

Invited Topical Review

Physiotherapy management of Parkinson's disease

Marco YC Pang

Department of Rehabilitation Sciences, Faculty of Health and Social Sciences, The Hong Kong Polytechnic University, Hong Kong

KEY WORDS

Parkinson's disease
Exercise
Review
Rehabilitation
Physical therapy

[Pang MYC (2021) Physiotherapy management of Parkinson's disease. *Journal of Physiotherapy* 67:163–176]

© 2021 Australian Physiotherapy Association. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease.¹ Physiotherapists play a very important role in the rehabilitation of people with PD, particularly in relation to the management of motor symptoms, promotion of regular physical exercise and prevention of secondary impairments and complications. This review summarises the: motor and non-motor impairments and secondary complications experienced by people with PD; research evidence about different interventions commonly used in the physiotherapy management of PD; and implications for research and practice.

Epidemiology of Parkinson's disease

Parkinson's disease affects over 6 million people globally,² with a prevalence of 51 to 439 per 100,000 people and an incidence of 2 to 28 per 100,000 people, based on door-to-door surveys.¹ Men are slightly more affected than women.³ Both the prevalence and incidence of PD increase with age, peaking in the seventh and eighth decades.¹ Available data also suggest higher prevalence and incidence of PD in western countries than eastern countries.^{1,4} Because of the rapidly ageing population, the number of people affected by PD is projected to double to over 12 million by 2040,² which will inevitably exacerbate the burden on healthcare systems and society.

Clinical features of Parkinson's disease

The cardinal motor symptoms of PD are bradykinesia, rigidity, tremor and postural instability.⁵ The onset of the cardinal motor symptoms arises from the loss of dopaminergic neurons of the substantia nigra pars compacta, leading to depletion of dopamine in the striatum. Therefore, the inhibitory influence from the basal ganglia to other brain regions that are involved in the control and execution of voluntary movements (eg, thalamus, brainstem and supplementary motor area) becomes exaggerated, which may account for bradykinesia and rigidity.⁶ On the other hand, balance impairment could be

caused by dysfunctions in the non-dopaminergic system, as it is often resistant to dopamine.⁷ The cardinal motor symptoms may give rise to a variety of secondary impairments such as muscle weakness (ie, reduced capacity of the muscles to generate force),^{8,9} altered gait (eg, reduced walking speed, stride length, cadence and level of independence in walking),^{9,10} reduced aerobic capacity (ie, reduced peak oxygen consumption rate and endurance)^{11–14} and falls.^{15,16} These secondary impairments, together with worsening of the motor symptoms as the disease progresses, may trigger a vicious cycle of further decline in physical activity level, activity and participation.

Apart from motor impairments, PD is also characterised by non-motor symptoms, including fatigue, depression, anxiety, sleep disturbance, cognitive impairments, behavioural issues and bladder/bowel dysfunction.¹⁷ While the basal ganglia are also involved in regulating the non-motor functions such as the behavioural, cognitive and emotional functions, increasing evidence suggests that the peripheral autonomic nervous system may be where the disease begins before the pathology spreads to the lower brainstem and eventually affects the substantia nigra.¹⁸ This may explain why some of the impairments in non-motor functions precede those of the motor functions by years or even decades.¹⁹ As the motor and non-motor impairments continue to worsen, there may be severe disabilities in different aspects of function, resulting in seriously compromised quality of life.²⁰

Physiotherapy management of Parkinson's disease

This section summarises the evidence for a range of physiotherapy interventions that have been investigated for their effect on PD. Where possible, the evidence from multiple similar trials has been meta-analysed. The resulting evidence has been summarised in [Figure 1](#).

Meta-analytic approach

In all meta-analyses presented in this review, only those trials with a comparison group that allowed the direct estimation of the

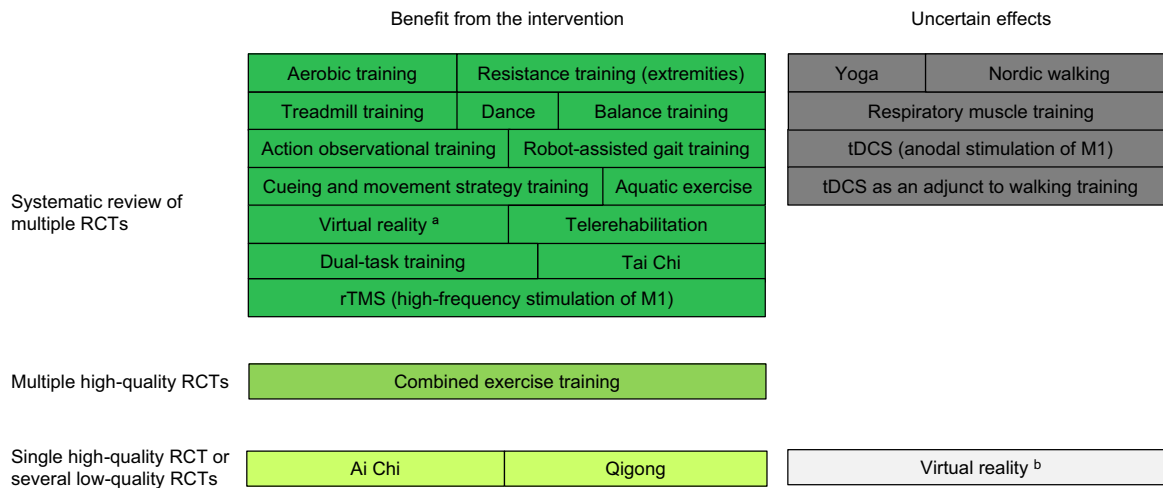


Figure 1. Interventions for management of Parkinson's disease with associated levels of evidence.

RCT = randomised controlled trials, M1 = primary motor cortex, rTMS = repetitive transcranial magnetic stimulation, tDCS = transcranial direct current stimulation.

^a centre-based, supervised.

^b home-based, minimally supervised.

effects of the experimental intervention were included (ie, experimental intervention versus no intervention/sham intervention/attentional control, or experimental intervention plus other intervention(s) versus the same other intervention(s) only). The mean difference (MD), rather than the standardised mean difference (SMD), was used in the analyses whenever possible because absolute measures of effect may be more easily interpreted by clinicians than relative effects. The random-effects model was used if the I^2 value was $> 50\%$ (ie, substantial heterogeneity); otherwise, the fixed-effect model was used.

As PD is chronic and progressive in nature, physiotherapy intervention involves management of motor impairments, promotion of regular physical exercise and prevention of secondary impairments and complications.^{21,22} Physiotherapy may also have an important role in delaying disease progression.²² Exercise intervention is a very important element in physiotherapy for people with PD.^{21,22}

Aerobic exercise

Aerobic capacity, as measured by the maximal oxygen consumption rate, is impaired in people with PD, particularly those with moderate to severe PD.^{12,14} Compromised aerobic capacity among people with PD is also reflected in reduced walking endurance on tests such as the 6-minute walk test (6MWT)¹¹ and increased physiologic cost when performing walking and other activities of daily living.^{23,24} Aerobic exercise may be a viable option to address these issues. Different modes of aerobic exercise have been studied in the PD population, with the most common ones being cycling on a stationary bicycle, followed by walking on a treadmill.²⁵ The final target exercise intensity was moderate to high, mostly at 50 to 80% heart rate reserve. The duration of each exercise session was 30 to 50 minutes for most studies, while the frequency and duration of the program was typically three to five sessions per week for 8 to 24 weeks.²⁵

A 2014 systematic review by Shu et al examined the effects of aerobic exercise in PD.²⁵ In the current review, updated meta-analyses were performed by first extracting the relevant trials from Shu et al's meta-analyses, and then adding the data obtained from aerobic exercise trials published after 2013.^{26–33} The updated meta-analyses estimated that aerobic exercise improved the peak oxygen consumption rate by 2.9 ml/kg/min (95% CI 1.6 to 4.3) (Figure 2A) and attenuated motor symptoms (ie, Unified Parkinson's Disease Rating Scale Part III (UPDRS-III) or Movement Disorder Society-Sponsored Revision of UPDRS Part III (MDS UPDRS-III)) by a SMD of -0.3 (95% CI -0.5 to -0.1) (Figure 2B). The effect of aerobic exercise on walking endurance (indicated by the 6MWT) was inconclusive due to the

wide confidence interval (Figure 2C). Aerobic exercise had little or no effect on quality of life, as measured by the Parkinson's Disease Questionnaire-39 (PDQ-39) (Figure 2D). For detailed forest plots, see Figure 3 on the eAddenda. In all the above meta-analyses, the methodological quality of the majority of the studies was good (PEDro scores ≥ 6). In addition to the effects on aerobic capacity and motor outcomes, a recent systematic review by Schootemeijer et al found that aerobic exercise improved bone health and decreased incidence of cardiovascular disease and mortality in people with PD;³⁴ however, its effects on non-motor impairments were conflicting.

The few aerobic exercise trials with a follow-up period had mixed results. Qutubuddin et al found no clear between-group difference in balance, motor symptoms and quality of life immediately after 8 weeks of training (intensity 61 to 80% of maximum heart rate, frequency two sessions per week) and also at a 4-month follow-up.³² However, the methodological quality was only fair (PEDro score = 5) and the sample size was small (23 participants). In a recent small-scale randomised trial by Arfa-Fatollahkhani et al with 20 participants,³⁵ 10 weeks of aerobic exercise at moderate intensity (intensity 60% heart rate reserve, frequency two sessions per week) resulted in improvements in the Timed Up and Go (TUG) test and 6MWT that were sustained for 2 months after the training had ended. More research is required to explore the long-term effects of aerobic exercise.

Graded resistance exercise training

People with PD have lower muscle strength than their peers without PD.^{8,36} Severe sarcopenia affects 20% of people with PD.³⁷ Loss of muscle mass and strength is a key factor in the development of secondary osteoporosis,³⁸ reduced functional performance³⁶ and falls in this population.³⁹ Graded resistance exercise training has been used to tackle the problem of muscle weakness and associated functional limitations in PD.^{40,41}

Updated meta-analyses were generated by adding the results of randomised trials published after 2013^{42–50} to the relevant studies extracted from the systematic reviews by Saltychev et al⁴⁰ and Chung et al.⁴¹ Most of the training programs consisted of 30 to 40 minutes of resistance exercises in each session on two to three non-consecutive days each week for 2 to 3 months, although a few studies had longer training durations up to 24 months. The initial resistance was typically set at 8 to 12 repetitions maximum (RM), which was then gradually increased by 2 to 10% if the participants were able to perform two to three sets of the same exercise at 8 to 12 RM with relative ease. The final target resistance at the end of the training

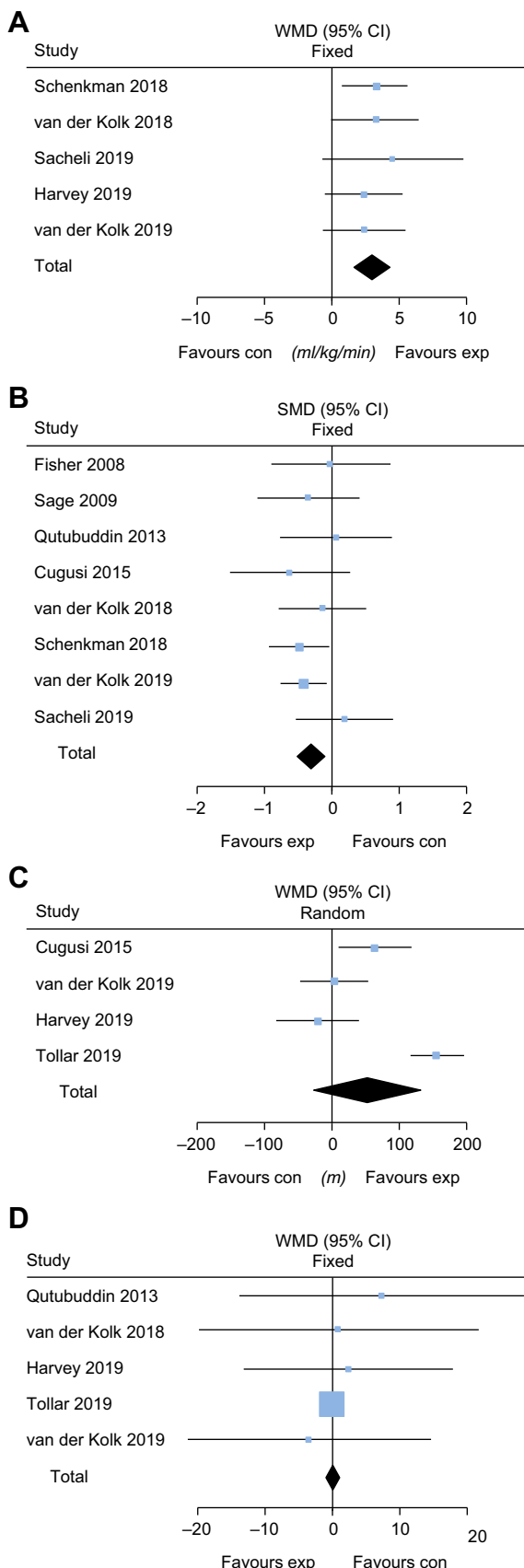


Figure 2. Effects of aerobic exercise compared with controls on (A) peak oxygen consumption rate, (B) Unified Parkinson's Disease Rating Scale Part III (UPDRS-III), (C) 6-minute walk test and (D) PDQ-39, modified from Shu et al.²⁵ Only the high-intensity group in Schenkman et al and only the cycling group in Tollar et al were used for meta-analyses. Only randomised controlled trials that clearly specified the target training intensity in the experimental group, and that the training intensity was distinct between the experimental and comparison groups were included. See the main text section 'Meta-analytic approach' for further details.

period was typically 70 to 80% of 1 RM. The updated meta-analyses, mostly consisting of good-quality studies (PEDro scores ≥ 6), showed that progressive resistance exercise improved leg extensor strength (SMD 0.71, 95% CI 0.21 to 1.21), TUG performance (MD -1.7 seconds, 95% CI -3.1 to -0.3), comfortable walking speed (SMD 0.39, 95% CI 0.12 to 0.66), fast walking speed (SMD 0.85, 95% CI 0.27 to 1.43), motor symptoms (SMD -0.46 , 95% CI -0.71 to -0.20), and PDQ-39 scores (MD -6 , 95% CI -10 to -3), as shown in Figure 4. For detailed forest plots, see Figure 5 on the eAddenda.

