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Evidence for Early and Regular Physical Therapy and Exercise in Parkinson's Disease

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Abstract

Advances in medical management of Parkinson's disease (PD) have resulted in living longer with disability. Although disability worsens over the course of the disease, there are signs of disability even in the early stages. Several studies reveal an early decline in gait and balance and a high prevalence of nonmotor signs in the prodromal period that contribute to early disability. There is a growing body of evidence revealing the benefits of physical therapy and exercise to mitigate motor and nonmotor signs while improving physical function and reducing disability. The presence of early disability coupled with the benefits of exercise suggests that physical therapy should be initiated earlier in the disease. In this review, we present the evidence revealing early disability in

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None declared.

PD and the effectiveness of physical therapy and exercise, followed by a discussion of a secondary prevention model of rehabilitation to reduce early disability and optimize long-term outcomes.

Keywords

Parkinson's disease; exercise; physical activity; physical therapy; rehabilitation

In 1817, Dr. James Parkinson's publication, "An Essay on the Shaking Palsy," documented a constellation of motor signs and symptoms that resulted in considerable morbidity and eventual mortality.[1] It was not until the late 1960s that dopamine replacement therapy became available, and not until the turn of the century that deep brain stimulation became a viable surgical treatment option. While these medical and surgical treatment options have dramatically improved longitudinal symptom control and have prolonged the average survival from diagnosis to death to decades, they have effectively prolonged the period of time people with Parkinson's disease (PD) live with disability.[2,3] Since no treatment for PD is curative and PD remains relentless in its progression toward substantial disability, the role of effective physical therapy (PT) and rehabilitative management has grown.

While the motor signs of PD have been recognized since James Parkinson's time, only over the past two decades has an understanding of the prodromal signs and symptoms and the constellation of nonmotor signs fully emerged.[4,5] For many years prior to the appearance of motor signs, nonmotor signs such as depression, anxiety, and disorders of sleep may accumulate. By the time the diagnosis of PD is determined, the presence of motor and nonmotor signs creates measurable disability that may be amenable to treatment. For this reason, optimizing status early in the course of the disease and delaying further disability should be the utmost priorities in the management of PD.

In this article, we provide a brief overview of PD and summarize the presence of disability at diagnosis and the natural history of progression of disability in PD. We review the evidence on the efficacy of PT, with a focus on important components of exercise early in the course of the disease. Mechanisms underlying these benefits are also discussed. Based on the evidence revealing early disability and efficacy of exercise in PD, we describe a secondary prevention model of rehabilitation in the comprehensive management of PD and present recommendations for clinical practice and research.

Overview of Parkinson's disease

Idiopathic PD affects approximately 1.6 to 1.8 percent of the population aged 65 years or older, as well as some younger individuals, with the prevalence projected to double by 2040.[6,7] The average age of onset is 61; however, up to 13% will be diagnosed before the age of 50 years.[8] Idiopathic PD is characterized by dopaminergic loss in the striatum and associated disruption of the basal ganglia and motor circuits.[9] A useful, although not universally accepted, conceptualization of PD pathology summarizes the progression of distinctive intraneuronal aggregation of α-synuclein in the form of globular Lewy bodies and spindle-like Lewy neurites that develop in vulnerable neurons.[10] Such pathology progresses from the lower brainstem through the midbrain and, ultimately, spreads to the

limbic and neocortical regions. Certain nonmotor symptoms (e.g., self-reported changes in olfaction, mood, sleep) may appear up to 20 years before motor symptoms, reflecting brainstem pathology that predates the involvement of the substantia nigra.[11,12] The clinical diagnosis of PD is usually made when the process reaches the substantia nigra and the classical motor signs emerge.

Currently, medical treatment of PD is purely symptomatic because no neuroprotective treatment is available. Pharmacologic treatment of PD focuses on dopamine replacement and relief of motor symptoms. Other pharmacologic interventions may be used to mitigate some of the nonmotor symptoms; however, the treatment of nonmotor symptoms is still limited and unsatisfactory because of the limited number of U.S. Food and Drug Administration (FDA)-approved medications for these problems.[13] The increasing evidence revealing the presence of early nonmotor and motor impairments supports the need for effective non-pharmacological interventions early in the course of disease.

Prior to a discussion of disability and the progression of the severity of the manifestations of PD, an explanation of the scales used by neurologists and researchers is necessary. First, to describe the body part distribution of signs and symptoms and difficulties with activities of daily living (ADLs) and instrumental ADLs (IADLs), an ordinal categorization is utilized (the Hoehn and Yahr scale [H&Y]).[14] Second, a more continuous measure of varied aspects of disease severity in several domains is widely utilized as a clinical and research outcome measure. The initial iteration, the Unified Parkinson Disease Rating Scale (UPDRS), was updated to a more contemporary version (the Movement Disorders Society-UPDRS or MDS-UPDRS[15]; ►Table 1). Both of these measures provide clarity to the amount of disability present in the samples and studies discussed in this review.[14,15]

Evidence of Early Disability/Natural History of Progression of Disability

Historically, the onset of disability in PD has been associated with moderate disease severity. However, careful examination of a variety of physiologic systems reveals the presence of measurable disability relative to age-matched neurologically healthy controls much earlier in the course of the disease, and in some cases even before diagnosis.

In a cross-sectional study of 618 persons with PD, even those in H&Y stages I to II described difficulty with ADLs and IADLs (►Table 1).[16] About 25% with mild disease severity (total UPDRS scores<20) reported difficulty walking (►Table 1). Difficulty with ambulation has been described as a clinical “red flag” signaling emerging disability in PD.[17] Early changes in gait are particularly concerning, as persons with PD have identified walking as the area of most concern yet least likely to improve.[18] For example, ambulatory activity studies point to early signs of decline. In a sample of 113 persons with de novo PD, the average daily step count measured over a 10-day period was 5,362 (±2,890) steps/day, indicating near sedentary levels of physical activity.[19] Persons with mild PD (H&Y I) accumulated approximately 20% fewer steps per day than controls over a 7-day period in a free-living environment.[20] In addition, these subjects performed fewer long bouts (> 2 minutes) of walking with less variable bout length compared with controls, indicating a more constrained pattern of ambulatory activity.[20] In a large study of individuals with PD

(*n*=699) and controls (*n*=1,959), self-reported physical activity was nearly 30% less in those with PD (57.8% in H&Y stages I–II).[21]

In a longitudinal study of ambulatory activity in PD, the overall amount of daily activity declined 12% over the course of a year.[22] Notably, the number of daily minutes of at least moderate-intensity ambulatory activity (i.e., step rate >100 steps per minute) declined by 40%, suggesting dramatic slowing of walking over 1 year. This decline represents a reduction in moderate-intensity physical activity to approximately 45 minutes per week, which is well below the recommended 150 minutes per week recommended by public health guidelines.[22,23] This rate of decline was steeper than the worsening of motor impairments, suggesting that natural ambulatory behavior may be a particularly robust indicator of decline and less responsive to dopaminergic replacement therapy.[16,22,24]

Gait speed has been referred to as a vital sign for recognizing imminent disability in older adults.[25] Studies in PD report clinically meaningful changes in gait speed that range from 0.02 to 0.06 m/s.[26] In a longitudinal study of persons with PD (*n*=266), a clinically meaningful decline of gait speed of 0.08 m/s over a 2-year period was observed.[27] Persons with PD walking slower than 0.88 m/s are less likely to be engaged in community walking.[28] These critical thresholds can provide important points of reference for interpreting the magnitude of gait disability in an individual patient.

Loss of postural control is an additional sign of early disability in PD. Even in persons with PD who report no balance or gait problems, deficits are recognized on clinical exam. For example, an increase in sway during static standing has been described in early PD.[29] Increased gait variability and impaired turning appear early in PD, and may indicate impaired dynamic balance.[30,31] Historically, falling has been thought to occur later in the course of PD. However, in a fall natural history study of 99 newly diagnosed persons with PD in the United Kingdom, 79.7% fell over a 54-month period.[32] Most striking, however, was that 26.2% reported retrospective falls at baseline (before being diagnosed). In addition, 30% experienced a fall within 18 months of the obtained baseline. These finding are similar to those reported in the Norwegian ParkWest Study, in which 181 drug-naive patients with incident PD were monitored prospectively over 7 years.[33] Approximately 64% reported falling over the study period, with 15% reporting falls prior to diagnosis and 13% falling within the first year. Collectively, these data suggest that screening for falls and balance training should occur early in the course of the disease.[31,32]

Beyond the motor concerns noted earlier, several non-motor signs are present during the prodromal period and/or at the point of diagnosis. In a study of de novo patients, 25% reported daytime sleepiness, suggesting early manifestations of sleep disturbance.[34] Depression and anxiety are relatively common features of PD that may suggest the need for interventions targeting mood early in the course of the disease.[5] The cognitive phenotype in early PD consists of mild deficits of attention, executive function, verbal fluency, and visuospatial function. The prevalence of cognitive deficits or mild cognitive impairment ranges from 19 to 36%.[5] Fatigue, characterized by the feeling of tiredness or exhaustion, has been identified by persons with PD as one of their most disabling symptoms with the greatest impact on quality of life.[35] Autonomic dysfunction may also be present

prior to diagnosis, as well as early in the postdiagnosis period. Common autonomic deficits include manifestations in the cardiovascular (e.g., orthostatic hypotension, supine hypertension, increased heart rate regularity), urinary (e.g., nocturia, urge incontinence), and gastrointestinal (e.g., dysphagia, constipation, bowel incontinence) systems.[36-39] Pain is another common nonmotor sign of PD and may predate motor symptoms by years.[40] In early-stage PD, pain is often rated as one of the most bothersome nonmotor symptoms which may contribute to functional decline.[40] In a study of 231 persons with PD, pain was reported by 81%, with 39% reporting pain of moderate severity or worse.[41] Increased rigidity was associated with higher pain frequency that interfered with ADLs and work. The most frequently occurring pain type in PD is musculoskeletal in nature, affecting 70% of patients.[42-45] Many studies have shown complaints of shoulder and hip pain that precede a diagnosis of PD for several months or years before the first motor symptoms develop.[43,46] Taken together, these studies suggest that a variety of nonmotor factors contribute to disability early in the disease process. Given that exercise has been shown to improve sleep[47] and cognition,[48] while reducing depression, anxiety,[49] and pain[50] among adults without PD, exercise studies targeting nonmotor signs, early in the disease progression in persons with PD, are warranted.

