Movement Disorders
CLINICAL PRACTICE

REVIEW

Prevention of Falls in Parkinson's Disease: Guidelines and Gaps

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ABSTRACT: Background: People living with Parkinson's disease (PD) have a high risk for falls.
Objective: To examine gaps in falls prevention targeting people with PD as part of the Task Force on Global Guidelines for Falls in Older Adults.
Methods: A Delphi consensus process was used to identify specific recommendations for falls in PD. The current narrative review was conducted as educational background with a view to identifying gaps in fall prevention.
Results: A recent Cochrane review recommended exercises and structured physical activities for PD; however, the types of exercises and activities to recommend and PD subgroups likely to benefit require further consideration. Freezing of gait, reduced gait speed, and a prior history of falls are risk factors for falls in PD and should be incorporated in assessments to identify fall risk and target interventions. Multimodal and multi-domain fall prevention interventions may be beneficial. With advanced or complex PD, balance and strength training should be administered under supervision. Medications, particularly cholinesterase inhibitors, show promise for falls prevention. Identifying how to engage people with PD, their families, and health professionals in falls education and implementation remains a challenge. Barriers to the prevention of falls occur at individual, environmental, policy, and health system levels.
Conclusion: Effective mitigation of fall risk requires specific targeting and strategies to reduce this debilitating and common problem in PD. While exercise is recommended, the types and modalities of exercise and how to combine them as interventions for different PD subgroups (cognitive impairment, freezing, advanced disease) need further study.

Most people living with idiopathic Parkinson's disease (PD) experience falls in the course of disease progression. Falls can adversely affect health and wellbeing,[1] and predispose to injuries and hospitalization.[2,3] A recent investigation on falls in people living with Parkinson's showed fall frequency to be double that of age-matched older people.[4] Using a digital device combined with telephone monitoring, Silva de Lima et al[4] showed that many falls in people with PD occur during spontaneous mobility tasks in the home and community and over half of people with PD are repeat fallers. There is a higher rate of injurious falls in people living with parkinsonism, compared to age-matched controls.[5] Recurrent falls are common in people with PD.[6,7] In addition fear of falling is common and debilitating.[6,7] Fear of falling can lead some people to restrict their

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physical activities which can in turn reduce their strength, balance and participation in social roles.

Frequent falls in people with PD are associated with the loss of motor automaticity that accompanies this chronic and progressive condition.[8] The basal ganglia and motor control mechanisms that regulate locomotion, balance and movement are disrupted, and this is associated with movement disorders such as freezing of gait (FOG), slowness, difficulties in turning when walking, and postural instability.[2,9] There are wide individual differences in the rate of disease progression and the combination of movement disorders and non-motor symptoms over time, adding complexity to the design of programs to prevent falls and associated injuries in people with PD.[9] In some individuals, there can be attentional deficits, sensory dysfunction or behavioral changes which interact with the motor decline.[10–13] Disease progression can also be accompanied by cognitive impairment, weakness, and fluctuations in relation to PD medications, complicating strategies to manage falls and other symptoms.[14] The extent of pathology and the neural reserve available to compensate for basal ganglia dysfunction also need to be taken into account when implementing fall prevention programs.[2,15]

Pharmacological therapies are a cornerstone of PD management and falls prevention strategies need to consider the locus of the medication cycle in relation to the performance of motor activities. Axial problems are partially responsive to dopaminergic treatment whereas posture and gait respond more variably.[16,17] As for FOG, dopaminergic medications can ameliorate the frequency and duration of episodes, yet FOG usually does not completely resolve.[18,19] Cholinesterase inhibitors are under investigation as a possible novel avenue for improving gait and balance, despite having comparatively low prescription rates to date.[20]

METHODS

Authors from across the globe were assembled with research and clinical expertise in both Parkinson's disease and falls prevention. They reviewed and critically analyzed key documents, including the world guidelines for falls prevention and management for older adults,[2] Cochrane reviews on exercise for Parkinson's disease[21] and falls prevention[22] and a recent meta-analysis on falls prevention in hospitals.[23] The authors also reviewed the findings from a prior Delphi process (see Montero-Odasso 2022[24]) and updated the literature review on evidence-based falls prevention for people living with Parkinson's disease. The new literature review had a particular focus on including new information on Parkinson's subgroups such as freezing of gait, young onset Parkinson's, and complex Parkinson's disease. Uni-modal, multimodal and multifactorial interventions for falls prevention in Parkinson's disease were also identified and new topics were included such as pharmacological interventions and barriers to falls prevention in people with movement disorders. After synthesizing the findings from these converging lines of evidence, recommendations were made for the prevention of falls in people at different stages of disease progression in Parkinson's disease.