Research on the long-term effects of resistance training is scarce. Among the studies included in the meta-analyses here, Santos et al⁴⁷ demonstrated that adding 8 weeks of progressive resistance training (two 60 to 70-minute sessions per week) to routine physiotherapy resulted in greater reduction in centre of pressure displacement during standing and greater improvements in fast walking speed and quality of life (PDQ-39) than routine physiotherapy alone, although only the effect on fast walking speed was sustained at 1-month follow-up. More studies are required to examine the effects of resistance exercise training on other important outcomes such as balance and walking endurance, as well as on the long-term effects.

One particular aspect of resistance exercise training in PD is the strengthening of respiratory muscles. This area has garnered attention in research because people with PD often have respiratory dysfunctions related to abnormal ventilator drive, restrictive changes, respiratory muscle weakness and upper airway obstruction.⁵¹ These may lead to impairments in swallowing and phonation.⁵¹ A 2020 systematic review only identified three randomised controlled trials of respiratory muscle strength training in PD. Although some positive effects on respiratory function were reported, two of these had PEDro scores < 6 .⁵² Therefore, the wide application of respiratory muscle training in PD cannot be supported until further high-quality research establishes its value.⁵²

Virtual reality and exergames

Exercise that incorporates virtual reality (VR) is also gaining popularity in the rehabilitation of people with PD. The intervention often involves the use of computer-based games in a virtual reality environment. Some examples include the Nintendo Wii or Xbox Kinect, which are commercially available, and other customised VR tools specifically designed to address PD impairments. Incorporating VR into exercise may have potential advantages over conventional exercise by providing an interesting and interactive environment, which may increase patient motivation and engagement.⁵³

Most of the VR intervention trials lasted 5 to 8 weeks (45 to 60 minutes per session, two to three sessions per week). A number of systematic reviews have addressed the use of VR in PD in recent years.^{53–58} A 2020 review by Canning et al⁵⁷ found that VR rehabilitation improved gait and balance when compared with inactive controls in three facility-based trials, but such beneficial effects were not apparent in a home-based trial (PEDro scores 6 to 8); this may have been related to exercise underdosing due to inadequate supervision in the home setting. A differential effect according to disease severity was also identified, with more beneficial effects for those with lower disease severity and potentially negative effects for those with higher disease severity.

Although previous systematic reviews have attempted to estimate the effects of VR rehabilitation compared with other non-VR interventions,^{53–56,58} the meta-analyses are very difficult to interpret because the type and dose of the non-VR interventions used in different studies varied. Canning et al⁵⁷ compared the effects of VR and non-VR rehabilitation of a similar type and dose based on the findings of 11 trials and found no consistent evidence of VR rehabilitation being more effective in improving gait or balance in PD.

Among the trials that compared VR rehabilitation and inactive control, only one incorporated a follow-up assessment after termination of training.⁵⁹ A high-quality study (V-TIME trial) demonstrated that participants in the VR treadmill training group had a lower

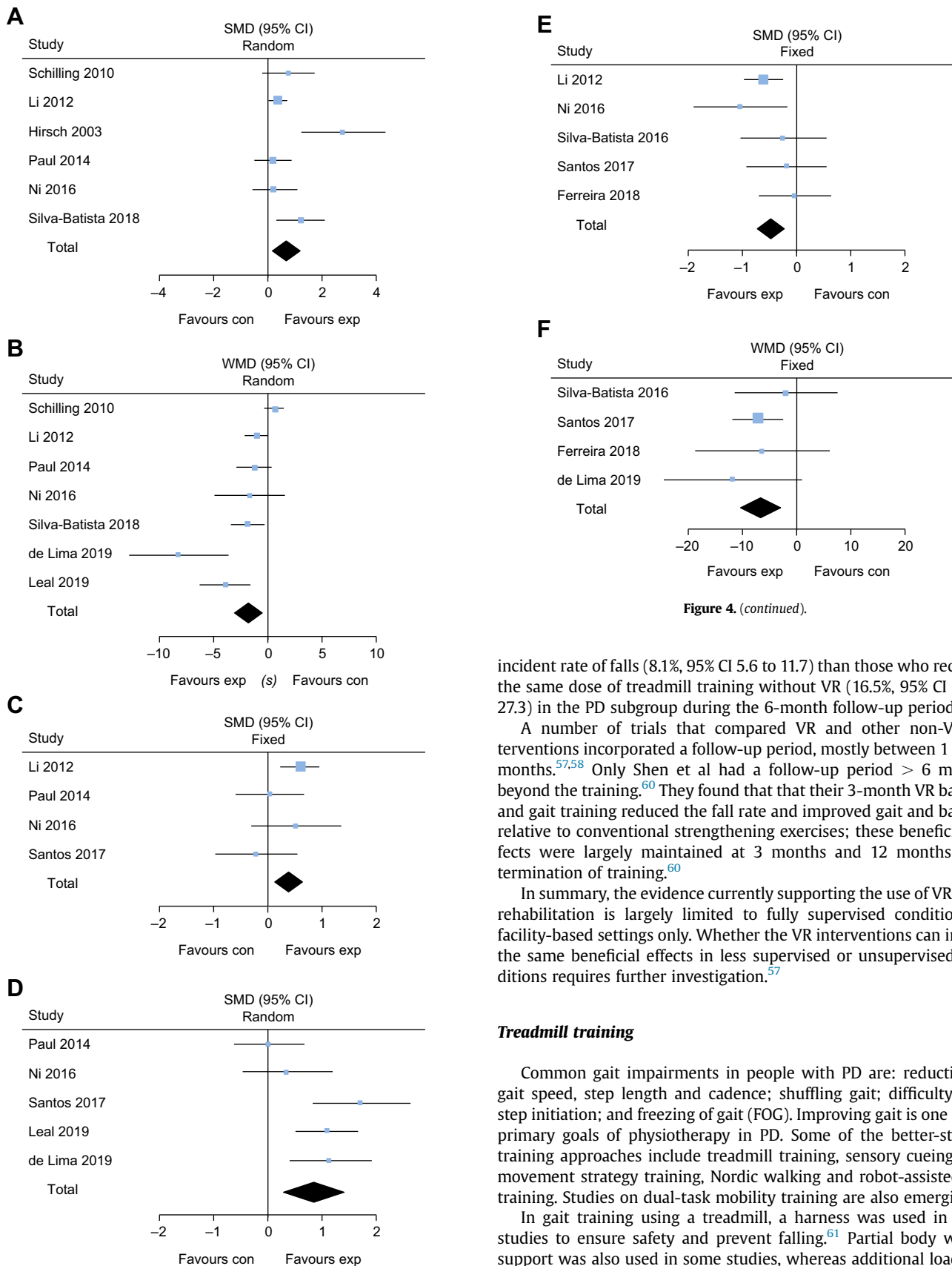


Figure 4. (continued).

incident rate of falls (8.1%, 95% CI 5.6 to 11.7) than those who received the same dose of treadmill training without VR (16.5%, 95% CI 9.9 to 27.3) in the PD subgroup during the 6-month follow-up period.⁵⁹

A number of trials that compared VR and other non-VR interventions incorporated a follow-up period, mostly between 1 and 3 months.^{57,58} Only Shen et al had a follow-up period > 6 months beyond the training.⁶⁰ They found that their 3-month VR balance and gait training reduced the fall rate and improved gait and balance relative to conventional strengthening exercises; these beneficial effects were largely maintained at 3 months and 12 months after termination of training.⁶⁰

In summary, the evidence currently supporting the use of VR in PD rehabilitation is largely limited to fully supervised conditions in facility-based settings only. Whether the VR interventions can induce the same beneficial effects in less supervised or unsupervised conditions requires further investigation.⁵⁷

Treadmill training

Common gait impairments in people with PD are: reduction in gait speed, step length and cadence; shuffling gait; difficulty with step initiation; and freezing of gait (FOG). Improving gait is one of the primary goals of physiotherapy in PD. Some of the better-studied training approaches include treadmill training, sensory cueing with movement strategy training, Nordic walking and robot-assisted gait training. Studies on dual-task mobility training are also emerging.

In gait training using a treadmill, a harness was used in some studies to ensure safety and prevent falling.⁶¹ Partial body weight support was also used in some studies, whereas additional load was used in others.⁶¹ Many of the studies adopted a 'speed-dependent treadmill approach', in which the belt speed was set as the highest speed at which the participant could walk safely without losing balance (ie, maximum achieved belt speed).⁶¹ Other studies used a constant walking speed during the same training session.⁶¹ The treadmill walking program typically lasted for 4 to 8 weeks, with three sessions (30 to 45 minutes) per week. The effects of treadmill training in PD were examined in a number of systematic reviews,^{61,62} including a 2015 Cochrane review of 18 randomised controlled

Figure 4. Effects of resistance exercise compared with control on (A) leg extensor strength, (B) Timed Up and Go Test, (C) comfortable walking speed, (D) fast walking speed, (E) motor symptoms and (F) quality of life, modified from the systematic reviews by Saltychev et al⁴⁰ and Chung et al.⁴¹ The resistance training group without added instability in Silva-Batista et al was used for analyses.⁴⁸ The SMD, rather than MD, was used in the analysis of leg extensor strength, comfortable walking speed, and fast walking speed because different outcome assessment methods involving different units of measurement were used. The SMD was also used in the analysis of motor symptoms because some studies used UPDRS III, while others used MDS UPDRS III as an outcome. See the main text section 'Meta-analytic approach' for further details.

trials.⁶¹ The Cochrane review concluded that treadmill training improved gait speed and stride length, with moderate and low quality of evidence, respectively.⁶¹ However, the cadence and distance did not improve with treadmill training.⁶¹ In the current review, the evidence was further updated by extracting relevant data from the Cochrane review and adding the relevant randomised trials published after September 2014.^{62–66} The results seemed to suggest that treadmill training had a more pronounced effect on fast walking speed than comfortable walking speed, as shown in Figure 6. For detailed forest plots, see Figure 7 on the eAddenda. Specifically, the fast walking speed was improved by treadmill training by an average of 0.16 m/s (95% CI 0.04 to 0.28) (Figure 6A), whereas the comfortable walking speed was improved by 0.11 m/s but the confidence interval (–0.05 to 0.27) revealed a small chance of a better outcome in the control group (Figure 6B). However, the interpretation of this result should recognise that the quality of most trials was only fair (PEDro score 5). In a systematic review by Ni et al, it was recommended that people with PD engage in treadmill training of 30 to 60 minutes per day, 2 to 3 days per week for more than 4 weeks.⁶⁷ A self-selected speed can be used initially, with gradual increases by 0.2 km/hour as tolerated.

Of the studies included in the meta-analyses, only Canning et al⁶³ assessed the long-term effect by incorporating a follow-up assessment. It was found that their moderate-intensity, home-based treadmill walking exercise program did not improve walking capacity but led to greater improvement in quality of life (PDQ-39) measured 6 weeks after termination of training. Further research is required to assess the long-term effects of treadmill training for people with PD.