Benefits of Exercise in Parkinson's Disease

Over the past two decades, there has been a significant increase in research examining exercise interventions in people with PD. This accumulation of primary research has more recently led to meta-analytic reviews of a variety of PT interventions.[51-53] Our coverage of the evidence base for these interventions focuses on selecting larger ($n \geq 40$), recent (2009 to present), randomized controlled trials (RCTs) of physical activity or exercise interventions in PD, in which the outcomes encompass motor and nonmotor symptoms, function and/or disability measures (►Table 2).

Aerobic Training

Epidemiological evidence suggests that higher levels of moderate to vigorous activity in mid or later life are associated with lower risk of PD.[54,55] Animal models of neurotoxin-induced parkinsonism provide evidence for both generalized and targeted effects of aerobic exercise on brain health.[56] Exercise increases dopamine release, alters synaptogenesis, increases regional cerebral blood flow, and increases endogenous brain neurotrophic levels (e.g., BDNF, GDNF), which are proposed to attenuate striatal dopamine loss.[56,57] Exercise also downregulates striatal dopamine transporter and vesicular monoamine transporter—markers for the integrity of striatal dopamine terminals.[58] The results of epidemiological and animal studies in PD suggest that aerobic exercise influences the underlying disease process, leading to a disease-modifying effect. However, in the absence of valid and reliable biomarkers of PD progression, conclusive evidence of the disease-modifying effects of aerobic exercise in humans with PD is lacking. Despite this, changes in the structural and functional integrity of the brain have been revealed in several small exercise studies in PD.[59] Increases in maximal corticomotor excitability, increases in BDNF, weakening of the overactive indirect striatal pathway DA-D2R expression, and changes in gray matter volume reveal the potential for exercise-induced neuroplasticity in the brains of people with PD.[59]

RCTs of aerobic exercise in PD reveal benefits at many levels (►Table 2). In a phase II RCT (SPARX trial) of 128 persons with de novo PD, high intensity aerobic treadmill training (4 days per week, 80–85% maximum heart rate), but not moderate intensity (4 days per week, 60–65% maximum heart rate), resulted in a significant attenuation of the progression of motor symptoms (UPDRS motor scores) and an increase in VO_2 max (maximum rate of oxygen consumption reflecting cardiorespiratory fitness) at 6 months compared with a wait-list control condition.[60] The results of a more recent double-blind RCT (Park-in-Shape) strengthen this body of evidence.[61] A home-based and remotely supervised moderate to high intensity aerobic cycling program (30–45 minutes, three times per week) was compared with an active control condition in 130 participants with PD in H&Y 1–2 over 6 months. Significant and clinically meaningful attenuation of off-state motor signs in the aerobic condition was revealed compared with the control condition at the 6-month endpoint.[61] Collectively, these results suggest the importance of high intensity aerobic training in the mitigation of motor symptoms in the early stages of PD. However, the effect of aerobic exercise on UPDRS motor scores is mixed when considering other studies.[62,63] This may be due to insufficient intensity, as the aerobic training was implemented in the low to moderate range in these studies. Notably, motor symptoms were assessed in the absence of dopamine replacement therapy in the SPARX trial[60] of de novo patients, and in the "off" medication state in the Park-in-Shape trial[61] as compared with during an "on" state in the other trials.[62,63] The confounding effects of dopamine replacement therapy may mask any exercise-related improvements in motor symptoms. In general, aerobic exercise studies consistently reveal improvements in VO_2 compared with other modes of exercise (i.e., resistance training, flexibility, and balance training).[60-64] Improvements in various gait parameters such as walking capacity (6-minute walk test), walking speed, and spatiotemporal variables (-step/stride length)[62-66] are most often reported in aerobic exercise trials which incorporate some form of walking (treadmill training, overground walking, Nordic walking) as the mode of exercise.[62,64,66] The recent Park-in-Shape trial failed to show improvements in gait and balance outcomes with cycling exercise.[61] Taken together, these findings suggest a specificity of training effect, as VO_2 consistently improves with all forms of aerobic training and walking improves with treadmill training, overground walking and Nordic walking but not with cycling. Cycling, however, may be a more viable option for those with postural instability or freezing, which may preclude safe walking on a treadmill or in the community.

Improvements in executive function, depression, and fatigue have been demonstrated following moderate intensity overground walking over 6 months[64] in those with mild to moderate PD (H&Y 1–3). In an RCT of persons with moderate disease severity (H&Y 3), significant improvements in executive function, attention, and memory were noted after 1 month (12 sessions, three times a week) of treadmill training compared with a control condition.[67] Improvements in sleep quality have been reported following 6 months of a multimodal exercise program that included aerobic, resistance, and balance training compared with a control condition.[68]

In summary, aerobic training is feasible in persons with PD. Among those meeting enrollment criteria across studies, no serious adverse events related to high or moderate intensity aerobic exercise have been reported, suggesting it is safe in persons with PD.

Moderate to high intensity aerobic exercise may be most beneficial in attenuating motor symptoms, improving physical function, and reducing disability; however, additional studies are needed. The effects of aerobic exercise on improving nonmotor signs are promising, but additional studies are needed. Long-term engagement in aerobic exercise is necessary to realize sustained benefits. Given the generalized effects of exercise on brain health, the potential for targeted effects on the underlying disease pathology and the reduced decline in motor signs in de novo PD, engagement in aerobic exercise early in the course of the disease is warranted.

Resistance Training

Hypokinesia and bradykinesia in PD are mediated by changes in basal ganglia function as well as the muscle atrophy and loss of strength associated with aging.[69] Such changes reinforce a positive feedback loop of reduced activity that leads to progressive deficits in muscle force production and increased difficulties with movement amplitude and speed. Given that skeletal muscle is the final effector of movement commands from the central nervous system, increasing muscle is targeted at minimizing both hypokinesia and bradykinesia.[70,71]

Cross-sectional studies comparing people with PD to neurologically healthy controls reveal a consistent reduction in strength in multiple modes of contraction, but appears worse at higher speeds of concentric contractions and in extensor muscles.[72-75] In addition, studies examining axial muscle function associated with cough suggest reduced strength of the accessory muscles of respiration responsible for contributing to forceful coughing.[76]

Well-controlled clinical studies of resistance training interventions in PD are fewer in number than aerobic exercise trials, but consistently demonstrate increased muscle force production and improved functional mobility acutely following training (►Table 2).[77-80] In one of the largest trials where resistance training was the primary intervention (the PRET-PD study), Corcos and colleagues followed an acute training period with guidance and support for continued training for 2 years.[78] Participants in the experimental group not only improved strength and mobility but also improved in their measures of disease severity (UPDRS) and cognition over the 2 years of the study, suggesting a longer term benefit when training was sustained.[81-83]

The mechanisms of force production improvements have not been comprehensively studied in a single study, but synthesis of results from several studies suggests both peripheral muscular and central neurologic adaptations occur. At a muscle cellular level, muscle biopsies show fiber hypertrophy following training.[79] At a macroscopic level, MRI measures of volume document muscle hypertrophy of trained muscles.[77] Electromyographic (EMG) measures of muscle contractions provide insight into neurologic improvements; reduced segmentation of muscle contractions and greater activation of muscles point to improvements in central nervous system–mediated efferent motor stimulation to the muscle.[79,84]

Regardless of the mechanisms of improvement, the functional improvements observed span tasks and muscle groups. While most studies have examined upper and lower limb

musculature and tasks, some studies have examined expiratory muscle strength training.[76] Important findings from these studies relevant to pulmonary function in PD are improved cough force and potential improvements in swallowing dynamics.[76] Collectively, these results suggest that the benefits of resistance training are enhanced when focused on targeted functional limitations that require muscle force production in finite time periods (i.e., sit to stand transfers, stair climbing, cough).

In summary, resistance training is safe and feasible in persons with PD. With the exception of delayed onset muscle soreness, no serious adverse events related to resistance training have been reported, suggesting it is also safe. Moderate to high intensity resistance exercise focused on movement speed or muscle power production may be beneficial in reducing UPDRS motor symptoms, improving physical function and reducing disability; however, additional studies are needed. Studies of resistance exercise effects on nonmotor signs are also greatly needed.

Balance Training

Fall occurs commonly in individuals with PD and is a significant contributor to injuries, mobility deficits, and self-reports of poor quality of life.[85] Given the heterogeneity of motor presentations of PD and postural instability, it is not surprising that there is no single research-validated program that specifically addresses all the causes of falls in people with PD. Despite this, high-quality evidence exists where balance programs may improve clinical postural task performance and reduce falls for subgroups of people with PD. Recent meta-analytic studies have documented pooled effect size estimates that suggest immediate post-program benefits and short-term follow-up benefits.[86]

In-depth consideration of the large RCTs published that use fall rates as primary outcomes reveals more detailed information about the relative efficacy of balance training (►Table 2).[87-92] Two trials utilized designs where balance training was compared with control groups receiving no balance training.[87,88] The balance training in these trials consisted of exercise interventions that included strength training components. One of these trials was conducted in a home,[87] while the other was delivered in a clinic.[88] In both of these trials, fall rates were reduced in the balance training group. Interestingly, the study conducted by Canning et al showed no reduction in fall rate for the experimental group as a whole. Subgroup analysis revealed substantial reductions in fall rates in lower disease severity participants (motor UPDRS score of 26 or less). Individuals with PD and low motor severity in the experimental group experienced a 69% reduction in falls, while the individuals with PD and a high disease severity (motor UPDRS score of 27 or greater) demonstrated a 61% increase in falls.[87]

Technologically more advanced interventions have begun to be utilized in an effort to address both physical and cognitive fall risk factors. In a multicenter trial, researchers utilized a virtual environment to train individuals on a treadmill to avoid virtual obstacles and to find their way on a virtual route, and compared this to treadmill training by itself. While training time was equivalent for the over 100 participants who took part in the study, the control group reduced their fall rate relative to the pre-study reported fall history, suggesting that treadmill training alone provided some fall rate improvements. However,

at the 6-month follow-up, persons with PD in the virtual training experimental group demonstrated a 55% reduction in falls compared with the control group.[89]

Most recently, a large trial in Europe (PDSAFE) was designed to examine more definitively the effects of a personalized and progressive home-based program, with fall rates as the primary outcome and several secondary outcomes (near fall rates, balance task performance, self-report measures).[90] Over 400 participants with varied levels of PD severity participated in a training program which included fall avoidance strategy training coupled with balance and strengthening exercises. Given the previous findings of varied effectiveness depending on disease severity, the authors prespecified subgroup comparisons. Their results were consistent with previous work, in that balance training was effective at reducing fall rates in individuals with PD of moderate disease severity, but increased the fall rate in individuals with higher levels of disease severity. Despite these findings on the primary outcomes, balance training was successful at addressing several secondary outcomes (near falls rate, balance task performance, and self-report measures of balance abilities) across the whole PDSAFE group—including those with mild, moderate, and severe disease. This suggests that all participants were able to adhere to and therefore benefit from the exercise program with regard to balance ability; however, these gains did not translate to mitigation of falls in those with the greatest disease severity during periods of instability in real-world situations.