RESULTS

Risk Factors for Falls in PD

Some of the factors that increase falls rates in people living with PD are the same as for community dwelling older people, such as advanced age, a prior history of falls, poly-pharmacy and multi-morbidity.[1,20] The motor and non-motor disorders specific to PD further increase the risk. In relation to non-motor symptoms, three factors are of particular importance in PD[2]: (1) orthostatic hypotension,[25] (2) fear of falling,[6,26] and (3) cognitive impairment.[27] Dementia, delirium, and impairments of executive function are closely associated with higher falls risk,[21,28–30] possibly related to defective movement automaticity.[15] In line with this suggestion, poor dual-tasking has been reported to increase falls risk in some people with PD.[31] In relation to motor symptoms, postural instability and lower limb muscle weakness increase falls risk, as they do in very old people.[32] Fall prevention strategies designed for community dwelling elderly people,[33,34] such as falls education, safe footwear, exercise, assistive devices, diet, medication review, management of cognitive impairment and environmental modifications[22] can be expected to reduce fall risk in PD as well. However, the unique and multi-faceted disease profile for each person with PD as well as their comorbidities, social circumstances, and caregiver support call for an individualized approach to fall prevention management in PD.[35] In this paper we focus on specific factors and modalities to mitigate falls in PD.

Guidelines proposed by the Task Force on Global Guidelines for Falls in Older Adults[2] were recently released. The guidelines incorporated a review of the literature on idiopathic PD and related disorders, and a Delphi consensus process on contemporary best practice. Here, the findings are expanded upon, and gaps in the assessment and prevention of falls in PD and related disorders are highlighted.[2] This builds on a Cochrane Collaborative review by Allen et al (2022)[21] that mostly focused on exercise. Therapeutic exercises incorporating uni-modal, multi-domain, or multi-modal interventions were considered. Randomized controlled clinical trials (RCT) that reported falls were also reviewed (refer to Table S1). *Uni-modal* interventions are single modalities such as treadmill training alone or leg power training exercises. *Multi-domain* interventions such as patient education, home hazard modification, exercises, and medication review are prescribed for each individual, matched to their falls risk profile.[2] As they are tailored, individuals are likely to receive different combinations of interventions. For *multi-modal* interventions, individuals receive a fixed combination of two or more therapies, such as exercise and education, balance training plus home safety, or exercise and psychological interventions. All individuals receive the same combination and dosage of therapies.

Freezing of Gait

A critical risk factor for falls in PD is freezing. Freezing of gait can be defined as a brief episodic absence or marked reduction of forward progression of the feet despite the intention to walk.[2,36] Recently, Pelicioni and colleagues[25] showed that 61% of falls in people with PD were freezing-related, when 2043 falls were analyzed prospectively by telephone interview. The sudden onset of a FOG-episode combined with the difficulties that people with FOG (freezers) experience with controlling their center of mass[37,38] may partly explain the strong association with falling. Several other studies have reported FOG to independently predict falls in PD, but the size of the impact of FOG on falls has only recently been fully uncovered.[18,32,39] Notably, freezing is one of the three criteria in a Parkinson's clinical tool used to predict falls.[2,40] The other criteria entail: (1) having a fall in the previous 12 months and (2) slowness of walking. Even after verification in a different cohort, this tool was shown to have excellent reliability and acceptable accuracy.[41] Such results highlight that FOG is an important predictor of falls and deserves to be at the forefront of clinical decision making to reduce risk.