Sensory cueing and movement strategy training

Gait hypokinesia in PD is thought to be attributable to the deficient formation of internal cues and reduced ability to activate the cortical motor set by the basal ganglia.⁶⁸ External cues have long been used in PD rehabilitation to overcome the deficits in internal rhythm generation, and activation of the motor control system may be key to facilitating a better gait pattern. Common types of cues that are used in PD rehabilitation of gait are largely auditory, visual and somatosensory in nature.^{68–73} Sensory cueing is sometimes combined with movement strategy training, which involves teaching people with PD to focus their attention on movement and respond to sensory cues to improve performance in activities such as walking, obstacle negotiation and turning.^{74,75} This includes learning to: plan in advance for movements to be performed, mentally rehearse the movements prior to their execution and consciously focus the attention on movements while they are being performed. Complex movement sequences are also broken down into several components to facilitate better learning. The goal is to form a mental picture of the desired movement (eg, optimal step length) before its actual execution.^{75,76}

A number of systematic reviews have examined the effects of sensory cueing on gait and falls in PD.^{69–73} The exercise interventions with sensory cueing typically consisted of 30 to 60 minutes of training per session, two to three sessions per week for a period of 4 to 12 weeks, although the studies by Martin et al⁷⁶ and Thaut et al⁷⁷ involved a longer training period of 6 months. The methodological quality of the reviewed studies varied (PEDro scores 2 to 8). Overall, both visual and auditory cues were found to be effective in improving the kinematic gait parameters and turning execution, while reducing the FOG and falls. The meta-analyses by Spaulding et al⁷² revealed some differences in results between visual and auditory cueing. While visual cueing improved stride length only, auditory cueing also improved cadence and speed. With auditory cueing, the effect was more pronounced when using high-intensity and high-frequency stimuli (10% above the patient's normal walking cadence). Proprioceptive cues in the form of rhythmic vibrations to the plantar surface of the foot skin synchronised with the step were shown to improve step length, speed, cadence and anticipatory postural adjustment (an important factor in step initiation).⁷¹ A number of studies also showed that the training effects from sensory cueing interventions can be largely maintained for a follow-up period varying from 1 to 6

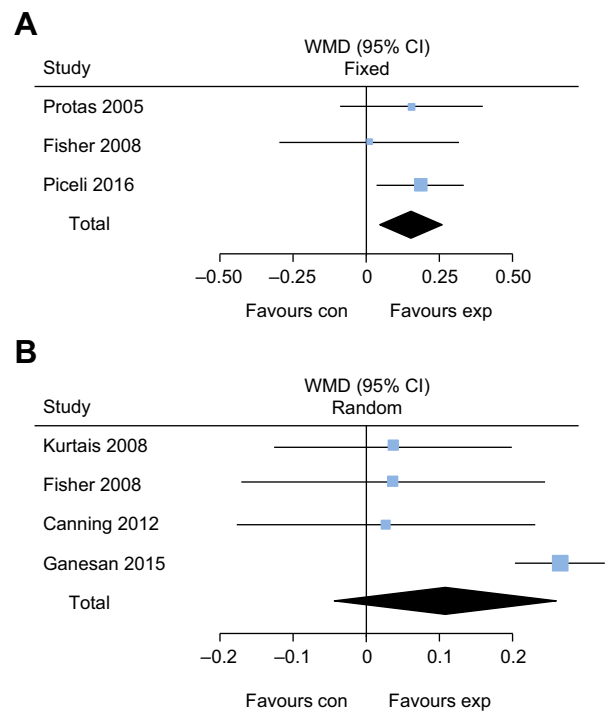


Figure 6. Effects of treadmill gait training on (A) fast walking speed and (B) comfortable walking speed, compared with controls. See the main text section 'Meta-analytic approach' for further details.

months.⁷² A recent systematic review by Radder et al showed that movement strategy training including cueing induced a moderate treatment effect on gait speed (six studies; SMD 0.45, 95% CI 0.13 to 0.76); however, only three of these six studies had PEDro scores ≥ 6 .⁷³ A moderately large effect on TUG performance was also found (six studies; SMD 0.53, 95% CI 0.23 to 0.82) in their meta-analysis of six studies (four with PEDro scores ≥ 6).⁷³

High-quality studies are needed to examine sensory cueing in PD and determine the most effective type of stimulus for different stages of the disease.²¹ With the development of wearable technology (eg, wearable sensors, laser, augmented reality via Google glasses and Halolens), there is much room for future research on their effectiveness on gait rehabilitation for people with PD.^{78,79}

Nordic walking

Nordic walking involves the use of two specially designed walking poles with rubber tips during walking. It requires the individual to perform arm swings using the poles as they move forward, similar to the movements observed in cross-country skiing.⁸⁰ The use of poles during walking may promote postural adjustment and dissociation of the shoulder and pelvic girdles, and lessen axial rigidity, which may facilitate a better gait pattern.⁸⁰ Based on the 2017 systematic review by Bombieri et al,⁸¹ only four randomised controlled trials were identified. Improvements in motor outcomes (eg, walking speed and endurance, leg muscle strength) and non-motor outcomes (eg, depression, fatigue) were reported after Nordic walking training. The same systematic review also suggested that people with mild disability or gait impairment seemed to benefit more from Nordic walking training.⁸¹ Their meta-analysis of these four randomised trials showed that Nordic walking was effective in reducing the UPDRS-III score (SMD –0.64, 95% CI –0.98 to –0.30).⁸¹ However, only two of these trials (PEDro scores of 4 and 6) could delineate the effects of Nordic walking by incorporating a relatively inactive control group. No definitive conclusion could be made, partly due to the low methodological quality of the studies and small sample sizes used.

Only two studies examined the long-term effects of Nordic walking training.^{80,82} Van Eihjkeren et al⁸⁰ demonstrated that the gain in gait velocity and functional mobility after 6 weeks of training (12 hours in total) was maintained for 5 months after the training had

ended. However, there was no control group and therefore any improvement can be explained by other extraneous factors. Ebersbach et al⁸² found that the benefits gained in cued reaction time after 4 weeks (16 hours in total) of Nordic walking was sustained for 16 weeks after program completion.

Robot-assisted gait training

Application of robot-assistive devices in gait training has gained increasingly wide application in the rehabilitation of people with PD and its effects were examined in systematic reviews by Alwardat and Etoom.^{83,84} The robot-assisted gait training programs usually lasted 4 weeks (30 to 45 minutes per session, three to five sessions per week).⁸³ The methodological quality of the reviewed trials was mostly good (PEDro scores ≥ 6 for six of seven studies).⁸³ There is high-quality evidence that robot-assisted gait training induced greater improvements in UPDRS-III score than conventional exercise (MD -5, 95% CI -3 to -8) but not treadmill training (MD 0, 95% CI -4 to 3).⁸⁴ Robot-assisted gait training also improved stride length (MD 9.3 cm, 95% CI 7.2 to 11.4; high-quality evidence) and gait speed (MD 0.17 m/s, 95% CI 0.09 to 0.24; low-quality evidence) and Berg Balance Scale (MD 3.6, 95% CI 0.4 to 6.7; moderate-quality evidence) when compared with conventional interventions.⁸³ The training effects on UPDRS-III and Berg Balance Scale were sustained at the 1-month follow-up but not at the 3-month follow-up. No clear treatment effects on stride time, cadence, TUG or balance confidence were detected.⁸³ The positive effect on FOG was supported by case studies and uncontrolled trials only.⁸⁴

Interventions for reducing freezing of gait

Various approaches have been used in attempts to reduce FOG, including balance exercises, treadmill training, sensory cueing, movement strategy training and action observation training. A 2020 systematic review by Consentino et al examined the effects of different physiotherapy interventions on FOG. Their primary analysis showed that physiotherapy interventions (nine trials examining cueing training/balance exercises/home-based exercises, with PEDro scores ≥ 6 in seven of nine trials) had an overall treatment effect on reducing FOG compared with no intervention (SMD -0.29, 95% CI -0.45 to -0.12).⁸⁵ In the sub-group analyses focusing on different categories of intervention, home-based exercise interventions of prolonged duration (ie, around 4 months), which included balance and gait exercises and cueing, showed a pronounced effect on FOG compared with no intervention (three studies; SMD -0.30; 95% CI -0.53 to -0.07) but the quality of evidence as determined by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) was low due to risk of bias. In contrast, there was very low-quality evidence that a shorter exercise program of 12 to 14 weeks in duration (three studies) or cueing training (two studies; mean duration six to nine sessions) generated no effect.⁸⁵ There was no evidence that the effects of the above interventions are sustained after termination of training.

In action observation training, the participant is asked to first observe single motor actions (eg, rise from a chair, turn, walk through a narrow space) performed by a physiotherapist and then repetitively practise the same movements.^{86,87} Therefore, action observation training is considered a combined motor-cognitive approach in PD rehabilitation. Adding action observation training to conventional exercises also led to greater reduction in FOG than the same exercises with sham or no action observation training (four studies; SMD -0.40, 95% CI -0.76 to -0.05), and the effect could be maintained for 4 weeks (four studies; SMD -0.56, 95% CI -0.91 to -0.21), with moderate-quality evidence.⁸⁵ However, adding visual/auditory cueing to treadmill or step training did not result in a better effect on FOG than treadmill or step training alone (very low quality of evidence).⁸⁵ Aquatic exercise also had no effect on FOG (very-low quality of evidence).⁸⁵ These findings are consistent with another systematic review by Delgado-Alvarado et al,⁸⁸ which showed that all available studies classified as cognitive training (ie, action observation training,

motor learning facilitated with cueing and movement strategies, and computerised training program such as Kinect) are effective in reducing FOG.⁸⁹ However, recent work showed no difference in cognitive function between those who have FOG and those who do not, after adjusting for covariates (particularly disease severity).⁸⁹ There was also no correlation between FOG severity and cognitive performance.⁸⁹ Thus, effective reduction in FOG may involve more complex strategies than a 'cognitive-motor' approach, but this will require more study.

Dual-task training

Ambulation in daily living requires the ability to perform a cognitive or motor task while walking (eg, carrying a glass of water or attending to traffic signals while walking). Relative to their peers without PD, dual-task conditions cause people with PD to have more exaggerated decreases in walking speed, stride length and cadence, along with an increase in stride variability.^{90,91} Dual-task exercise training in PD has gained increasing attention in recent years. It typically involves performing various walking and balance activities concurrently with cognitive tasks or upper limb motor tasks (eg, carrying an object).⁹²

The effects of dual-task training were examined in a recent systematic review of 11 randomised trials by Li et al.⁹² The majority of these trials had a training duration of 6 to 12 weeks (45 to 60-minute sessions, two to three sessions per week). All but one study had a PEDro score of ≥ 6 . Their meta-analyses showed that dual-task training improved gait speed in single-task conditions (SMD -0.29, 95% CI -0.47 to -0.10) but not in dual-task conditions (SMD -0.13, 95% CI -0.38 to 0.12) when compared with the control group (usual care or single-task training). The improvement was attributable to increase in cadence rather than step length. Dual-task training also improved motor symptoms, as measured by the UPDRS-III (SMD 0.56, 95% CI 0.18 to 0.94) and Mini-BESTest score (SMD -0.44, 95% CI -0.84 to -0.05). However, the data of the control group in their meta-analyses were derived from a combination of studies that used a no-intervention control group and those that used a conventional/single-task training group. As the conventional/single-task training may have a beneficial effect on the outcomes, as clearly shown by Strouwen et al in their DUALITY trial,⁹³ their meta-analyses may have underestimated the treatment effect of dual-task training.

Regarding the long-term effects of dual-task training, the DUALITY trial demonstrated that both dual-task training and single-task training led to similar improvements in dual-task walking speed, which were sustained at the 12-week follow-up.⁹³ Their study was also the only high-quality trial that measured falls and found no between-group difference in fall rate during the 24-week follow-up period after training.⁹³ In summary, more high-quality research is needed to investigate whether dual-task training is beneficial for improving gait and balance under dual-task conditions, and fall incidence.

Overall, the gait training methods reviewed above have beneficial effects on certain aspects of gait, particularly walking speed, stride length and endurance. Ni et al⁶⁷ examined different types of exercise training in their systematic review of 40 randomised trials and, based on the calculated effect sizes, the treatment effect from a task-specific exercise (eg, walking exercise, treadmill training) was generally greater than that from a general exercise program (eg, cycling). Therefore, gait-specific training, rather than a general exercise program, may be required if gait is the outcome of interest.

Balance training

People with PD may show deficits in different aspects of balance function, as described by Horak et al,⁹⁴ namely: biomechanical constraints and postural orientation (ie, impaired flexibility, muscle weakness, stooped posture); limits of stability and verticality (ie, camptocormia, lateral trunk flexion, inability to hold an inclined posture); anticipatory postural adjustments (ie, diminished and delayed adjustments); reactive postural responses (ie, excessive

muscle co-activations, decreased stepping reactions); sensorimotor integration (ie, over-dependence on visual cues, impaired processing of proprioceptive input); and dynamic control of gait (ie, hypokinetic, shuffling gait, deficits in dual-task mobility).²¹ Thus, multidimensional balance/agility exercise training is the most common physiotherapy intervention to improve balance performance for people with PD.^{31,95–99} Examples of balance exercises typically included flexibility/joint mobility exercises (ie, targeting biomechanical constraints), weight shifting exercises (ie, limits of stability), exercises of self-destabilisation of the centre of mass (ie, anticipatory postural adjustments), tasks that involve external destabilisation of the centre of mass (ie, reactive postural responses), balance exercises on unstable support surfaces (ie, sensory orientation), balance activities during walking (eg, obstacle courses) that require continuous feedback and feedforward postural adjustments (ie, dynamic control of gait).^{95–99} Other types of balance training methods that have been studied include aquatic therapy, movement strategy training, motor-cognitive dual-task training, technology-assisted balance training, trunk/core exercises, treadmill walking with added perturbations, biofeedback and strengthening exercises with added instability.^{100–102}

The training programs were typically 4 to 12 weeks in duration (40 to 60 minutes per session, two to three sessions per week), although a few studies involved a longer training period of ≥ 6 months. An earlier systematic review by Allen et al¹⁰⁰ found that balance training was effective in improving balance-related activity performance in PD, and that programs that involved highly challenging balance activities had a tendency to induce greater improvement in balance. A more recent meta-analysis, by Shen et al,¹⁰¹ of trials with moderate-to-high methodological quality found that exercise training generated significant short-term and long-term improvements (up to 12 months) in balance performance (short-term effect: Hedges' $g = 0.303$; long-term effect: Hedges' $g = 0.419$). On the other hand, a more recent systematic review by Flynn et al showed that home-based standing balance and/or gait exercises improved balance (SMD 0.21, 95% CI 0.10 to 0.32) and gait speed (SMD 0.30, 95% CI 0.12 to 0.49) but not quality of life, when compared with no or sham intervention. Home-based exercise practice also induced similar improvement in balance to centre-based exercises (SMD -0.04 , 95% CI -0.36 to 0.27).¹⁰² Recent studies by Capato et al demonstrated that both people who freeze and non-freezers benefit equally from the training.^{97–99} The treatment effect was greater and lasted longer when the multidimensional balance exercises were supported by rhythmic auditory stimuli.^{97–99} Multidimensional balance exercise training induced improvement in balance not only in those with mild-to-moderate disease (Hoehn and Yahr stage 1 to 3)^{96–98} but also those with advanced PD (Hoehn and Yahr stage 4).⁹⁹

Dance exercise therapy

Dance exercise therapy in PD is an emerging area of research.^{103,104} Different types of dance have been studied, including Tango, Irish dance, waltz, ballet, Turo PD (a qigong dance hybrid), Ballu Sardu (a Sardinian folk dance), ballroom dancing, dance therapy specifically designed to address the PD symptoms, and a mixed genre. Most dance therapy programs lasted for 8 to 13 weeks. Each session was typically 1 to 1.5 hour in duration, with training frequency at one to two sessions per week. Argentine Tango was the most studied among the various dance programs. A 2020 systematic review of 16 trials (five trials having low risk of bias in ≥ 6 of 10 categories described in the Cochrane Collaboration risk of bias assessment tool) by Carapelloti et al revealed that dance exercise had favourable treatment effect on MDS UPDRS-III (MD -2 , 95% CI -4 to -1), balance (SMD 0.50, 95% CI 0.21 to 0.79), 6MWT (MD 50 m, 95% CI 15 to 85), TUG (MD -1.1 seconds, 95% CI -2.1 to 0.2) and depressive symptoms, as measured by the Beck Depression Inventory II (MD -5.1 , 95% CI -7.7 to -2.4).¹⁰⁴ There was a tendency for dance exercise to improve the forward and backward gait speed and stride length, but the confidence intervals did not exclude the possibility that usual care was slightly superior. The effect of dance exercise on PDQ-39 was not apparent. Another 2020 systematic review by

Barnish et al indicated that Tango dance induced an overall treatment effect on UPDRS-III (MD -10 , 95% CI -17 to -3) and that PD-specific dance improved PDQ-39 (MD -8 , 95% CI -12 to -4) but not performance in TUG (MD -2.1 seconds, 95% CI -6.3 to 2.1).¹⁰³ Finally, the systematic review by de Almeida et al specifically assessed the effect of dance on postural control in PD and revealed a large effect size in their meta-analysis (SMD 0.82, 95% CI 0.52 to 1.12).¹⁰⁵ In summary, sustained dance practice is beneficial in improving various aspects of motor function – including balance, mobility and walking endurance – and delays the progression of motor symptoms.

