's disease*, 9(1), 153. <https://doi.org/10.1038/s41531-023-00585-y>
- Morgan, C., Jameson, J., Craddock, I., Tonkin, E. L., Oikonomou, G., Isotalus, H. K., Heidarvinch, F., McConville, R., Tourte, G. J. L., Kinnunen, K. M., & Whone, A. (2022). Understanding how people with Parkinson's disease turn in gait from a real-world in-home dataset. *Parkinsonism & Related Disorders*, 105, 114–122. <https://doi.org/10.1016/j.parkreldis.2022.11.007>
- Morris, R., Martini, D. N., Madhyastha, T., Kelly, V. E., Grabowski, T. J., Nutt, J., & Horak, F. (2019). Overview of the cholinergic contribution to gait, balance and falls in Parkinson's disease. *Parkinsonism & Related Disorders*, 63, 20–30. <https://doi.org/10.1016/j.parkreldis.2019.02.017>
- Morris, R., Martini, D. N., Smulders, K., Kelly, V. E., Zabetian, C. P., Poston, K., Hiller, A., Chung, K. A., Yang, L., Hu, S.-C., Edwards, K. L., Cholerton, B., Grabowski, T. J., Montine, T. J., Quinn, J. F., & Horak, F. (2019). Cognitive associations with comprehensive gait and static balance measures in Parkinson's disease. *Parkinsonism & Related Disorders*, 69, 104–110. <https://doi.org/10.1016/j.parkreldis.2019.06.014>
- Motl, R. W., Pilutti, L. A., Learmonth, Y. C., Goldman, M. D., & Brown, T. (2013). Clinical importance of steps taken per day among persons with multiple sclerosis. *PLoS One*, 8(9), e73247. <https://doi.org/10.1371/journal.pone.0073247>
- Motl, R. W., Zhu, W., Park, Y., McAuley, E., Scott, J. A., & Snook, E. M. (2007). Reliability of scores from physical activity monitors in adults with multiple sclerosis. *Adapted physical activity quarterly: APAQ*, 24(3), 245–253. <https://doi.org/10.1123/apaq.24.3.245>
- Mudge, S., Stott, N. S., & Walt, S. E. (2007). Criterion validity of the StepWatch Activity Monitor as a measure of walking activity in patients after stroke. *Archives of Physical Medicine and Rehabilitation*, 88(12), 1710–1715. <https://doi.org/10.1016/j.apmr.2007.07.039>
- Nagaki, K., Fujioka, S., Sasai, H., Yamaguchi, Y., & Tsuboi, Y. (2022). Physical Activity and Its Diurnal Fluctuations Vary by Non-Motor Symptoms in Patients with Parkinson's Disease: An Exploratory Study. *Healthcare (Basel, Switzerland)*, 10(4), 749. <https://doi.org/10.3390/healthcare10040749>
- Nakagata, T., Murakami, H., Kawakami, R., Tripette, J., Nakae, S., Yamada, Y., Ishikawa-Takata, K., Tanaka, S., & Miyachi, M. (2022). Step-count outcomes of 13 different activity trackers: Results from laboratory and free-living experiments. *Gait & Posture*, 98, 24–33. <https://doi.org/10.1016/j.gaitpost.2022.08.004>
- Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53(4), 695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>
- Nemanich, S. T., Duncan, R. P., Dibble, L. E., Cavanaugh, J. T., Ellis, T. D., Ford, M. P., Foreman, K. B., & Earhart, G. M. (2013). Predictors of Gait Speeds and the Relationship of Gait Speeds to Falls in Men and Women with Parkinson Disease. *Parkinson's Disease*, 2013, 141720. <https://doi.org/10.1155/2013/141720>
- Nieuwboer, A., Rochester, L., Herman, T., Vandenberghe, W., Emil, G. E., Thomaes, T., & Giladi, N. (2009). Reliability of the new freezing of gait questionnaire: Agreement between patients with Parkinson's disease and their carers. *Gait & Posture*, 30(4), 459–463. <https://doi.org/10.1016/j.gaitpost.2009.07.108>
- Nóbrega-Sousa, P., Gobbi, L. T. B., Orcioli-Silva, D., Conceição, N. R. d., Beretta, V. S., & Vitorio, R. (2020). Prefrontal Cortex Activity During Walking: Effects of Aging and Associations With Gait and Executive Func-

- tion. *Neurorehabilitation and Neural Repair*, 34(10), 915–924. <https://doi.org/10.1177/1545968320953824>
- Norris, M., Anderson, R., Motl, R. W., Hayes, S., & Coote, S. (2017). Minimum number of days required for a reliable estimate of daily step count and energy expenditure, in people with MS who walk unaided. *Gait & Posture*, 53, 201–206. <https://doi.org/10.1016/j.gaitpost.2017.02.005>
- Nutt, J. G., Siderowf, A. D., Guttman, M., Schmidt, P. N., Zamudio, J. I., Wu, S. S., Okun, M. S., Simuni, T., Parashos, S. A., Dahodwala, N. A., Davis, T. L., Giladi, N., Gurevich, T., Hauser, R. A., Jankovic, J., Lyons, K. E., Marsh, L., Miyasaki, J. M., Morgan, J. C., ... Nelson, E. C. (2014). Mobility, mood and site of care impact health related quality of life in Parkinson's disease. *Parkinsonism & Related Disorders*, 20(3), 274–279. <https://doi.org/10.1016/j.parkreldis.2013.10.004>
- Nutt, J. G., Bloem, B. R., Giladi, N., Hallett, M., Horak, F. B., & Nieuwboer, A. (2011). Freezing of gait: Moving forward on a mysterious clinical phenomenon. *The Lancet. Neurology*, 10(8), 734–744. [https://doi.org/10.1016/S1474-4422\(11\)70143-0](https://doi.org/10.1016/S1474-4422(11)70143-0)
- Nwogo, R. O., Kammermeier, S., & Singh, A. (2022). Abnormal neural oscillations during gait and dual-task in Parkinson's disease. *Frontiers in Systems Neuroscience*, 16, 995375. <https://doi.org/10.3389/fnsys.2022.995375>
- O' Donnell, D., Moriarty, F., Lavan, A., Kenny, R. A., & Briggs, R. (2025). The Association Between Psychotropic Medication Use and Gait and Mobility Impairment in Community-Dwelling Older People: Data From The Irish Longitudinal Study on Ageing (TILDA). *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 80(5), glae263. <https://doi.org/10.1093/gerona/glae263>
- O'Gorman Tuura, R. L., Baumann, C. R., & Baumann-Vogel, H. (2018). Beyond Dopamine: GABA, Glutamate, and the Axial Symptoms of Parkinson Disease. *Frontiers in Neurology*, 9, 806. <https://doi.org/10.3389/fneur.2018.00806>
- Organization, W. H. (2002). Towards a common language for functioning, disability, and health : ICF [Publisher: World Health Organization]. *The International Classification of Functioning, Disability and Health*. Retrieved May 30, 2025, from <https://cir.nii.ac.jp/crid/1573668925447490176>
- Ortega-Bastidas, P., Gómez, B., Aqueveque, P., Luarte-Martínez, S., & Cano-de-la-Cuerda, R. (2023). Instrumented Timed Up and Go Test (iTUG)-More Than Assessing Time to Predict Falls: A Systematic Review. *Sensors (Basel, Switzerland)*, 23(7), 3426. <https://doi.org/10.3390/s23073426>
- Outeiro, T. F., Alcalay, R. N., Antonini, A., Attems, J., Bonifati, V., Cardoso, F., Chesselet, M.-F., Hardy, J., Madeo, G., McKeith, I., Mollenhauer, B., Moore, D. J., Rascol, O., Schlossmacher, M. G., Soreq, H., Stefanis, L., & Ferreira, J. J. (2023). Defining the Riddle in Order to Solve It: There Is More Than One "Parkinson's Disease". *Movement Disorders: Official Journal of the Movement Disorder Society*, 38(7), 1127–1142. <https://doi.org/10.1002/mds.29419>
- Oyama, G., Burq, M., Hatano, T., Marks, W. J., Kapur, R., Fernandez, J., Fujikawa, K., Furusawa, Y., Nakatome, K., Rainaldi, E., Chen, C., Ho, K. C., Ogawa, T., Kamo, H., Oji, Y., Takeshige-Amano, H., Taniguchi, D., Nakamura, R., Sasaki, F., ... Hattori, N. (2023). Analytical and clinical validity of wearable, multi-sensor technology for assessment of motor function in patients with Parkinson's disease in Japan. *Scientific Reports*, 13(1), 3600. <https://doi.org/10.1038/s41598-023-29382-6>
- Packer, E., DeBelle, H., Bailey, H. G. B., Rehman, R. Z. U., Yarnall, A. J., Rochester, L., Alcock, L., & Del Din, S. (2025). Systematic review of wearables assessing medication effect on motor function and symptoms in Parkinson's disease. *NPJ Parkinson's disease*, 11(1), 135. <https://doi.org/10.1038/s41531-025-00943-y>
- Paker, N., Bugdayci, D., Goksenoglu, G., Demircioğlu, D. T., Kesiktaş, N., & Ince, N. (2015). Gait speed and related factors in Parkinson's disease. *Journal of Physical Therapy Science*, 27(12), 3675–3679. <https://doi.org/10.1589/jpts.27.3675>