Balance training may also contribute to improvements in nonmotor signs. A 10-week RCT comparing land-based to aquatic exercise revealed significant reductions in pain across both groups.[93] An RCT of a sensorimotor-based balance exercise program revealed significant reductions in depression and apathy in those receiving individual but not group treatment.[94] In an 8-week RCT (n=138), mindfulness yoga training resulted in significantly more improvement in depression and anxiety symptoms, compared with those in the stretching and resistance training group.[95]

In summary, the highest quality evidence available to date suggests significant ability to reduce fall rates for those with mild to moderate disease. In addition, those studies that are clinic-based and not home-based provide greater levels of supervision and more intensive training, and have resulted in greater reductions in fall rate.[88,92,96] In these studies, those with more severe disease did not benefit and even appeared to have increased fall rates as a result of training. The origins of this increased risk are not clear, but may include increased gait-related mobility without improving postural competence, thus increasing the frequency of exposure to postural challenges without the postural skills to deal with these challenges. In addition, the role of declining cognitive status contributing to poor carryover of fall prevention strategies and lower adherence to the exercise program may contribute. Finally, those with greater disease severity are likely to have more complex symptoms such as freezing of gait, which is associated with reduced motor learning capacity and diminished retention. Those with freezing of gait may also require different strategies (i.e., external cueing) which may not be encompassed in a balance training program. Such findings reflect the initial steps of lines of research that are needed to clarify which subgroups of individuals (just diagnosed individuals, those who demonstrate freezing of gait, intermittent fallers, recurrent fallers) may benefit from specific types of interventions. Studies are ongoing to examine the efficacy of alternate interventions in these individuals. Just as the heterogeneity

of PD motor symptoms necessitates variations in pharmacologic and surgical treatments, current research clearly indicates that a “one-size-fits-all” rigidly controlled balance training intervention is inappropriate for all those with PD.

Gait training

Given the evidence revealing early declines in gait speed and ambulatory activity, treatment geared toward increasing walking velocity and amount of walking is critical to improve function and reduce disability.[97] Numerous studies reveal the effectiveness of treadmill training in improving gait speed in persons with PD (►Table 2).[51,53,98] The increase in gait speed with treadmill training is also associated with improved stride length, arm swing, and stride time variability.[65] The treadmill may serve as an external pacer, overcoming the hypokinesia that leads to gait slowing with continuous walking. Treadmill walking has also been associated with reductions in depression.[98] Improvements in walking have also resulted following moderate intensity overground walking in the community setting, using either a heart rate monitor or step activity tracker to facilitate adherence to a moderate intensity pace.[64,97] Several studies suggest the benefits of Nordic walking in improving gait in persons with PD.[66,99,100] Most reveal increases in gait speed and walking capacity, with some revealing a reduction in motor symptoms or pain.[66,99,100]

There is a robust body of literature revealing the benefits of external cueing to improve various aspects of gait in PD.[101] Rhythmic auditory stimulation is particularly effective in improving gait speed during continuous walking. External cueing is also effective in discontinuous gait impairments such as freezing of gait. Both visual and auditory cues have been shown to reduce freezing of gait during discrete tasks such as turning, walking over a threshold, or through a doorway.[102] There do not appear to be lasting effects once the cues are withdrawn. Despite the lack of persistent effects, cueing is a very effective means of improving various aspects of gait and should be recommended to improve immediate functional capacity. Several wearable cueing devices show promise for use at home to overcome freezing of gait; however, additional studies are needed to improve usability and effectiveness.[103,104]

Difficulty with dual-task walking is also evident early in the course of the disease.[105] Due to the reduction in automaticity of movement associated with basal ganglia dysfunction, persons with PD often allocate attention resources to the task of walking to improve walking ability. When engaging in dual tasks, such as walking and talking or walking and carrying an object, attentional resources are allocated to the secondary cognitive or motor task and subsequently drawn away from the walking task.[106] This often leads to a degradation in walking ability. A recent multicenter RCT investigated whether improvements in dual tasking were possible in persons with PD (N=121) compared with a control period without training.[107] Results revealed that dual-task training over 6 weeks led to improvements in dual-task gait velocity and select gait parameters across both trained and untrained dual tasks.[107,108] The gains were retained at the 12-week follow-up. There was no increase in fall risk, suggesting that dual-task training is safe as well as effective and should be included as part of PT interventions.

In summary, gait training is effective in improving various aspects of walking in persons with PD. This is particularly important given that many aspects of gait do not improve with dopamine replacement therapy.[24] Treadmill training and moderate intensity over ground walking have been shown to improve gait speed, walking capacity, and step/stride length. Rhythmic auditory cueing is particularly effective in improving gait speed, whereas discrete auditory and visual cues are effective in overcoming freezing of gait. Dual-task training is safe and effective in improving walking under dual-task conditions.

Suboptimal Standard of Physical Therapy Care

Ironically, despite the increased understanding of early disability in PD and the evidence supporting early and regular exercise interventions, utilization of PT services for persons with PD in the United States is remarkably low. In a study examining outpatient rehabilitation utilization for PD, only 14.2% of 174,643 Medicare beneficiaries with a diagnosis of PD in 2007 had claims for PT.[109] Those patients with PD who had at least one neurologist visit per year were 43% more likely to have a claim for a PT evaluation compared with patients without neurologist care. Rehabilitation utilization in other countries far exceeds that of the United States. In the Netherlands, referral rates to PT in 2009 were 63%,[110] and 54% in the United Kingdom.[111] A wide variety of factors may explain the low physical therapy utilization rates among those with PD in the United States. Care by a primary care physician (rather than a neurologist) may reduce referral rates due to a lack of awareness of the evidence supporting physical therapy and exercise in PD.[109] In addition, physicians have traditionally waited for the presence of overt disability associated with the moderate to severe stages of PD to refer patients to physical therapy. Lack of appreciation of early disability and/or the value of PT and exercise during early disease stages may also contribute to later referrals. Physicians also may be recommending community-based exercise programs (tai chi, dance, boxing) during the early stages, rather than physical therapy services, given the lack of substantial disability or an awareness of the role of PT at the point of diagnosis. Previous Medicare policy requiring that patients demonstrate functional improvements to continue with PT may have led to denials of PT services and therefore fewer claims.

Guidelines and policy changes may help increase the utilization of PT services for persons with PD. In 2010, the American Academy of Neurology published the first set of quality measures for the treatment of patients with PD[112] and these include a recommendation to discuss the need for physical, occupational, and speech therapy on an annual basis. The UK National Institute for Health and Care Excellence (NICE) guidelines go a step further, recommending referral to physiotherapists *early* in the course of the disease.[113] Lastly, in 2014, Medicare policy changed to allow access to PT services when the goal is to maintain functional status or prevent a decline in functional status, as long as the need for skilled intervention could be justified.

Traditionally, when patients with PD are referred to PT, this occurs many years into the disease when there is overt disability such as falling, freezing of gait, difficulty moving in bed or rising from a chair (►Fig. 1). At this point, an episode of PT is typically provided and the patient often experiences improvements in functional outcomes. However, there is

a lost opportunity to take more preventative measures in the early stages of the disease. In addition, a discrete episode of care without regular follow-up visits results in decreased adherence to treatment recommendations and a worsening of disability. Often patients with PD return to PT only after an acute event, such as a hip fracture, that results in significant disability and poor quality of life. A secondary prevention approach to rehabilitation is needed to address signs of disability and physical inactivity early and regularly over the course of the disease.

Secondary Prevention Model

In a secondary prevention model, patients with PD consult with a physical therapist with expertise in PD at the point of diagnosis (►Fig. 2). A standardized battery of clinical measures are implemented to characterize baseline functional status, burden of disability, and quality of life. Motor and nonmotor impairments contributing to functional limitations are also measured. In addition, the contributions of cardiopulmonary, orthopaedic, and/or other neurologic conditions to the functional deficits are ascertained. Overall physical activity level and engagement in exercise are captured. Detailed characterization of functional status at baseline using standardized, psychometrically strong clinical measures allows for careful monitoring of the progression of disability over the disease continuum. Comparisons to natural history data in PD and age-matched normative data provide the physical therapist with the essential data needed to tailor the exercise prescription to each individual with the goal of optimizing outcome through prevention and/or mitigation of functional deficits.

During this initial consultation period, only a few visits to a physical therapist are typically needed to characterize baseline status and to prescribe an exercise program tailored to the individual. These visits encompass teaching patients how to properly perform the exercises in addition to ensuring the exercise program is implemented at the optimal dose (i.e., frequency, duration, and intensity). In addition, time is spent helping patients develop a plan as to how to successfully integrate exercise into their daily routines over the long term. Barriers and motivators of exercise and strategies to facilitate behavioral change are discussed.[114,115] This is particularly important given the prevalence of depression and apathy that may reduce motivation to engage in exercise over the long term.[116,117] Some have suggested the benefits of an intensive bout of therapy during the early stages to reduce long-term disability.[118] For example, the long-term effect of an intensive, multidisciplinary, inpatient rehabilitation preventative approach applied 5 days per week for 4 weeks in newly diagnosed persons with PD was examined. The 4-week intervention was provided early in the diagnosis and again 1 year later. At 2 years, results revealed less disability, less disease progression, and improved mobility in the intervention group compared with a usual care control group.[118]

A critical element of this secondary prevention approach is regular follow-up visits to a physical therapist over the continuum of the disease. Just as regular visits to a neurologist are necessary to allow for reassessment of PD signs and adjustments to the medication regimen, regular visits to a physical therapist allow for reassessment of functional status and adjustments to the exercise program as necessary. An exercise program must be sufficiently

challenging and targeted to optimize benefits. The mode and intensity of the exercise needs to be adapted over the course of the disease as symptom profiles change. This approach is analogous to the “Dental Model” in which regular visits occur every 6 months or annually, aligning with the AAN guidelines.[112] Small changes in status (i.e., slower walking speed, decline in balance) can be detected and treated early, leading to improvements (i.e., faster walking, reduced fall risk) rather than a continued decline in function.[27,119] These follow-up visits could trigger an episode of care in the form of a series of PT visits if a significant decline in function has occurred. This episode of care may include treatment beyond exercise, such as gait training with cueing, balance retraining, and strategies to overcome freezing of gait, among others, depending on the profile of each individual.