Several mechanisms underlying the observed improvement following dance therapy have been proposed. First, the external cues involved in dancing (eg, music with strong beats, physical contact with partner, seeing the movements of partner, hearing the dance steps) may enable the participants to bypass the impaired basal ganglia and access the cortical circuitry, thereby facilitating a better gait pattern and reducing FOG.¹⁰⁶ Dance often involves frequent stepping in different directions, turning, sudden cessation of stepping, shifting of centre of mass, and movements of varying speeds coordinated with arm movements. These may explain why sustained dance practice may result in improvement in balance and mobility. If the dance movements are intensive enough, they also impose a considerable demand on aerobic capacity and induce a training effect on endurance.

Dance practice makes the exercise more enjoyable and also promotes social interaction.^{107,108} A qualitative research study has provided important insights into the design and implementation of dance therapy classes in PD.¹⁰⁹ It is important to consider the disease severity of the participants. One possible strategy is to stratify the dance groups according to individual ability level. It is critical that the therapist is able to tailor the activities to the ability of the participants. Another important factor is the choice of music. Music with clear and strong beats is preferable because it helps participants to focus on movement and enables them to execute the movement sequences more smoothly.¹⁰⁹

Tai Chi, Qigong and yoga

Chinese traditional mind-body exercises, such as Qigong and Tai Chi, have become increasingly popular in neurological rehabilitation, including for PD. There are two theories underpinning these techniques. The first is related to the concept of 'qi': in traditional Chinese medicine, qi is an energy that flows through the meridian system in the body.¹¹⁰ The blockage of the flow of qi is thought to contribute to illness. According to traditional Chinese medicine philosophies, Qigong facilitates the movement of qi throughout the body so that health can be promoted.¹¹¹ The second theory is related to the concept of 'yin and yang': they are the two complementary and opposing elements that comprise the universe that needs to be maintained in harmony. Through practising Qigong, the yin and yang of the body become balanced, thereby improving health.¹¹²

Tai Chi is a specific branch of Qigong and involves more martial arts features, and involves the execution of slow and controlled body movements coordinated with deep diaphragmatic breathing.²¹ The most common form used is the Yang style. The movements involved often require shifting of the centre of gravity to the individual's stability limit, reaching beyond the base of support, shifting of the body weight from one leg to another, changing the base of support from bilateral to unilateral stance, and sustained squatting movements. With these manoeuvres, Tai Chi has the potential to improve balance and muscle strength, which may in turn improve related functions such as mobility and endurance.²¹ Three systematic reviews were published to examine the effect of Tai Chi in PD between 2014 and 2015.^{113–115} All three reviews concluded that Tai Chi was effective in improving balance and motor function for people with PD.

To provide a more comprehensive picture of the therapeutic value of Tai Chi in PD based on the latest evidence, the meta-analyses presented in Yang et al¹¹⁴ were updated by including relevant randomised controlled trials that were published after 2013.^{116–120} Most trials involved regular Tai Chi practice for 30 to 60 minutes per

session, three times a week for 8 to 24 weeks. The updated meta-analysis (PEDro scores 5 to 7) showed that Tai Chi improved balance function as measured by the Berg Balance Scale (MD 4, 95% CI 1 to 6) (Figure 8A) and functional reach test (MD 5 cm, 95% CI 3 to 7) (Figure 8B). Tai Chi also improved the TUG performance by 1.1 seconds (95% CI -0.4 to -1.8) (Figure 8C), and the 6MWT by 41 m (95% CI 3 to 78) (Figure 8D). It also attenuated the motor symptoms (SMD -0.7, 95% CI -1.2 to -0.2) (Figure 8E). However, its effect on walking speed was inconclusive (Figure 8F). For detailed forest plots, see Figure 9 on the eAddenda. As for the long-term effects of Tai Chi, Li et al reported that the effect from 6 months of Tai Chi practice led to sustained effects for 3 months.¹²¹ Tai Chi also reduced the incidence of falls after 12 weeks¹¹⁷ and 24 weeks¹²¹ of practice during a 3 to 6-month follow-up period (RR 0.33 to 0.44).

Baduanjin is a popular form of Qigong that involves fewer exercises and is easier to master than Tai Chi.¹²² A few studies have examined the effect of Qigong for people with PD and identified beneficial effects on balance,^{122,123} mobility^{122,123} and motor function¹²⁴ after 8 to 24 weeks of Qigong practice (45 to 60 minutes per session, two to four sessions per week); however, there was one high-quality trial¹²² and the others either have poor methodological quality (PEDro score 3)¹²³ or a small sample size (< 40 participants).¹²⁴

A peaceful mind and focused attention are required during Qigong and Tai Chi practice, leading researchers to postulate that these exercise approaches may have a positive impact on non-motor outcomes. The effects of these techniques on depression,^{119,125-127} cognition,^{119,126,127} sleep quality^{122,128} and quality of life (PDQ-39)^{120,124,126} have been examined in a number of studies. The estimated effects on these outcomes were mostly positive.

The application of yoga in PD has also garnered attention. Yoga consists of prolonged muscle-stretching postures, diaphragmatic breathing and meditation.¹²⁹ As a mind-body exercise intervention, yoga also encourages body awareness and kinesthetic sense. A recent systematic review by Jin et al did not find strong enough evidence to support the use of yoga to reduce the risk of falls for people with PD.¹³⁰ The benefits of yoga on motor impairments, gait, muscle strength and quality of life were supported by pilot studies or low-quality randomised trials. The study of yoga in PD is only emerging and more research is required to examine its health benefits.

Aquatic exercise

The use of aquatic exercise in PD has been examined in several studies.¹³¹ The duration of the exercise programs varied between 4 and 10 weeks, with each session typically lasting 45 to 60 minutes at a frequency of 2 to 5 days per week. The exercises involved were usually a mix of mobility, balance, strengthening and endurance exercises. One specific type of aquatic exercise is Ai Chi,^{125,132,133} which is a combination of Tai Chi and Qigong performed in the water rather than on land. The Ai Chi trials were of good methodological quality (PEDro scores 6 to 7), although the sample sizes were relatively small (29 to 40 participants in each study).^{125,132,133} Improvements in balance (Berg Balance Scale, Single-leg-standing, Tinetti scores), TUG and motor function (UPDRS-III) were reported after 5 to 11 weeks (45 to 60 minutes per session, two to five sessions weekly) of Ai Chi practice.^{125,132,133}

A 2019 systematic review by Cugusi et al examined the effects of aquatic exercises in PD.¹³¹ Most of the trials compared the effects of aquatic exercise versus land-based exercise and were of good quality (all but one trial having PEDro scores \geq 6).¹³¹ Their meta-analysis revealed that aquatic exercise was superior to land-based exercise in improving the Berg Balance Scale score (MD 2.7, 95% CI 1.6 to 3.9), Fall Efficacy Scale (MD -4.0, 95% CI -6.1 to -1.8) and PDQ-39 (MD -6.0, 95% CI -11.3 to -0.6). There was a trend for aquatic exercise to be more beneficial than land-based exercise in reducing the UPDRS-III scores but the size of any additional benefit would be small (MD -1, 95% CI -2 to 0). The effects of aquatic exercise on the TUG and Activities-specific Balance Confidence Scale were similar to that of land-based exercise. However, the quality of evidence was

considered to be low or very low, except for the Berg Balance Scale (high quality) and PDQ-39 (moderate quality).¹³¹

Combined exercise training

As the motor impairments and activity limitations are multifaceted among people with PD, the exercise training in the overall physiotherapy intervention may be multidimensional, with incorporation of different types of exercises (eg, aerobic, resistance, balance training).^{43,134-142} Most of the trials of combined exercise training are of good methodological quality (PEDro scores \geq 6).^{43,134,135,137,139-140,142} The exercise sessions were typically conducted at a frequency of two to three times per week for a duration of 4 to 16 weeks, although a few trials studied an exercise protocol of much longer duration (6 to 24 months).¹³⁷⁻¹³⁹ Most trials reported beneficial effects on strength, gait, balance and endurance. Combined exercise training has also been shown to have benefits on slowing the progression of motor impairments, as reflected by the change in MDS UPDRS-III scores.¹³⁶ A few trials also reported positive impacts on the non-motor impairments of fatigue,¹³⁶ sleep quality,¹³⁴ bone density¹³⁶ and quality of life.⁴³

Prevention of falls

Balance impairments are associated with falls in PD.¹⁰⁰ Falls are very common among people with PD, with an incidence rate of 343 per 100,000 people, representing more than twice the risk of falls than the reference population without PD.¹⁴³ A systematic review of 22 PD studies showed that an average of 60.5% of participants experienced at least one fall, with 39% reporting recurrent falls.⁹⁵ One of the detrimental consequences of falls is fragility fractures. After adjusting for potential confounders, the incidence rate of fractures remained much greater among people with PD than their non-PD counterparts (adjusted incidence rate ratio: 1.73), regardless of sex and age groups.¹⁴³ The prevention of falls is thus a very important goal of physiotherapy for PD.

A number of intervention studies used fall rate or number of fallers as an outcome measure.^{60,101,117,137,142,144-151} The intervention methods included balance/gait exercises,^{60,117,146,147,150} strengthening exercises,¹⁴⁹ a combination of balance/gait and strengthening exercises,^{137,142,144} Tai Chi,¹⁵¹ movement strategy training or exercise program combined with fall prevention education.^{137,146,148,149} The program duration showed great diversity, varying from 8 weeks to 6 months. The duration and frequency of the supervised sessions was usually 1 to 2 hours and one to two sessions per week, respectively. The supervised sessions were often supplemented with a home exercise program. In some studies, the participants were required to perform the exercises unsupervised following the intervention period;^{60,137,145,148} in other studies, home-based exercise programs were supplemented with home visits or telephone calls.^{137,149} The meta-analysis by Shen et al¹⁰¹ showed that exercise training reduced the rate of falls (rate ratio 0.485 in the short term and 0.413 in the long term) but not the number of fallers in the short or long term. Influence of disease severity seems to have an important association with the outcome after exercise training. Those who have less severe disease (UPDRS-III scores of 23 to 28 in Chivers-Seymour et al¹³⁷ or \leq 26 in Canning et al¹⁴⁶, or Hoehn and Yahr scale 2 to 3 in Ashburn et al¹⁴⁸) experienced a reduction of fall rate with exercise intervention, while those with more severe disease had a higher fall rate after training when compared with the control group.