- Paluch, A. E., Bajpai, S., Bassett, D. R., Carnethon, M. R., Ekelund, U., Evenson, K. R., Galuska, D. A., Jefferis, B. J., Kraus, W. E., Lee, I.-M., Matthews, C. E., Omura, J. D., Patel, A. V., Pieper, C. F., Rees-Punia, E., Dallmeier, D., Klenk, J., Whincup, P. H., Dooley, E. E., ... Fulton, J. E. (2022). Daily steps and all-cause mortality: A meta-analysis of 15 international cohorts [Publisher: Elsevier]. *The Lancet Public Health*, 7(3), e219–e228. [https://doi.org/10.1016/S2468-2667\(21\)00302-9](https://doi.org/10.1016/S2468-2667(21)00302-9)
- Paluch, A. E., Gabriel, K. P., Fulton, J. E., Lewis, C. E., Schreiner, P. J., Sternfeld, B., Sidney, S., Siddique, J., Whitaker, K. M., & Carnethon, M. R. (2021). Steps per Day and All-Cause Mortality in Middle-aged Adults in the Coronary Artery Risk Development in Young Adults Study. *JAMA network open*, 4(9), e2124516. <https://doi.org/10.1001/jamanetworkopen.2021.24516>
- Paul, S. S., Ellis, T. D., Dibble, L. E., Earhart, G. M., Ford, M. P., Foreman, K. B., & Cavanaugh, J. T. (2016). Obtaining Reliable Estimates of Ambulatory Physical Activity in People with Parkinson's Disease. *Journal of Parkinson's Disease*, 6(2), 301–305. <https://doi.org/10.3233/JPD-160791>
- Pecoraro, P. M., Marsili, L., Espay, A. J., Bologna, M., & di Biase, L. (2025). Computer Vision Technologies in Movement Disorders: A Systematic Review. *Movement Disorders Clinical Practice*. <https://doi.org/10.1002/mdc3.70123>
- Pedersen, B. S., Kristensen, M. T., Josefsen, C. O., Lykkegaard, K. L., Jønsson, L. R., & Pedersen, M. M. (2022). Validation of Two Activity Monitors in Slow and Fast Walking Hospitalized Patients. *Rehabilitation Research and Practice*, 2022, 9230081. <https://doi.org/10.1155/2022/9230081>
- Perera, S., Mody, S. H., Woodman, R. C., & Studenski, S. A. (2006). Meaningful change and responsiveness in common physical performance measures in older adults. *Journal of the American Geriatrics Society*, 54(5), 743–749. <https://doi.org/10.1111/j.1532-5415.2006.00701.x>
- Peters, D. M., O'Brien, E. S., Kamrud, K. E., Roberts, S. M., Rooney, T. A., Thibodeau, K. P., Balakrishnan, S., Gell, N., & Mohapatra, S. (2021). Utilization of wearable technology to assess gait and mobility post-stroke: A systematic review. *Journal of Neuroengineering and Rehabilitation*, 18(1), 67. <https://doi.org/10.1186/s12984-021-00863-x>
- Peterson, D. S., & Horak, F. B. (2016). Neural Control of Walking in People with Parkinsonism. *Physiology (Bethesda, Md.)*, 31(2), 95–107. <https://doi.org/10.1152/physiol.00034.2015>
- Peto, V., Jenkinson, C., Fitzpatrick, R., & Greenhall, R. (1995). The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, 4(3), 241–248. <https://doi.org/10.1007/BF02260863>
- Pilotto, A., Rizzardi, A., Zatti, C., Hansen, C., Donini, A., Romijnders, R., Maetzler, W., & Padovani, A. (2023). Unsupervised but not supervised gait parameters are related to fatigue in Parkinson's disease: A pilot study. *Frontiers in Aging Neuroscience*, 15, 1279722. <https://doi.org/10.3389/fnagi.2023.1279722>
- Poewe, W., Seppi, K., Tanner, C. M., Halliday, G. M., Brundin, P., Volkman, J., Schrag, A.-E., & Lang, A. E. (2017). Parkinson disease. *Nature Reviews. Disease Primers*, 3, 17013. <https://doi.org/10.1038/nrdp.2017.13>
- Politis, M., & Niccolini, F. (2015). Serotonin in Parkinson's disease. *Behavioural Brain Research*, 277, 136–145. <https://doi.org/10.1016/j.bbr.2014.07.037>
- Pongmala, C., Stonsaovapak, C., van Emde Boas, M., & Bohnen, N. I. (2025). Differential associations between retro walking versus forward walking, axial motor features and body composition in Parkinson's disease. *Parkinsonism & Related Disorders*, 137, 107924. <https://doi.org/10.1016/j.parkreldis.2025.107924>
- Porta, M., Pilloni, G., Aripa, F., Casula, C., Cossu, G., & Pau, M. (2019). Similarities and Differences of Gait Patterns in Women and Men With Parkinson Disease With Mild Disability. *Archives of Physical Medicine and Rehabilitation*, 100(11), 2039–

2045. <https://doi.org/10.1016/j.apmr.2019.04.010>
- Postuma, R. B., Berg, D., Stern, M., Poewe, W., Olanow, C. W., Oertel, W., Obeso, J., Marek, K., Litvan, I., Lang, A. E., Halliday, G., Goetz, C. G., Gasser, T., Dubois, B., Chan, P., Bloem, B. R., Adler, C. H., & Deuschl, G. (2015). MDS clinical diagnostic criteria for Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 30(12), 1591–1601. <https://doi.org/10.1002/mds.26424>
- Powers, R., Etezadi-Amoli, M., Arnold, E. M., Kianian, S., Mance, I., Gibiansky, M., Trietsch, D., Alvarado, A. S., Kretlow, J. D., Herrington, T. M., Brillman, S., Huang, N., Lin, P. T., Pham, H. A., & Ullal, A. V. (2021). Smartwatch inertial sensors continuously monitor real-world motor fluctuations in Parkinson's disease. *Science Translational Medicine*, 13(579), eabd7865. <https://doi.org/10.1126/scitranslmed.abd7865>
- Prakash, K. M., Nadkarni, N. V., Lye, W.-K., Yong, M.-H., & Tan, E.-K. (2016). The impact of non-motor symptoms on the quality of life of Parkinson's disease patients: A longitudinal study. *European Journal of Neurology*, 23(5), 854–860. <https://doi.org/10.1111/ene.12950>
- Prange, S., Danaila, T., Laurencin, C., Caire, C., Metereau, E., Merle, H., Broussole, E., Maucourt-Boulch, D., & Thobois, S. (2019). Age and time course of long-term motor and nonmotor complications in Parkinson disease. *Neurology*, 92(2), e148–e160. <https://doi.org/10.1212/WNL.0000000000006737>
- Prime, M., McKay, J. L., Bay, A., Hart, A., Kim, C., Abraham, A., & Hackney, M. E. (2020). Differentiating Parkinson Disease Subtypes Using Clinical Balance Measures. *Journal of neurologic physical therapy : JNPT*, 44(1), 34–41. <https://doi.org/10.1097/NPT.0000000000000297>
- Ray Chaudhuri, K., Leta, V., Bannister, K., Brooks, D. J., & Svenningsson, P. (2023). The noradrenergic subtype of Parkinson disease: From animal models to clinical practice. *Nature Reviews. Neurology*, 19(6), 333–345. <https://doi.org/10.1038/s41582-023-00802-5>
- Ray Chaudhuri, K., Poewe, W., & Brooks, D. (2018). Motor and Nonmotor Complications of Levodopa: Phenomenology, Risk Factors, and Imaging Features. *Movement Disorders: Official Journal of the Movement Disorder Society*, 33(6), 909–919. <https://doi.org/10.1002/mds.27386>
- Revicki, D., Hays, R. D., Cella, D., & Sloan, J. (2008). Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *Journal of Clinical Epidemiology*, 61(2), 102–109. <https://doi.org/10.1016/j.jclinepi.2007.03.012>
- Rizos, A., Martinez-Martin, P., Odin, P., Antonini, A., Kessel, B., Kozul, T. K., Todorova, A., Douiri, A., Martin, A., Stocchi, F., Dietrichs, E., Chaudhuri, K. R., & EUROPAR and the IPDMDS non-Motor PD Study Group. (2014). Characterizing motor and non-motor aspects of early-morning off periods in Parkinson's disease: An international multicenter study. *Parkinsonism & Related Disorders*, 20(11), 1231–1235. <https://doi.org/10.1016/j.parkreldis.2014.09.013>
- Romijnders, R., Atrsaei, A., Rehman, R. Z. U., Strehlow, L., Massoud, J., Hinchliffe, C., Macrae, V., Emmert, K., Reilmann, R., Janneke van der Woude, C., Van Gassen, G., Baribaud, F., Ahmaniemi, T., Chatterjee, M., Vitturi, B. K., Pinaud, C., Kalifa, J., Avey, S., Ng, W.-F., ... Maetzler, W. (2025). Association of real life postural transitions kinematics with fatigue in neurodegenerative and immune diseases [Publisher: Nature Publishing Group]. *npj Digital Medicine*, 8(1), 12. <https://doi.org/10.1038/s41746-024-01386-0>
- Rosenfeldt, A. B., Jansen, A. E., Lopez-Lennon, C., Zimmerman, E., Imrey, P. B., Dibble, L. E., & Alberts, J. L. (2024). Physical Activity Declines over a 12-Month Period in Parkinson's Disease: Considerations for Longitudinal Activity Monitoring. *Medicine and Science in Sports and Exercise*. <https://doi.org/10.1249/MSS.0000000000003615>
- Rousham, E. K., Clarke, P. E., & Gross, H. (2006). Significant changes in physical activity among pregnant women in the UK as assessed by accelerometry and self-reported activity. *European Journal of Clinical Nu-*