A recent study showed the first occurrence of FOG to be a milestone in the evolution of PD, and this was related to several motor and non-motor determinants of falling.[42] As discussed in the world falls guidelines,[2] these factors included lower limb symptoms,[43] more severe axial symptoms,[43] a higher daily dose of levodopa,[44] poor balance,[41,45] and cognitive disturbance.[46] Specific FOG-related predictors were also found, such as gait festination,[47] hallucinations,[44] depression,[45] anxiety,[46] and motor breakdown of repetitive limb motion.[2,43,47] Classifying PD-fallers into freezers or non-freezers could potentially help to identify optimal strategies to prevent falls that take into account effective management of FOG.[21] The assessment of FOG can also benefit from specialized clinical testing supported by expert video ratings, given that recollection of freezing by patients may not always be accurate.[48] Future methods based on wearables could also improve detection.[49]

Bradykinesia, Weakness, Cognitive Impairment

Freezing of gait is not the only risk factor for falls in PD and related disorders.[50–52] Especially when very old or with multimorbidity, people with PD can experience bradykinesia as well as weakness secondary to reduced activity levels.[51] Weakness and marked slowness of gait, are closely related to the rate of falls and associated injuries, particularly when people are hospitalized or living in aged care.[22,23] Cognitive impairment increases falls and injuries even further because it restricts opportunities for patient education, which is shown to be a powerful determinant of falls mitigation in care settings.[53–56] For those with cognitive impairment, dementia, or delirium; environmental modifications, regular toileting, vitamin D, and medication optimization are some of the options to reduce risk.[22]

Exercise and Medication Interventions for Falls in PD

The recent Cochrane review by Allen et al (2022)[21] evaluated the effectiveness of a range of non-pharmacological interventions, mainly exercises, to reduce falls in PD. Thirteen trials (1652 participants) were included when fall prevention was compared with control treatments. The results revealed consistently that exercise reduced falls rates by around 35% (Rate Ratio = 0.65 [0.53–0.80]). This was provided that people were in the early to mid-stages of disease progression, when most of the trials were conducted. Exercise reduced the proportion of people with one or more falls by around 10% (Risk Ratio = 0.90 [0.82–1.00]). No evidence was found to support a specific mode of exercise above others, such as balance, functional mobility, strength, or Tai Chi training. Fully supervised exercises were more effective in ameliorating falls (Rate Ratio = 0.56 [0.41–0.77]) compared to partially supervised interventions or independent exercise (Rate Ratio = 0.85 [0.75–0.97]). Data from two studies included subgroup analyses by disease severity and showed differential effects of exercise. Falls were less for those with lower disease severity, in contrast to people with more severe disease (Rate Ratio = 1.19 [1.00–1.41]). Adverse events reported in four studies included non-injurious falls and reduced physical activity.

Although fall prevention education may reduce fear of falling, it can sometimes inadvertently lead some patients to over-compensate by restricting their activities.[57] Likewise, when activity levels increase, falls increase because people often take more risks when they engage in more physical activities. Noting the trade-off between physical activity levels and falls rates, we still recommend exercise as an important fall prevention strategy in mild to moderately affected people with PD. Assistive devices such as wheeled walking frames can add stability, and cueing can further facilitate safe movement.[51] For people with late-stage PD, the focus is typically on preserving quality of life, comfort, and wellbeing.[58]

The review by Allen (2022)[21] included exercise trials on falls and mostly focused on balance training, walking, and various physical activity and exercise therapy programs. Next, two specific training categories, targeting freezing of gait and motor-cognitive interplay, will be discussed.

Exercise for Freezing of Gait

A recent PD meta-analysis pooled 41 exercise studies (1838 participants), showing positive effects for various exercise training modes on FOG, albeit of a moderate size (ES = −0.37).[59] This review included a wide variety of training interventions which were designed to reduced FOG-severity. Sub-analysis showed that general exercise for fitness and health did not impact FOG. In contrast, specific FOG-prevention interventions reduced FOG-severity (ES = −0.35 [−0.56 to −0.13]). The interventions incorporated cueing and teaching FOG-prevention strategies at home. The largest effect sizes (ES = −0.40 [−0.64 to −0.16]) were found for exercises targeting FOG-relevant compensatory systems. As discussed in the world falls guidelines,[2] helpful therapies included cognitive training, dual-task training, balance training, curved treadmill training, regular treadmill training with cueing, and obstacle avoidance. The review also examined 10 studies with freezers alone, thus addressing those with more advanced disease profiles. Even in this sub-group, there were beneficial effects of exercise on FOG (ES = −0.46 [−0.76 to −0.17]). Although no direct link with fall outcomes was confirmed, we do recommend adopting exercise programs for FOG as a useful strategy for falls prevention in PD.