Effect of physical exercise on non-motor impairments

While the effects of specific types of exercise on non-motor impairments were discussed in the respective sections above, a number of systematic reviews have attempted to synthesise the evidence related to the effect of physical exercise training as a whole on non-motor impairments in PD. Cusso et al showed that the effects of exercise therapy on global non-motor impairments (indicated by UPDRS-I) and depressive symptoms were conflicting.¹⁵² The evidence

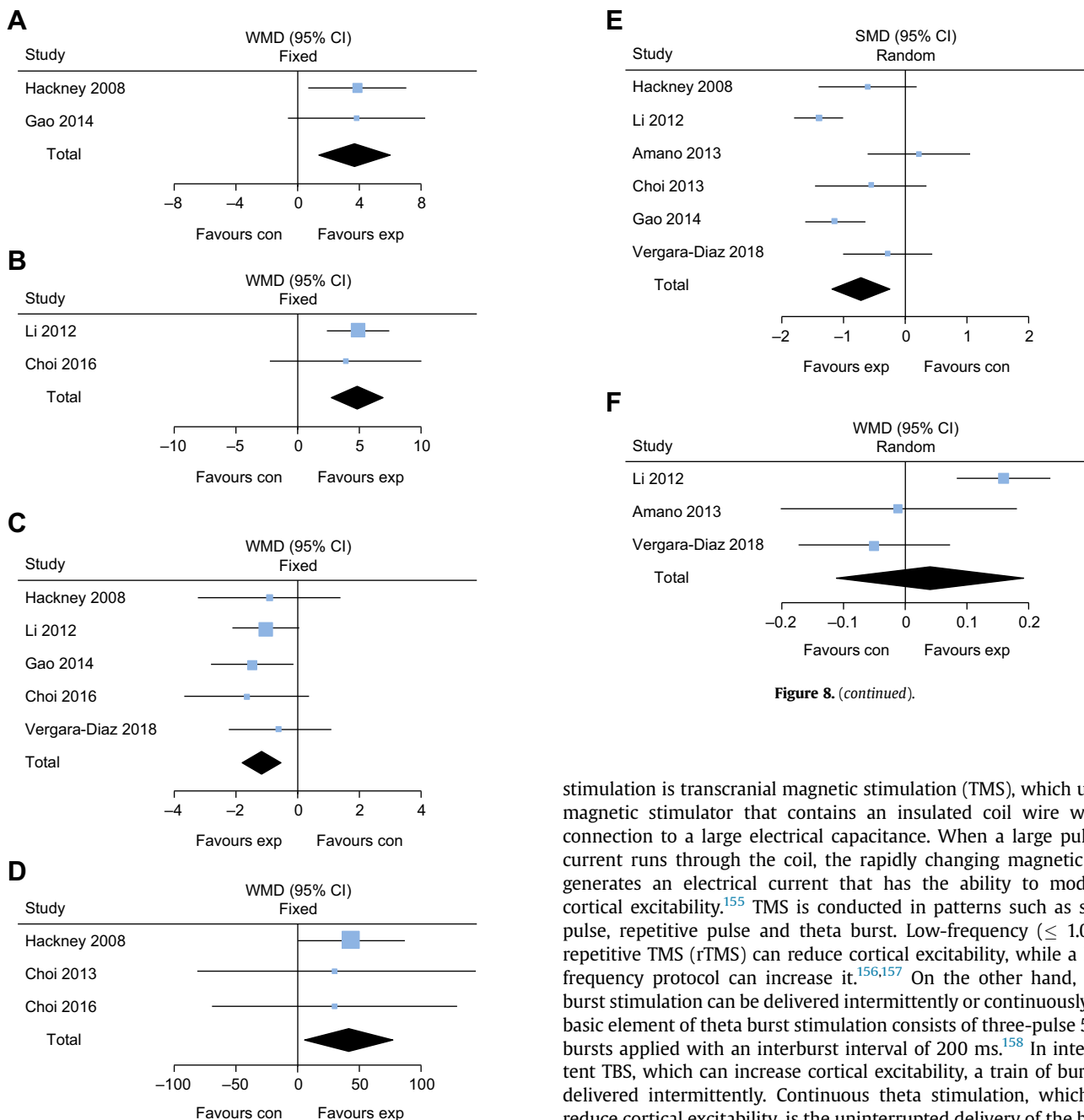


Figure 8. (continued).

Figure 8. Effects of Tai Chi compared with controls on (A) Berg Balance Scale score, (B) Functional Reach, (C) Timed Up and Go, (D) 6-minute walk test, (E) Unified Parkinson's Disease Rating Scale Part III (UPDRS-III) and (F) walking speed. The SMD was used in the analysis of motor symptoms because some studies used UPDRS III, while others used MDS UPDRS III as an outcome. See the main text section 'Meta-analytic approach' for further details.

related to daytime sleepiness, fatigue, apathy and sleep quality was sparse and thus inconclusive.¹⁵² Another systematic review by da Silva et al¹⁵³ revealed that adapted Tango, exergames^a, and treadmill training maintained or improved cognitive function among people at a mild or moderate stage of PD. One common feature of these interventions is their substantial demand on aerobic capacity. This is consistent with findings that moderate-intensity aerobic exercise led to a more pronounced effect on improving global cognition among people with mild cognitive impairment or dementia.¹⁵⁴

Transcranial magnetic stimulation

Increasing research has explored the use of brain stimulation for people with PD. One of the more investigated methods of brain

stimulation is transcranial magnetic stimulation (TMS), which uses a magnetic stimulator that contains an insulated coil wire with a connection to a large electrical capacitance. When a large pulse of current runs through the coil, the rapidly changing magnetic field generates an electrical current that has the ability to modulate cortical excitability.¹⁵⁵ TMS is conducted in patterns such as single pulse, repetitive pulse and theta burst. Low-frequency (≤ 1.0 Hz) repetitive TMS (rTMS) can reduce cortical excitability, while a high-frequency protocol can increase it.^{156,157} On the other hand, theta burst stimulation can be delivered intermittently or continuously. The basic element of theta burst stimulation consists of three-pulse 50 Hz bursts applied with an interburst interval of 200 ms.¹⁵⁸ In intermittent TBS, which can increase cortical excitability, a train of bursts is delivered intermittently. Continuous theta stimulation, which can reduce cortical excitability, is the uninterrupted delivery of the bursts for a short period of time (eg, 20 seconds).¹⁵⁸ Apart from its impact on cortical excitability, rTMS can also affect the excitability of brain regions that are related to the site of stimulation, probably via the cortico-striato-thalamocortical circuitry, thus pointing to potential utility of rTMS in improving motor performance in PD.^{159,160}

A 2019 systematic review by Yang et al (23 studies, most with good methodological quality) showed that high-frequency rTMS, but not low-frequency rTMS, was effective in improving motor performance (SMD 0.48, 95% CI 0.32 to 0.64).¹⁶¹ The frequency used in the high-frequency rTMS protocol was typically between 5 and 10 Hz, and the intensity was 80 to 110% of the resting motor threshold. The frequency of treatment sessions varied between two sessions per day to once a week. Multi-sessions of rTMS (typically three to ten sessions) were found to have stronger effects than a single session of treatment. The stimulation site had an impact on the outcome. High-frequency rTMS only yielded a therapeutic effect on motor performance when the stimulation was applied to the primary motor cortex (M1) but not the other brain regions. In addition, bilateral M1 stimulation yielded a greater treatment effect than unilateral M1 stimulation. The outcome was also affected by the stimulation dosage. The effect of high-frequency rTMS applied to M1 was stronger when 18,000 to 20,000 pulses were delivered, compared with other

dosages. However, the medication state did not affect the magnitude of improvement.¹⁶¹

Another systematic review by Chung et al (22 trials) examined not only motor impairments in general (eg, UPDRS-III) but also specific aspects of motor activities (eg, upper limb function, walking).¹⁶² The methodological quality of the studies varied, but more than half of the criteria described in the Cochrane risk-of-bias checklist were fulfilled in 10 of the 22 trials reviewed. Their results revealed that rTMS induced improvements in: upper limb motor performance in the short term (Hedges' g 0.40); walking performance in the short term (Hedges' g 0.61) and long term (Hedges' g 0.89) and UPDRS-III scores in the short term (Hedges' g 0.31) and long term (Hedges' g 0.54). Consistent with the meta-analysis by Yang et al,¹⁶¹ a stronger effect was observed with stimulation at M1. Long-term improvement in UPDRS-III score was also associated with a greater number of total stimulation pulses.¹⁶²

In a 2020 systematic review of 14 trials (13 with PEDro scores ≥ 7), Xie et al examined the effect of TMS specifically on gait and found improvement in walking speed after rTMS treatment, but only when the walking speed was assessed in the 'on' state.¹⁶³ In addition, the improvement in walking speed was not retained at 1 month follow-up. FOG and TUG were not improved with rTMS. The meta-analysis by Goodwill et al revealed no effect of rTMS on cognition (five studies, four with PEDro scores ≥ 7).¹⁶⁴ Overall, rTMS does show some promise in improving motor performance, but the optimal protocol for people with different levels of disability requires further research.

Transcranial direct current stimulation

Another form of brain stimulation studied in PD is transcranial direct current stimulation (tDCS), which involves the delivery of a constant low-amplitude electric current (generally between 1 and 2 mA) via scalp electrodes. It can modulate excitability in both cortical and subcortical brain regions.^{165,166} Anodal tDCS can increase neuronal excitability, while cathodal tDCS can decrease it.¹⁶⁵ tDCS may have relevance to the treatment of PD symptoms because anodal tDCS can enhance extracellular dopamine levels in the striatum¹⁶⁷ and inhibit GABAergic neurons.^{168,169}

A systematic review by Broeder et al¹⁷⁰ investigated the effects of tDCS on different aspects of motor activities and cognition in PD (10 studies). Two studies (PEDro scores 7 and 8) found that anodal tDCS over M1 reduced UPDRS-III scores compared to sham stimulation. The other studies did not find significant results on UPDRS, but the stimulation sites were different (dorsolateral prefrontal cortex, or a combination of premotor cortex, prefrontal cortex and M1). Of the seven studies (the majority with high quality, PEDro scores ≥ 7) that examined gait parameters, five reported beneficial effects. The results on upper limb activity were conflicting. Of the four included studies (the majority with high quality, PEDro scores ≥ 7), two reported positive effects of anodal tDCS. A more recent systematic review by Goodwill et al¹⁶⁴ revealed an overall improvement of motor activity with tDCS based on the results of nine studies (eight with PEDro scores ≥ 7) and the degree of improvement was similar to that induced by rTMS.

The effects of tDCS on cognitive function was mixed. Some studies showed that anodal tDCS applied over the dorsolateral prefrontal cortex improved working memory^{171,172} and phonemic verbal fluency,¹⁷¹ but this was not observed in other studies.^{173,174} The systematic review by Goodwill et al¹⁶⁴ revealed no effect of tDCS on cognition but the meta-analysis was based on the findings of three studies.

In clinical practice, tDCS is often combined with other physiotherapy interventions. Beretta et al¹⁷⁵ showed in their 2020 systematic review of randomised trials that tDCS combined with cognitive and/or motor training may induce more pronounced treatment effects on motor performance (gait, posture, upper limb activity) and cognition, suggesting a possible synergistic effect. However, the methodological quality of the studies was not evaluated. Similar to the rTMS trials, the stimulation protocol varied greatly in terms of the

number of treatment sessions, and tDCS intensity and duration. To enhance the clinical utility of tDCS, more research is required to identify the optimal protocols for improving different aspects of motor performance and also the neurophysiological mechanisms underlying the change in cortical excitability after tDCS intervention.¹⁶⁹

Telerehabilitation

Telehealth involves the use of electronic information and telecommunication technologies to deliver healthcare services. It is particularly relevant to patients who have limited access to conventional face-to-face rehabilitation services for a variety of reasons, including financial burden, lack of required services locally, and difficulties with travel due to long distance, impaired mobility or pandemic restrictions.¹⁷⁶ A 2020 systematic review showed that telehealth interventions significantly lowered the degree of motor impairment (UPDRS-III).¹⁷⁷ The interventions were either phone-based or computer-based and involved a wide variety of arrangements: motor monitoring using wireless sensor technology, exercise DVD with weekly phone calls, gait training/feedback via a smartphone application, virtual visits/care from a remote specialist, use of a Parkinson's tracker app that enabled tracking of different self-monitoring measures (eg, cognition, movement, mood) and medications, and delivery of a web-based course.¹⁷⁷

Two trials directly involved the participation of physiotherapists.^{178,179} Ginis et al¹⁷⁸ found that their Smartphone-delivered gait training system led to similar improvement in gait as standard physiotherapy after 6 weeks of training (30 minutes, three sessions per week) and the effects were retained after another 4 weeks. Their system also induced more gain in balance ability (mini-BESTest) than standard physiotherapy, but the effect was not maintained at follow-up. In a pilot study, Khalil et al¹⁷⁹ studied the effects of an 8-week program that involved the home use of an exercise DVD (three times a week, 24 sessions) and walking program (once weekly, eight sessions). Of the 32 sessions, eight sessions within the first 4 weeks were supervised by a physiotherapist. The participants received a weekly phone call from the physiotherapist to check the adherence to exercises and also to address areas of concern raised by the patients. The intervention was found to cause a greater reduction in MDS UPDRS-III score than usual care. The retention rate and adherence to the above interventions were quite high, at 87 to 91% and 70 to 77%, respectively.^{178,179} However, there is a lack of economic analysis of these telerehabilitation interventions compared with conventional physiotherapy.

More recently, Gandolfi et al addressed this limitation by comparing both the therapeutic effects and cost of a home-based telerehabilitation virtual reality balance training program with an in-clinic sensory integration balance training regimen.¹⁸⁰ After 7 weeks of training (50 minutes per session, 3 days per week) that was remotely supervised by a physiotherapist, their post-hoc analysis showed similar improvement in balance (Berg Balance Scale, Dynamic Gait Index), balance confidence (Activities-specific Balance Confidence Scale) and quality of life (PDQ-8) in both groups immediately after training and at 1-month follow-up. The total cost per patient was €384 for the telerehabilitation, which was considerably lower than the in-clinic intervention (€602). An important point to note is that the caregiver was always present during the training sessions to ensure safety. This may be a key limitation of some telerehabilitation interventions, especially those that require a higher degree of monitoring of performance and safety.

Overall, while home-based telerehabilitation may be a viable alternative to traditional face-to-face physiotherapy service delivery, there is scarcity of research in this area. The search for innovative methods of physiotherapy service delivery has never been so relevant because of the current COVID-19 pandemic. More research on PD telerehabilitation is urgently needed.