There has been a substantial increase in the number of community-based exercise programs available for people with PD. These may include tai chi, boxing, dance, cycling, among others. This has been a positive development in that they allow greater access to exercise programs and provide a sense of camaraderie and social support, which may increase adherence to exercise. Physical therapists are well positioned to determine the types of programs that may be most beneficial to patients given their particular profile. However, patients need a comprehensive, adequately dosed exercise program, which is often only partially achieved through participation in community-based exercise programs. For example, it is typical for persons with PD to participate in community exercise programs one to two times per week. In addition, a particular type of exercise class may address some of their needs (i.e., balance exercise) but not all. There is also a tendency for people to overestimate the intensity at which they exercise. In addition, autonomic dysfunction early in the course of the disease is common and may lead to blunted heart rate responses as well as affect the overall response to exercise interventions.[36-38] Education is needed as to how to accurately determine optimal exercise intensity so that persons with PD can ensure optimal benefit while exercising within an exercise class or while exercising independently. In summary, a physical therapist can prescribe an appropriately dosed exercise program tailored to an individual, which may include recommendations for participation in community-based exercise classes as part of a comprehensive exercise program.

Summary and Future Directions

While the epidemiologic evidence suggesting that exercise may reduce the risk of developing PD coupled with evidence of the beneficial effects of exercise in toxin-induced animal models of PD has generated significant interest in exercise and physical activity research for people with PD, there is much work that remains to be done. At a basic science level, the neural/physiologic mechanisms underlying the benefits of various types of exercise are not fully understood. However, the majority of well-controlled exercise studies reveal benefits across a variety of behavioral outcomes, suggesting a central role for exercise in the management of PD. However, these results reflect group means. Not all participants improve and some improve more than others. Personalization of interventions to specific motor phenotypes has not been explored and could optimize outcomes. Additional studies are also needed to examine the effects of exercise on physiologic measures of nonmotor features such as cognition, depression, fatigue, pain, and autonomic dysfunction.

Importantly, numerous studies reveal the presence of early disability in PD. Given the benefits of exercise in improving many of the early signs (i.e., gait, balance, and cognitive impairments), physical therapy should be recommended at the point of diagnosis to establish a long-term, ongoing exercise plan of care. However, from a health services/health outcomes standpoint, more studies are needed to determine the benefits of early rehabilitation interventions (i.e., secondary prevention approach) on reducing health care costs, slowing the progression of disability and enhancing quality of life in persons with PD over the long term. Future research is needed to examine PT utilization rates given the growth of evidence demonstrating the benefits of PT, the increased awareness of early disability in PD, the changes to Medicare policy, and the more recent AAN quality measures for the treatment of PD.

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References

1. Parkinson J An essay on the shaking palsy. 1817. J Neuropsychiatry Clin Neurosci 2002;14(02):223–236, discussion 222 [PubMed: 11983801]
2. De Pablo-Fernandez E, Tur C, Revesz T, Lees AJ, Holton JL, Warner TT. Association of autonomic dysfunction with disease progression and survival in Parkinson disease. JAMA Neurol 2017;74(08):970–976 [PubMed: 28655059]
3. Golbe LI, Leyton CE. Life expectancy in Parkinson disease. Neurology 2018;91(22):991–992 [PubMed: 30381371]
4. Marras C, Chaudhuri KR. Nonmotor features of Parkinson's disease subtypes. Mov Disord 2016;31(08):1095–1102 [PubMed: 26861861]
5. Goldman JG, Postuma R. Premotor and nonmotor features of Parkinson's disease. Curr Opin Neurol 2014;27(04):434–441 [PubMed: 24978368]
6. Kowal SL, Dall TM, Chakrabarti R, Storm MV, Jain A. The current and projected economic burden of Parkinson's disease in the United States. Mov Disord 2013;28(03):311–318 [PubMed: 23436720]
7. Willis AW, Evanoff BA, Lian M, et al. Metal emissions and urban incident Parkinson disease: a community health study of Medicare beneficiaries by using geographic information systems. Am J Epidemiol 2010;172(12):1357–1363 [PubMed: 20959505]
8. Pagano G, Ferrara N, Brooks DJ, Pavese N. Age at onset and Parkinson disease phenotype. Neurology 2016;86(15):1400–1407 [PubMed: 26865518]
9. Rodriguez-Oroz MC, Jahanshahi M, Krack P, et al. Initial clinical manifestations of Parkinson's disease: features and pathophysiological mechanisms. Lancet Neurol 2009;8(12):1128–1139 [PubMed: 19909911]
10. Braak H, Ghebremedhin E, Rüb U, Bratzke H, Del Tredici K. Stages in the development of Parkinson's disease-related pathology. Cell Tissue Res 2004;318(01):121–134 [PubMed: 15338272]
11. Kalia LV, Lang AE. Parkinson's disease. Lancet 2015;386(9996):896–912 [PubMed: 25904081]
12. Olanow CWM, Stern MB, Sethi K. The scientific and clinical basis for the treatment of Parkinson disease. Neurology 2009;72(21, Suppl 4):S1–136

13. Titova N, Chaudhuri KR. Nonmotor Parkinson's and future directions. Int Rev Neurobiol 2017;134:1493–1505 [PubMed: 28805581]
14. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967;17(05):427–442 [PubMed: 6067254]
15. Goetz CG, Tilley BC, Shaftman SR, et al. ; Movement Disorder Society UPDRS Revision Task Force. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. Mov Disord 2008;23(15):2129–2170 [PubMed: 19025984]
16. Shulman LM, Gruber-Baldini AL, Anderson KE, et al. The evolution of disability in Parkinson disease. Mov Disord 2008;23(06):790–796 [PubMed: 18361474]
17. Shulman LM. Understanding disability in Parkinson's disease. Mov Disord 2010;25(Suppl 1):S131–S135 [PubMed: 20187231]
18. Nisenzon AN, Robinson ME, Bowers D, Banou E, Malaty I, Okun MS. Measurement of patient-centered outcomes in Parkinson's disease: what do patients really want from their treatment? Parkinsonism Relat Disord 2011;17(02):89–94 [PubMed: 20952243]
19. Christiansen C, Moore C, Schenkman M, et al. Factors associated with ambulatory activity in de novo Parkinson disease. J Neurol Phys Ther 2017;41(02):93–100 [PubMed: 28263256]
20. Lord S, Godfrey A, Galna B, Mhiripiri D, Burn D, Rochester L. Ambulatory activity in incident Parkinson's: more than meets the eye? J Neurol 2013;260(12):2964–2972 [PubMed: 23900754]
21. van Nimwegen M, Speelman AD, Hofman-van Rossum EJ, et al. Physical inactivity in Parkinson's disease. J Neurol 2011;258(12):2214–2221 [PubMed: 21614433]
22. Cavanaugh JT, Ellis TD, Earhart GM, Ford MP, Foreman KB, Dibble LE. Capturing ambulatory activity decline in Parkinson's disease. J Neurol Phys Ther 2012;36(02):51–57 [PubMed: 22592060]
23. Cavanaugh JT, Ellis TD, Earhart GM, Ford MP, Foreman KB, Dibble LE. Toward Understanding Ambulatory Activity Decline in Parkinson Disease. Phys Ther 2015;95(08):1142–1150 [PubMed: 25858971]
24. Smulders K, Dale ML, Carlson-Kuhta P, Nutt JG, Horak FB. Pharmacological treatment in Parkinson's disease: effects on gait. Parkinsonism Relat Disord 2016;31:3–13 [PubMed: 27461783]
25. Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. J Am Geriatr Soc 2003;51(03):314–322 [PubMed: 12588574]
26. Hass CJ, Bishop M, Moscovich M, et al. Defining the clinically meaningful difference in gait speed in persons with Parkinson disease. J Neurol Phys Ther 2014;38(04):233–238 [PubMed: 25198866]
27. Ellis TD, Cavanaugh JT, Earhart GM, et al. Identifying clinical measures that most accurately reflect the progression of disability in Parkinson disease. Parkinsonism Relat Disord 2016;25:65–71 [PubMed: 26876037]
28. Elbers RG, van Wegen EE, Verhoef J, Kwakkel G. Is gait speed a valid measure to predict community ambulation in patients with Parkinson's disease? J Rehabil Med 2013;45(04):370–375 [PubMed: 23450464]
29. Mancini M, Fling BW, Gendreau A, et al. Effect of augmenting cholinergic function on gait and balance. BMC Neurol 2015;15:264 [PubMed: 26697847]
30. Hausdorff JM, Doniger GM, Springer S, Yogev G, Simon ES, Giladi N. A common cognitive profile in elderly fallers and in patients with Parkinson's disease: the prominence of impaired executive function and attention. Exp Aging Res 2006;32(04):411–429 [PubMed: 16982571]
31. Mancini M, El-Gohary M, Pearson S, et al. Continuous monitoring of turning in Parkinson's disease: rehabilitation potential. NeuroRehabilitation 2015;37(01):3–10 [PubMed: 26409689]
32. Lord S, Galna B, Yarnall AJ, et al. Natural history of falls in an incident cohort of Parkinson's disease: early evolution, risk and protective features. J Neurol 2017;264(11):2268–2276 [PubMed: 28948348]
33. Hiorth YH, Alves G, Larsen JP, Schulz J, Tysnes O-B, Pedersen KF. Long-term risk of falls in an incident Parkinson's disease cohort: the Norwegian ParkWest study. J Neurol 2017;264(02):364–372 [PubMed: 28000003]