- trition*, 60(3), 393–400. <https://doi.org/10.1038/sj.ejcn.1602329>
- Roussos, G., Herrero, T. R., Hill, D. L., Dowling, A. V., L T M Müller, M., Evers, L. J. W., Burton, J., Derungs, A., Fisher, K., Kilambi, K. P., Mehrotra, N., Bhatnagar, R., Sardar, S., Stephenson, D., Adams, J. L., Ray Dorsey, E., & Cosman, J. (2022). Identifying and characterising sources of variability in digital outcome measures in Parkinson's disease. *NPJ digital medicine*, 5(1), 93. <https://doi.org/10.1038/s41746-022-00643-4>
- Ryder-Burbidge, C., Wieler, M., Nykiforuk, C. I. J., & Jones, C. A. (2022). Life-Space Mobility and Parkinson's Disease. A Multiple-Methods Study. *Movement Disorders Clinical Practice*, 9(3), 351–361. <https://doi.org/10.1002/mdc3.13406>
- Safarpour, D., Dale, M. L., Shah, V. V., Talman, L., Carlson-Kuhta, P., Horak, F. B., & Mancini, M. (2022). Surrogates for rigidity and PIGD MDS-UPDRS subscores using wearable sensors. *Gait & Posture*, 91, 186–191. <https://doi.org/10.1016/j.gaitpost.2021.10.029>
- Saint-Maurice, P. F., Troiano, R. P., Bassett, D. R., Graubard, B. I., Carlson, S. A., Shihrom, E. J., Fulton, J. E., & Matthews, C. E. (2020). Association of Daily Step Count and Step Intensity With Mortality Among US Adults. *JAMA*, 323(12), 1151–1160. <https://doi.org/10.1001/jama.2020.1382>
- Salazar, R. D., Ren, X., Ellis, T. D., Toraif, N., Barthelemy, O. J., Neargarder, S., & Cronin-Golomb, A. (2017). Dual tasking in Parkinson's disease: Cognitive consequences while walking. *Neuropsychology*, 31(6), 613–623. <https://doi.org/10.1037/neu0000331>
- San Martín Valenzuela, C., Moscardó, L. D., López-Pascual, J., Serra-Añó, P., & Tomás, J. M. (2020). Effects of Dual-Task Group Training on Gait, Cognitive Executive Function, and Quality of Life in People With Parkinson Disease: Results of Randomized Controlled DUALGAIT Trial. *Archives of Physical Medicine and Rehabilitation*, 101(11), 1849–1856.e1. <https://doi.org/10.1016/j.apmr.2020.07.008>
- Scarpina, F., & Tagini, S. (2017). The Stroop Color and Word Test. *Frontiers in Psychology*, 8, 557. <https://doi.org/10.3389/fpsyg.2017.00557>
- Schalkamp, A.-K., Harrison, N. A., Peall, K. J., & Sandor, C. (2024). Digital outcome measures from smartwatch data relate to non-motor features of Parkinson's disease. *NPJ Parkinson's disease*, 10(1), 110. <https://doi.org/10.1038/s41531-024-00719-w>
- Schapira, A. H. V., Chaudhuri, K. R., & Jenner, P. (2017). Non-motor features of Parkinson disease. *Nature Reviews. Neuroscience*, 18(7), 435–450. <https://doi.org/10.1038/nrn.2017.62>
- Schimpl, M., Moore, C., Lederer, C., Neuhaus, A., Sambrook, J., Danesh, J., Ouwehand, W., & Daumer, M. (2011). Association between walking speed and age in healthy, free-living individuals using mobile accelerometry—a cross-sectional study. *PloS One*, 6(8), e23299. <https://doi.org/10.1371/journal.pone.0023299>
- Schlachetzki, J. C. M., Barth, J., Marxreiter, F., Gossler, J., Kohl, Z., Reinfelder, S., Gassner, H., Aminian, K., Eskofier, B. M., Winkler, J., & Klucken, J. (2017). Wearable sensors objectively measure gait parameters in Parkinson's disease. *PloS One*, 12(10), e0183989. <https://doi.org/10.1371/journal.pone.0183989>
- Schmidt, A. L., Pennypacker, M. L., Thrush, A. H., Leiper, C. I., & Craik, R. L. (2011). Validity of the StepWatch Step Activity Monitor: Preliminary findings for use in persons with Parkinson disease and multiple sclerosis. *Journal of Geriatric Physical Therapy* (2001), 34(1), 41–45. <https://doi.org/10.1519/JPT.0b013e31820aa921>
- Sedaghat, A. R. (2019). Understanding the Minimal Clinically Important Difference (MCID) of Patient-Reported Outcome Measures. *Otolaryngology-Head and Neck Surgery: Official Journal of American Academy of Otolaryngology-Head and Neck Surgery*, 161(4), 551–560. <https://doi.org/10.1177/0194599819852604>
- Shearin, S., Medley, A., Trudelle-Jackson, E., Swank, C., & Querry, R. (2021). Differences in predictors for gait speed and gait endurance in Parkinson's disease. *Gait & Posture*, 87, 49–53. <https://doi.org/10.1016/j.gaitpost.2021.04.019>

- Shen, L., Xu, H., Wang, K., Cui, X., & Ye, J. (2025). Global, Regional, and National Burdens of Parkinson's Disease in Adults Aged 20–50 Years, 1990–2021: A Cross-Sectional Study [eprint: <https://onlinelibrary.wiley.com/doi/pdf/10.1002/hsr2.71326>]. *Health Science Reports*, 8(10), e71326. <https://doi.org/10.1002/hsr2.71326>
- Shen, X., & Mak, M. K. Y. (2012). Repetitive step training with preparatory signals improves stability limits in patients with Parkinson's disease. *Journal of Rehabilitation Medicine*, 44(11), 944–949. <https://doi.org/10.2334/16501977-1056>
- Shokouhi, N., Khodakarami, H., Fernando, C., Osborn, S., & Horne, M. (2022). Accuracy of Step Count Estimations in Parkinson's Disease Can Be Predicted Using Ambulatory Monitoring. *Frontiers in Aging Neuroscience*, 14, 904895. <https://doi.org/10.3389/fnagi.2022.904895>
- Siciliano, M., Chiorri, C., De Micco, R., Russo, A., Tedeschi, G., Trojano, L., & Tesitore, A. (2019). Fatigue in Parkinson's disease: Italian validation of the Parkinson Fatigue Scale and the Fatigue Severity Scale using a Rasch analysis approach. *Parkinsonism & Related Disorders*, 65, 105–110. <https://doi.org/10.1016/j.parkreldis.2019.05.028>
- Sigmundová, D., Vašíčková, J., Stelzer, J., & Repka, E. (2013). The influence of monitoring interval on data measurement: An analysis of step counts of university students. *International Journal of Environmental Research and Public Health*, 10(2), 515–527. <https://doi.org/10.3390/ijerph10020515>
- Silva de Lima, A. L., Hahn, T., Evers, L. J. W., de Vries, N. M., Cohen, E., Afek, M., Bataille, L., Daeschler, M., Claes, K., Boroojerdi, B., Terricabras, D., Little, M. A., Baldus, H., Bloem, B. R., & Faber, M. J. (2017). Feasibility of large-scale deployment of multiple wearable sensors in Parkinson's disease. *PloS One*, 12(12), e0189161. <https://doi.org/10.1371/journal.pone.0189161>
- Silva de Lima, A. L., Smits, T., Darweesh, S. K. L., Valenti, G., Milosevic, M., Pijl, M., Baldus, H., de Vries, N. M., Meinders, M. J., & Bloem, B. R. (2020). Home-based monitoring of falls using wearable sensors in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 35(1), 109–115. <https://doi.org/10.1002/mds.27830>
- Skidmore, F. M., Mackman, C. A., Pav, B., Shulman, L. M., Garvan, C., Macko, R. F., & Heilman, K. M. (2008). Daily ambulatory activity levels in idiopathic Parkinson disease. *Journal of Rehabilitation Research and Development*, 45(9), 1343–1348.
- Smith, L., Hamer, M., Ucci, M., Marmot, A., Gardner, B., Sawyer, A., Wardle, J., & Fisher, A. (2015). Weekday and weekend patterns of objectively measured sitting, standing, and stepping in a sample of office-based workers: The active buildings study. *BMC public health*, 15, 9. <https://doi.org/10.1186/s12889-014-1338-1>
- Smulders, K., Dale, M. L., Carlson-Kuhta, P., Nutt, J. G., & Horak, F. B. (2016). Pharmacological treatment in Parkinson's disease: Effects on gait. *Parkinsonism & related disorders*, 31, 3–13. <https://doi.org/10.1016/j.parkreldis.2016.07.006>
- Soileau, M. J., Aldred, J., Budur, K., Fisseha, N., Fung, V. S., Jeong, A., Kimber, T. E., Klos, K., Litvan, I., O'Neill, D., Robieson, W. Z., Spindler, M. A., Standaert, D. G., Talapala, S., Vaou, E. O., Zheng, H., Facheris, M. F., & Hauser, R. A. (2022). Safety and efficacy of continuous subcutaneous foslevodopa-foscarbidopa in patients with advanced Parkinson's disease: A randomised, double-blind, active-controlled, phase 3 trial. *The Lancet. Neurology*, 21(12), 1099–1109. [https://doi.org/10.1016/S1474-4422\(22\)00400-8](https://doi.org/10.1016/S1474-4422(22)00400-8)
- Sommerauer, M., Werth, E., Poryazova, R., Gavrilov, Y. V., Hauser, S., & Valko, P. O. (2015). Bound to supine sleep: Parkinson's disease and the impact of nocturnal immobility. *Parkinsonism & Related Disorders*, 21(10), 1269–1272. <https://doi.org/10.1016/j.parkreldis.2015.08.010>
- Soulard, J., Carlin, T., Knitza, J., & Vuillerme, N. (2022). Wearables for Measuring the Physical Activity and Sedentary Behavior of Patients With Axial Spondyloarthritis: Systematic Review. *JMIR mHealth and uHealth*, 10(8), e34734. <https://doi.org/10.2196/34734>