Fall Prevention Exercises for Different PD Profiles

Prediction studies based on supervised individually-dosed exercise trials targeting risk factors for falls or fall frequency as outcomes will be considered in this section.[39,60–62] Two multivariable prediction studies showed that baseline levels of physical deconditioning targeted with the type of exercise intervention, predicted the size of training outcomes. The effects of challenging balance training were predicted by worse perceived health at baseline, the extent of cognitive impairment, and poor performance on the Timed Up & Go test.[62] In contrast, the effects of dual task training was predicted by milder disease and better cognitive capacity. The ability to compensate for loss of function appeared to be specifically relevant for the response to multi-modal rehabilitation.[63]

Three studies compared the effects of fall-related training comparing subgroups of PD. Freezers versus non-freezers were compared in the V-Time study.[60] The patients received either standard treadmill training or complex treadmill training with cognitive exercises delivered via a virtual reality screen. Both groups reduced fall rates at 6 months. This was despite the finding that baseline fall rates were higher in the people with FOG. Of note, fall frequency reduced more in the training arm with virtual reality, yet FOG did not. In a different cross-over trial that evaluated cognitive-motor circuit training (including boxing, dual task balance exercises, and obstacle negotiation) versus a control arm receiving education,[61] freezers demonstrated larger effect sizes in dual task walking than non-freezers. Lower dual task capacity at baseline in freezers appeared to afford greater changes. The same participants were also classified into subgroups according to the severity of PD and the severity of cognitive impairment. Similar to the dual task capacity results, groups with worse clinical profiles showed better balance entrainment.[61] Finally, in the PD-SAFE trial,[39] a fall prevention intervention delivered at home was compared to a usual care program combined with fall prevention education. Fall rates only improved in those with moderate disease severity, although PD-SAFE enhanced balance capacity and reduced fear of falling in the full cohort. Importantly, there was an increase in falls associated with the PD-SAFE program in the group with FOG. Thus, the heightened fall risk in freezers warrants a cautious approach to fall prevention exercise, a conclusion that was also drawn by the Cochrane review.[21]

Perturbation training, often delivered using treadmills coupled with virtual reality or split-belts, is being studied in healthy older adults,[64] and people with PD.[43] Advantages of such paradigms are that subjects wear a harness during training and the training dose can be varied according to the needs of participants. Perturbation training is thought to tackle true fall-resisting skills, which may transfer to daily life when applied with the correct dose.[64] A drawback is the availability and accessibility of the specific equipment.[65] Also, the implementation of perturbation training not only requires additional infrastructure for healthcare but also thoughtful measures to deal with the consequences of high-risk patients becoming more mobile. Regardless of the intervention, PD disease severity may influence outcomes.[66] Close supervision is needed to ensure both safety and appropriate practice dosage in patients with advanced PD.

Multi-Domain and Multi-Modal Falls Prevention Interventions for PD

Many factors contribute to fall risk in PD and multi-domain and multi-modal interventions have the potential to target more than one factor at a time. Table S1 summarizes key PD RCTs on therapeutic exercises and other interventions to reduce falls in PD. Trials included combined cognitive and motor tasks, combined methods for improving balance (eg, reaching, enhancing participant anticipatory postural adjustments, stepping), or targeted training such virtual reality training, cognitive strategies, strength training, treadmill training, therapeutic dance, environmental adaptations, and medication reviews. Some multi-domain and multi-modal studies focused on falls prevention education coupled with either cueing, strategy training, exercise programs, or progressive resistance training.[51,52,67]