34. Duncan GW, Khoo TK, Yarnall AJ, et al. Health-related quality of life in early Parkinson's disease: the impact of nonmotor symptoms. Mov Disord 2014;29(02):195–202 [PubMed: 24123307]
35. Dogan VB, Koksal A, Dirican A, Baybas S, Dirican A, Dogan GB. Independent effect of fatigue on health-related quality of life in patients with idiopathic Parkinson's disease. Neurol Sci 2015;36(12):2221–2226 [PubMed: 26198763]
36. Asahina M, Vichayanrat E, Low DA, Iodice V, Mathias CJ. Autonomic dysfunction in parkinsonian disorders: assessment and pathophysiology. J Neurol Neurosurg Psychiatry 2013;84(06):674–680 [PubMed: 22942216]
37. Liepelt-Scarfone I, Pilotto A, Müller K, et al. Autonomic dysfunction in subjects at high risk for Parkinson's disease. J Neurol 2015;262(12):2643–2652 [PubMed: 26530505]
38. Fasano A, Visanji NP, Liu LWC, Lang AE, Pfeiffer RF. Gastrointestinal dysfunction in Parkinson's disease. Lancet Neurol 2015;14(06):625–639 [PubMed: 25987282]
39. Pfeiffer RF. Gastrointestinal dysfunction in Parkinson's disease. Curr Treat Options Neurol 2018;20(12):54 [PubMed: 30361783]
40. Tseng M-T, Lin C-H. Pain in early-stage Parkinson's disease: implications from clinical features to pathophysiology mechanisms. J Formos Med Assoc 2017;116(08):571–581 [PubMed: 28532582]
41. Allen NE, Moloney N, van Vliet V, Canning CG. The rationale for exercise in the management of pain in Parkinson's disease. J Parkinsons Dis 2015;5(02):229–239 [PubMed: 25649828]
42. Beiske AG, Loge JH, Rønningen A, Svensson E. Pain in Parkinson's disease: prevalence and characteristics. Pain 2009;141(1-2):173–177 [PubMed: 19100686]
43. Riley D, Lang AE, Blair RD, Birnbaum A, Reid B. Frozen shoulder and other shoulder disturbances in Parkinson's disease. J Neurol Neurosurg Psychiatry 1989;52(01):63–66 [PubMed: 2709037]
44. Schott GD. Pain in Parkinson's disease. Pain 1985;22(04):407–411 [PubMed: 4047709]
45. Stamey W, Davidson A, Jankovic J. Shoulder pain: a presenting symptom of Parkinson disease. J Clin Rheumatol 2008;14(04):253–254 [PubMed: 18766134]
46. Defazio G, Berardelli A, Fabbrini G, et al. Pain as a nonmotor symptom of Parkinson disease: evidence from a case-control study. Arch Neurol 2008;65(09):1191–1194 [PubMed: 18779422]
47. Kelley GA, Kelley KS. Exercise and sleep: a systematic review of previous meta-analyses. J Evid Based Med 2017;10(01):26–36 [PubMed: 28276627]
48. Neviani F, Belvederi Murri M, Mussi C, et al. Physical exercise for late life depression: effects on cognition and disability. Int Psychogeriatr 2017;29(07):1105–1112 [PubMed: 28412979]
49. Wegner M, Helmich I, Machado S, Nardi AE, Arias-Carrion O, Budde H. Effects of exercise on anxiety and depression disorders: review of meta- analyses and neurobiological mechanisms. CNS Neurol Disord Drug Targets 2014;13(06):1002–1014 [PubMed: 24923346]
50. O'Connor SR, Tully MA, Ryan B, et al. Walking exercise for chronic musculoskeletal pain: systematic review and meta-analysis. Arch Phys Med Rehabil 2015;96(04):724–734.e3 [PubMed: 25529265]
51. Mak MK, Wong-Yu IS, Shen X, Chung CL. Long-term effects of exercise and physical therapy in people with Parkinson disease. Nat Rev Neurol 2017;13(11):689–703 [PubMed: 29027544]
52. Tomlinson CL, Patel S, Meek C, et al. Physiotherapy versus placebo or no intervention in Parkinson's disease. Cochrane Database Syst Rev 2013;9(09):CD002817
53. Mehrholz J, Friis R, Kugler J, Twork S, Storch A, Pohl M. Treadmill training for patients with Parkinson's disease. Cochrane Database Syst Rev 2010;(01):CD007830 [PubMed: 20091652]
54. Fang X, Han D, Cheng Q, et al. Association of levels of physical activity with risk of Parkinson disease: a systematic review and meta-analysis. JAMA Netw Open 2018;1(05):e182421 [PubMed: 30646166]
55. Xu Q, Park Y, Huang X, et al. Physical activities and future risk of Parkinson disease. Neurology 2010;75(04):341–348 [PubMed: 20660864]
56. Ahlskog JE. Aerobic exercise: evidence for a direct brain effect to slow Parkinson disease progression. Mayo Clin Proc 2018;93(03):360–372 [PubMed: 29502566]

57. Petzinger GM, Holschneider DP, Fisher BE, et al. The effects of exercise on dopamine neurotransmission in Parkinson's disease: targeting neuroplasticity to modulate basal ganglia circuitry. Brain Plast 2015;1(01):29–39 [PubMed: 26512345]
58. Petzinger GM, Fisher BE, McEwen S, Beeler JA, Walsh JP, Jakowec MW. Exercise-enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's disease. Lancet Neurol 2013;12(07):716–726 [PubMed: 23769598]
59. Hirsch MA, Iyer SS, Sanjak M. Exercise-induced neuroplasticity in human Parkinson's disease: What is the evidence telling us? Parkinsonism Relat Disord 2016;22(Suppl 1):S78–S81 [PubMed: 26439945]
60. Schenkman M, Moore CG, Kohrt WM, et al. Effect of high-intensity treadmill exercise on motor symptoms in patients with de novo Parkinson disease: a phase 2 randomized clinical trial. JAMA Neurol 2018;75(02):219–226 [PubMed: 29228079]
61. van der Kolk NM, de Vries NM, Kessels RPC, et al. Effectiveness of home-based and remotely supervised aerobic exercise in Parkinson's disease: a double-blind, randomised controlled trial. Lancet Neurol 2019;18(11):998–1008 [PubMed: 31521532]
62. Shulman LM, Katzel LI, Ivey FM, et al. Randomized clinical trial of 3 types of physical exercise for patients with Parkinson disease. JAMA Neurol 2013;70(02):183–190 [PubMed: 23128427]
63. Schenkman M, Hall DA, Barón AE, Schwartz RS, Mettler P, Kohrt WM. Exercise for people in early- or mid-stage Parkinson disease: a 16-month randomized controlled trial. Phys Ther 2012;92(11):1395–1410 [PubMed: 22822237]
64. Uc EY, Doerschug KC, Magnotta V, et al. Phase I/II randomized trial of aerobic exercise in Parkinson disease in a community setting. Neurology 2014;83(05):413–425 [PubMed: 24991037]
65. Mirelman A, Bonato P, Camicioli R, et al. Gait impairments in Parkinson's disease. Lancet Neurol 2019;18(07):697–708 [PubMed: 30975519]
66. Cugusi L, Solla P, Serpe R, et al. Effects of a Nordic Walking program on motor and non-motor symptoms, functional performance and body composition in patients with Parkinson's disease. NeuroRehabilitation 2015;37(02):245–254 [PubMed: 26484516]
67. Picelli A, Varalta V, Melotti C, et al. Effects of treadmill training on cognitive and motor features of patients with mild to moderate Parkinson's disease: a pilot, single-blind, randomized controlled trial. Funct Neurol 2016;31(01):25–31 [PubMed: 27027891]
68. Amara AW, Memon AA. Effects of exercise on non-motor symptoms in Parkinson's disease. Clin Ther 2018;40(01):8–15 [PubMed: 29198450]
69. Falvo MJ, Schilling BK, Earhart GM. Parkinson's disease and resistive exercise: rationale, review, and recommendations. Mov Disord 2008;23(01):1–11 [PubMed: 17894327]
70. Allen NE, Canning CG, Sherrington C, Fung VSC. Bradykinesia, muscle weakness and reduced muscle power in Parkinson's disease. Mov Disord 2009;24(09):1344–1351 [PubMed: 19425085]
71. Allen NE, Sherrington C, Canning CG, Fung VSC. Reduced muscle power is associated with slower walking velocity and falls in people with Parkinson's disease. Parkinsonism Relat Disord 2010;16(04):261–264 [PubMed: 20117036]
72. Chung CLH, Thilarajah S, Tan D. Effectiveness of resistance training on muscle strength and physical function in people with Parkinson's disease: a systematic review and meta-analysis. Clin Rehabil 2016;30(01):11–23 [PubMed: 25691582]
73. Ramazzina I, Bernazzoli B, Costantino C. Systematic review on strength training in Parkinson's disease: an unsolved question. Clin Interv Aging 2017;12:619–628 [PubMed: 28408811]
74. Roeder L, Costello JT, Smith SS, Stewart IB, Kerr GK. Effects of resistance training on measures of muscular strength in people with Parkinson's disease: a systematic review and meta-analysis. PLoS One 2015;10(07):e0132135 [PubMed: 26146840]
75. Cruickshank TM, Reyes AR, Ziman MR. A systematic review and meta-analysis of strength training in individuals with multiple sclerosis or Parkinson disease. Medicine (Baltimore) 2015;94(04):e411 [PubMed: 25634170]
76. Troche MS, Okun MS, Rosenbek JC, et al. Aspiration and swallowing in Parkinson disease and rehabilitation with EMST: a randomized trial. Neurology 2010;75(21):1912–1919 [PubMed: 21098406]

77. Dibble LE, Foreman KB, Addison O, Marcus RL, LaStayo PC. Exercise and medication effects on persons with Parkinson disease across the domains of disability: a randomized clinical trial. J Neurol Phys Ther 2015;39(02):85–92 [PubMed: 25742370]

78. Corcos DM, Robichaud JA, David FJ, et al. A two-year randomized controlled trial of progressive resistance exercise for Parkinson's disease. Mov Disord 2013;28(09):1230–1240 [PubMed: 23536417]

79. Kelly NA, Ford MP, Standaert DG, et al. Novel, high-intensity exercise prescription improves muscle mass, mitochondrial function, and physical capacity in individuals with Parkinson's disease. J Appl Physiol (1985) 2014;116(05):582–592 [PubMed: 24408997]

80. Paul SS, Canning CG, Song J, Fung VS, Sherrington C. Leg muscle power is enhanced by training in people with Parkinson's disease: a randomized controlled trial. Clin Rehabil 2014;28(03):275–288 [PubMed: 24188914]

81. David FJ, Robichaud JA, Leurgans SE, et al. Exercise improves cognition in Parkinson's disease: the PRET-PD randomized, clinical trial. Mov Disord 2015;30(12):1657–1663 [PubMed: 26148003]

82. Prodoehl J, Rafferty MR, David FJ, et al. Two-year exercise program improves physical function in Parkinson's disease: the PRET-PD randomized clinical trial. Neurorehabil Neural Repair 2015;29(02):112–122 [PubMed: 24961994]

83. Rafferty MR, Prodoehl J, Robichaud JA, et al. Effects of 2 years of exercise on gait impairment in people with Parkinson disease: the PRET-PD randomized trial. J Neurol Phys Ther 2017;41(01):21–30 [PubMed: 27977518]

84. David FJ, Robichaud JA, Vaillancourt DE, et al. Progressive resistance exercise restores some properties of the triphasic EMG pattern and improves bradykinesia: the PRET-PD randomized clinical trial. J Neurophysiol 2016;116(05):2298–2311 [PubMed: 27582297]

85. Allen NE, Schwarzel AK, Canning CG. Recurrent falls in Parkinson's disease: a systematic review. Parkinsons Dis 2013;2013:906274 [PubMed: 23533953]

86. Shen X, Wong-Yu ISK, Mak MKY. Effects of exercise on falls, balance, and gait ability in Parkinson's disease: a meta-analysis. Neurorehabil Neural Repair 2016;30(06):512–527 [PubMed: 26493731]