- Souza, R. J. d., Shigaki, I. A. d. A., Terra, M. B., Barboza, N. M., Bueno, M. E. B., Mesas, A. E., & Smaili, S. M. (2023). Effectiveness of Neurofunctional Physical Therapy on the Quality of Sleep of Individuals with Parkinson's Disease: Case Series. *Sleep Science*, 16(2), 206–215. <https://doi.org/10.1055/s-0043-1770801>
- Sringean, J., Anan, C., & Bhidayasiri, R. (2020). Impaired ability to turn in bed in parkinson's disease as a potential rare cause of positional asphyxia: A sensor-based analysis. *Clinical Neurology and Neurosurgery*, 192, 105713. <https://doi.org/10.1016/j.clineuro.2020.105713>
- Sringean, J., Anan, C., Thanawattano, C., & Bhidayasiri, R. (2017). Time for a strategy in night-time dopaminergic therapy? An objective sensor-based analysis of nocturnal hypokinesia and sleeping positions in Parkinson's disease. *Journal of the Neurological Sciences*, 373, 244–248. <https://doi.org/10.1016/j.jns.2016.12.045>
- Sringean, J., Taechalertpaisarn, P., Thanawattano, C., & Bhidayasiri, R. (2016). How well do Parkinson's disease patients turn in bed? Quantitative analysis of nocturnal hypokinesia using multisite wearable inertial sensors. *Parkinsonism & Related Disorders*, 23, 10–16. <https://doi.org/10.1016/j.parkreldis.2015.11.003>
- Sringean, J., Udomsirithamrong, O., & Bhidayasiri, R. (2024). Too little or too much nocturnal movements in Parkinson's disease: A practical guide to managing the unseen. *Clinical Parkinsonism & Related Disorders*, 10, 100258. <https://doi.org/10.1016/j.prdoa.2024.100258>
- Stack, E., & Ashburn, A. (2008). Dysfunctional turning in Parkinson's disease. *Disability and Rehabilitation*, 30(16), 1222–1229. <https://doi.org/10.1080/09638280701829938>
- Stebbins, G. T., Goetz, C. G., Burn, D. J., Jankovic, J., Khoo, T. K., & Tilley, B. C. (2013). How to identify tremor dominant and postural instability/gait difficulty groups with the movement disorder society unified Parkinson's disease rating scale: Comparison with the unified Parkinson's disease rating scale. *Movement Disorders: Official Journal of the Movement Disorder Society*, 28(5), 668–670. <https://doi.org/10.1002/mds.25383>
- Stefani, A., Tessitore, A., Tambasco, N., Cossu, G., Ceravolo, M. G., Defazio, G., Morgante, F., Ramat, S., Melzi, G., Gualberti, G., Merolla, R., Onuk, K., & Lopiano, L. (2022). Criteria for identification of advanced Parkinson's disease: The results of the Italian subgroup of OBSERVE-PD observational study. *BMC neurology*, 22(1), 41. <https://doi.org/10.1186/s12883-022-02554-z>
- Steiger, M. J., Thompson, P. D., & Marsden, C. D. (1996). Disordered axial movement in Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, 61(6), 645–648. <https://doi.org/10.1136/jnnp.61.6.645>
- Stellmann, J. P., Neuhaus, A., Götze, N., Briken, S., Lederer, C., Schimpl, M., Heesen, C., & Daumer, M. (2015). Ecological validity of walking capacity tests in multiple sclerosis. *PloS One*, 10(4), e0123822. <https://doi.org/10.1371/journal.pone.0123822>
- Still, A., Hale, L., Alam, S., Morris, M. E., & Jayakaran, P. (2024). Relationships between physical activities performed under free-living conditions and non-motor symptoms in people with Parkinson's: A systematic review and meta-analysis. *Clinical Rehabilitation*, 38(11), 1534–1551. <https://doi.org/10.1177/02692155241272967>
- Straiton, N., Alharbi, M., Bauman, A., Neubeck, L., Gullick, J., Bhindi, R., & Gallagher, R. (2018). The validity and reliability of consumer-grade activity trackers in older, community-dwelling adults: A systematic review. *Maturitas*, 112, 85–93. <https://doi.org/10.1016/j.maturitas.2018.03.016>
- Stroop, J. R. (1935). Studies of interference in serial verbal reactions [Place: US Publisher: Psychological Review Company]. *Journal of Experimental Psychology*, 18(6), 643–662. <https://doi.org/10.1037/h0054651>
- Strouwen, C., Molenaar, E. A. L. M., Munks, L., Keus, S. H. J., Zijlmans, J. C. M., Vandenberghe, W., Bloem, B. R., & Nieuwboer, A. (2017). Training dual tasks together or apart in Parkinson's disease: Results from the DUALITY trial. *Movement Disorders: Official Journal of the Movement Disorder Society*

- Society*, 32(8), 1201–1210. <https://doi.org/10.1002/mds.27014>
- Studenski, S., Perera, S., Patel, K., Rosano, C., Faulkner, K., Inzitari, M., Brach, J., Chandler, J., Cawthon, P., Connor, E. B., Nevitt, M., Visser, M., Kritchevsky, S., Badinelli, S., Harris, T., Newman, A. B., Cauley, J., Ferrucci, L., & Guralnik, J. (2011). Gait speed and survival in older adults. *JAMA*, 305(1), 50–58. <https://doi.org/10.1001/jama.2010.1923>
- Su, D., Cui, Y., He, C., Yin, P., Bai, R., Zhu, J., Lam, J. S. T., Zhang, J., Yan, R., Zheng, X., Wu, J., Zhao, D., Wang, A., Zhou, M., & Feng, T. (2025). Projections for prevalence of Parkinson's disease and its driving factors in 195 countries and territories to 2050: Modelling study of Global Burden of Disease Study 2021. *BMJ (Clinical research ed.)*, 388, e080952. <https://doi.org/10.1136/bmj-2024-080952>
- Sun, Y., Chen, J., Ji, M., & Li, X. (2025). Wearable Technologies for Health Promotion and Disease Prevention in Older Adults: Systematic Scoping Review and Evidence Map. *Journal of Medical Internet Research*, 27, e69077. <https://doi.org/10.2196/69077>
- Suri, A., VanSwearingen, J., Dunlap, P., Redfern, M. S., Rosso, A. L., & Sejdíć, E. (2022). Facilitators and barriers to real-life mobility in community-dwelling older adults: A narrative review of accelerometry- and global positioning system-based studies. *Aging Clinical and Experimental Research*, 34(8), 1733–1746. <https://doi.org/10.1007/s40520-022-02096-x>
- Suzuki, K., Miyamoto, T., Miyamoto, M., Suzuki, S., Numao, A., Watanabe, Y., Tatsumoto, M., Sakuta, H., Watanabe, Y., Fujita, H., Iwanami, M., Sada, T., Kadowaki, T., Hashimoto, K., Trenkwalder, C., & Hirata, K. (2015). Evaluation of cutoff scores for the Parkinson's disease sleep scale-2. *Acta Neurologica Scandinavica*, 131(6), 426–430. <https://doi.org/10.1111/ane.12347>
- Svarre, F. R., Jensen, M. M., Nielsen, J., & Villumsen, M. (2020). The validity of activity trackers is affected by walking speed: The criterion validity of Garmin Vivosmart® HR and StepWatch™ 3 for measuring steps at various walking speeds under controlled conditions. *PeerJ*, 8, e9381. <https://doi.org/10.7717/peerj.9381>
- Taniguchi, S., D'cruz, N., Nakagoshi, M., Osaki, T., & Nieuwboer, A. (2022). Determinants of impaired bed mobility in Parkinson's disease: Impact of hip muscle strength and motor symptoms. *NeuroRehabilitation*, 50(4), 445–452. <https://doi.org/10.3233/NRE-210301>
- Tanji, H., Gruber-Baldini, A. L., Anderson, K. E., Pretzer-Abhoff, I., Reich, S. G., Fishman, P. S., Weiner, W. J., & Shulman, L. M. (2008). A comparative study of physical performance measures in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(13), 1897–1905. <https://doi.org/10.1002/mds.22266>
- Taylor, N., Carroll, A., & Gifford, R. M. (2025). Five-day evaluation of the acceptability and comfort of wearable technology at four anatomical locations during military training. *BMJ military health*, 171(3), 245–249. <https://doi.org/10.1136/military-2023-002524>
- Timblin, H., Rahmani, E., Ryczek, C. A., Hill, C. R., & Jones, J. D. (2022). Physical Inactivity Links Depressive Symptoms and Cognitive Functioning among Individuals with Parkinson's Disease. *Neuropsychology*, 36(6), 505–512. <https://doi.org/10.1037/neu0000837>
- Timurtas, E., Sharkh, A.-A., Mate, K. K. V., Dawes, H., & Mayo, N. E. (2025). Evidence for the Link Between Non-Motor Symptoms, Kinematic Gait Parameters, and Physical Function in People with Parkinson's Disease. *Bioengineering*, 12(5), 551. <https://doi.org/10.3390/bioengineering12050551>
- Toosizadeh, N., Mohler, J., Lei, H., Parvaneh, S., Sherman, S., & Najafi, B. (2015). Motor Performance Assessment in Parkinson's Disease: Association between Objective In-Clinic, Objective In-Home, and Subjective/Semi-Objective Measures. *PLoS ONE*, 10(4), e0124763. <https://doi.org/10.1371/journal.pone.0124763>
- Topalidis, P., Florea, C., Eigl, E.-S., Kurapov, A., Leon, C. A. B., & Schabus, M. (2021). Evaluation of a Low-Cost Commercial Actigraph and Its Potential Use in Detecting Cultural Variations in Physical Ac-