Future directions for clinical practice and research

A clinical regimen should be selected for each patient after consideration of the therapist time required for equipment set up and the cost-effectiveness and sustainability of the program. As PD is chronic and progressive in nature, patients should be equipped with the necessary skills to perform the exercises in home-based or community-based settings in the long run so that the therapeutic effects can be sustained. Therefore, delivery of physiotherapy service through telecommunication technologies should be further explored. Considering the promising preliminary results, more efforts should be directed towards developing innovative telerehabilitation services for people with PD delivered by physiotherapists and evaluating their efficacy and cost-effectiveness. The use of Qigong, yoga and respiratory muscle training requires further research due to the limited evidence. Future research is also warranted to identify the optimal exercise protocols for improving more complex walking tasks (eg, dual tasking) and FOG. The use of rTMS and tDCS shows some promising results, but should undergo more research to identify the optimal protocols for different outcomes and PD subgroups. More work is also needed to investigate the effects of different types of exercise training on non-motor outcomes in PD.

Footnotes: ^a Wii Fit, Nintendo, Kyoto, Japan.

eAddenda: Figures 3, 5, 7 and 9 can be found online at <https://doi.org/10.1016/j.jphys.2021.06.004>

Ethics approval: Nil.

Competing interests: Nil.

Source(s) of support: Nil.

Acknowledgements: The author would like to thank Miss Ouyang Huixi for assistance in data curation, and Dr Raymond Chung for assistance in statistical analysis.

Provenance: Invited. Peer reviewed.

Correspondence: Marco YC Pang, Department of Rehabilitation Sciences, Faculty of Health and Social Sciences, The Hong Kong Polytechnic University, Hong Kong. Email: marco.pang@polyu.edu.hk

References

- Abbas MM, Xu Z, Tan LCS. Epidemiology of Parkinson's Disease-East Versus West. *Mov Disord Clin Pract*. 2017;5:14–28.
- Dorsey ER, Sherer T, Okun MS, Bloem BR. The emerging evidence of the Parkinson pandemic. *J Parkinsons Dis*. 2018;8:S3–S8.
- Pringsheim T, Jette N, Frolkis A, Steeves TD. The prevalence of Parkinson's disease: a systematic review and meta-analysis. *Mov Disord*. 2014;29:1583–1590.
- Muangpaisan W, Hori H, Brayne C. Systematic review of the prevalence and incidence of Parkinson's disease in Asia. *J Epidemiol*. 2009;19:281–293.
- Kalia LV, Lang AE. Parkinson's disease. *Lancet*. 2015;386:896–912.
- Albin RL. The pathophysiology of chorea/ballism and Parkinsonism. *Parkinsonism Relat Disord*. 1995;1:3–11.
- Horak FB, Frank J, Nutt J. Effects of dopamine on postural control in parkinsonian subjects: scaling, set, and tone. *J Neurophysiol*. 1996;75:2380–2396.
- Pang MY, Mak MK. Influence of contraction type, speed, and joint angle on ankle muscle weakness in Parkinson's disease: implications for rehabilitation. *Arch Phys Med Rehabil*. 2012;93:2352–2359.
- Mak MK, Pang MY, Mok V. Gait difficulty, postural instability, and muscle weakness are associated with fear of falling in people with Parkinson's disease. *Parkinsons Dis*. 2012;2012:901721.
- Mak MK, Pang MY. Balance confidence and functional mobility are independently associated with falls in people with Parkinson's disease. *J Neurol*. 2009;256:742–749.
- Mak MK, Pang MY. Balance self-efficacy determines walking capacity in people with Parkinson's disease. *Mov Disord*. 2008;23:1936–1939.
- Saltin B, Landin S. Work capacity, muscle strength and SDH activity in both legs of hemiparetic patients and patients with Parkinson's disease. *Scand J Clin Lab Invest*. 1975;35:531–538.
- Protas EJ, Stanley RK, Jankovic J, MacNeill B. Cardiovascular and metabolic responses to upper- and lower-extremity exercise in men with idiopathic Parkinson's disease. *Phys Ther*. 1996;76:34–40.
- Mavrommati F, Collett J, Franssen M, Meaney A, Sexton C, Dennis-West A, et al. Exercise response in Parkinson's disease: insights from a cross-sectional comparison with sedentary controls and a per-protocol analysis of a randomised controlled trial. *BMJ Open*. 2017;7:e017194.
- Mak MK, Pang MY. Parkinsonian single fallers versus recurrent fallers: different fall characteristics and clinical features. *J Neurol*. 2010;257:1543–1551.
- Chou KL, Elm JJ, Wielinski CL, Simon DK, Aminoff MJ, Christine CW, et al. Factors associated with falling in early, treated Parkinson's disease: the NET-PD LSI cohort. *J Neurol Sci*. 2017;377:137–143.
- Poewe W. Non-motor symptoms in Parkinson's disease. *Eur J Neurol*. 2008;15(Suppl 1):14–20.
- Katzenschlager R, Head J, Schrag A, Ben-Shlomo Y, Evans A, Lees AJ, et al. Fourteen-year final report of the randomized PDRC-UK trial comparing three initial treatments in PD. *Neurology*. 2008;71:474–480.
- Postuma RB, Aarsland D, Barone P, Burn DJ, Hawkes CH, Oertel W, et al. Identifying prodromal Parkinson's disease: pre-motor disorders in Parkinson's disease. *Mov Disord*. 2012;27:617–626.
- Song W, Guo X, Chen K, Chen X, Cao B, Wei Q, et al. The impact of non-motor symptoms on the health-related quality of life of Parkinson's disease patients from Southwest China. *Parkinsonism Relat Disord*. 2014;20:149–152.
- Mak MKY, Wong-Yu ISK. Exercise for Parkinson's disease. *Int Rev Neurobiol*. 2019;147:1–44.
- 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;13:689–703.
- Katzel LI, Ivey FM, Sorkin JD, Macko RF, Smith B, Shulman LM. Impaired economy of gait and decreased six-minute walk distance in Parkinson's disease. *Parkinsons Dis*. 2012;2012:241754.
- Christiansen CL, Schenkman ML, McFann K, Wolfe P, Kohrt WM. Walking economy in people with Parkinson's disease. *Mov Disord*. 2009;24:1481–1487.
- Shu HF, Yang T, Yu SX, Huang HD, Jiang LL, Gu JW, et al. Aerobic exercise for Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials. *PLoS One*. 2014;9:e100503.
- Cugusi L, Solla P, Serpe R, Carzedda T, Piras L, Oggianu M, 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;37:245–254.
- Harvey M, Weston KL, Gray WK, O'Callaghan A, Oates LL, Davidson R, et al. High-intensity interval training in people with Parkinson's disease: a randomized, controlled feasibility trial. *Clin Rehabil*. 2019;33:428–438.
- Schenkman M, Moore CG, Kohrt WM, Hall DA, Delitto A, Comella CL, 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;75:219–226.
- van der Kolk NM, de Vries NM, Penko AL, van der Vlugt M, Mulder AA, Post B, et al. A remotely supervised home-based aerobic exercise programme is feasible for patients with Parkinson's disease: results of a small randomised feasibility trial. *J Neurol Neurosurg Psychiatry*. 2018;89:1003–1005.
- van der Kolk NM, de Vries NM, Kessels RPC, Joosten H, Zwiderman AH, Post B, et al. Effectiveness of home-based and remotely supervised aerobic exercise in Parkinson's disease: a double-blind, randomised controlled trial. *Lancet Neurol*. 2019;18:998–1008.
- Tollár J, Nagy F, Hortobágyi T. Vastly different exercise programs similarly improve parkinsonian symptoms: a randomized clinical trial. *Gerontology*. 2019;65:120–127.
- Qutubuddin A, Reis T, Alramadhani R, Cifu DX, Towne A, Carne W. Parkinson's disease and forced exercise: a preliminary study. *Rehabil Res Pract*. 2013;2013:375267.
- Sacheli MA, Neva JL, Lakhani B, Murray DK, Vafai N, Shahinfard E, et al. Exercise increases caudate dopamine release and ventral striatal activation in Parkinson's disease. *Mov Disord*. 2019;34:1891–1900.
- Schootemeijer S, van der Kolk NM, Bloem BR, de Vries NM. Current perspectives on aerobic exercise in people with Parkinson's disease. *Neurotherapeutics*. 2020;17:1418–1433.
- Arfa-Fatollahkhani P, Safar Cherati A, Habibi SAH, Shahidi GA, Sohrabi A, Zamani B. Effects of treadmill training on the balance, functional capacity and quality of life in Parkinson's disease: a randomized clinical trial. *J Complement Integr Med*. 2019;17:20180245.
- Inkster LM, Eng JJ, MacIntyre DL, Stoessel AJ. Leg muscle strength is reduced in Parkinson's disease and relates to the ability to rise from a chair. *Mov Disord*. 2003;18:157–162.
- Vetrano DL, Pisciotto MS, Laudisio A, Lo Monaco MR, Onder G, Brandi V, et al. Sarcopenia in Parkinson disease: comparison of different criteria and association with disease severity. *J Am Med Dir Assoc*. 2018;19:523–527.
- Pang MY, Mak MK. Muscle strength is significantly associated with hip bone mineral density in women with Parkinson's disease: a cross-sectional study. *J Rehabil Med*. 2009;41:223–230.
- Pelicioni PHS, Menant JC, Latt MD, Lord SR. Falls in Parkinson's disease subtypes: risk factors, locations and circumstances. *Int J Environ Res Public Health*. 2019;16:2216.
- Saltychev M, Bärlund E, Paltamaa J, Katajapuu N, Laimi K. Progressive resistance training in Parkinson's disease: a systematic review and meta-analysis. *BMJ Open*. 2016;6:e008756.
- Chung CL, 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;30:11–23.
- Ni M, Signorile JF, Mooney K, Balachandran A, Potiaumpai M, Luca C, et al. Comparative effect of power training and high-speed yoga on motor function in older patients with Parkinson Disease. *Arch Phys Med Rehabil*. 2016;97:345–354.
- Ni M, Signorile JF, Balachandran A, Potiaumpai M. Power training induced change in bradykinesia and muscle power in Parkinson's disease. *Parkinsonism Relat Disord*. 2016;23:37–44.
- Paul SS, Canning CG, Song J. Leg muscle power is enhanced by training in people with Parkinson's disease: a randomized controlled trial. *Clin Rehabil*. 2014;28:275–288.
- de Lima TA, Ferreira-Moraes R, Alves WMGDC, Alves TGG, Pimentel CP, Sousa EC, et al. Resistance training reduces depressive symptoms in elderly people with Parkinson disease: a controlled randomized study. *Scand J Med Sci Sports*. 2019;29:1957–1967.