87. Canning CG, Sherrington C, Lord SR, et al. Exercise for falls prevention in Parkinson disease: a randomized controlled trial. Neurology 2015;84(03):304–312 [PubMed: 25552576]

88. Morris ME, Menz HB, McGinley JL, et al. A randomized controlled trial to reduce falls in people with Parkinson's disease. Neurorehabil Neural Repair 2015;29(08):777–785 [PubMed: 25567121]

89. Mirelman A, Rochester L, Maidan I, et al. Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial. Lancet 2016;388(10050):1170–1182 [PubMed: 27524393]

90. Chivers Seymour K, Pickering R, Rochester L, et al. Multicentre, randomised controlled trial of PDSAFE, a physiotherapist-delivered fall prevention programme for people with Parkinson's. J Neurol Neurosurg Psychiatry 2019;90(07):774–782 [PubMed: 30944149]

91. Goodwin VA, Richards SH, Henley W, Ewings P, Taylor AH, Campbell JL. An exercise intervention to prevent falls in people with Parkinson's disease: a pragmatic randomised controlled trial. J Neurol Neurosurg Psychiatry 2011;82(11):1232–1238 [PubMed: 21856692]

92. Li F, Harmer P, Fitzgerald K, et al. Tai chi and postural stability in patients with Parkinson's disease. N Engl J Med 2012;366(06):511–519 [PubMed: 22316445]

93. Pérez de la Cruz S. Effectiveness of aquatic therapy for the control of pain and increased functionality in people with Parkinson's disease: a randomized clinical trial. Eur J Phys Rehabil Med 2017;53(06):825–832 [PubMed: 28627861]

94. King LA, Wilhelm J, Chen Y, et al. ; Effects of Group. Effects of group, individual, and home exercise in persons with Parkinson disease: a randomized clinical trial. J Neurol Phys Ther 2015;39(04):204–212 [PubMed: 26308937]

95. Kwok JYY, Kwan JCY, Auyeung M, et al. Effects of mindfulness yoga vs stretching and resistance training exercises on anxiety and depression for people with Parkinson disease: a randomized clinical trial. JAMA Neurol 2019;76(07):755–763 [PubMed: 30958514]

96. Conradsson D, Löfgren N, Nero H, et al. The effects of highly challenging balance training in elderly with Parkinson's disease: a randomized controlled trial. Neurorehabil Neural Repair 2015;29(09):827–836 [PubMed: 25608520]

97. Ellis TD, Cavanaugh JT, DeAngelis T, et al. Comparative effectiveness of mHealth-supported exercise compared with exercise alone for people with Parkinson disease: randomized controlled pilot study. Phys Ther 2019;99(02):203–216 [PubMed: 30715489]

98. Nadeau A, Pourcher E, Corbeil P. Effects of 24 wk of treadmill training on gait performance in Parkinson's disease. Med Sci Sports Exerc 2014;46(04):645–655 [PubMed: 24002341]

99. Bombieri F, Schena F, Pellegrini B, Barone P, Tinazzi M, Erro R. Walking on four limbs: a systematic review of Nordic walking in Parkinson disease. Parkinsonism Relat Disord 2017;38:8–12 [PubMed: 28202374]

100. Reuter I, Mehnert S, Leone P, Kaps M, Oechsner M, Engelhardt M. Effects of a flexibility and relaxation programme, walking, and Nordic walking on Parkinson's disease. J Aging Res 2011;2011:232473 [PubMed: 21603199]

101. Ghai S, Ghai I, Schmitz G, Effenberg AO. Effect of rhythmic auditory cueing on parkinsonian gait: a systematic review and meta-analysis. Sci Rep 2018;8(01):506 [PubMed: 29323122]

102. Ginis P, Nackaerts E, Nieuwboer A, Heremans E. Cueing for people with Parkinson's disease with freezing of gait: a narrative review of the state-of-the-art and novel perspectives. Ann Phys Rehabil Med 2018;61(06):407–413 [PubMed: 28890341]

103. Sweeney D, Quinlan LR, Browne P, Richardson M, Meskell P, ÓLaighin G. A technological review of wearable cueing devices addressing freezing of gait in Parkinson's disease. Sensors (Basel) 2019;19(06):E1277 [PubMed: 30871253]

104. Ginis P, Nieuwboer A, Dorfman M, et al. Feasibility and effects of home-based smartphone-delivered automated feedback training for gait in people with Parkinson's disease: a pilot randomized controlled trial. Parkinsonism Relat Disord 2016;22:28–34 [PubMed: 26777408]

105. Raffegeau TE, Krehbiel LM, Kang N, et al. A meta-analysis: Parkinson's disease and dual-task walking. Parkinsonism Relat Disord 2019;62:28–35 [PubMed: 30594454]

106. Bloem BR, Grimbergen YAM, van Dijk JG, Munneke M. The "posture second" strategy: a review of wrong priorities in Parkinson's disease. J Neurol Sci 2006;248(1-2):196–204 [PubMed: 16806270]

107. Strouwen C, Molenaar EALM, Münks L, et al. Training dual tasks together or apart in Parkinson's disease: results from the DUALITY trial. Mov Disord 2017;32(08):1201–1210 [PubMed: 28440888]

108. Geroin C, Nonnekes J, de Vries NM, et al. Does dual-task training improve spatiotemporal gait parameters in Parkinson's disease? Parkinsonism Relat Disord 2018;55:86–91 [PubMed: 29802080]

109. Fullard ME, Thibault DP, Hill A, et al. ; Parkinson Study Group Healthcare Outcomes and Disparities Working Group. Utilization of rehabilitation therapy services in Parkinson disease in the United States. Neurology 2017;89(11):1162–1169 [PubMed: 28835397]

110. Nijkrake MJ, Keus SHJ, Oostendorp RAB, et al. Allied health care in Parkinson's disease: referral, consultation, and professional expertise. Mov Disord 2009;24(02):282–286 [PubMed: 19170189]

111. Parkinson's UK. Life with Parkinson's today–room for improvement. London:: Parkinson's UK; 2007

112. Cheng EM, Tonn S, Swain-Eng R, Factor SA, Weiner WJ, Bever CT JrAmerican Academy of Neurology Parkinson Disease Measure Development Panel. Quality improvement in neurology: AAN Parkinson disease quality measures: report of the Quality Measurement and Reporting Subcommittee of the American Academy of Neurology. Neurology 2010;75(22):2021–2027 [PubMed: 21115958]

113. Rogers G, Davies D, Pink J, Cooper P. Parkinson's disease: summary of updated NICE guidance. BMJ 2017;358:j1951 [PubMed: 28751362]

114. Ellis T, Cavanaugh JT, Earhart GM, et al. Factors associated with exercise behavior in people with Parkinson disease. Phys Ther 2011;91(12):1838–1848 [PubMed: 22003171]

115. Ellis T, Boudreau JK, DeAngelis TR, et al. Barriers to exercise in people with Parkinson disease. Phys Ther 2013;93(05):628–636 [PubMed: 23288910]

116. den Brok MGHE, van Dalen JW, van Gool WA, Moll van Charante EP, de Bie RMA, Richard E. Apathy in Parkinson's disease: a systematic review and meta-analysis. Mov Disord 2015;30(06):759–769 [PubMed: 25787145]

117. Reijnders JSAM, Ehrt U, Weber WEJ, Aarsland D, Leentjens AFG. A systematic review of prevalence studies of depression in Parkinson's disease. Mov Disord 2008;23(02):183–189, quiz 313 [PubMed: 17987654]

118. Frazzitta G, Maestri R, Bertotti G, et al. Intensive rehabilitation treatment in early Parkinson's disease: a randomized pilot study with a 2-year follow-up. Neurorehabil Neural Repair 2015;29(02):123–131 [PubMed: 25038064]

119. Duncan RP, Leddy AL, Cavanaugh JT, et al. Detecting and predicting balance decline in Parkinson disease: a prospective cohort study. J Parkinsons Dis 2015;5(01):131–139 [PubMed: 25514984]

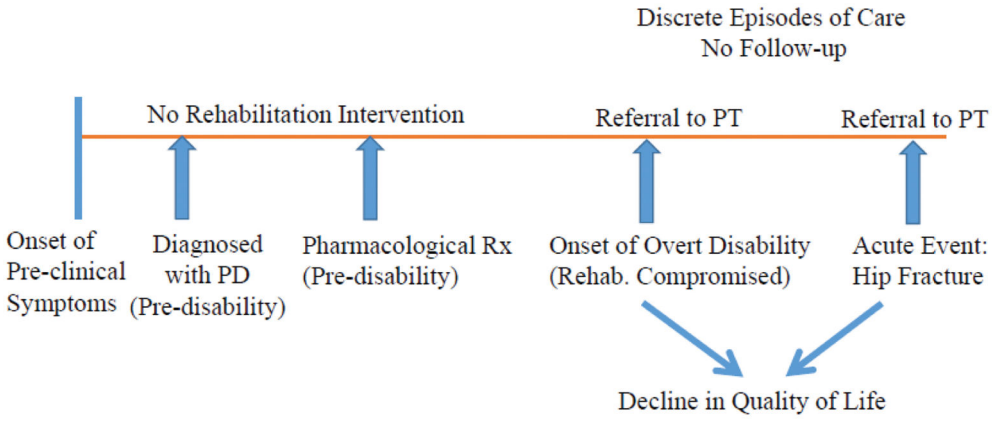


Fig. 1.
Suboptimal model of rehabilitation in Parkinson's disease (PD).

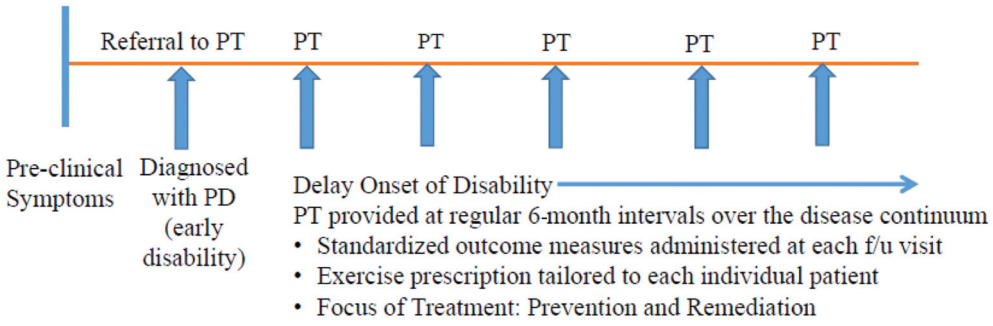


Fig. 2.

Secondary prevention model of care (Dental Model). PD, Parkinson's disease; PT, physical therapy.