- tivity and Sleep. *Sensors (Basel, Switzerland)*, 21(11), 3774. <https://doi.org/10.3390/s21113774>
- Tosserams, A., Bloem, B. R., Ehgoetz Martens, K. A., Helmich, R. C., Kessels, R. P. C., Shine, J. M., Taylor, N. L., Weinstein, G., Lewis, S. J. G., & Nonnekes, J. (2023). Modulating arousal to overcome gait impairments in Parkinson's disease: How the noradrenergic system may act as a double-edged sword. *Translational Neurodegeneration*, 12(1), 15. <https://doi.org/10.1186/s40035-023-00347-z>
- Treacy, D., Hassett, L., Schurr, K., Chagpar, S., Paul, S. S., & Sherrington, C. (2017). Validity of Different Activity Monitors to Count Steps in an Inpatient Rehabilitation Setting. *Physical Therapy*, 97(5), 581–588. <https://doi.org/10.1093/ptj/pzx010>
- Trenkwalder, C., Kohnen, R., Högl, B., Metta, V., Sixel-Döring, F., Frauscher, B., Hülsmann, J., Martinez-Martin, P., & Chaudhuri, K. R. (2011). Parkinson's disease sleep scale—validation of the revised version PDSS-2. *Movement Disorders: Official Journal of the Movement Disorder Society*, 26(4), 644–652. <https://doi.org/10.1002/mds.23476>
- Uchino, K., Shiraishi, M., Tanaka, K., Akamatsu, M., & Hasegawa, Y. (2017). Impact of inability to turn in bed assessed by a wearable three-axis accelerometer on patients with Parkinson's disease. *PloS One*, 12(11), e0187616. <https://doi.org/10.1371/journal.pone.0187616>
- Uekermann, J., Daum, I., Peters, S., Wiebel, B., Przuntek, H., & Müller, T. (2003). Depressed mood and executive dysfunction in early Parkinson's disease. *Acta Neurologica Scandinavica*, 107(5), 341–348. <https://doi.org/10.1034/j.1600-0404.2003.02155.x>
- van Schooten, K. S., Rispens, S. M., Elders, P. J., Lips, P., van Dieën, J. H., & Pijnappels, M. (2015). Assessing physical activity in older adults: Required days of trunk accelerometer measurements for reliable estimation. *Journal of Aging and Physical Activity*, 23(1), 9–17. <https://doi.org/10.1123/japa.2013-0103>
- van Uem, J. M. T., Cerff, B., Kampmeyer, M., Prinzen, J., Zuidema, M., Hobert, M. A., Gräber, S., Berg, D., Maetzler, W., & Liepelt-Scarfone, I. (2018). The association between objectively measured physical activity, depression, cognition, and health-related quality of life in Parkinson's disease. *Parkinsonism & Related Disorders*, 48, 74–81. <https://doi.org/10.1016/j.parkreldis.2017.12.023>
- Varghese, J., Alen, C. M. v., Fujarski, M., Schlake, G. S., Sucker, J., Warnecke, T., & Thomas, C. (2021). Sensor Validation and Diagnostic Potential of Smartwatches in Movement Disorders. *Sensors (Basel, Switzerland)*, 21(9), 3139. <https://doi.org/10.3390/s21093139>
- Venables, W. N., & Ripley, B. D. (2002, August). *Modern Applied Statistics with S* (4th edition). Springer.
- Vignatelli, L., Plazzi, G., Barbato, A., Ferini-Strambi, L., Manni, R., Pompei, F., D'Alessandro, R., & GINSEN (Gruppo Italiano Narcolessia Studio Epidemiologico Nazionale). (2003). Italian version of the Epworth sleepiness scale: External validity. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, 23(6), 295–300. <https://doi.org/10.1007/s100720300004>
- Vítečková, S., Horáková, H., Poláková, K., Krupička, R., Růžicka, E., & Brožová, H. (2020). Agreement between the GAITRite® System and the Wearable Sensor BTS G-Walk® for measurement of gait parameters in healthy adults and Parkinson's disease patients. *PeerJ*, 8, e8835. <https://doi.org/10.7717/peerj.8835>
- Vivosmart 4 - Introduction. (n.d.). Retrieved July 16, 2025, from <https://www8.garmin.com/manuals/webhelp/vivosmart4/EN-US/GUID-8B9070D6-C0EA-45EE-8F62-1602492BF264.html>
- Walton, C. C., Shine, J. M., Hall, J. M., O'Callaghan, C., Mowszowski, L., Gilat, M., Szeto, J. Y. Y., Naismith, S. L., & Lewis, S. J. G. (2015). The major impact of freezing of gait on quality of life in Parkinson's disease. *Journal of Neurology*, 262(1), 108–115. <https://doi.org/10.1007/s00415-014-7524-3>

- Wang, Y.-C., Hart, D. L., Stratford, P. W., & Mioduski, J. E. (2011). Baseline dependency of minimal clinically important improvement. *Physical Therapy*, 91(5), 675–688. <https://doi.org/10.2522/ptj.20100229>
- Warmerdam, E., Hausdorff, J. M., Atrsaei, A., Zhou, Y., Mirelman, A., Aminian, K., Espay, A. J., Hansen, C., Evers, L. J. W., Keller, A., Lamoth, C., Pilotto, A., Rochester, L., Schmidt, G., Bloem, B. R., & Maetzler, W. (2020). Long-term unsupervised mobility assessment in movement disorders. *The Lancet. Neurology*, 19(5), 462–470. [https://doi.org/10.1016/S1474-4422\(19\)30397-7](https://doi.org/10.1016/S1474-4422(19)30397-7)
- Warmerdam, E., Romijnders, R., Hansen, C., Elshehabi, M., Zimmermann, M., Metzger, F. G., von Thaler, A.-K., Berg, D., Schmidt, G., & Maetzler, W. (2021). Arm swing responsiveness to dopaminergic medication in Parkinson's disease depends on task complexity. *NPJ Parkinson's disease*, 7(1), 89. <https://doi.org/10.1038/s41531-021-00235-1>
- Welzel, J., Wendtland, D., Warmerdam, E., Romijnders, R., Elshehabi, M., Geritz, J., Berg, D., Hansen, C., & Maetzler, W. (2021). Step Length Is a Promising Progression Marker in Parkinson's Disease. [Place: Switzerland]. *Sensors (Basel, Switzerland)*, 21(7). <https://doi.org/10.3390/s21072292>
- Wendel, N., Macpherson, C. E., Webber, K., Hendron, K., DeAngelis, T., Colon-Semenza, C., & Ellis, T. (2018). Accuracy of Activity Trackers in Parkinson Disease: Should We Prescribe Them? [Place: United States]. *Physical therapy*, 98(8), 705–714. <https://doi.org/10.1093/ptj/pzy054>
- Wilson, J., Alcock, L., Yarnall, A. J., Lord, S., Lawson, R. A., Morris, R., Taylor, J.-P., Burn, D. J., Rochester, L., & Galna, B. (2020). Gait Progression Over 6 Years in Parkinson's Disease: Effects of Age, Medication, and Pathology. *Frontiers in Aging Neuroscience*, 12, 577435. <https://doi.org/10.3389/fnagi.2020.577435>
- Winogrodzka, A., Wagenaar, R. C., Booij, J., & Wolters, E. C. (2005). Rigidity and bradykinesia reduce interlimb coordination in Parkinsonian gait [Publisher: Elsevier]. *Archives of Physical Medicine and Rehabilitation*, 86(2), 183–189. <https://doi.org/10.1016/j.apmr.2004.09.010>
- Wright, A., Hannon, J., Hegedus, E. J., & Kavchak, A. E. (2012). Clinimetrics corner: A closer look at the minimal clinically important difference (MCID). *The Journal of Manual & Manipulative Therapy*, 20(3), 160–166. <https://doi.org/10.1179/2042618612Y.0000000001>
- Wüllner, U., Borghammer, P., Choe, C.-U., Csoti, I., Falkenburger, B., Gasser, T., Lingor, P., & Riederer, P. (2023). The heterogeneity of Parkinson's disease. *Journal of Neural Transmission (Vienna, Austria: 1996)*, 130(6), 827–838. <https://doi.org/10.1007/s00702-023-02635-4>
- Xue, F., Wang, F.-Y., Mao, C.-J., Guo, S.-P., Chen, J., Li, J., Wang, Q.-J., Bei, H.-Z., Yu, Q., & Liu, C.-F. (2018). Analysis of nocturnal hypokinesia and sleep quality in Parkinson's disease. *Journal of Clinical Neuroscience: Official Journal of the Neurosurgical Society of Australasia*, 54, 96–101. <https://doi.org/10.1016/j.jocn.2018.06.016>
- Yang, F. (2025). What determines gait speed in community-living older adults? A relative weight analysis. *European Geriatric Medicine*, 16(3), 1045–1054. <https://doi.org/10.1007/s41999-025-01208-w>
- Yao, J., Tan, C. S., Lim, N., Tan, J., Chen, C., & Müller-Riemenschneider, F. (2021). Number of daily measurements needed to estimate habitual step count levels using wrist-worn trackers and smartphones in 212,048 adults. *Scientific Reports*, 11(1), 9633. <https://doi.org/10.1038/s41598-021-89141-3>
- Yi, Q., Yu-Peng, C., Jiang-Ting, L., Jing-Yi, L., Qi-Xiong, Q., Dan-Lei, W., Jing-Wei, Z., Zhi-Juan, M., Yong-Jie, X., Zhe, M., & Zheng, X. (2022). Worse Sleep Quality Aggravates the Motor and Non-Motor Symptoms in Parkinson's Disease. *Frontiers in Aging Neuroscience*, 14, 887094. <https://doi.org/10.3389/fnagi.2022.887094>
- Yilmaz, N. H., Saricaoglu, M., Eser, H. Y., Düz, Ö. A., Polat, B., & Özer, F. F. (2019). The Relationship Between Pain, and Freezing of Gait and Falls in Parkinson's Disease. *Archives of Neuropsychiatry*, 57(1), 56–60. <https://doi.org/10.29399/npa.24716>