Studies that incorporated dual task activities that were cognitively and physically challenging showed better results for falls, near falls, and falls risk compared to regular physiotherapy.[51,68–70] In a small RCT by Penko et al,[69] participants in a multimodal training group that received treatment three times a week for 8 weeks showed positive results for falls. The multi-modal training included a fixed set of dual task gait activities coupled with cognitive tasks directed towards executive function, attention, memory, and language tasks. The control group received unimodal therapies such as stretching or lower limb strength training and did not show comparable improvements in falling. Other multi-modal studies combined training such as anticipatory postural adjustments,[70] reaching, and rapid stepping and showed improvements in balance confidence and step length. Outdoor multi-modal training,[71] such walking on different surfaces and practicing tasks that challenged balance (ie, pulling or pushing doors, exiting or entering an escalator, fast walking) had positive effects on gait and balance.

Mirelman et al[15] and Feng et al[72] examined the outcomes of virtual reality training (VR) on balance and falls in PD. Mirelman reported that training incorporating VR reduced the number of people who reported two or more falls in 6 months. Falls rates after training were 42% lower in a group that received treadmill training plus VR, compared with a group that received treadmill training alone. Capato et al[73] investigated a multi-modal balance training program supported by rhythmical auditory stimulation yet did not measure falls. The combined intervention showed benefits for falls self-efficacy. The authors hypothesized that multi-modal balance training supported by auditory stimulation could optimize attention and task prioritization in PD. This awaits verification in controlled clinical trials.

Other interventions such as agility boot camps[74] and Tai Chi[75,76] have reported benefits for balance, falls, and gait in people with PD. Tai Chi is often viewed as a multi-domain mind–body intervention. A study by Li et al,[76] aimed to improve balance and fall rates using Tai Chi to enhance postural stability. Compared to strength training or stretching, Tai Chi was associated with fewer falls. The ABC-C trial[74] did not measure falls yet improved anticipatory postural adjustments. Dual-task cost on gait speed showed positive results. Interestingly, participants with severe cognitive or motor impairments showed greater improvements. The PD-SAFE RCT did not show improvements in falls with a fixed multi-modal intervention.[39] This was a multi-center, multi-dimensional, physiotherapist delivered, individually tailored, trial. Of note, people with moderately severe parkinsonism had reduced fall incidence and those with more severe disease had increased falls. The results raised questions about dosage necessary to reduce falls, which PD patients benefit the most, and the role of multi-morbidity.

Overall, the literature showed trends in favor of multi-modal and multi-domain interventions to reduce falls in PD. However, while balance tests reflect fall risk, they do not fully capture the risk of falls in daily life. Most published RCTs had follow-up periods of only 6 to 12 months. In the future, it will be important to evaluate the effects over longer time periods, supported by digital fall detection methods. Investigation of the determinants of falls program compliance and the PD populations who benefit the most is also warranted.

Medications for Falls Prevention in PD

Pharmacological interventions were recently addressed in a Cochrane review.[21] The effectiveness of two classes of non-dopaminergic medications were examined, as no studies existed on the effects of levodopa on falls risk.[77] Nevertheless, levodopa has been shown to ameliorate some components of gait and balance dysfunction and may mediate fall risk indirectly.[17] Direct studies of other agents on falls (including dopamine agonists, COMT-inhibitors, amantadine, rasagiline, selegiline, methylphenidate) did not yield any studies examining falls as a primary outcome. Optimizing motoric response, while minimizing adverse effects, is a fundamental tenet of management. Cholinergic dysfunction is common in people with PD and is associated with impaired cognition, leading to study of cholinesterase inhibitors for cognitive enhancement.[78] Cholinergic mechanisms have also been implicated in gait and balance impairment.[79,80] The Cochrane review[21] found anticholinesterase medication (eg, rivastigmine) versus placebo probably reduced the rate of falls by 50%, based on evidence with moderate certainty evaluated in three trials with 242 participants. No effect of anticholinesterase medication was found on the number of fallers. Also, these findings need to be balanced against the concern that anticholinesterase medication may increase (moderate certainty evidence) the rate of non-fall related adverse effects by 60%. As only one trial (225 participants) was evaluated that examined the effects of alpha- and beta-adrenergic agonists (droxidopa), which also contained a risk of industry bias, the effects on falls outcomes in people with PD and neurogenic orthostatic hypotension are currently uncertain.