Table 1

Parkinson's disease rating scales

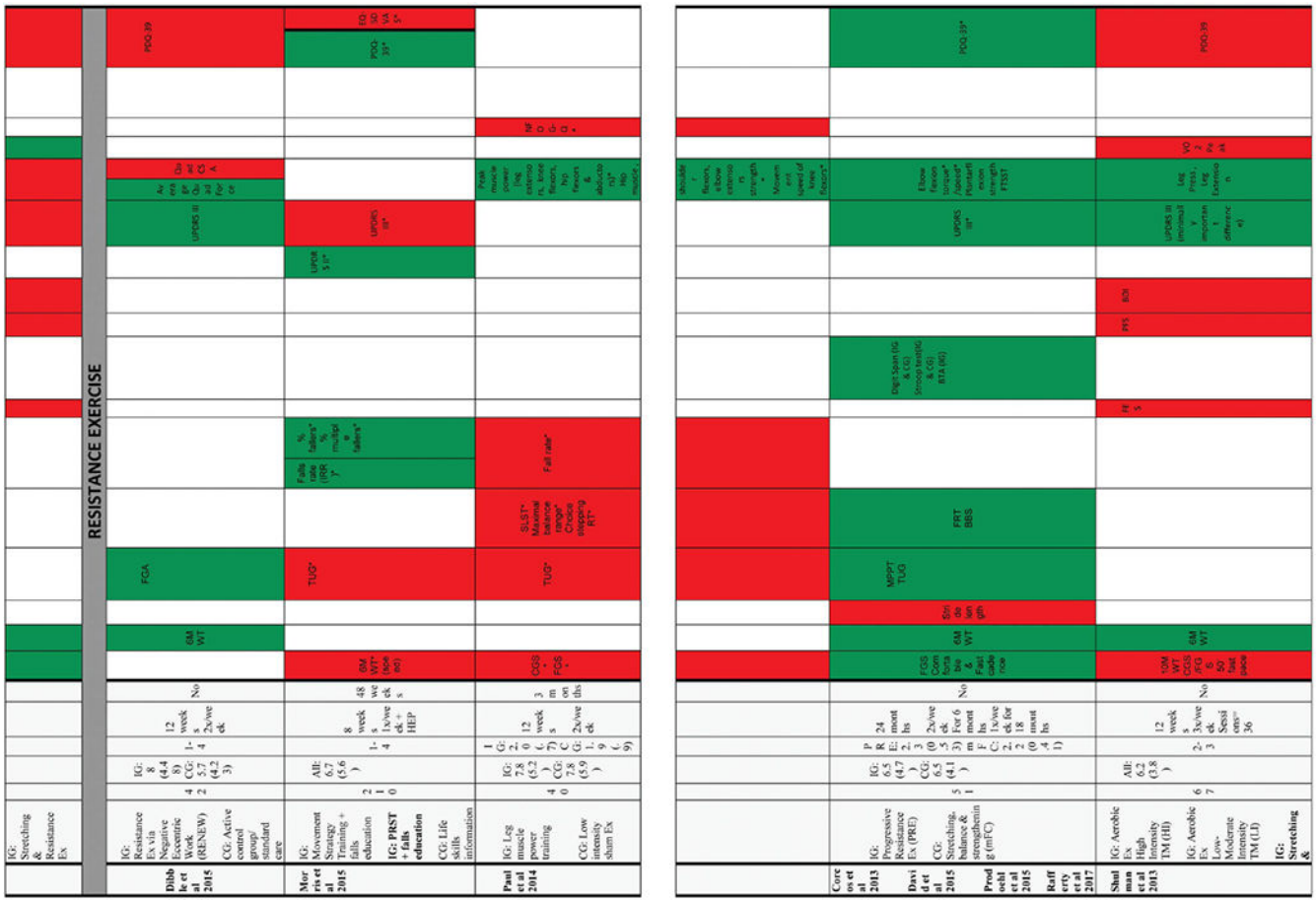
Hoehn and Yahr scale			
1: Unilateral involvement only usually with minimal or no functional disability			
2: Bilateral or midline involvement without impairment of balance			
3: Bilateral disease: mild to moderate disability with impaired postural reflexes; physically independent			
4: Severely disabling disease; still able to walk or stand unassisted			
5: Confinement to bed or wheelchair unless aided			
Comparison of scoring of original UPDRS with MDS-UPDRS			
	Original UPDRS score range		MDS-UPDRS score range
Part I: mentation, behavior and mood	0–16 (4 items)	Part I: nonmotor experiences of daily living	0–52 (13 items)
Part II: activities of daily living	0–52 (13 items)	Part II: motor experiences of daily living	0–52 (13 items)
Part III: motor examination	0–108 (14 items)	Part III: motor examination	0–132 (18 items, some with several parts)

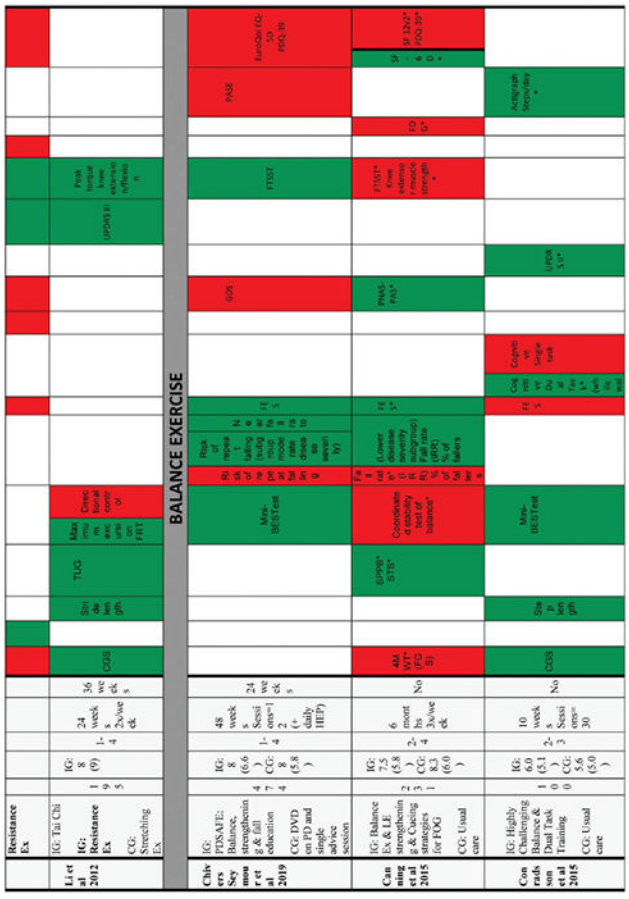
Source: Adapted from Hoehn and Yahr[14]; UPDRS and MDS-UPDRS.[15]

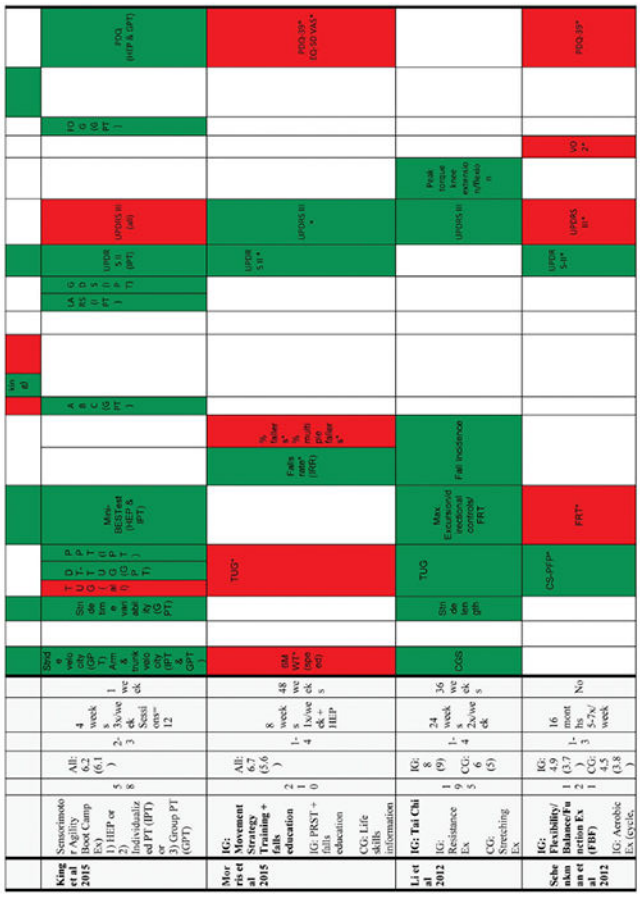
Table 2

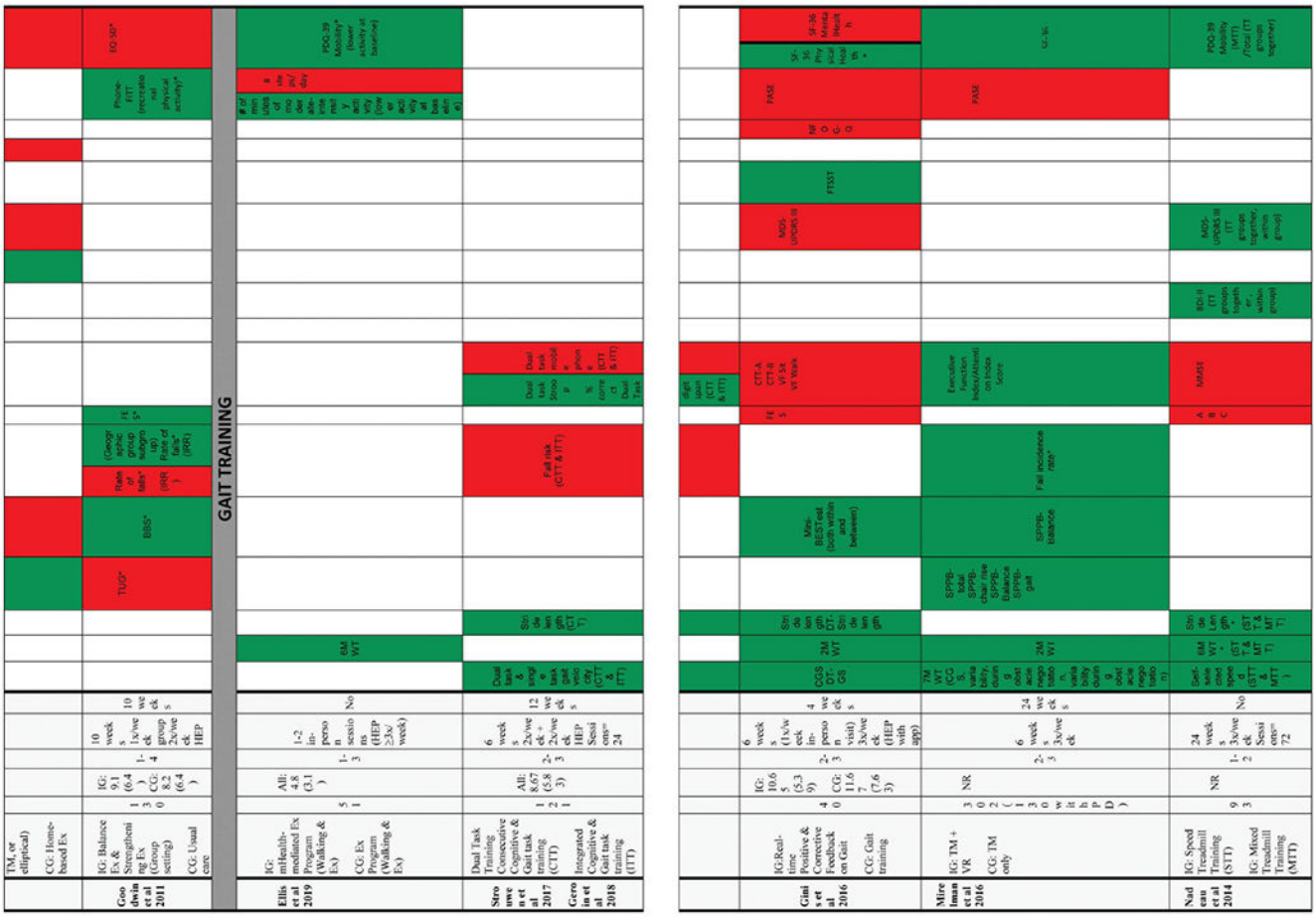
RCTs examining the effect of exercise interventions in people with Parkinson's disease