- Yogev-Seligmann, G., Hausdorff, J. M., & Giladi, N. (2008). The role of executive function and attention in gait. *Movement Disorders: Official Journal of the Movement Disorder Society*, 23(3), 329–342, quiz 472. <https://doi.org/10.1002/mds.21720>
- Yoneyama, M., Mitoma, H., & Okuma, Y. (2013). Accelerometry-based long-term monitoring of movement disorders: From diurnal gait behavior to nocturnal bed mobility [Publisher: World Scientific Publishing Co.]. *Journal of Mechanics in Medicine and Biology*, 13(02), 1350041. <https://doi.org/10.1142/S0219519413500413>
- Zajac, J. A., Cavanaugh, J. T., Baker, T., Duncan, R. P., Fulford, D., Giris, J., LaValley, M., Nordahl, T., Porciuncula, F., Rawson, K. S., Saint-Hilaire, M., Thomas, C. A., Earhart, G. M., & Ellis, T. D. (2022). Does clinically measured walking capacity contribute to real-world walking performance in Parkinson's disease? *Parkinsonism & Related Disorders*, 105, 123–127. <https://doi.org/10.1016/j.parkreldis.2022.11.016>
- Zampogna, A., Manoni, A., Asci, F., Liguori, C., Irrera, F., & Suppa, A. (2020). Shedding Light on Nocturnal Movements in Parkinson's Disease: Evidence from Wearable Technologies. *Sensors (Basel, Switzerland)*, 20(18). <https://doi.org/10.3390/s20185171>
- Zeileis, A., & Hothorn, T. (2002). Diagnostic Checking in Regression Relationships. *R News*, 2(3), 7–10. <https://CRAN.R-project.org/doc/Rnews>
- Zeileis, A., Köll, S., & Graham, N. (2020). Various Versatile Variances: An Object-Oriented Implementation of Clustered Covariances in R. *Journal of Statistical Software*, 95, 1–36. <https://doi.org/10.18637/jss.v095.i01>
- Zetusky, W. J., Jankovic, J., & Pirozzolo, F. J. (1985). The heterogeneity of Parkinson's disease: Clinical and prognostic implications. *Neurology*, 35(4), 522–526. <https://doi.org/10.1212/wnl.35.4.522>
- Zhang, Y., Xi, X., & Huang, Y. (2023). The anchor design of anchor-based method to determine the minimal clinically important difference: A systematic review. *Health and Quality of Life Outcomes*, 21(1), 74. <https://doi.org/10.1186/s12955-023-02157-3>
- Zhang, Y., Folarin, A. A., Sun, S., Cummins, N., Vairavan, S., Qian, L., Ranjan, Y., Rashid, Z., Conde, P., Stewart, C., Laiou, P., Sankesara, H., Matcham, F., White, K. M., Oetzmann, C., Ivan, A., Lamers, F., Siddi, S., Simblett, S., ... Dobson, R. J. B. (2022). Associations Between Depression Symptom Severity and Daily-Life Gait Characteristics Derived From Long-Term Acceleration Signals in Real-World Settings: Retrospective Analysis. *JMIR mHealth and uHealth*, 10(10), e40667. <https://doi.org/10.2196/40667>
- Zhou, J., Cattaneo, G., Yu, W., Lo, O.-Y., Gouskova, N. A., Delgado-Gallén, S., Redondo-Camós, M., España-Irla, G., Solana-Sánchez, J., Tormos, J. M., Lipsitz, L. A., Bartres-Faz, D., Pascual-Leone, A., & Manor, B. (2023). The age-related contribution of cognitive function to dual-task gait in middle-aged adults in Spain: Observations from a population-based study. *The lancet. Healthy longevity*, 4(3), e98–e106. [https://doi.org/10.1016/S2666-7568\(23\)00009-0](https://doi.org/10.1016/S2666-7568(23)00009-0)
- Zou, H., Goetz, C. G., Stebbins, G. T., Schrag, A., Mestre, T. A., & Luo, S. (2023). Summing MDS-UPDRS Parts 1 + 2 (Non-motor and Motor Experience of Daily Living): The Patient's Voice. *Movement disorders : official journal of the Movement Disorder Society*, 38(7), 1363–1364. <https://doi.org/10.1002/mds.29417>

APPENDICES

Résumé

Évaluation de la mobilité dans la maladie de Parkinson : de l'étude de la maladie à l'application thérapeutique

La maladie de Parkinson (MP) est la deuxième maladie neurodégénérative la plus fréquente. Les troubles de la marche représentant un des symptômes moteurs (SM) les plus invalidants, leur étude est essentielle pour améliorer le suivi et le la prise en charge des personnes atteintes. Les symptômes de la MP sont connus pour fluctuer d'un jour à l'autre, et au cours d'une même journée ; donct, évaluer la mobilité uniquement à travers des tests supervisés en laboratoire, qui fournissent un instantané de la dite 'capacité' d'une personne à un moment précis, s'avère insuffisant. Il est dès lors nécessaire d'intégrer une évaluation de la dite 'performance', réalisée dans des conditions de vie réelle, sur de plus longues périodes.

L'utilisation d'outils numériques et d'objets connectés tels que les montres rend aujourd'hui cette évaluation de la mobilité possible mais peu de ces nouvelles technologies ont été validés. De plus, l'influence présumée des SM et surtout des symptômes non moteurs (SNM) sur la capacité et la performance reste à ce jour peu étudiée. Ce travail doctoral a abordé ces enjeux à travers trois chapitres complémentaires :

- Validation d'une montre connectée commercialisée pour le comptage de pas quotidiens (4 études originales).
- Évaluation des relations entre les paramètres de mobilité mesurés en laboratoire et en condition de vie réelle, et de la contribution des SM et SNM (3 études originales).
- Analyse de la mobilité nocturne, de son association avec la mobilité diurne et de la réponse au traitement dopaminergique (2 études originales).

Pour répondre à ces objectifs, nous avons constitué une base de données de 121 personnes atteintes de MP, comprenant des données démographiques, anthropométriques et cliniques explorant à la fois les SM et les SNM, ainsi que des mesures de tests de mobilité réalisées en laboratoire (marche avant, arrière, rotation) et des mesures de mobilité réalisée en condition de vie réelle.

Dans un premier temps, nous avons démontré que le nombre moyen de pas quotidiens (AvDS) mesuré chez les personnes de MP légère à modérée au moyen d'une montre connectée sont précis et fiable, et que ces propriétés métrologiques soit influencés par le stade de la maladie, le phénotype et l'état pharmacologique du patient notamment. Nous avons en outre établi, pour la première fois, la différence minimale cliniquement importante pour AvDS, fournissant une référence pour interpréter les résultats d'études interventionnelles entre autre. Dans leur ensemble, ces résultats confirment l'intérêt des mesures fournies pas des montres connectées comme biomarqueurs numériques de mobilité, tout en soulignant leurs limites liées à la MP.

Dans un second temps, nous avons montré que les paramètres de capacité prédisent très faiblement ceux de performance. Nos analyses ont en outre souligné le rôle majeur des SNM, notamment les troubles exécutifs, la dépression et la fatigue, souvent

plus importants que celui des SM. La mobilité dans la MP apparaît en définitive comme un phénomène multidimensionnel façonné par l'interaction de facteurs moteurs, non moteurs et environnementaux.

Dans une troisième et dernière section, nous avons montré que les personnes atteintes de MP présentant une mobilité nocturne altérée avaient également une mobilité diurne réduite, suggérant que les limitations motrices s'étendent sur les 24 heures de la journée. Enfin, si le traitement dopaminergique a amélioré la qualité subjective du sommeil, aucune amélioration n'a été observée sur les paramètres objectifs de mobilité nocturne, suggérant l'existence des mécanismes distincts.

Dans leur ensemble, les résultats de ce travail doctoral soutiennent le développement de biomarqueurs digitaux nécessaires pour mettre en œuvre des stratégies de suivi et de prise en charge personnalisée de la mobilité des personnes atteintes de MP, susceptibles de guider les décisions cliniques, et importantes pour améliorer l'autonomie et la qualité de vie des personnes atteintes de MP.

Riassunto

Valutazione della mobilità nella malattia di Parkinson: dallo studio della malattia alle applicazioni terapeutiche

La malattia di Parkinson (MP) è la seconda malattia neurodegenerativa più frequente. Il declino della mobilità rappresenta una delle principali cause di disabilità; pertanto, studiare come le persone con MP si muovono è essenziale per la valutazione e la gestione della malattia. I sintomi della MP possono fluttuare nel corso della giornata o tra giorni diversi. Dunque, valutare la mobilità solo attraverso test di laboratorio (capacità) può essere insufficiente e richiede l'integrazione di un monitoraggio in condizioni reali (performance), lungo l'intero arco di 24.

L'avvento dei dispositivi indossabili commerciali, come gli smartwatch, ha reso questa valutazione possibile, ma la maggior parte di tali dispositivi necessita di validazione. Inoltre, la mobilità non è determinata unicamente dalla funzione motoria, ma è influenzata da fattori personali e ambientali. Ciò è particolarmente vero nella MP, in cui i sintomi non motori (NMS) hanno un impatto rilevante. Tuttavia, la misura in cui i sintomi motori (MS) e NMS influenzano la capacità e la performance rimane ancora poco chiara.

Questa tesi di dottorato ha affrontato tali domande nella MP attraverso tre sezioni complementari:

- Validazione di uno smartwatch commerciale per il conteggio dei passi giornalieri (4 contributi originali).
- Valutazione della relazione tra la capacità di cammino in clinica e la performance di cammino nel mondo reale, e del contributo di MS e NMS alla mobilità (3 contributi originali).
- Valutazione della mobilità notturna, della sua associazione con la mobilità diurna e della risposta al trattamento dopaminergico (2 contributi originali).

Abbiamo costruito un dataset multimodale di 121 persone con MP, includendo misure demografiche, antropometriche e cliniche che esplorano sia i MS che i NMS oltre a misure di mobilità supervisionata (inclusi cammino in avanti, indietro e rotazioni) e non supervisionata. Nella prima sezione abbiamo dimostrato che il numero medio di passi giornalieri (AvDS) è accurato e affidabile nei pazienti con MP lieve-moderata in condizioni ecologiche, pur essendo influenzato da stadio di malattia, fenotipo, posizionamento del dispositivo e stato farmacologico. Inoltre, abbiamo definito per la prima volta la minima differenza clinicamente significativa (MCID) per AvDS nella MP, fornendo un riferimento per interpretare le variazioni nel tempo o in risposta a interventi. Nel complesso, questi risultati confermano la fattibilità dell'uso degli smartwatch come strumenti di misura digitale della mobilità, pur evidenziando i limiti legati alla malattia.

La seconda sezione, mediante modelli bayesiani, ha evidenziato il potere limitato dei test di mobilità supervisionata nel predire la mobilità non supervisionata. Inoltre, le analisi multivariate hanno mostrato che i NMS, in particolare disfunzione esecutiva, depressione e astenia, rappresentano i determinanti principali della mobilità

supervisionata e non supervisionata. La loro influenza è risultata più marcata nei compiti complessi, ma evidente anche in AvDS, talvolta più dei MS. Questi risultati sottolineano che la mobilità nella MP è un fenomeno multidimensionale, modellato da MS, NMS e fattori ambientali.

Nella terza sezione abbiamo osservato che i pazienti con mobilità notturna ridotta mostravano anche una peggiore mobilità diurna, indicando che le limitazioni motorie si estendono lungo l'intero arco di 24 ore. La terapia dopaminergica migliorava la qualità soggettiva del sonno ma non la mobilità notturna oggettiva, suggerendo meccanismi distinti.

In conclusione, i risultati della presente tesi di dottorato aprono la strada a strategie di monitoraggio della mobilità più ecologicamente valide, multidimensionali e centrate sul paziente. Tali risultati possono supportare la decisione clinica, guidare le strategie terapeutiche e contribuire alla definizione di indicatori digitali di mobilità, migliorando l'autonomia e la qualità di vita delle persone con MP.