46. Leal LC, Abrahim O, Rodrigues RP, da Silva MC, Araújo AP, de Sousa EC, et al. Low-volume resistance training improves the functional capacity of older individuals with Parkinson's disease. *Geriatr Gerontol Int*. 2019;19:635–640.
47. Santos L, Fernandez-Rio J, Winge K, Barragán-Pérez B, González-Gómez L, Rodríguez-Pérez V, et al. Effects of progressive resistance exercise in akinetic-rigid Parkinson's disease patients: a randomized controlled trial. *Eur J Phys Rehabil Med*. 2017;53:651–663.
48. Silva-Batista C, Corcos DM, Roschel H, Kanegusuku H, Gobbi LT, Piemonte ME, et al. Resistance training with instability for patients with Parkinson's disease. *Med Sci Sports Exerc*. 2016;48:1678–1687.
49. Silva-Batista C, Corcos DM, Kanegusuku H, Piemonte MEP, Gobbi LTB, de Lima-Pardini AC, et al. Balance and fear of falling in subjects with Parkinson's disease is improved after exercises with motor complexity. *Gait Posture*. 2018;61:90–97.
50. Ferreira RM, Alves WMGDC, de Lima TA, Alves TGG, Alves Filho PAM, Pimentel CP, et al. The effect of resistance training on the anxiety symptoms and quality of life in elderly people with Parkinson's disease: a randomized controlled trial. *Arq Neuropsiquiatr*. 2018;76:499–506.
51. Torsney KM, Forsyth D. Respiratory dysfunction in Parkinson's disease. *J R Coll Physicians Edinb*. 2017;47:35–39.
52. Rodríguez MÁ, Crespo I, Del Valle M, Olmedillas H. Should respiratory muscle training be part of the treatment of Parkinson's disease? A systematic review of randomized controlled trials. *Clin Rehabil*. 2020;34:429–437.
53. Dockx K, Bekkers EM, Van den Bergh V, Ginis P, Rochester L, Hausdorff JM, et al. Virtual reality for rehabilitation in Parkinson's disease. *Cochrane Database Syst Rev*. 2016;12:CD010760.
54. Lei C, Sunzi K, Dai F, Liu X, Wang Y, Zhang B, et al. Effects of virtual reality rehabilitation training on gait and balance in patients with Parkinson's disease: a systematic review. *PLoS One*. 2019;14:e0224819.
55. Chen Y, Gao Q, He CQ, Bian R. Effect of virtual reality on balance in individuals with Parkinson disease: a systematic review and meta-analysis of randomized controlled trials. *Phys Ther*. 2020;100:933–945.
56. Triegaardt J, Han TS, Sada C, Sharma S, Sharma P. The role of virtual reality on outcomes in rehabilitation of Parkinson's disease: meta-analysis and systematic review in 1031 participants. *Neuro Sci*. 2020;41:529–536.
57. Canning CG, Allen NE, Nackaerts E, Paul SS, Nieuwboer A, Gilat M. Virtual reality in research and rehabilitation of gait and balance in Parkinson disease. *Nat Rev Neurol*. 2020;16:409–425.
58. Wang B, Shen M, Wang YX, He ZW, Chi SQ, Yang ZH. Effect of virtual reality on balance and gait ability in patients with Parkinson's disease: a systematic review and meta-analysis. *Clin Rehabil*. 2019;33:1130–1138.
59. Mirelman A, Rochester L, Maidan I, Del Din S, Alcock L, Nieuwhof F, 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;388:1170–1182.
60. Shen X, Mak MKY. Technology-assisted balance and gait training reduces falls in patients with Parkinson's disease: a randomised controlled trial with 12 month follow-up. *Neurorehabil Neural Repair*. 2015;29:103–111.
61. Mehrholz J, Kugler J, Storch A, Pohl M, Elsner B, Hirsch K. Treadmill training for patients with Parkinson's disease. *Cochrane Database Syst Rev*. 2015;8:CD007830.
62. Robinson AG, Dennett AM, Snowdon DA. Treadmill training may be an effective form of task-specific training for improving mobility in people with Parkinson's disease and multiple sclerosis: a systematic review and meta-analysis. *Physiotherapy*. 2019;105:174–186.
63. Canning CG, Allen NE, Dean CM, Goh L, Fung VS. Home-based treadmill training for individuals with Parkinson's disease: a randomized controlled pilot trial. *Clin Rehabil*. 2012;26:817–826.
64. Protas EJ, Mitchell K, Williams A, Qureshy H, Caroline K, Lai EC. Gait and step training to reduce falls in Parkinson's disease. *NeuroRehabilitation*. 2005;20:183–190.
65. Kurtais Y, Kutlay S, Tur BS, Gok H, Akbostanci C. Does treadmill training improve lower-extremity tasks in Parkinson disease? A randomized controlled trial. *Clin J Sport Med*. 2008;18:289–291.
66. Picelli A, Varalta V, Melotti C, Zatezalo V, Fonte C, Amato S, 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;31:25–31.
67. Ni M, Hazzard JB, Signorile JF, Luca C. Exercise guidelines for gait function in Parkinson's disease: a systematic review and meta-analysis. *Neurorehabil Neural Repair*. 2018;32:872–886.
68. Morris ME, Iansek R, Matyas TA, Summers JJ. The pathogenesis of gait hypokinesia in Parkinson's disease. *Brain*. 1994;117:1169–1181.
69. Muñoz-Hellín E, Cano-de-la-Cuerda R, Miangolarra-Page JC. Guías visuales como herramienta terapéutica en la enfermedad de Parkinson. Una revisión sistemática [Visual cues as a therapeutic tool in Parkinson's disease. A systematic review]. *Rev Esp Geriatr Gerontol*. 2013;48:190–197.
70. Gómez-González J, Martín-Casas P, Cano-de-la-Cuerda R. Effects of auditory cues on gait initiation and turning in patients with Parkinson's disease. *Neurologia*. 2019;34:396–407.
71. Rocha PA, Porfirio GM, Ferraz HB, Trevisani VF. Effects of external cues on gait parameters of Parkinson's disease patients: a systematic review. *Clin Neurol Neurosurg*. 2014;124:127–134.
72. Spaulding SJ, Barber B, Colby M, Cormack B, Mick T, Jenkins ME. Cueing and gait improvement among people with Parkinson's disease: a meta-analysis. *Arch Phys Med Rehabil*. 2013;94:562–570.
73. Radder DLM, Lígia Silva de Lima A, Domingos J, Keus SHJ, van Nimwegen M, Bloem BR, et al. Physiotherapy in Parkinson's disease: a meta-analysis of present treatment modalities. *Neurorehabil Neural Repair*. 2020;34:871–880.
74. Morris ME, Iansek R, Matyas TA, Summers JJ. Stride length regulation in Parkinson's disease. Normalization strategies and underlying mechanisms. *Brain*. 1996;119:551–568.
75. Morris ME, Iansek R, Kirkwood B. A randomized controlled trial of movement strategies compared with exercise for people with Parkinson's disease. *Mov Disord*. 2009;24:64–71.
76. Martin T, Weatherall M, Anderson TJ, MacAskill MR. A randomized controlled feasibility trial of a specific cueing program for falls management in persons with Parkinson disease and freezing of gait. *J Neurol Phys Ther*. 2015;39:179–184.
77. Thaut MH, Rice RR, Braun Janzen T, Hurt-Thaut CP, McIntosh GC. Rhythmic auditory stimulation for reduction of falls in Parkinson's disease: a randomized controlled study. *Clin Rehabil*. 2019;33:34–43.
78. Carpinella I, Cattaneo D, Bonora G, Bowman T, Martina L, Montesano A, et al. Wearable sensor-based biofeedback training for balance and gait in Parkinson disease: a pilot randomized controlled trial. *Arch Phys Med Rehabil*. 2017;98:622–630.
79. 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;61:407–413.
80. van Eijkeren FJ, Reijmers RS, Kleinveld MJ, Minten A, Bruggen JP, Bloem BR. Nordic walking improves mobility in Parkinson's disease. *Mov Disord*. 2008;23:2239–2243.
81. 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.
82. Ebersbach G, Ebersbach A, Gandor F, Wegner B, Wissel J, Kupsch A. Impact of physical exercise on reaction time in patients with Parkinson's disease-data from the Berlin BIG Study. *Arch Phys Med Rehabil*. 2014;95:996–999.
83. Alwardat M, Etoom M, Al Dajah S, Schirinzi T, Di Lazzaro G, et al. Effectiveness of robot-assisted gait training on motor impairments in people with Parkinson's disease: a systematic review and meta-analysis. *Int J Rehabil Res*. 2018;41:287–296.
84. Alwardat M, Etoom M. Effectiveness of robot-assisted gait training on freezing of gait in people with Parkinson disease: evidence from a literature review. *J Exerc Rehabil*. 2019;15:187–192.
85. Cosentino C, Baccini M, Putzolu M, Ristori D, Avanzino L, Pelosin E. Effectiveness of physiotherapy on freezing of gait in Parkinson's disease: a systematic review and meta-analyses. *Mov Disord*. 2020;35:523–536.
86. Pelosin E, Barella R, Bet C, Magioncalda E, Putzolu M, Di Biasio F, et al. Effect of group-based rehabilitation combining action observation with physiotherapy on freezing of gait in Parkinson's disease. *Neural Plast*. 2018;2018:4897276.
87. Di Iorio W, Ciarrimboli A, Ferriero G, Feleppa M, Baratto L, Matarazzo G, et al. Action observation in people with Parkinson's disease. A motor-cognitive combined approach for motor rehabilitation. A preliminary report. *Diseases*. 2018;6:58.
88. Delgado-Alvarado M, Marano M, Santurtún A, Urriaga-Gallano A, Tordesillas-Gutierrez D, Infante J. Nonpharmacological, nonsurgical treatments for freezing of gait in Parkinson's disease: a systematic review. *Mov Disord*. 2020;35:204–214.
89. Morris R, Smulders K, Peterson DS, Mancini M, Carlson-Kuhta P, Nutt JG, et al. Cognitive function in people with and without freezing of gait in Parkinson's disease. *NPJ Parkinsons Dis*. 2020;6:9.
90. Wild LB, de Lima DB, Balardin JB, Rizzi L, Giacobbo BL, Oliveira HB, et al. Characterization of cognitive and motor performance during dual-tasking in healthy older adults and patients with Parkinson's disease. *J Neurol*. 2013;260:580–589.
91. Kleiner AFR, Pagnussat AS, Prisco GD, Vagnini A, Stocchi F, De Pandis MF, et al. Analyzing gait variability and dual task interference in patients with Parkinson's disease and freezing by means of the wordcolor Stroop test. *Aging Clin Exp Res*. 2018;30:1137–1142.
92. Li Z, Wang T, Liu H, Jiang Y, Wang Z, Zhuang J. Dual-task training on gait, motor symptoms, and balance in patients with Parkinson's disease: a systematic review and meta-analysis. *Clin Rehabil*. 2020;34:1355–1367.
93. Strouwen C, Molenaar EALM, Munks L, Keus SHJ, Zijlmans JCM, Vandenberghe W, et al. Training dual tasks together or apart in Parkinson's disease: results from the DUALITY trial. *Mov Disord*. 2017;32:1201–1210.
94. Horak FB, Wrisley DM, Frank J. The Balance Evaluation Systems Test (BESTest) to differentiate balance deficits. *Phys Ther*. 2009;89:484–498.
95. Allen NE, Schwarzel AK, Canning CG. Recurrent falls in Parkinson's disease: a systematic review. *Parkinsons Dis*. 2013;2013:906274.
96. Wong-Yu IS, Mak MK. Multi-dimensional balance training programme improves balance and gait performance in people with Parkinson's disease: a pragmatic randomized controlled trial with 12-month follow-up. *Parkinsonism Relat Disord*. 2015;21:615–621.
97. Capato TTC, de Vries NM, Int'Hout J, Ramjith J, Barbosa ER, Nonnekes J, et al. Multimodal balance training supported by rhythmic auditory stimuli in Parkinson disease: effects in freezers and nonfreezers. *Phys Ther*. 2020;100:2023–2034.
98. Capato TTC, de Vries NM, Int'Hout J, Barbosa ER, Nonnekes J, Bloem BR. Multimodal balance training supported by rhythmical auditory stimuli in Parkinson's disease: a randomized clinical trial. *J Parkinsons Dis*. 2020;10:333–346.
99. Capato TTC, Nonnekes J, de Vries NM, Int'Hout J, Barbosa ER, Bloem BR. Effects of multimodal balance training supported by rhythmical auditory stimuli in people with advanced stages of Parkinson's disease: a pilot randomized clinical trial. *J Neurol Sci*. 2020;418:117086.
100. Allen NE, Sherrington C, Paul SS, Canning CG. Balance and falls in Parkinson's disease: a meta-analysis of the effect of exercise and motor training. *Mov Disord*. 2011;26:1605–1615.
101. Shen X, Wong-Yu IS, Mak MK. Effects of exercise on falls, balance, and gait ability in Parkinson's disease: a meta-analysis. *Neurorehabil Neural Repair*. 2016;30:512–527.
102. Flynn A, Allen NE, Dennis S, Canning CG, Preston E. Home-based prescribed exercise improves balance-related activities in people with Parkinson's disease and has benefits similar to centre-based exercise: a systematic review. *J Physiother*. 2019;65:189–199.