AUTHOR AND YEAR OF PUBLICATION	CHARACTERISTICS of the STUDIES						CLINICAL OUTCOMES																	
	INTERVENTION	SUBJ #	DISEASE DURATION (years)	H & Y stage	INTERVENTION DURATION	F. U.	GAIT VELOCITY	GAIT DISTANCE	STEP/STRIDE LENGTH	MOBILITY	BALANCE	FALLS	FEAR of FALLS	COGNITION	FATIGUE	DEPRESSION APATHY AFFECT ANXIETY	MOTOR EXPERIENCES of DAILY LIVING (UPDRS II)	MOTOR SYMPTOMS (MDS-UPDRS III or UPDRS) Or UPDRS Total	MUSCLE STRENGTH/ POWER	FITNESS	FOG	PHYSICAL ACTIVITY	QOL DISABILITY
AEROBIC EXERCISE																								
Van der Kolk et al 2019	IG: Aerobic Ex (stationary home-trainer) CG: Stretching	130	IG: 3.4(1.3-7.3) CG: 3.2(1.6-6.8)	1-2	6 months 3x/week	No		6MWT*		TUG*	Mini BESTest*	Number of falls*		TMT-A&B*/TAP*/MoCA*	FSS*	HADS*		MDS-UPDRS III (off state)* MDS-UPDRS III (on state)*		VO2 Max*			PDQ-39*
Coll et al 2017	IG: Aerobic Ex (cycle, TM, mix, or other) & Resistance Ex CG: Handwriting group	105	IG: 4.8(4.1) CG: 5.3(4.1)	NR	6 months 2x/week	48 weeks		2MWT*		TUG*					FSS*			MDS-UPDRS III*	Leg Power/Grip Strength*	VO2 Max* RER*		PASE*	EQ5D-5L* SF-36*
Schenkman et al 2018	IG: Aerobic Ex High Intensity(HI) TM or	128	High: 0.3 (IQR	1-2	26 weeks 4x/week	No												UPDRS III* UPDRS total*(HI		VO2 Max*(HI)		Total step count*(HI & MI)	
	IG: Moderate Intensity(MI) TM CG: Ususal care		0.1-1.3) Moderate: 0.3 (IQR 0.2-0.8) CG: 04 (0.1-0.8)															(HI) & MI)					
Uc et al 2014	IG: Aerobic Ex (TM)	49	All: 5.5 (4.9)	1-3	6 months 3x/week	No	7MWT				FRT			Inhibition (flanker task) General/other (MoCA)	FSS	GDS	UPDRS II	UPDRS III		VO2 Max			PD-QUALIF (total)
Schenkman et al 2012	IG: Flexibility/Balance/Function Ex (FBF) **IG: Aerobic Ex (cycle, TM, or elliptical)** CG: Home-based Ex	121	IG: 3.9 (4.2) CG: 4.5 (3.8)	1-3	16 months 5-7x/week	No				CS-PFP*	FRT*						UPDRS II*	UPDRS III*		VO2*			PDQ-39*
Shulman et al 2013	**IG: Aerobic Ex High Intensity TM (HI)** **IG: Aerobic Ex Low-Moderate Intensity TM (LI)**	67	All: 6.2 (3.8)	2-3	12 weeks 3x/week Sessions=36	No	CGS (LI) FGS (HI & LI)	6MWT (LI)					FES		PFS	BDI		UPDRS III	Leg Press, Leg Extension	VO2 Peak (LI & HI)			PDQ-39









	CG: No Treadmill training; Light Ex																							
Reuter et al 2011	IG: Nordic Walking(NW) IG: Walking (W) CG: Flexibility & Relaxation (FR)	90	IG: NW, 5.34 (4.06) IG: W, 5.99 (4.21) CG: FR, 5.19 (3.18)	2-3	IG (NW & W) 24 weeks 3x/week CG (1x/week)		12 and 24 meter Webster walking test (NW vs FR & W vs FR)*		Stride length (NW vs W)* (NW vs FR)*		Postural stability item on UPDRS(NW)*	BBS (NW, W, FR)							UPDRS total (NW & W)		Systolic BP during exercise testing (NW & W)		Activity Log (Time spent sitting /Doing heavy work) (NW & W)	PDQ-39 (NW, W, FR)
MULTIMODAL TRAINING																								
Kwok et al 2019	IG: Mindfulness Yoga CG: Stretching & Resistance Training	138	NR	1-3	8 weeks 1x/week	12 weeks				TUG*								HADS*		MDS-UPDRS III*						
Stozek et al 2015	IG: Multimodal (Balance, gait, motor performance & trunk rotation) CG: Control group	64	IG: 4.6 (2.7) CG: 4.3 (2.6)	1.5-3	4 weeks (2x/day for 2 weeks/ 11days) 3x/week for 2 weeks) Sessions=28	4 weeks	10MWT*			Timed activities* PPT*	Tandem stance* Pastor test*														
Frazziata et al 2015	IG: Multi-disciplinary intensive inpatient rehabilitation CG: Usual care	40	NR	1-1.5	4 weeks 5x/week (3 sessions/day) + repeated at 1 year	2 years		6MWT		TUG*									UPDRS II*	UPDRS III*					PDDS*

Green cells- significant improvement after training, Red cells - no significant improvement, White cells- not tested or not reported; Bolded intervention reflects intervention under consideration in that row; * between group difference, otherwise within group difference

SUBJ, Subjects; (m)H&Y, (modified) Hoehn and Yahr scale; #, Number; F.U., Follow Up; Min, Minutes; Ex, Exercise; FoG, Freezing of Gait; QoL, Quality of Life;

2MWT, 2 minute walk test; 6MWT, 6 minute walk test; 7MWT, 7 meter walk time; 10MWT, 10 meter walk test; ABC(−16), Activities-specific Balance Confidence (16 item); BBS, Berg Balance Scale; BDI (II), Beck Depression Inventory (second version); BTA, Brief Test of Attention; CG, Control group; CGS, Comfortable Gait Speed; CSI, Carer Strain Index; CS-PFP, Continuous Scale-Physical Functional Performance Test; CST, Chair Stand Test; CTT (A/B), Color Trail Test (A/B); DT-TUG, Dual-task Timed Up & Go; EQ5D-5L, (VAS), Health-related quality of life Euro-QOL (visual analogue scale); FAB-it, Frontal Assessment Battery-Italian version; FES, Falls Efficacy Scale; FGA, Functional Gait Assessment; FGS, Fast Gait speed; FoG (-S), Freezing of Gait (Score); (N) FoG-Q, (New) Freezing of Gait Questionnaire; FRT, Functional Reach Test; FSS, Fatigue Severity Scale; FTSST, Five Time Sit to Stand; GDS, Geriatric Depression Scale; GF-Q, Gait and Falls Questionnaire; HADS, Hospital Anxiety and Depression Scale; HEP, Home exercise program; IG, Intervention group; IRR, Incidence rate ratio; LARS, Lille Apathy Rating Scale; LRI, Locomotor rehabilitation index; MDS-UPDRS, Movement Disorder Society-Sponsored revision of the Unified Parkinson's Disease Rating Scale; mFC, Modified Fitness Counts; MFI, Modified Figure-of-Eight test; mHealth, mobile health; MI, memory interference test; MMSE, Mini-Mental State Exam; MoCA, Montreal Cognitive Assessment; MPPT, Modified Physical Performance Test; MST, Movement Strategy Training; NFOGQ, New Freezing of Gait Questionnaire; NR, not rated; OLS, One Leg Stance time; Other (set shifting, verbal & visual memory, language, visuospatial); PASE, Physical Activity Scale for the Elderly; PDDS, Parkinson Disease Disability Scale;PDQ-8, 8-item Parkinson's Disease Questionnaire; PDQ-39, Parkinson's Disease Questionnaire 39-Item; PD-QUALIF, Parkinson's Disease Quality of Life Scale; PFS (−16), Parkinson Fatigue Scale; PPT, Physical Performance Test; PRST, Progressive Resistance Strength Training; PT, Physical Therapy; Quad (CSA), Quadriceps (cross-sectional area); RBP, resting blood pressure; RST, Rapid step test; RT, Reaction Time; SF-6D, Short Form, 6 dimensions; SF 12 v2, Short Form 12, version 2; SF-36, Short Form 36 Health Survey; SLST, Single-limb stand test; SOT, Sensory Orientation Test; SPPB, Short Physical Performance Battery; TAP, Test of Attentional Performance; TM, Treadmill; TMT-A & B, Trail Making Test A & B; TUG(SS/FS), Timed Up and Go (Self-selected speed, Forced speed); UPDRS II, Unified Parkinson's Disease Rating Scale, Activities of Daily Living; UPDRS III, Unified Parkinson's Disease Rating Scale, Motor Section; UPDRS total, Unified Parkinson's Disease Rating Scale, Total sum score; VF, Verbal fluency; V02 (max) /(peak), (maximal)/(peak) oxygen uptake; VR, Virtual reality