Scientific contributions

Papers published in peer-reviewed international scientific journals (n=30)

1. Iodice, F., Cuffaro, L., Romoli, M., Bianchini, E., Sparaco, M., Arighi, A., Cerami, C., Salemme, S., Reale, G., Orologio, I., Lavorgna, L., & Padovani, A. (2025). A comprehensive guide to digital neurology. An update on current development on digital neurology derived from the Digital Neuro Hub project. *Neurological Sciences*. <https://doi.org/10.1007/s10072-025-08428-9>
2. Sergi, G., Yekutieli, Z., Meloni, M., Bianchini, E., Vivacqua, G., Di Lazzaro, V., & Marano, M. (2025). Sympathetic Burden Measured Through a Chest-Worn Sensor Correlates with Spatiotemporal Gait Performances and Global Cognition in Parkinson's Disease. *Sensors*, 25(18), 5756. <https://doi.org/10.3390/s25185756>
3. Bianchini, E., Alborghetti, M., Galli, S., Hansen, C., Zampogna, A., Suppa, A., Salvetti, M., Pontieri, F. E., Rinaldi, D., & Vuillerme, N. (2025). Minimal Clinically Important Difference of Average Daily Steps Measured Through a Consumer Smartwatch in People With Mild-to-Moderate Parkinson Disease: Cross-Sectional Study. *JMIR mHealth and uHealth*, 13(1), e64213. <https://doi.org/10.2196/64213>
4. Milane, T., Vuillerme, N., Petit, P., Warmerdam, E., Romijnders, R., Bianchini, E., Maetzel, W., & Hansen, C. (2025). Impact of forward and backward walking on gait parameters across parkinson's disease stages and severity: A prospective observational study. *BMC Neurology*, 25(1), 379. <https://doi.org/10.1186/s12883-025-04321-2>
5. Milane, T., Bianchini, E., Chardon, M., Barbieri, F. A., Hansen, C., & Vuillerme, N. (2025). Associations Between Daily Step Counts and Sleep Parameters in Parkinson's Disease: A Scoping Review. *Sensors*, 25(14). <https://doi.org/10.3390/s25144447>
6. Alborghetti, M., Lionetto, L., Lombardoizzi, G., Montaguti, L., Trovini, G., Donato, D., Costanzi, G., Bernardini, D. D., Catapano, F., Surano, M., Pagano, I., Ceccherelli, A., Bianchini, E., Lorenzo, G. D., Simmaco, M., Martinotti, G., Kotzalidis, G. D., Nicoletti, F., & Filippis, S. D. (2025). The Potential Influence of Associated Antidepressants on the Pharmacokinetic Profile of Esketamine in Patients Affected by Treatment-resistant Depression. *Current Neuropharmacology*. <https://doi.org/10.2174/011570159X356952241216172603>
7. Bianchini, E., Rinaldi, D., Carolis, L. D., Galli, S., Alborghetti, M., Hansen, C., Suppa, A., Salvetti, M., Pontieri, F. E., & Vuillerme, N. (2025). Reliability of Average Daily Steps Measured Through a Consumer Smartwatch in Parkinson Disease Phenotypes, Stages, and Severities: Cross-Sectional Study. *JMIR Formative Research*, 9(1), e63153. <https://doi.org/10.2196/63153>
8. Patera, M., Zampogna, A., Pietrosanti, L., Asci, F., Falletti, M., Pinola, G., Bianchini, E., Di Lazzaro, G., Rosati, V., Grillo, P., Giannini, F., Fattapposta, F., Costantini, G., Pisani, A., Saggio, G., & Suppa, A. (2025). Abnormal arm swing movements in Parkinson's disease: Onset, progression and response to L-Dopa. *Journal of NeuroEngineering and Rehabilitation*, 22(1), 47. <https://doi.org/10.1186/s12984-025-01589-w>
9. Di Menna, L., Alborghetti, M., De Bartolo, M. I., Borro, M., Gentile, G., Zinni, M., Bologna, M., Cutrona, C., D'Errico, G., Imbriglio, T., Bucci, D., Merlo, S., Ginerete, R. P., Orlando, R., Carrillo, F., Fortunato, G., Cannella, M., Sortino, M. A., Pansiot, J., ... Battaglia, G. (2025). Preclinical and clinical study on type 3 metabotropic glutamate receptors in Parkinson's disease. *Npj Parkinson's Disease*, 11(1), 1–14. <https://doi.org/10.1038/s41531-024-00860-6>

10. Galli, S., Pacilio, P., Bianchini, E., Alborghetti, M., De Carolis, L., Lombardo, P., Garramone, F., Salvetti, M., & Rinaldi, D. (2025). The Role of MAO-B Inhibitors in Fatigue in Parkinson's Disease: A Narrative Review. *Journal of Clinical Medicine*, 14(8), Articolo 8. <https://doi.org/10.3390/jcm14082598>
11. De Blasiis, P., Fullin, A., De Girolamo, C. I., Bianchini, E., Miele, G., Setola, N., & Melone, M. A. B. (2025). Postural Abnormalities on the Sagittal Plane in Parkinson's Disease and Therapeutic Role of the K1 Posture Keeper Shirt Evaluated by 3D Motion Analysis. *Applied Sciences*, 15(5), Articolo 5. <https://doi.org/10.3390/app15052255>
12. De Blasiis, P., Massimiani, A., Inglese, C., Bianchini, E., Fullin, A., De Girolamo, C. I., Giovannelli, M., Pau, M., Cocco, E., Salvetti, M., & Lus, G. (2024). Spasticity patterns assessment and recognition for therapeutic approaches (SPARTA) in multiple sclerosis: A multicenter epidemiological study. *Journal of Neurology*, 272(1), 34. <https://doi.org/10.1007/s00415-024-12750-1>
13. Galli, S., De Carolis, L., Bianchini, E., Alborghetti, M., Calì, B., Pacilio, P., Fanciulli, A., Pontieri, F. E., & Rinaldi, D. (2024). Effects of levodopa/carbidopa intestinal gel infusion on autonomic symptoms in advanced Parkinson's disease: A systematic review. *Clinical Autonomic Research: Official Journal of the Clinical Autonomic Research Society*. <https://doi.org/10.1007/s10286-024-01090-9>
14. Milane, T., Hansen, C., Correno, M. B., Chardon, M., Barbieri, F. A., Bianchini, E., & Vuillerme, N. (2024a). Comparison of number of people with freezing of gait in Parkinson's disease with and without sleep disturbances: A systematic review. *Sleep Medicine*, 121, 32–41. <https://doi.org/10.1016/j.sleep.2024.06.001>
15. Milane, T., Hansen, C., Correno, M. B., Chardon, M., Barbieri, F. A., Bianchini, E., & Vuillerme, N. (2024b). Comparison of sleep characteristics between Parkinson's disease with and without freezing of gait: A systematic review. *Sleep Medicine*, 114, 24–41. <https://doi.org/10.1016/j.sleep.2023.11.021>
16. Zerbinati, P., Bemporad, J., Massimiani, A., Bianchini, E., Mazzoli, D., Glorioso, D., della Vecchia, G., De Luca, A., & De Blasiis, P. (2024). Lateral Pectoral Nerve Identification through Ultrasound-Guided Methylene Blue Injection during Selective Peripheral Neurectomy for Shoulder Spasticity: Proposal for a New Procedure. *Journal of Personalized Medicine*, 14(1). <https://doi.org/10.3390/jpm14010116>
17. Suau, Q., Bianchini, E., Bellier, A., Chardon, M., Milane, T., Hansen, C., & Vuillerme, N. (2024). Current Knowledge about ActiGraph GT9X Link Activity Monitor Accuracy and Validity in Measuring Steps and Energy Expenditure: A Systematic Review. *Sensors*, 24(3). <https://doi.org/10.3390/s24030825>
18. Bianchini, E., Rinaldi, D., Alborghetti, M., Simonelli, M., D'Audino, F., Onelli, C., Pegolo, E., & Pontieri, F. E. (2024). The Story behind the Mask: A Narrative Review on Hypomimia in Parkinson's Disease. *Brain Sciences*, 14(1), Articolo 1. <https://doi.org/10.3390/brainsci14010109>
19. Alborghetti, M., Bianchini, E., De Carolis, L., Galli, S., Pontieri, F. E., & Rinaldi, D. (2024). Type-B monoamine oxidase inhibitors in neurological diseases: Clinical applications based on preclinical findings. *Neural Regeneration Research*, 19(1), 16–21. <https://doi.org/10.4103/1673-5374.375299>
20. Bianchini, E., Massimiani, A., Bemporad, J., & Giovannelli, M. (2023). A case of idiopathic lower limb dystonia treated with combined botulinum toxin and phenol nerve block. *Acta Neurologica Belgica*. <https://doi.org/10.1007/s13760-023-02458-w>
21. Sforza, M., Bianchini, E., Alivernini, D., Spalloni, A., Teresi, V., Madonia, I., Salvetti, M., Pontieri, F. E., & Sette, G. (2023). Cerebral hemodynamics and cognitive functions