The Cochrane review by Allen et al (2022)[21] was supplemented with an additional literature search on medications, which we report on in Table 1. A subsequent systematic review summarized the extant data.[81] Three studies examined the effects of cholinesterase inhibitors on falls. One showed a reduction in falls with donepezil,[82] but this relatively small study excluded participants with freezing of gait. Two investigations examined rivastigmine[83,84] and suggested a reduction in falls, noting that falls were a secondary outcome. The study by Li et al[84] examined mildly cognitively impaired participants while that of Henderson et al[83] excluded cognitively impaired participants. Although the meta-analysis showed no significant impact on falls risk, there were promising trends. A recent phase 3 clinical trial has been described that will further examine this issue.[85] One additional study examined the role of nicotinergic cholinergic enhancement using nicotine, and noted an improvement in freezing and falls.[86] Recently, additional trials have examined the impact of cholinergic medications on surrogate predictors of falls, such as gait speed or gait variability,[87] or balance[88] (Table 1). While encouraging, surrogate markers do not always translate into lower falls rates or reduced falls related injuries. Many studies of falls rely on self-report, which might underestimate falls incidence and are imprecise (Table 1). Home monitoring using body worn or other sensors are in development. Given the paucity of data in this domain, the Delphi consensus reported in the world guidelines[2] did not make specific recommendations on medications to reduce falls in PD. An adequately powered ($n = 450$) multicenter placebo controlled double blind randomized controlled trial is in progress examining the impact of cholinergic medications on falls risk.[85]

Barriers to Falls Prevention in PD

Despite potentially helpful interventions such as exercise, structured physical activities, patient education, medication modification, diet, environmental adaptions, complementary therapies such as dance, physical therapy, and occupational therapy to reduce falls[89]; barriers can preclude participation or diminish efficacy. For example, fear of falling is one risk factor for future falls that might lead to avoidance of interventions.[90] In addition to patient-centered factors, extrinsic factors such as staffing, non-evidence-based health facility policies, or failure to adequately engage consumers in therapy co-design[53,56,91] can interfere with falls prevention.[55] During the pandemic many service providers pivoted to online PD interventions aimed at improving access and safety.[92] Digital delivery of falls prevention interventions is a promising intervention for the future yet the systems supporting it are still under development. Another barrier to receiving

TABLE 1 *Clinical trials evaluating the effect of cholinesterase inhibitors or cholinergic agonists on falls in Parkinson's disease*

Author and journal	Study design	Aim	Drug class	Participant characteristics	Outcome/measures	Findings
Chung et al (2010)[82]	Randomized controlled crossover trial Intervention period for each treatment: 6 weeks Washout period: 3 weeks	Investigate whether a central cholinesterase inhibitor can reduce falling frequency in PD with advanced postural instability, compared to placebo.	Cholinesterase inhibitors (Donepezil)	N = 23 Women, n (%): 8 (35%) PD with HY stage <5, 2 or more falls per week, and normal cognition (MMSE>25), but without freezing or non-CNS contributors to falls	Primary: falls and near falls reported prospectively on daily falls recording postcards Secondary: Subject-completed global impression of improvement, the Activities of Balance Confidence Scale, balance measured the Berg Balance Scale, UPDRS, MMSE	Falling frequency was lower when taking donepezil: 0.25 falls per day on placebo versus 0.13 falls per day on treatment ($P = 0.049$). Six participants had deep brain stimulation.
Li et al (2015)[84]	Randomized controlled trial Follow-up period: 12 months	Determine the effects of cholinesterase inhibitors on cognitive function and falling in PD, compared to placebo.	Cholinesterase inhibitors (Rivastigmine)	N = 81 Women, n (%): 19 in placebo (48%) and 11 in treatment (27%) PD with cognitive impairment	MoCA, falls recorded using weekly phone calls or follow-up	Rivastigmine significantly lowered the incidence of falls: 4.26 falls per year in placebo versus 1.82 falls per year in treatment group ($P < 0.01$).
Henderson et al (2013)[83]	Randomized controlled trial Follow-up period: 32 weeks	Assess whether acetylcholinesterase inhibitor rivastigmine can improve gait variability in PD, compared to placebo.	Cholinesterase inhibitors (Rivastigmine)	N = 130 Women, n (%): 19 (29%) in placebo and 30 (46%) in treatment PD with HY stage 2–3, and the ability to walk 18 m without walking aid	Primary: gait variability Secondary: falls recorded prospectively with self-completed monthly diaries, gait speed, balance, freezing, cognition, disease severity, levodopa dose, moods, quality of life	Rivastigmine significantly reduced falls rate: 2.4 falls per month in placebo versus 1.4 in treatment group ($P < 0.002$).