103. Barnish MS, Barran SM. A systematic review of active group-based dance, singing, music therapy and theatrical interventions for quality of life, functional communication, speech, motor function and cognitive status in people with Parkinson's disease. *BMC Neurol.* 2020;20:371.
104. Carapellotti AM, Stevenson R, Doumas M. The efficacy of dance for improving motor impairments, non-motor symptoms, and quality of life in Parkinson's disease: a systematic review and meta-analysis. *PLoS One.* 2020;15:e0236820.
105. de Almeida HS, Porto F, Porretti M, Lopes G, Fiorot D, Bunn PDS, et al. Effect of dance on postural control in people with Parkinson's disease: a meta-analysis review. *J Aging Phys Act.* 2020;31:1–11.
106. Hackney ME, Earhart GM. Effects of dance on movement control in Parkinson's disease: a comparison of Argentine tango and American ballroom. *J Rehabil Med.* 2009;41:475–481.
107. Hackney ME, Earhart GM. Health-related quality of life and alternative forms of exercise in Parkinson disease. *Parkinsonism Relat Disord.* 2009;15:644–648.
108. McGill A, Houston S, Lee RY. Dance for Parkinson's: a new framework for research on its physical, mental, emotional, and social benefits. *Complement Ther Med.* 2014;22:426–432.
109. Rocha PA, Slade SC, McClelland J, Morris ME. Dance is more than therapy: qualitative analysis on therapeutic dancing classes for Parkinson's. *Complement Ther Med.* 2017;34:1–9.
110. Tsang HW, Cheung L, Lak DC. Qigong as a psychosocial intervention for depressed elderly with chronic physical illnesses. *Int J Geriatr Psychiatry.* 2002;17:1146–1154.
111. Kemp CA. Qigong as a therapeutic intervention with older adults. *J Holist Nurs.* 2004;22:351–373.
112. Seki K, Chisaka M, Eriguchi M, Yanagie H, Hisa T, Osada I, et al. An attempt to integrate Western and Chinese medicine: rationale for applying Chinese medicine as chronotherapy against cancer. *Biomed Pharmacother.* 2005;59(S1):S132–S140.
113. Ni X, Liu S, Lu F, Shi X, Guo X. Efficacy and safety of Tai Chi for Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials. *PLoS One.* 2014;9:e99377.
114. Yang Y, Li XY, Gong L, Zhu YL, Hao YL. Tai Chi for improvement of motor function, balance and gait in Parkinson's disease: a systematic review and meta-analysis. *PLoS One.* 2014;9:e102942.
115. Zhou J, Yin T, Gao Q, Yang XC. A meta-analysis on the efficacy of tai chi in patients with Parkinson's disease between 2008 and 2014. *Evid Based Complement Alternat Med.* 2015;2015:593263.
116. Choi HJ. Effects of therapeutic Tai chi on functional fitness and activities of daily living in patients with Parkinson disease. *J Exerc Rehabil.* 2016;12:499–503.
117. Gao Q, Leung A, Yang Y, Wei Q, Guan M, Jia C, et al. Effects of Tai Chi on balance and fall prevention in Parkinson's disease: a randomized controlled trial. *Clin Rehabil.* 2014;28:748–753.
118. Amano S, Nocera JR, Vallabhajosula S, Juncos JL, Gregor RJ, Waddell DE, et al. The effect of Tai Chi exercise on gait initiation and gait performance in persons with Parkinson's disease. *Parkinsonism Relat Disord.* 2013;19:955–960.
119. Choi HJ, Garber CE, Jun TW, Jin YS, Chung SJ, Kang HJ. Therapeutic effects of tai chi in patients with Parkinson's disease. *ISRN Neuro.* 2013;2013:548240.
120. Vergara-Diaz C, Osypiuk K, Hausdorff JM, Bonato P, Gow BJ, Miranda JG, et al. Tai Chi for reducing dual-task gait variability, a potential mediator of fall risk in Parkinson's disease: a pilot randomized controlled trial. *Glob Adv Health Med.* 2018;7:216495611875385.
121. Li F, Harmer P. Economic Evaluation of a Tai Ji Quan intervention to reduce falls in people with Parkinson disease, Oregon, 2008–2011. *Prev Chronic Dis.* 2015;12:E120.
122. Xiao CM, Zhuang YC. Effect of health Baduanjin Qigong for mild to moderate Parkinson's disease. *Geriatr Gerontol Int.* 2016;16:911–919.
123. Liu XL, Chen S, Wang Y. Effects of health qigong exercises on relieving symptoms of Parkinson's disease. *Evid Based Complement Alternat Med.* 2016;2016:5935782.
124. Lee HJ, Kim SY, Chae Y, Kim MY, Yin C, Jung WS, et al. Turo (Qi Dance) program for Parkinson's disease patients: randomized, assessor blind, waiting-list control, partial crossover study. *Explore.* 2018;14:216–223.
125. Pérez-de la Cruz S. A bicentric controlled study on the effects of aquatic Ai Chi in Parkinson disease. *Complement Ther Med.* 2018;36:147–153.
126. Nocera JR, Amano S, Vallabhajosula S, Hass CJ. Tai Chi exercise to improve non-motor symptoms of Parkinson's disease. *J Yoga Phys Ther.* 2013;3:10.
127. Zhu M, Zhang Y, Pan J, Fu C, Wang Y. Effect of simplified Tai Chi exercise on relieving symptoms of patients with mild to moderate Parkinson's disease. *J Sports Med Phys Fitness.* 2020;60:282–288.
128. Moon S, Schmidt M, Smirnova IV, Colgrove Y, Liu W. Qigong exercise may reduce serum TNF- α levels and improve sleep in people with Parkinson's disease: a pilot study. *Medicine.* 2017;4:23.
129. Van Puymbroeck M, Walter AA, Hawkins BL, Sharp JL, Woschkolup K, Urrea-Mendoza E, et al. Functional improvements in Parkinson's disease following a randomized trial of yoga. *Evid Based Complement Alternat Med.* 2018;2018:8516351.
130. Jin X, Wang L, Liu S, Zhu L, Loprinzi PD, Fan X. The impact of mind-body exercises on motor function, depressive symptoms, and quality of life in Parkinson's disease: a systematic review and meta-analysis. *Int J Environ Res Public Health.* 2019;17:31.
131. Cugusi L, Manca A, Bergamin M, Di Blasio A, Monticone M, Deriu F, et al. Aquatic exercise improves motor impairments in people with Parkinson's disease, with similar or greater benefits than land-based exercise: a systematic review. *J Physiother.* 2019;65:65–74.
132. 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;53:825–832.
133. Kurt EE, Büyükturan B, Büyükturan Ö, Erdem HR, Tuncay F. Effects of Ai Chi on balance, quality of life, functional mobility, and motor impairment in patients with Parkinson's disease. *Disabil Rehabil.* 2018;40:791–797.
134. Amara AW, Wood KH, Joop A, Memon RA, Pilkington J, Tuggle SC, et al. Randomized, controlled trial of exercise on objective and subjective sleep in Parkinson's disease. *Mov Disord.* 2020;35:947–958.
135. Serrao M, Pierelli F, Sinibaldi E, Chini G, Castiglia SF, Priori M, et al. Progressive modular rebalancing system and visual cueing for gait rehabilitation in Parkinson's disease: a pilot, randomized, controlled trial with crossover. *Front Neurol.* 2019;10:902.
136. Landers MR, Navalta JW, Murtishaw AS, Kinney JW, Pirio Richardson S. A high-intensity exercise boot camp for persons with Parkinson disease: a phase II, pragmatic, randomized clinical trial of feasibility, safety, signal of efficacy, and disease mechanisms. *J Neurol Phys Ther.* 2019;43:12–25.
137. Chivers Seymour K, Pickering R, Rochester L, Roberts HC, Ballinger C, Hulbert S, et al. Multicentre, randomised controlled trial of PDSAFE, a physiotherapist-delivered fall prevention programme for people with Parkinson's. *J Neurol Neurosurg Psychiatry.* 2019;90:774–782.
138. Coe S, Franssen M, Collett J, Boyle D, Meaney A, Chantry R, et al. Physical activity, fatigue, and sleep in people with Parkinson's disease: a secondary per protocol analysis from an intervention trial. *Parkinsons Dis.* 2018;2018:1517807.
139. Rafferty MR, Prodoehl J, Robichaud JA, David FJ, Poon C, Goelz LC, 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;41:21–30.
140. Winward C, Sackley C, Meek C, Izadi H, Barker K, Wade D, et al. Weekly exercise does not improve fatigue levels in Parkinson's disease. *Mov Disord.* 2012;27:143–146.
141. DiFrancisco-Donoghue J, Lamberg EM, Rabin E, Elokda A, Fazzini E, Werner WG. Effects of exercise and B vitamins on homocysteine and glutathione in Parkinson's disease: a randomized trial. *Neurodegener Dis.* 2012;10:127–134.
142. Ashburn A, Fazakarley L, Ballinger C, Pickering R, McLellan LD, Fitton C. A randomised controlled trial of a home based exercise programme to reduce the risk of falling among people with Parkinson's disease. *J Neurol Neurosurg Psychiatry.* 2007;78:678–684.
143. Kalilani L, Asgharnejad M, Palokangas T, Durgin T. Comparing the incidence of falls/fractures in Parkinson's disease patients in the US population. *PLoS One.* 2016;11:e0161689.
144. 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;82:1232–1238.
145. Wong-Yu ISK, Mak MKY. Multisystem balance training reduces injurious fall risk in Parkinson disease: a randomized trial. *Am J Phys Med Rehabil.* 2019;98:239–244.
146. Canning CG, Sherrington C, Lord SR, Close JC, Heritier S, Heller GZ, et al. Exercise for falls prevention in Parkinson disease: a randomized controlled trial. *Neurology.* 2015;84:304–312.
147. Smania N, Corato E, Tinazzi M, Stanzani C, Fiaschi A, Girardi P, et al. Effect of balance training on postural instability in patients with idiopathic Parkinson's disease. *Neurorehabil Neural Repair.* 2010;24:826–834.
148. Ashburn A, Pickering R, McIntosh E, Hulbert S, Rochester L, Roberts HC, et al. Exercise- and strategy-based physiotherapy-delivered intervention for preventing repeat falls in people with Parkinson's: the PDSAFE RCT. *Health Technol Assess.* 2019;23:1–150.
149. Morris ME, Menz HB, McGinley JL, Watts JJ, Huxham FE, Murphy AT, et al. A randomized controlled trial to reduce falls in people with Parkinson's disease. *Neurorehabil Neural Repair.* 2015;29:777–785.
150. Nieuwboer A, Kwakkel G, Rochester L, Jones D, van Wegen E, Willems AM, et al. Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. *J Neurol Neurosurg Psychiatry.* 2007;78:134–140.
151. Li F, Harmer P, Fitzgerald K, Eckstrom E, Stock R, Galver J, et al. Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med.* 2012;366:511–519.
152. Cusso ME, Donald KJ, Khoo TK. The impact of physical activity on non-motor symptoms in Parkinson's disease: a systematic review. *Front Med.* 2016;3:35.
153. da Silva FC, Iop RDR, de Oliveira LC, Boll AM, de Alvarenga JGS, Gutierrez Filho PJB, et al. 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.* 2018;13:e0193113.
154. Law CK, Lam FM, Chung RC, Pang MY. Physical exercise attenuates cognitive decline and reduces behavioural problems in people with mild cognitive impairment and dementia: a systematic review. *J Physiother.* 2020;66:9–18.
155. Rothwell J. Transcranial brain stimulation: past and future. *Brain Neurosci Adv.* 2018;2:2398212818818070.
156. Maeda F, Keenan JP, Tormos JM, Topka H, Pascual-Leone A. Modulation of corticospinal excitability by repetitive transcranial magnetic stimulation. *Clin Neurophysiol.* 2000;111:800–805.
157. Peinemann A, Reimer B, Löer C, Quartarone A, Münchau A, Conrad B, et al. Long-lasting increase in corticospinal excitability after 1800 pulses of subthreshold 5 Hz repetitive TMS to the primary motor cortex. *Clin Neurophysiol.* 2004;115:1519–1526.
158. Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of the human motor cortex. *Neuron.* 2005;45:201–206.
159. González-García N, Armony JL, Soto J, Trejo D, Alegría MA, Drucker-Colín R. Effects of rTMS on Parkinson's disease: a longitudinal fMRI study. *J Neurol.* 2011;258:1268–1280.
160. Strafella AP, Paus T, Barrett J, Dagher A. Repetitive transcranial magnetic stimulation of the human prefrontal cortex induces dopamine release in the caudate nucleus. *J Neurosci.* 2001;21:RC157.
161. Yang C, Guo Z, Peng H, Xing G, Chen H, McClure MA, et al. Repetitive transcranial magnetic stimulation therapy for motor recovery in Parkinson's disease: a meta-analysis. *Brain Behav.* 2018;8:e01132.

162. Chung CL, Mak MK. Effect of repetitive transcranial magnetic stimulation on physical function and motor signs in Parkinson's disease: a systematic review and meta-analysis. *Brain Stimul.* 2016;9:475–487.
163. Xie YJ, Gao Q, He CQ, Bian R. Effect of repetitive transcranial magnetic stimulation on gait and freezing of gait in Parkinson disease: a systematic review and meta-analysis. *Arch Phys Med Rehabil.* 2020;101:130–140.
164. Goodwill AM, Lum JAG, Hendy AM, Muthalib M, Johnson L, Albein-Urios N, et al. Using non-invasive transcranial stimulation to improve motor and cognitive function in Parkinson's disease: a systematic review and meta-analysis. *Sci Rep.* 2017;7:14840.
165. Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol.* 2000;527:633–639.
166. Bolzoni F, Pettersson LG, Jankowska E. Evidence for long-lasting subcortical facilitation by transcranial direct current stimulation in the cat. *J Physiol.* 2013;591:3381–3399.
167. Tanaka T, Takano Y, Tanaka S, Hironaka N, Kobayashi K, Hanakawa T, et al. Transcranial direct-current stimulation increases extracellular dopamine levels in the rat striatum. *Front Syst Neurosci.* 2013;7:6.
168. Stagg CJ, O'Shea J, Kincses ZT, Woolrich M, Matthews PM, Johansen-Berg H. Modulation of movement-associated cortical activation by transcranial direct current stimulation. *Eur J Neurosci.* 2009;30:1412–1423.
169. Filmer HL, Dux PE, Mattingley JB. Applications of transcranial direct current stimulation for understanding brain function. *Trends Neurosci.* 2014;37:742–753.
170. Broeder S, Nackaerts E, Heremans E, Vervoort G, Meesen R, Verheyden G, et al. Transcranial direct current stimulation in Parkinson's disease: neurophysiological mechanisms and behavioral effects. *Neurosci Biobehav Rev.* 2015;57:105–117.
171. Pereira JB, Junqué C, Bartrés-Faz D, Martí MJ, Sala-Llonch R, Compta Y, et al. Modulation of verbal fluency networks by transcranial direct current stimulation (tDCS) in Parkinson's disease. *Brain Stimul.* 2013;6:16–24.
172. Boggio PS, Ferrucci R, Rigonatti SP, Covre P, Nitsche M, Pascual-Leone A, et al. Effects of transcranial direct current stimulation on working memory in patients with Parkinson's disease. *J Neurol Sci.* 2006;249:313–318.
173. Doruk D, Gray Z, Bravo GL, Pascual-Leone A, Fregni F. Effects of tDCS on executive function in Parkinson's disease. *Neurosci Lett.* 2014;582:27–31.
174. Ferrucci R, Cortese F, Bianchi M, Pittera D, Turrone R, Bocci T, et al. Cerebellar and motor cortical transcranial stimulation decrease levodopa-induced dyskinesias in Parkinson's disease. *Cerebellum.* 2016;15:43–47.
175. Beretta VS, Conceição NR, Nóbrega-Sousa P, Orcioli-Silva D, Dantas LKBF, Gobbi LTB, et al. Transcranial direct current stimulation combined with physical or cognitive training in people with Parkinson's disease: a systematic review. *J Neuroeng Rehabil.* 2020;17:74.
176. Samii A, Ryan-Dykes P, Tsukuda RA, Zink C, Franks R, Nichol WP. Telemedicine for delivery of health care in Parkinson's disease. *J Telemed Telecare.* 2006;12:16–18.
177. Chen YY, Guan BS, Li ZK, Yang QH, Xu TJ, Li HB, et al. Application of telehealth intervention in Parkinson's disease: a systematic review and meta-analysis. *J Telemed Telecare.* 2020;26:3–13.
178. Ginis P, Nieuwboer A, Dorfman M, Ferrari A, Gazit E, Canning CG, 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.
179. Khalil H, Busse M, Quinn L, Nazzal M, Batyha W, Alkhazaleh S, et al. A pilot study of a minimally supervised home exercise and walking program for people with Parkinson's disease in Jordan. *Neurodegener Dis Manag.* 2017;7:73–84.
180. Gandolfi M, Geroïn C, Dimitrova E, Boldrini P, Waldner A, Bonadiman S, et al. Virtual reality telerehabilitation for postural instability in Parkinson's disease: a multicenter, single-blind, randomized, controlled trial. *Biomed Res Int.* 2017;2017:7962826.