- in the acute and subacute stage of mild ischemic stroke: A longitudinal pilot study. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*. <https://doi.org/10.1007/s10072-023-07260-3>
22. Bianchini, E., Galli, S., Alborghetti, M., De Carolis, L., Zampogna, A., Hansen, C., Vuillerme, N., Suppa, A., & Pontieri, F. E. (2023). Four Days Are Enough to Provide a Reliable Daily Step Count in Mild to Moderate Parkinson's Disease through a Commercial Smartwatch. *Sensors*, *23*(21), Articolo 21. <https://doi.org/10.3390/s23218971>
 23. Asci, F., Di Stefano, G., Di Santo, A., Bianchini, E., Leone, C., La Cesa, S., Zampogna, A., Cruccu, G., & Suppa, A. (2023). Pain-motor integration in chronic pain: A neurophysiological study. *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology*, *154*, 107–115. <https://doi.org/10.1016/j.clinph.2023.07.010>
 24. Bianchini, E., Warmerdam, E., Romijnders, R., Stürner, K. H., Baron, R., Heinzel, S., Pontieri, F. E., Hansen, C., & Maetzler, W. (2023). Turning When Using Smartphone in Persons With and Those Without Neurologic Conditions: Observational Study. *Journal of Medical Internet Research*, *25*, e41082. <https://doi.org/10.2196/41082>
 25. Rinaldi, D., Imbalzano, G., Galli, S., Bianchini, E., Ledda, C., De Carolis, L., Zibetti, M., Lopiano, L., Pontieri, F. E., & Artusi, C. A. (2023). The impact of dysphagia in Parkinson's disease patients treated with levodopa/carbidopa intestinal gel. *Parkinsonism & Related Disorders*, *109*, 105368. <https://doi.org/10.1016/j.parkreldis.2023.105368>
 26. Hansen, C., Chebil, B., Cockroft, J., Bianchini, E., Romijnders, R., & Maetzler, W. (2023). Changes in Coordination and Its Variability with an Increase in Functional Performance of the Lower Extremities. *Biosensors*, *13*(2), Articolo 2. <https://doi.org/10.3390/bios13020156>
 27. De Carolis, L., Galli, S., Bianchini, E., Rinaldi, D., Raju, M., Calì, B., Alborghetti, M., & Pontieri, F. E. (2023). Age at Onset Influences Progression of Motor and Non-Motor Symptoms during the Early Stage of Parkinson's Disease: A Monocentric Retrospective Study. *Brain Sciences*, *13*(2), Articolo 2. <https://doi.org/10.3390/brainsci13020157>
 28. Milane, T., Hansen, C., Chardon, M., Bianchini, E., & Vuillerme, N. (2023). Comparing Backward Walking Performance in Parkinson's Disease with and without Freezing of Gait-A Systematic Review. *International Journal of Environmental Research and Public Health*, *20*(2), 953. <https://doi.org/10.3390/ijerph20020953>
 29. Bianchini, E., Calì, B., Alborghetti, M., Rinaldi, D., Hansen, C., Vuillerme, N., Maetzler, W., & Pontieri, F. E. (2022). Step-Counting Accuracy of a Commercial Smartwatch in Mild-to-Moderate PD Patients and Effect of Spatiotemporal Gait Parameters, Laterality of Symptoms, Pharmacological State, and Clinical Variables. *Sensors (Basel, Switzerland)*, *23*(1), 214. <https://doi.org/10.3390/s23010214>
 30. Sforza, M., Bianchini, E., Alivernini, D., Salvetti, M., Pontieri, F. E., & Sette, G. (2022). The impact of cerebral vasomotor reactivity on cerebrovascular diseases and cognitive impairment. *Journal of Neural Transmission (Vienna, Austria: 1996)*, *129*(11), 1321–1330. <https://doi.org/10.1007/s00702-022-02546-w>

Papers submitted in peer-reviewed scientific journals (n=4)

1. Bianchini E, Lombardo P, Milane T, Rinaldi D, De Carolis L, Alborghetti M, Suppa A, Salvetti M, Hansen C, Vuillerme N. The impact of nocturnal hypokinesia on supervised and unsupervised mobility in people with Parkinson's disease. *npj Parkinson disease*.

Submitted.

2. Bianchini E, Garramone F, Rinaldi D, Alborghetti M, De Carolis L, Galli S, Suppa A, Salvetti M, Hansen C, Vuillerme N. Does cognition affect supervised and unsupervised mobility differently in people with Parkinson's Disease? A Cross-Sectional Study. *Journal of NeuroEngineering and Rehabilitation*. Submitted.
3. Bianchini E, Petit P, Chardon M, Rinaldi D, Alborghetti M, Galli S, Suppa A, Hansen C, Salvetti M, Vuillerme N. A Bayesian model averaging analysis to compare in-clinic walking capacity versus real-world walking performance in people with Parkinson's disease from digital health technologies. *JMIR mHealth uHealth*. Submitted.
4. Bianchini E, Petit P, Chardon M, Rinaldi D, Alborghetti M, Galli S, Suppa A, Hansen C, Salvetti M, Vuillerme N. Motor and non-motor symptoms impact on different domains of capacity- and performance-based mobility measures in Parkinson's disease. *npj Parkinson disease*. Submitted.

Communications in national and international congresses (n=13)

1. Pacilio P, Bianchini E, Galli S, De Carolis L, Hansen C, Alborghetti M, Milane T, Pontieri FE, Rinaldi D, Vuillerme N. Mobility differs in people with Parkinson's disease with and without nocturnal hypokinesia: a propensity score-matched study. *11th Congress of the European Academy of Neurology (EAN)*. 2025. 21-24 Jun. Helsinki.
2. Bianchini E, Hansen C, Alborghetti M, De Carolis L, Galli S, Pacilio P, Garramone F, Lombardo P, Rinaldi D, Vuillerme N. Objective evaluation of nocturnal movements in people with Parkinson's disease and association with clinical parameters. *11th Congress of the Italian Parkinson Society (LIMPE-DISMOV)*. 2025. 14-16 May. Rome.
3. Lombardo P, Guerriero M, Mauro C, Galli S, De Carolis L, Alborghetti M, Rinaldi D, Bianchini E. Combined physiotherapy and occupational therapy in people with Parkinson's disease: a pilot study. *11th Congress of the Italian Parkinson Society (LIMPE-DISMOV)*. 2025. 14-16 May. Rome.
4. De Carolis L, Pacilio P, Alborghetti M, Rinaldi D, Galli S, Garramone F, Lombardo P, Salvetti M, Bianchini E. The hidden face of hypomimia in Parkinson's disease: exploring clinical motor and non-motor symptoms correlates. *54th Congress of the Italian Society of Neurology (SIN)*. 2025. 24-28 Oct. Padova.
5. Bianchini E, Petit P, Rinaldi D, De Carolis L, Galli S, Alborghetti M, Pacilio P, Milane T, Hansen C, Garramone F, Lombardo P, Salvetti M, Vuillerme N. Non-motor symptoms impact on different domains of supervised and unsupervised mobility in Parkinson disease. *54th Congress of the Italian Society of Neurology (SIN)*. 2025. 24-28 Oct. Padova.
6. Bianchini E, Defilippi F, Rinaldi D, De Carolis L, Galli S, Pacilio P, Marano M, Hansen C, Salvetti M, Vuillerme N. Impact of Opicapone and Foslevodopa/Foscarbidopa on sleep quality and mobility in Fluctuating Parkinson's Disease: preliminary insights from a longitudinal pilot study. *54th Congress of the Italian Society of Neurology (SIN)*. 2025. 24-28 Oct. Padova.
7. Bianchini E, Rinaldi D, Alborghetti M, Galli S, De Carolis L, Pacilio P, Hansen C, Pontieri FE, Vuillerme N. Defining the Minimal Clinically Important Difference of average daily steps measured through a commercial smartwatch in people with Parkinson disease. *10th Congress of the Italian Parkinson Society (LIMPE-DISMOV)*. 2024. 10-12 Apr. Milan.

8. Garramone F, Bianchini E, Milane T, Rinaldi D, Alborghetti M, Galli S, De Carolis L, Pacilio P, Lombardo P, Hansen C, Pontieri FE, Vuillerme N. The association between questionnaires-based and smartwatch-based sleep parameters in people with Parkinson's disease. *10th Congress of the Italian Parkinson Society (LIMPE-DISMOV)*. 2024. 10-12 Apr. Milan.
9. Pacilio P, Bianchini E, Rinaldi D, Alborghetti M, Galli S, De Carolis L, Milane T, Hansen C, Pontieri FE, Vuillerme N. Association between cognitive functions and supervised mobility parameters in people with Parkinson's disease: the added value of backward walking assessment. *10th Congress of the Italian Parkinson Society (LIMPE-DISMOV)*. 2024. 10-12 Apr. Milan.
10. Bianchini E, Hansen C, Rinaldi D, Alborghetti M, Galli S, De Carolis L, Pacilio P, Pontieri FE, Vuillerme N. Clinically Assessed Walking Capacity Versus Real-World Walking Performance in People with Parkinson's disease. *10th Congress of the European Academy of Neurology (EAN)*. 2024. 29 Jun – 02 Jul. Helsinki.
11. Bianchini E, Rinaldi D, Galli S, Alborghetti M, De Carolis L, Petit P, Pacilio P, Milane T, Hansen C, Pontieri FE, Vuillerme N. Exploring Supervised and Real-World Mobility in People with Parkinson's Disease with and without Nocturnal Hypokinesia. *2024 International Congress of Parkinson's Disease and Movement Disorders*. 2024. 28 Sept – 01 Oct. Philadelphia.
12. Bianchini E, Di Pietro G, Galli S, Alborghetti M, Rinaldi D, De Carolis L, Pacilio P, Hansen C, Vuillerme N, Pontieri FE. Association between average daily steps measured through a commercial smartwatch and clinical parameters in Parkinson's Disease. *XXIII National Congress of the Italian Society of Movement Analysis in Clinic (SIAMOC)*. 2023. 4-7 Oct. Rome.
13. Bianchini E, Di Pietro G, Galli S, Alborghetti M, Rinaldi D, De Carolis L, Pacilio P, Hansen C, Vuillerme N, Pontieri FE. Association between average daily steps measured through a commercial smartwatch and clinical parameters in Parkinson's disease in different disease phenotypes. *53rd Congress of the Italian Society of Neurology (SIN)*. 2023. 21-24 Oct. Naples.

Book chapters (n=1)

1. Bianchini, E., & Maetzler, W. (2023). Chapter Five—Wearable systems in movement disorders. In A. Sánchez Ferro & M. H. G. Monje (A c. Di), *International Review of Movement Disorders* (Vol. 5, pp. 93–113). Academic Press. <https://doi.org/10.1016/bs.irmvd.2023.04.002>

This doctoral thesis explores mobility in Parkinson's disease as a multidimensional phenomenon, bridging laboratory-based assessments and real-world motor behavior. By integrating the use and validation of commercial wearable technology with advanced analytical approaches, it examines how motor and non-motor factors shape daily and nocturnal mobility across the 24-hour cycle and how movement reflects disease mechanisms and therapeutic potential. The work aims to contribute to a more ecological and patient-centered evaluation of mobility, with implications for clinical practice and the development of meaningful digital outcomes.