(Continues)

TABLE 1 *Continued*

Author and journal	Study design	Aim	Drug class	Participant characteristics	Outcome/measures	Findings
Lieberman et al. (2019)[86]	Randomized trial Follow-up period: 10 weeks. (Study duration was 17 weeks as it included additional 3 weeks of transition period and 4 weeks of postintervention period)	Re-analyze effects of nicotine bitartrate dihydrate (NC001) on falls and freezing of gaits in PD, compared to placebo. Study was originally designed to analyze its effect on levodopa-induced dyskinesias.	Cholinergic agonist (nicotine bitartrate)	N = 65 Women, n (%): 13 (43%) in placebo and 21 (60%) in treatment PD with HY stage 2–3, moderate-to-severely disabling levodopa-induced dyskinesias, and normal cognition (MMSE > 25)	Falls measured with UPDRS Part II Question 13, freezing of gait measured with UPDRS Part II Question 14, retropulsion measured with UPDRS Part III Item 30, UPDRS Part II and III scores, and UDysRS ambulation subtest score	Significant difference between groups in proportion of patients with reduction in falls score: falls score reduced in 11% of placebo versus 47% of treatment group ($P = 0.004$).

Note: PubMed was searched using the following keywords: Parkinson's disease and falls and prevention; Parkinson's disease and falls and cholinesterase inhibitors (as well as specific medications: donepezil, rivastigmine, galantamine). Randomized controlled studies that include falls as an outcome measure were selected. Case reports were excluded. Human clinical trials or systematic reviews were identified. Parkinson's disease and falls and prevention and medication were also used as broader search terms but did not yield additional articles.
Abbreviations: HY, Hoehn and Yahr stage; MMSE, Mini-Mental state exam; MoCA, montreal cognitive assessment; UPDRS, unified Parkinson's disease rating scale.

evidence-based therapy is the parkinsonism subgroup. Little is known about how best to prevent falls in people with Progressive Supranuclear Palsy, Multiple System Atrophy, Cortico-basal degeneration, and other forms of atypical parkinsonism.[93,94] We did not specifically evaluate the impact of deep brain stimulation (DBS) on falls; however patients undergoing DBS may share risk factors for falls with PD patients under medical management, including age, axial features, and disease duration.[95] Novel targets, such as the pedunculopontine nucleus (and other areas) are being investigated as potential targets that might improve axial features and falls risk.[96]

Poor access to exercise or poor understanding of the benefits of exercise is another barrier to falls prevention in PD. In one PD survey, low expectations from exercise and lack of time were reported as barriers to exercise.[97,98] Health care professionals are arguably in a position to assist by informing patients of the benefits of exercise.[99] In a study by Afshari et al[100] participants who engaged in exercise habitually were less likely to need added motivation to exercise, and all participants with PD benefited from a training partner or trainer. Once engaged in a fall prevention activity, adherence over the long term can be a challenge. People with PD often live for many years with the condition, and it can be challenging to continually engage in exercise and physical activities over such a long period of time. Allen and colleagues examined adherence to a 6-month weight-bearing exercise intervention in medically stable people with PD with a history of one or more falls.[33] Predictors of increased adherence included shorter disease duration, less pain, and better wellbeing. Much of the variance in adherence was unexplained, highlighting the need to identify person-centered factors that can be modified to reduce the risk of falls and associated injuries.

A qualitative study by O'Brien et al (2016)[101] highlighted that non-motor factors such as apathy and fatigue can also be barriers to exercise in PD. Participant perceptions of finite energy availability was a determinant of exercise engagement. On a similar theme, a survey by Prakash et al (2021)[102] identified that low energy, physical symptoms, and anxiety regarding falls risk were barriers to participating in physical activities in people living with PD. Lower levels of exercise were also associated with concerns about the impact of exercise on physical symptoms and energy levels. Of note, when participants were referred to physiotherapy or community-based exercise programs, many continued the activity.

Cognitive impairment, including attentional problems, executive dysfunction, and dementia, are also barriers to exercise and risk factors for falls[103–105]; yet cognitive impairment is often an exclusion for PD intervention studies.[106] Cognitive impairment can affect participation due to the inability to follow instructions and to set goals. One trial showed that PD participants with mild cognitive impairment had challenges in understanding scenarios outlining goals of care.[107] Additional non-motor symptoms, especially anxiety, depression, and psychotic features may also affect participation in falls prevention. Fear of falling is a common risk factor for falls in PD.[108] Falls efficacy is associated with depression, balance impairment, and use of assistive devices.[109] The degree to which people perceive falls risk can influence participation in falls prevention activities.[110] Falls-related activity avoidance is a consequence of concern about falling that can lead to decreased overall activity and increased falls risk.[90] Strategies for the management of fear of falling and other factors that affect participation in exercise and other fall prevention activities require further study.

In PD, pain, fatigue and other neurological, musculoskeletal or cardio-pulmonary conditions can be barriers to participation. Pain is common in PD although a study by Greene et al (2007)[111] showed that older participants with PD had a similar level of pain compared to age-matched older people. Pain can be undertreated in PD[112] and occurs worldwide.[113] Pain represents a potentially treatable barrier to participation in exercise, falls prevention, and activity programs.[114]

People have individual preferences and goals regarding the type of exercise or physical activity to engage in to prevent falls. For example, a study by Terrens et al (2021)[115] reported an aquatic exercise program was acceptable to some yet not all people with PD, albeit with post-session fatigue. Extrinsic factors such as care-giver support, resource availability, access to facilities and transportation, and cost can all be barriers or facilitators to falls prevention. Such factors may vary in different geographical locations and cultures.[116] Access to informational resources may not be equally available in all languages and referral to physiotherapy and other therapists is variable.[117] Technology can sometimes facilitate improved dissemination of information and improved access to programs, although these resources currently appear to be underdeveloped.[118] Finally, during the pandemic there was a rapid pivot to online education and physical therapy programs for people living with PD.[92] Digital modes of falls prevention education and training, together with the adoption of remote monitoring and sensors hold promise for the future.

CONCLUSIONS

This review supplements the recent world guidelines[2] for the management of falls in older people. People living with PD and related disorders have disproportionally high falls rates and falls-related injuries. On average, they fall 4 to 6 times per year although some people with PD fall multiple times every day, especially if they have freezing of gait, slow walking, or a history of falling. A range of exercise, physical activity, virtual reality, and patient education methods exist to mitigate falls in PD. Environmental modifications, assistive devices, footwear, and healthcare policy setting adjustments can also be implemented as multi-modal interventions or single therapies. When prescribing multi-domain, multi-modal, or uni-modal interventions to reduce falls and injuries, individual differences in PD symptoms need to be considered, as well as variability associated with medication status and disease stage. The person living with PD is central to setting falls prevention goals, in conjunction with health professional team, given the trade-off between increasing physical activity levels and falls rates.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript: A. Writing of the first draft, B. Review and Critique.

R.C.: 1A, 1B, 1C, 2A, 2B, 3A, 3B
M.E.M.: 1C, 2C, 3B
F.P-F.: 1C, 2C, 3B
M.M-O.: 1A, 1B, 1C, 2B, 2C, 3B
S.S.: 1C, 2C, 3B
D.B.: 1C, 2B, 3B
J.M.H.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B
A.N.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

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Supporting Information

Supporting information may be found in the online version of this article.

TABLE S1. Key Multi-domain, multi-modal and uni-modal falls prevention RCTs for Parkinson's disease